CYTOKINETICS INC
Form 10-K
March 07, 2019

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K

(Mark One)

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2018

or

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
From the transition period from to

Commission file number: 000-50633

CYTOKINETICS, INCORPORATED

(Exact name of registrant as specified in its charter)

Delaware	94-3291317
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
280 East Grand Avenue	
South San Francisco, CA	94080
(Address of principal executive offices)	(Zip Code)

(650) 624-3000

(Registrant's telephone number, including area code)

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

Title of each class	Name of each exchange on which registered
Common Stock, $0.001 par value	The Nasdaq Global Select Market

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

None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes No

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes No

Indicate by check mark whether the Registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes No

Indicate by check mark whether the Registrant has submitted electronically Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405 of this chapter) is not contained herein, and will not be contained, to the best of the Registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

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

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

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

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates was $449.7 million, computed by reference to the last sales price of $8.30 as reported by the Nasdaq Market as of June 29, 2018. This

calculation does not reflect a determination that certain persons are affiliates of the Registrant for any other purpose. The number of shares of common stock held by non-affiliates excluded 415,221 shares of common stock held by directors, officers and affiliates of directors. The number of shares owned by affiliates of directors was determined based upon information supplied by such persons and upon Schedules 13D and 13G, if any, filed with the SEC. Exclusion of shares held by any person should not be construed to indicate that such person possesses the power, direct or indirect, to direct or cause the direction of the management or policies of the Registrant, that such person is controlled by or under common control with the Registrant, or that such persons are affiliates for any other purpose.

The number of shares outstanding of the Registrant's common stock on March 5, 2019 was 54,888,369 shares.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's Proxy Statement for its 2019 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission, no later than 120 days after the end of the fiscal year, are incorporated by reference into Part III of this Annual Report on Form 10-K.

CYTOKINETICS, INCORPORATED

FORM 10-K

Year Ended December 31, 2018

INDEX

PART I

This report contains forward-looking statements indicating expectations about future performance and other forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and the Private Securities Litigation Reform Act of 1995, that involve risks and uncertainties. We intend that such statements be protected by the safe harbor created thereby. Forward-looking statements involve risks and uncertainties and our actual results and the timing of events may differ significantly from the results discussed in the forward-looking statements. Examples of such forward-looking statements include, but are not limited to, statements about or relating to:

- guidance concerning revenues, research and development expenses and general and administrative expenses in 2019;
- the sufficiency of existing resources to fund our operations for at least the next 12 months;
- our capital requirements and needs for additional financing;
- the initiation, design, conduct, enrollment, progress, timing and scope of clinical trials and development activities for our drug candidates conducted by ourselves or our partners, Amgen Inc. ("Amgen") and Astellas Pharma Inc. ("Astellas"), including the anticipated timing for initiation of clinical trials, anticipated rates of enrollment for clinical trials and anticipated timing of results becoming available or being announced from clinical trials;
- the results from the clinical trials, the non-clinical studies and chemistry, manufacturing, and controls ("CMC") activities of our drug candidates and other compounds, and the significance and utility of such results;
- anticipated interactions with regulatory authorities;
- our and our partners' plans or ability to conduct the continued research and development of our drug candidates and other compounds;
- the advancement of omecamtiv mecarbil in Phase 3 clinical development;
- our expected roles in research, development or commercialization under our strategic alliances with Amgen and Astellas;
    - the properties and potential benefits of, and the potential market opportunities for, our drug candidates and other compounds, including the potential indications for which they may be developed;
- the sufficiency of the clinical trials conducted with our drug candidates to demonstrate that they are safe and efficacious;
- our receipt of milestone payments, royalties, reimbursements and other funds from current or future partners under strategic alliances, such as with Amgen or Astellas;
- our ability to continue to identify additional potential drug candidates that may be suitable for clinical development;
- our plans or ability to commercialize drugs, with or without a partner, including our intention to develop sales and marketing capabilities;
- the focus, scope and size of our research and development activities and programs;
- the utility of our focus on the biology of muscle function, and our ability to leverage our experience in muscle contractility to other muscle functions;
- our ability to protect our intellectual property and to avoid infringing the intellectual property rights of others;
- future payments and other obligations under loan and lease agreements;
- potential competitors and competitive products;
- retaining key personnel and recruiting additional key personnel; and
- the potential impact of recent accounting pronouncements on our financial position or results of operations.

Such forward-looking statements involve risks and uncertainties, including, but not limited to:

- Amgen's decisions with respect to the timing, design and conduct of research and development activities for omecamtiv mecarbil and related compounds, including decisions to postpone or discontinue research or development activities relating to such compounds;

1

- Astellas' decisions with respect to the timing, design and conduct of research and development activities for reldesemtiv and other skeletal muscle activators, including decisions to postpone or discontinue research or development activities relating to reldesemtiv and other skeletal muscle activators, as well as Astellas' decisions with respect to its option to enter into a global collaboration for the development and commercialization of tirasemtiv;
- our ability to enter into strategic partnership agreements for any of our programs on acceptable terms and conditions or in accordance with our planned timelines;
- our ability to obtain additional financing on acceptable terms, if at all;
- our receipt of funds and access to other resources under our current or future strategic alliances;
- difficulties or delays in the development, testing, manufacturing or commercialization of our drug candidates;
- difficulties or delays, or slower than anticipated patient enrollment, in our or our partners' clinical trials;
- difficulties or delays in the manufacture and supply of clinical trial materials;
- failure by our contract research organizations, contract manufacturing organizations and other vendors to properly fulfill their obligations or otherwise perform as expected;
- results from non-clinical studies that may adversely impact the timing or the further development of our drug candidates and other compounds;
- the possibility that the US Food and Drug Administration ("FDA") or foreign regulatory agencies may delay or limit our or our partners' ability to conduct clinical trials or may delay or withhold approvals for the manufacture and sale of our or our partners' products;
- changing standards of care and the introduction of products by competitors or alternative therapies for the treatment of indications we target that may limit the commercial potential of our drug candidates;
- difficulties or delays in achieving market access and reimbursement for our drug candidates and the potential impacts of health care reform;
- changes in laws and regulations applicable to drug development, commercialization or reimbursement;
- the uncertainty of protection for our intellectual property, whether in the form of patents, trade secrets or otherwise;
- potential infringement or misuse by us of the intellectual property rights of third parties;
- activities and decisions of, and market conditions affecting, current and future strategic partners;
- accrual information provided by our contract research organizations ("CROs"), contract manufacturing organizations ("CMOs"), and other vendors;
- potential ownership changes under Internal Revenue Code Section 382; and
- the timeliness and accuracy of information filed with the U.S. Securities and Exchange Commission (the "SEC") by third parties.

In addition, such statements are subject to the risks and uncertainties discussed in the "Risk Factors" section and elsewhere in this document. Such statements speak only as of the date on which they are made, and, except as required by law, we undertake no obligation to update any forward-looking statement to reflect events or circumstances after the date on which the statement is made or to reflect the occurrence of unanticipated events. New factors emerge from time to time, and it is not possible for us to predict which factors will arise. In addition, we cannot assess the impact of each factor on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements.

Item 1. Business

When used in this report, unless otherwise indicated, "Cytokinetics," "the Company," "we," "our" and "us" refers to Cytokinetics, Incorporated. CYTOKINETICS, and our logo used alone and with the mark CYTOKINETICS, are registered service marks and trademarks of Cytokinetics. Other service marks, trademarks and trade names referred to in this report are the property of their respective owners.

Overview

We are a late-stage biopharmaceutical company focused on discovering, developing and commercializing first-in-class muscle activators and best-in-class muscle inhibitors as potential treatments for debilitating diseases in which muscle performance is compromised and/or declining. We have discovered and are developing muscle-directed investigational medicines that may potentially improve the healthspan of people with devastating cardiovascular and neuromuscular diseases of impaired muscle function. Our research and development activities relating to the biology of muscle function have evolved from our knowledge and expertise regarding the cytoskeleton, a complex biological infrastructure that plays a fundamental role within every human cell. As a leader in muscle biology and the mechanics of muscle performance, we are developing small molecule drug candidates specifically engineered to impact muscle function and contractility.

Our drug candidates currently in clinical development are: omecamtiv mecarbil, a novel cardiac myosin activator which we are developing for the potential treatment of heart failure, reldesemtiv, a novel fast skeletal muscle troponin activator ("FSTA") which we are developing for the potential treatment of amyotrophic lateral sclerosis ("ALS") and spinal muscular atrophy ("SMA"), CK-3773274 ("CK-274"), a novel cardiac myosin inhibitor, which we are developing for the potential treatment of hypertrophic cardiomyopathy ("HCM") and AMG 594, a novel cardiac troponin activator which is the subject of a Phase 1 clinical study.

Omecamtiv mecarbil is being evaluated for the potential treatment of heart failure under a strategic alliance with Amgen established in 2006 to discover, develop, and commercialize novel small molecule therapeutics designed to activate cardiac muscle contractility pursuant to the collaboration and option agreement dated December 29, 2006, as amended (the "Amgen Agreement"). Amgen, in collaboration with Cytokinetics, is conducting GALACTIC-HF (Global Approach to Lowering Adverse Cardiac Outcomes Through Improving Contractility in Heart Failure), a Phase 3 cardiovascular outcomes clinical trial of omecamtiv mecarbil in heart failure. In collaboration with Amgen, we are conducting METEORIC-HF (Multicenter Exercise Tolerance Evaluation of Omecamtiv Mecarbil Related to Increased Contractility in Heart Failure), a second Phase 3 clinical trial intended to evaluate its potential to increase exercise performance.

Reldesemtiv selectively activates the fast skeletal muscle troponin complex in the sarcomere by increasing its sensitivity to calcium, leading to an increase in skeletal muscle contractility. Cytokinetics and Astellas are developing reldesemtiv under the Amended and Restated License and Collaboration Agreement dated December 22, 2014, as amended (the "Astellas Agreement"). Astellas holds an exclusive license to develop and commercialize reldesemtiv worldwide, subject to our development and commercialization participation rights. In collaboration with Astellas, we conducted a Phase 2 clinical trial of reldesemtiv in patients with SMA and we are conducting a Phase 2 clinical trial of reldesemtiv in patients with ALS, called FORTITUDE-ALS (Functional Outcomes in a Randomized Trial of Investigational Treatment with CK-2127107 to Understand Decline in Endpoints – in ALS). Astellas, in collaboration with us, conducted a Phase 2 clinical trial of reldesemtiv in patients with chronic obstructive pulmonary disease ("COPD") and a Phase 1b clinical trial of reldesemtiv in elderly subjects with limited mobility.

CK-274 is a novel, oral, small molecule cardiac myosin inhibitor that we discovered independent of our collaborations. CK-274 arose from an extensive chemical optimization program conducted with careful attention to therapeutic index and pharmacokinetic properties that may translate into best-in-class potential in clinical development. CK-274 was designed to reduce the hypercontractility that is associated with HCM. In preclinical models, CK-274 reduces myocardial contractility by binding directly to cardiac myosin at a distinct and selective allosteric binding site, thereby preventing myosin from entering a force producing state. CK-274 reduces the number of active actin-myosin cross bridges during each cardiac cycle and consequently reduces myocardial contractility. This mechanism of action may be therapeutically effective in conditions characterized by excessive hypercontractility, such as HCM. We are conducting a Phase 1 double-blind, randomized, placebo-controlled, multi-part, single and multiple

ascending dose clinical trial of CK-274 in healthy adult subjects.

AMG 594 was discovered under our joint research program with Amgen. In collaboration with Cytokinetics, Amgen is conducting a randomized, placebo-controlled, double-blind, single and multiple ascending dose, single-center Phase 1 study to assess the safety and tolerability, pharmacokinetics and pharmacodynamics of AMG 594 in healthy subjects.

Our research continues to drive innovation and leadership in muscle biology, evidenced by three new muscle biology directed compounds advancing from research to development in 2018. All of our drug candidates have arisen from our cytoskeletal research activities. Our focus on the biology of the cytoskeleton distinguishes us from other biopharmaceutical companies, and potentially positions us to discover and develop novel therapeutics that may be useful for the treatment of severe diseases and medical conditions. Each of our drug candidates has a novel mechanism of action compared to currently marketed drugs, which we believe validates our focus on the cytoskeleton as a productive area for drug discovery and development. We intend to leverage our experience in muscle contractility to expand our current pipeline and expect to identify additional potential drug candidates that may be suitable for clinical development.

Corporate Strategy

We are a late-stage biopharmaceutical company focused on discovering, developing and commercializing first-in-class muscle activators and best-in-class muscle inhibitors as potential treatments for debilitating diseases in which muscle performance is compromised and/or declining. As a leader in muscle biology and the mechanics of muscle performance, we are developing small molecule drug candidates specifically engineered to impact muscle function and contractility. Our goal is to discover, develop and commercialize novel drug products that modulate muscle function that may benefit people living with serious diseases or medical conditions, with the intent of establishing a fully-integrated biopharmaceutical company.

The key components of our Corporate Strategy are:

- Progress proprietary research programs focused on muscle into development. We believe that our extensive understanding of muscle biology and our proprietary research technologies should enable us to discover and potentially to develop drug candidates with novel mechanisms of action that may offer potential benefits not provided by existing drugs and which may have application across a broad array of diseases and medical conditions. We expect that we may be able to leverage our expertise in muscle contractility to expand programs related to other areas of muscle function and which may extend to the potential treatment of other serious medical diseases and conditions. Progressing related programs in parallel may afford us an opportunity to build a broader business that could benefit from multiple products that serve related clinical and commercial needs associated with impaired muscle function, muscle weakness and fatigue. In addition, this strategy may enable us to diversify certain technical, financial and operating risks by advancing several drug candidates in parallel.
- Advance next-generation skeletal and cardiac muscle-directed compounds into clinical development. We take a purpose-driven approach by leveraging our extensive muscle biology expertise to engineer compounds with specific characteristics aimed at treating diseases that impact muscle function. By increasing muscle strength and performance, our drug candidates may preserve and extend independence and self-reliance in people suffering from debilitating diseases. We have established select strategic alliances to support certain drug development programs while preserving significant development and commercialization rights. We believe that such alliances may allow us to obtain financial support and to capitalize on the therapeutic area expertise and resources of our partners that can potentially accelerate the development and commercialization of our drug candidates. Where we deem appropriate, we plan to retain certain rights to participate in the development and commercialization of drug candidates arising from our programs and alliances, so that we can expand and capitalize on our own internal development capabilities and build our commercialization capabilities.
- Conduct clinical development of novel, first-in-class and/or best-in-class muscle activators/inhibitors for the potential treatment of ALS, SMA, heart failure, HCM and other diseases impacting muscle function. Our portfolio consists of drug candidates that are in clinical development in principally four therapeutic areas, namely ALS, SMA, heart failure and HCM which may also inform their further development in other diseases characterized by either limited or excessive muscle function. We believe that by focusing on these disease areas that are associated with well-organized physician-investigator groups, significant unmet clinical needs, and strong patient and disease advocacy, we may enhance our effectiveness in enrolling and conducting clinical trials to answer important questions about the dosing, tolerability, pharmacokinetics and pharmacodynamics as well as the potential safety and efficacy of our drug candidates. We believe that our development programs can improve our ability to realize value from our and our partners' clinical development activities. As we advance our drug candidates into later-stage clinical development, we extensively evaluate previous clinical trial designs and results to assess key learnings that may be applied to our late-stage clinical development activities. We believe this may result in more successful later-stage clinical development activities that may increase the likelihood of developing effective therapies that can address the needs of people living with these devastating diseases.
- Collaborate with patient communities to support the urgent development of new medicines for diseases of impaired muscle function with pressing unmet medical needs. Central to our corporate strategy are the people living with a

disease or medical condition characterized by impaired muscle function. We focus our development and commercialization activities on diseases that lack effective therapies and, in some cases, those with no approved medicines. We recognize that by applying our extensive knowledge of muscle biology towards the development of novel therapies for the people living with these diseases, we aim to improve lives of not only patients but also their caregivers and families. We collaborate with these individuals and their communities to ensure our potential drugs address their urgent needs and that we understand and appreciate the issues associated with these diseases and conditions. We work collaboratively with entities, such as patient advocacy groups, that focus on policies, guidelines and practices to accelerate development and commercialization of novel therapies, when possible and appropriate, and on ensuring that the voice of their constituencies are heard.

- Mature our company's operations to enable development, registration and commercialization of muscle biology drug candidates across North America and Europe. With a focus on disease areas for which there are serious unmet medical needs, we direct our activities to potential commercial opportunities in concentrated and tractable customer segments, such as hospital specialists and disease-specific centers of excellence, which may be addressed by smaller, targeted sales

forces. In preparing for the potential commercialization of our drug candidates directed to these markets, we are focusing our activities on the key issues facing patients and payors, including the principal drivers of clinical and economic burdens associated with these diseases. We also focus on opportunities that multiple stakeholders may recognize as creating value. Accordingly, targeting unmet medical needs in these areas may provide us competitive advantages and support our development of a potential franchise in diseases involving muscle function. In these markets, we believe that a company with limited resources may be able to compete effectively against larger, more established companies with greater financial and commercial resources. For these opportunities, we intend to develop clinical development and sales and marketing capabilities in North America and Europe with the goal of becoming a fully-integrated biopharmaceutical company.

Research and Development Programs

Our long-standing interest in the cytoskeleton has led us to focus our research and development activities on the biology of muscle function and, in particular, small molecule modulation of muscle contractility. We believe that our expertise in the modulation of muscle contractility is an important differentiator for us. Our preclinical and clinical experience in muscle contractility may position us to discover and develop additional novel therapies that have the potential to improve the health of patients with severe and debilitating diseases or medical conditions.

Small molecules that affect muscle contractility may have several applications for a variety of serious diseases and medical conditions. For example, heart failure is a disease often characterized by impaired cardiac muscle contractility which may be treated by modulating the contractility of cardiac muscle. Similarly, certain diseases and medical conditions associated with muscle weakness may be amenable to treatment by enhancing the contractility of skeletal muscle. Because the modulation of the contractility of different types of muscle, such as cardiac and skeletal muscle, may be relevant to multiple diseases or medical conditions, we believe we can leverage our expertise in these areas to more efficiently discover and develop potential drug candidates that modulate the applicable muscle type for multiple indications.

We segment our research and development activities related to muscle contractility by our cardiac muscle contractility program and our skeletal muscle contractility program. We also conduct research and development on novel treatments for disorders involving muscle function beyond muscle contractility.

Our research and development expenses were $89.1 million for 2018, $90.3 million for 2017 and $59.9 million for 2016.

Cardiac Muscle Program

Our cardiac muscle contractility program is focused on the cardiac sarcomere, the basic unit of muscle contraction in the heart. The cardiac sarcomere is a highly ordered cytoskeletal structure composed of cardiac myosin, actin and a set of regulatory proteins. Cardiac myosin is the cytoskeletal motor protein in the cardiac muscle cell. It is directly responsible for converting chemical energy into the mechanical force, resulting in cardiac muscle contraction. Our most advanced cardiac program is based on the hypothesis that activators of cardiac myosin may address certain adverse properties of existing positive inotropic agents. Current positive inotropic agents, such as beta-adrenergic receptor agonists or inhibitors of phosphodiesterase activity, increase the concentration of intracellular calcium, thereby increasing cardiac sarcomere contractility. The effect on calcium levels, however, also has been linked to potentially life-threatening side effects. In contrast, our novel cardiac myosin activators work by a mechanism that directly stimulates the activity of the cardiac myosin motor protein, without increasing the intracellular calcium concentration. They accelerate the rate-limiting step of the myosin enzymatic cycle and shift it in favor of the force-producing state. Rather than increasing the velocity of cardiac contraction, this mechanism instead lengthens the

systolic ejection time, which results in increased cardiac function in a potentially more oxygen-efficient manner.

Our earlier stage cardiac program is based on the hypothesis that inhibitors of hyperdynamic contraction and obstruction of left ventricular blood flow may counteract the pathologic effects of mutations in the sarcomere that lead to hypertrophic cardiomyopathies. A targeted oral therapy addressing this disease etiology may improve symptoms, exercise capacity and potentially slow disease progression.

Omecamtiv mecarbil

Our lead drug candidate from our cardiac contractility program is omecamtiv mecarbil, a novel cardiac myosin activator. We expect omecamtiv mecarbil to be developed as a potential treatment across the continuum of care in heart failure both for use in the hospital setting and for use in the outpatient setting. Omecamtiv mecarbil is the subject of a Phase 3 development program in patients with heart failure with reduced ejection fraction under our strategic alliance with Amgen.

Amgen Strategic Alliance

Our strategic alliance with Amgen to discover, develop, and commercialize novel small molecule therapeutics designed to activate cardiac muscle, including omecamtiv mecarbil, for the potential treatment of heart failure is governed by the Amgen Agreement. Amgen has exclusive, worldwide rights to develop and commercialize omecamtiv mecarbil and related compounds

subject to our specified development and commercial participation rights. Amgen has also entered an alliance with Les Laboratoires Servier and Institut de Recherches Internationales Servier ("Servier") for exclusive commercialization rights in Europe as well as the Commonwealth of Independent States ("CIS"), including Russia. Servier contributes funding for development and provides strategic support to the program.

Under the Amgen Agreement we are eligible for potential additional pre-commercialization and commercialization milestone payments of over $600.0 million in the aggregate on omecamtiv mecarbil and other potential products arising from research under the collaboration, and royalties that escalate based on increasing levels of annual net sales of products commercialized under the agreement.

The Amgen Agreement provided for us to receive increased royalties by co-funding the Phase 3 development program for omecamtiv mecarbil and other drug candidates under the collaboration. We fully exercised this option and co-invested $40.0 million in the Phase 3 development program of omecamtiv mecarbil in exchange for a total incremental royalty from Amgen of up to 4% on increasing worldwide sales of omecamtiv mecarbil outside Japan and the right to co-promote omecamtiv mecarbil in institutional care settings in North America, with reimbursement by Amgen for certain sales force activities (the "Co-Invest Option"). A joint commercial operating team comprising representatives of Cytokinetics and Amgen will be responsible for the day-to-day management of the commercialization program of omecamtiv mecarbil.

Amgen generally has discretion to elect whether to pursue or abandon the development of omecamtiv mecarbil and may terminate our strategic alliance for any reason upon six months' prior notice. With our consent, Amgen granted Servier an option to commercialize omecamtiv mecarbil in Europe and the CIS, including Russia, which Servier decided to exercise. In August 2016, we entered into a letter agreement with Amgen and Servier, which provides that if Amgen's rights to omecamtiv mecarbil are terminated with respect to the territory subject to Servier's sublicense, the sublicensed rights previously granted by Amgen to Servier with respect to omecamtiv mecarbil, will remain in effect and become a direct license or sublicense of such rights by us to Servier, on substantially the same terms as those in the Option, License and Collaboration Agreement between Amgen and Servier.

Omecamtiv Mecarbil: Clinical Development

GALACTIC-HF: GALACTIC-HF (Global Approach to Lowering Adverse Cardiac Outcomes Through Improving Contractility in Heart Failure) is a Phase 3 cardiovascular outcomes clinical trial of omecamtiv mecarbil which is being conducted by Amgen, in collaboration with Cytokinetics. The primary objective of this double-blind, randomized, placebo-controlled multicenter clinical trial is to determine if treatment with omecamtiv mecarbil when added to standard of care is superior to standard of care plus placebo in reducing the risk of cardiovascular death or heart failure events in patients with high risk chronic heart failure and reduced ejection fraction. GALACTIC-HF is being conducted under a Special Protocol Assessment ("SPA") with the FDA. GALACTIC-HF is planned to enroll approximately 8,000 symptomatic chronic heart failure patients in over 900 sites in 35 countries who are either currently hospitalized for a primary reason of heart failure or have had a hospitalization or admission to an emergency room for heart failure within one year prior to screening. Patients are randomized to either placebo or omecamtiv mecarbil with dose titration up to a maximum dose of 50 mg twice daily based on the plasma concentration of omecamtiv mecarbil after initiation of drug therapy. The primary endpoint is a composite of time to cardiovascular death or first heart failure event, whichever occurs first, with heart failure event defined as hospitalization, emergency room visit, or urgent unscheduled clinic visit for heart failure. Secondary endpoints include time to cardiovascular death; patient reported outcomes as measured by the Kansas City Cardiomyopathy Questionnaire Total Symptom Score; time to first heart failure hospitalization; and all-cause death.

METEORIC-HF: In collaboration with Amgen, we are conducting METEORIC-HF (Multicenter Exercise Tolerance Evaluation of Omecamtiv Mecarbil Related to Increased Contractility in Heart Failure), a second Phase 3 clinical trial

intended to evaluate its potential to increase exercise performance. Patients will be randomized in a 2:1 fashion to omecamtiv mecarbil, which will be started at 25 mg twice daily and titrated to 25, 37.5 or 50 mg twice daily based on the same PK-guided dosing regimen as is used in GALACTIC-HF, or to placebo. METEORIC-HF is planned to enroll approximately 270 symptomatic chronic heart failure patients in nine countries. The primary endpoint of METEORIC-HF is change in peak oxygen uptake on Cardio-Pulmonary Exercise Testing ("CPET") from baseline to Week 20. Secondary endpoints include change in total workload during CPET from baseline to Week 20, change in ventilatory efficiency during CPET from baseline to Week 20 and change in the average daily activity units measured over 2 weeks from baseline to Week 18-20.

AMG 594

AMG 594 is a novel, selective, oral, small molecule cardiac troponin activator which was discovered under our joint research program with Amgen. In preclinical models, AMG 594 increases myocardial contractility by binding to cardiac troponin through an allosteric mechanism that sensitizes the cardiac sarcomere to calcium, facilitating more actin-myosin cross bridge formation during each cardiac cycle thereby resulting in increased myocardial contractility. Similar to cardiac myosin activation, preclinical research has shown that cardiac troponin activation does not change the calcium transient of cardiac myocytes. In collaboration with Cytokinetics, Amgen is conducting a randomized, placebo-controlled, double-blind, single and multiple ascending dose, single-center Phase 1 study to assess the safety and tolerability, pharmacokinetics and pharmacodynamics of AMG 594 in healthy subjects. The study design includes several single ascending dose cohorts and three multiple ascending dose cohorts, with eight healthy subjects per cohort.

Omecamtiv Mecarbil: Heart Failure Commercial Market

Heart failure is a widespread and debilitating syndrome affecting millions of people in the United States. The high and rapidly growing prevalence of heart failure translates into significant hospitalization rates and associated societal costs. About 6.4 million people in the United States have heart failure (approximately half with reduced ejection fraction), resulting in nearly one million hospital discharges with the primary diagnosis of heart failure and approximately 300,000 deaths each year. For people over 65 years of age, heart failure incidences approach 10 per 1000 and approximately 50% of people diagnosed with heart failure will die within 5 years of diagnosis. These numbers are increasing due to the aging of the U.S. population and an increased likelihood of survival following acute myocardial infarctions.

The costs to society attributable to heart failure are high, especially as many chronic heart failure patients suffer repeated acute episodes. Despite currently available therapies, readmission rates for heart failure patients remain high. In general, the mortality following hospitalization for patients with heart failure is approximately 10% at 30 days, 22% at one year and 42% at 5 years, despite the availability of therapeutic alternatives for treatment of these patients. These poor outcomes in the setting of current therapies point to the need for novel therapeutics that may offer further reductions in morbidity and mortality. The annual cost of heart failure to the U.S. health care system is estimated to be $32 billion and is predicted to grow to almost $70 billion by the year 2030. Approximately 70% of those costs are due to hospitalization, home health and physician care. In the U.S., Medicare is one of the largest payors for heart failure related costs. Approximately 50% of Medicare beneficiaries with heart failure are concentrated in the top 20% of the hospital referral regions in the U.S. New drug therapies that could reduce the number of hospitalizations could decrease the cost to the health care system.

CK-274

CK-274 is a novel, oral, small molecule cardiac myosin inhibitor that our company scientists discovered independent of our collaborations. CK-274 arose from an extensive chemical optimization program conducted with careful attention to therapeutic index and pharmacokinetic properties that may translate into best-in-class potential in clinical development. CK-274 was designed to reduce the hypercontractility that is associated with HCM. In preclinical models, CK-274 reduces myocardial contractility by binding directly to cardiac myosin at a distinct and selective allosteric binding site, thereby preventing myosin from entering a force producing state. CK-274 reduces the number of active actin-myosin cross bridges during each cardiac cycle and consequently reduces myocardial contractility. This mechanism of action may be therapeutically effective in conditions characterized by excessive hypercontractility, such as HCM.

In preclinical models of cardiac function, CK-274 reduced cardiac contractility in a predictable dose and exposure dependent fashion. In preclinical models of disease, CK-274 reduced compensatory cardiac hypertrophy and cardiac fibrosis. The preclinical pharmacokinetics of CK-274 were characterized, evaluated and optimized for potential ease-of-use in the clinical setting. The initial focus of our development program for CK-274 will include an extensive characterization of its pharmacokinetics/pharmacodynamic (PK/PD) relationship as has been a hallmark of our development programs in muscle pharmacology. The overall development program will assess the potential of CK 274 to improve exercise capacity and relieve symptoms in patients with hyperdynamic ventricular contraction due to HCM.

CK-274: Clinical Development

We are conducting a Phase 1 double-blind, randomized, placebo-controlled, multi-part, single and multiple ascending dose clinical trial of CK-274 to assess the safety and tolerability, pharmacokinetics and pharmacodynamics of CK-274 in healthy subjects.

CK-274: HCM Commercial Market

HCM is the most common inherited cardiovascular disorder. HCM is a disease in which the heart muscle (myocardium) becomes abnormally thick (hypertrophied). The thickening of cardiac muscle leads to the inside of the left ventricle becoming smaller and stiffer, and thus the ventricle becomes less able to relax and fill with blood. This ultimately limits the heart's pumping function, resulting in symptoms including chest pain, dizziness, shortness of breath, or fainting during physical activity. A subset of patients with HCM are at high risk of progressive disease which can lead to atrial fibrillation, stroke and death due to arrhythmias. There are no current medical treatments that directly address the hypercontractility that underlies HCM.

Skeletal Muscle Contractility Program

Our skeletal muscle contractility program is focused on the activation of the skeletal sarcomere, the basic unit of skeletal muscle contraction. The skeletal sarcomere is a highly ordered cytoskeletal structure composed of skeletal muscle myosin, actin, and a set of regulatory proteins, which include the troponins and tropomyosin. This program leverages our expertise developed in our ongoing discovery and development of cardiac sarcomere activators, including the cardiac myosin activator, omecamtiv mecarbil.

We believe that our skeletal sarcomere activators may lead to new therapeutic options for diseases and medical conditions associated with neuromuscular dysfunction and potentially also conditions associated with aging and muscle weakness and wasting. The clinical effects of muscle weakness and wasting, fatigue and loss of mobility can range from decreased quality of life to, in some instances, life-threatening complications. By directly improving skeletal muscle function, a small molecule activator of the skeletal sarcomere potentially could enhance functional performance and quality of life in patients suffering from diseases or medical

conditions associated with skeletal muscle weakness or wasting, such as ALS, SMA, COPD or sarcopenia (general frailty associated with aging).

Reldesemtiv

Reldesemtiv selectively activates the fast skeletal muscle troponin complex in the sarcomere by increasing its sensitivity to calcium, leading to an increase in skeletal muscle contractility. Reldesemtiv has demonstrated pharmacological activity in preclinical models and evidence of potentially clinically relevant pharmacodynamic effects in humans. The FDA has granted reldesemtiv orphan drug designation for the potential treatment of SMA.

Astellas Strategic Alliance

Our strategic alliance with Astellas to advance novel therapies for diseases and medical conditions associated with muscle impairment and weakness is governed by the Astellas Agreement. We initially exclusively licensed to Astellas rights to co-develop and potentially co-commercialize reldesemtiv and other FSTAs in non-neuromuscular indications and to develop and commercialize other novel mechanism skeletal muscle activators in all indications, subject to certain Cytokinetics' development and commercialization rights. Subsequently, we and Astellas expanded the strategic alliance to include certain neuromuscular indications, including SMA, for reldesemtiv and other FSTAs and to advance reldesemtiv into Phase 2 clinical development, initially in SMA. In 2016, we and Astellas further expanded the strategic alliance to include the development of reldesemtiv for the potential treatment of ALS, as well as the possible development in ALS of other FSTAs previously licensed by us to Astellas, and granted Astellas an option for a global collaboration for the development and commercialization of our first-generation FSTA, tirasemtiv (the "Option on Tirasemtiv").

The strategic alliance with Astellas includes a joint research program focused on the discovery of additional next-generation skeletal muscle activators, including sponsored research at Cytokinetics. This research program has been extended through 2019.

We have options to conduct early-stage development for certain agreed indications at our initial expense, subject to reimbursement if development continues under the strategic alliance; to co-promote collaboration products containing FSTAs for neuromuscular indications in the U.S., Canada and Europe; and to co-promote other collaboration products in the U.S. and Canada. Astellas will reimburse us for certain expenses associated with our co-promotion activities.

Astellas is primarily responsible for the development of reldesemtiv in ALS, but we are conducting FORTITUDE-ALS and will share in the operational responsibility for subsequent clinical trials. Subject to specified guiding principles, decision making will be by consensus, subject to escalation and, if necessary, Astellas' final decision-making authority on the development (including regulatory affairs), manufacturing, medical affairs and commercialization of reldesemtiv and other FSTAs in ALS. We and Astellas share equally the costs of developing reldesemtiv in ALS for potential registration and marketing authorization in the U.S. and Europe, provided that (i) Astellas has agreed to solely fund Phase 2 development costs of reldesemtiv in ALS subject to a right to recoup our share of such costs plus a 100% premium on such amounts by reducing future milestone and royalty payments to us and (ii) we may defer (but not eliminate) a portion of our co-funding obligation for development activities after Phase 2 for up to 18 months, subject to certain conditions. We have the right to co-fund our share of such Phase 2 development costs on a current basis, in which case there would not be a premium due to Astellas.

Based on the achievement of pre-specified criteria, we may receive over $600.0 million in milestone payments relating to the development and commercial launch of collaboration products, including up to $112.0 million (of which we have received $17.0 million) relating to early development of reldesemtiv and for later-stage development and commercial launch milestones for reldesemtiv in non-neuromuscular indications, and over $100.0 million in

development and commercial launch milestones for reldesemtiv in each of SMA and other neuromuscular indications. We may also receive up to $200.0 million in payments for achievement of pre-specified sales milestones related to net sales of all collaboration products.

If Astellas commercializes any collaboration products, we will also receive royalties on sales of such collaboration products, including royalties ranging from the high single digits to the high teens on sales of products containing reldesemtiv. We can co-fund certain development costs for reldesemtiv and other compounds in exchange for increased milestone payments and royalties; such royalties may increase under certain scenarios to exceed twenty percent. In addition to the foregoing development, commercial launch and sales milestones, we may also receive payments for the achievement of pre-specified milestones relating to the joint research program.

Astellas generally has discretion to elect whether to pursue or abandon the development of reldesemtiv and other collaboration products, in whole or in part. Astellas may terminate our strategic alliance in whole or in part for any reason upon six months' prior notice at any time following expiration of the strategic alliance's research term, which will expire December 31, 2019.

Reldesemtiv: Clinical Development

SMA: In June 2018, we announced data from a hypothesis-generating, Phase 2 double-blind, randomized, placebo-controlled clinical study in patients with SMA which was designed to determine potential pharmacodynamic effects of a suspension formulation of reldesemtiv following 8 weeks of oral dosing in each of two cohorts of 36 patients with Type II, Type III, or Type IV disease were

presented at the 2018 Annual Cure SMA Conference in Dallas. Secondary objectives were to evaluate the safety, tolerability and pharmacokinetics of reldesemtiv. The study showed statistically significant concentration-dependent increases in changes from baseline in Six Minute Walk Distance ("6MWD"), a sub-maximal exercise test of aerobic capacity and endurance. The study also showed statistically significant increases for Maximal Expiratory Pressure ("MEP"), a measure of strength of respiratory muscles. Other assessments, including the Hammersmith Functional Motor Score - Extended, Revised Upper Limb Module, Timed Up-and-Go, Forced Vital Capacity, and the SMA Health Index ("SMA-HI"), a patient reported outcome measure ("PROM") developed to comply with FDA standards for PROMs, did not demonstrate differences between reldesemtiv versus placebo. Adverse events were similar between groups receiving reldesemtiv and placebo.

Additional results presented at the 2018 Muscle Study Group Scientific Meeting in Oxford, U.K. showed sustained increases in 6MWD and MEP four weeks after discontinuation of study drug (i.e., follow-up). A post-hoc analysis also showed that changes from baseline in the 6MWD at 450 mg twice daily were significantly correlated with changes from baseline on certain domains of the SMA-HI intended to reflect improved endurance, especially Fatigue and Activity Participation. Decreases in SMA-HI scores reflect reduced disease burden as measured by that PROM, indicating that as 6MWD increases, disease burden assessed by that domain of the SMA-HI is reduced.

In January 2019, we announced that we received feedback from the FDA that the Six Minute Walk Test (6MWT) is an acceptable primary efficacy endpoint for a potential registration program for reldesemtiv in patients with SMA who have maintained ambulatory function. The FDA also recommended adding a global function scale as a secondary endpoint.

ALS: In collaboration with Astellas, we are conducting FORTITUDE-ALS. This trial was designed to enroll approximately 450 eligible ALS patients to be randomized (1:1:1:1) to receive either 150 mg, 300 mg or 450 mg of reldesemtiv or placebo dosed orally twice daily for 12 weeks. The primary efficacy endpoint of FORTITUDE-ALS is the change from baseline in the percent predicted slow vital capacity ("SVC") at 12 weeks. Secondary endpoints include slope of the change from baseline in the mega-score of muscle strength measured by hand held dynamometry ("HHD") and handgrip dynamometry in patients on reldesemtiv; change from baseline in the ALS Functional Rating Scale – Revised ("ALSFRS-R"); incidence and severity of treatment-emergent adverse events ("TEAEs"); and plasma concentrations of reldesemtiv at the sampled time points during the study. Exploratory endpoints will be measured including the effect of reldesemtiv versus placebo on self-assessments of respiratory function made at home by the patient with help as needed by the caregiver; disease progression through quantitative measurement of speech production characteristics over time; disease progression through quantitative measurement of handwriting abilities over time; and change from baseline in quality of life (as measured by the ALSAQ-5) in patients on reldesemtiv. In November 2018, we announced completion of enrollment in FORTITUDE-ALS. We expect results from this trial in the second quarter of 2019.

COPD: Astellas, in collaboration with Cytokinetics, conducted a Phase 2 clinical trial of reldesemtiv in patients with COPD designed to assess the effect of reldesemtiv on physical function in patients with COPD. In October 2018, we announced that this trial did not meet the primary endpoint and did not demonstrate a statistically significant treatment difference in any of the secondary endpoints. Adverse events were similar between groups receiving reldesemtiv and placebo.

Frailty: Astellas, in collaboration with Cytokinetics, conducted a Phase 1b clinical trial of reldesemtiv in elderly subjects with limited mobility. In October 2018, we announced that an interim analysis of this study had been conducted, the Independent Data Monitoring Committee for this trial determined that the pre-defined criteria for lack of efficacy of reldesemtiv had been met and Astellas had notified investigators to halt further enrollment in the trial.

The clinical trials program for reldesemtiv may proceed for several years, and we may not generate any revenues or material net cash flows from sales of this drug candidate until the program is successfully completed, regulatory approval is achieved, and the drug is commercialized. We cannot predict if or when this may occur.

Our expenditures will increase if Astellas terminates development of reldesemtiv or related compounds and we elect to develop them independently, or if we conduct early-stage development for certain agreed indications at our initial expense, subject to reimbursement if development continues under the collaboration.

CK-3762601

In October 2018, we announced that we and Astellas are advancing CK-3762601 (“CK-601”), a next-generation FSTA, into IND-enabling studies, which triggered a $2 million milestone payment from Astellas to us. CK-601 was designed in a joint research program conducted by the companies’ scientists to have different pharmacokinetics and physicochemical properties than reldesemtiv which may inform its development for the treatment of diseases and conditions associated with both neuromuscular and non-neuromuscular etiology and pathogenesis.

Ongoing Research in Skeletal Muscle Activators

Our research program with Astellas has been extended through 2019. Our research on the direct activation of skeletal muscle continues in two areas. We are conducting translational research in preclinical models of disease and muscle function with FSTAs to explore the potential clinical applications of this novel mechanism in diseases or conditions associated with skeletal muscle dysfunction. We also intend to conduct preclinical research on other chemically and pharmacologically distinct mechanisms to activate the skeletal sarcomere.

Commercial Market for SMA: SMA is a severe neuromuscular disease that occurs in 1 in every 6,000 to 10,000 live births each year resulting in a prevalence of 10,000 to 15,000 patients in the U.S. and is one of the most common fatal genetic disorders. SMA manifests in various degrees of severity as progressive muscle weakness resulting in respiratory and mobility impairment. There are four types of SMA, distinguished by the time of the initial onset of muscle weakness and the severity of related symptoms: Type I (severe), Type II (intermediate), Type III (juvenile) and Type IV (adult onset). Life expectancy and disease severity varies by type of SMA from Type I, who have the worst prognosis and a life expectancy of approximately two years from birth, to Type IV, who have a normal life span but with gradual weakness in the proximal muscles of the extremities resulting in mobility issues. Type II, III and IV patients are often characterized by their ambulatory status as it is an important driver of clinical decisions and care and constitute 50% of the incident patient population but as much as 90% of the prevalent patient population. Few treatment options exist for these patients, resulting in a high unmet need for new therapeutic options to ameliorate symptoms, improve muscle function and modify disease progression.

Commercial Market for ALS: Limited options exist for the treatment of patients with ALS, which affects as many as 30,000 Americans, with an estimated 5,600 new cases diagnosed each year in the U.S. Based on our primary market research, the per capita prevalence and incidence appears similar in the major European markets. ALS is 20% more common in men than women; however, with increasing age, the prevalence becomes more equal between men and women. The life expectancy of an ALS patient averages two to five years from the time of diagnosis, mostly due to respiratory issues. Of the patients diagnosed with ALS, 5 to 10% have a family history of the disease (familial ALS) and remaining 90 to 95% have the sporadic form. The majority of patients with ALS in the U.S. and Europe receive treatment at a concentrated number of multidisciplinary centers that specialize in the unique needs of these patients. In the U.S., there are approximately 150 ALS multidisciplinary clinics, according to either the ALS Association or the Muscular Dystrophy Association. For most patients with ALS, death is usually due to respiratory failure because of diminished strength in the skeletal muscles responsible for breathing. We believe that there is an urgent need for novel therapies to address the unmet medical issues of this patient population which could be addressed by a small, targeted sales force.

Other Commercial Markets for Skeletal Muscle Activators: We continue to evaluate potential commercial markets for other potential indications for skeletal muscle activators.

Tirasemtiv

In November 2017, we announced that VITALITY-ALS, a Phase 3 clinical trial of tirasemtiv in patients with ALS, did not meet its primary endpoint of change from baseline in SVC and we suspended development of tirasemtiv. After consulting with an advisory board of ethicists, patient advocates, trial investigators and experts in pre-approval access to assess whether and how best to continue providing tirasemtiv to those people living with ALS participating in VIGOR-ALS, an open-label extension clinical trial designed to assess the long-term safety and tolerability of tirasemtiv in patients with ALS, we closed VIGOR-ALS and established a Managed Access Program for patients previously enrolled in VIGOR-ALS to remain on tirasemtiv.

Beyond Muscle Contractility

We developed preclinical expertise in the mechanics of skeletal, cardiac and smooth muscle that extends from proteins to tissues to intact animal models. Our translational research in muscle contractility has enabled us to better understand the potential impact of small molecule compounds that increase skeletal or cardiac muscle contractility and to apply those findings to the further evaluation of our drug candidates in clinical populations. In addition to contractility, other major functions of muscle play a role in certain diseases that could benefit from novel mechanism treatments. Accordingly, our knowledge of muscle contractility may serve as an entry point to the discovery of novel treatments for disorders involving muscle functions other than muscle contractility. We are leveraging our current understandings of muscle biology to investigate new ways of modulating these other aspects of muscle function for other potential therapeutic applications.

Intellectual Property

Our policy is to seek patent protection for the technologies, inventions and improvements that we develop that we consider important to the advancement of our business. As of December 31, 2018, we owned, co-owned or licensed 96 issued U.S. patents, over 360 issued patents in various foreign jurisdictions, and over 225 additional pending U.S. and foreign patent applications. We also rely on trade secrets, technical know-how and continuing innovation to develop and maintain our competitive position. Our commercial success will depend on obtaining and maintaining patent protection and trade secret protection for our drug candidates and

technologies and our successfully defending these patents against third-party challenges. We will only be able to protect our technologies from unauthorized use by third parties to the extent that valid and enforceable patents cover them or we maintain them as trade secrets.

With regard to our drug candidates directed to muscle biology targets, we have a U.S. patent covering omecamtiv mecarbil and U.S. patents covering our skeletal muscle sarcomere activators including, but not limited to reldesemtiv, which expire in 2027 and 2031, respectively, unless extended or otherwise adjusted. We also have issued patents in various foreign jurisdictions and additional U.S. and foreign patent applications pending for these drug candidates. It is not known or determinable whether other patents will issue from any of our other pending applications or what the expiration dates would be for any other patents that do issue.

Our drug candidates are still in clinical development and have not yet been approved by the FDA. If any of these drug candidates are approved, then pursuant to federal law, we may apply for an extension of the U.S. patent term for one patent covering the approved drug, which could extend the term of the applicable patent by up to a maximum of five additional years.

The degree of future protection of our proprietary rights is uncertain because legal means may not adequately protect our rights or permit us to gain or keep our competitive advantage. Due to evolving legal standards relating to the patentability, validity and enforceability of patents covering pharmaceutical inventions and the claim scope of these patents, our ability to enforce our existing patents and to obtain and enforce patents that may issue from any pending or future patent applications is uncertain and involves complex legal, scientific and factual questions. The standards that the U.S. Patent and Trademark Office and its foreign counterparts use to grant patents are not always applied predictably or uniformly and are subject to change. To date, no consistent policy has emerged regarding the breadth of claims allowed in biotechnology and pharmaceutical patents. Thus, we cannot be sure that any patents will issue from any pending or future patent applications owned by, co-owned, or licensed to us. Even if patents do issue, we cannot be sure that the claims of these patents will be held valid or enforceable by a court of law, will provide us with any significant protection against competitive products, or will afford us a commercial advantage over competitive products. For example:

- we or our licensors might not have been the first to make the inventions covered by each of our pending patent applications or issued patents;
- we or our licensors might not have been the first to file patent applications for the inventions covered by our pending patent applications or issued patents;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- some or all of our or our licensors' pending patent applications may not result in issued patents or the claims that issue may be narrow in scope and not provide us with competitive advantages;
- our and our licensors' issued patents may not provide a basis for commercially viable drugs or therapies or may be challenged and invalidated by third parties;
- our or our licensors' patent applications or patents may be subject to interference, post-grant proceedings, opposition or similar legal and administrative proceedings that may result in a reduction in their scope or their loss altogether;
- we may not develop additional proprietary technologies or drug candidates that are patentable; or
- the patents of others may prevent us or our partners from discovering, developing or commercializing our drug candidates.

The defense and prosecution of intellectual property infringement suits, interferences, post-grant proceedings, oppositions and related legal and administrative proceedings are costly, time-consuming to pursue and divert resources. The outcome of these types of proceedings is uncertain and could significantly harm our business.

Our ability to commercialize drugs depends on our ability to use, manufacture and sell those drugs without infringing the patents or other proprietary rights of third parties. U.S. and foreign issued patents and pending patent applications owned by third parties exist that may be relevant to the therapeutic areas and chemical compositions of our drug candidates. While we are aware of certain relevant patents and patent applications owned by third parties, there may be issued patents or pending applications of which we are not aware that could cover our drug candidates. Because patent applications are often not published immediately after filing, there may be currently pending applications, unknown to us, which could later result in issued patents that our activities with our drug candidates could infringe.

The development of our drug candidates and the commercialization of any resulting drugs may be impacted by patents of companies engaged in competitive programs with significantly greater resources. This could result in the expenditure of significant legal fees and management resources.

We also rely on trade secrets to protect our technology, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are often difficult to protect, especially outside of the United States. While we believe that we use reasonable efforts to protect our trade secrets, our employees, consultants, contractors, partners and other advisors may unintentionally or willfully disclose our trade secrets to competitors. Enforcing a claim that a third party had illegally obtained and is using our trade

secrets would be expensive and time-consuming, and the outcome would be unpredictable. Even if we are able to maintain our trade secrets as confidential, our competitors may independently develop information that is equivalent or similar to our trade secrets.

We seek to protect our intellectual property by requiring our employees, consultants, contractors and other advisors to execute nondisclosure and invention assignment agreements upon commencement of their employment or engagement, through which we seek to protect our intellectual property. Agreements with our employees also preclude them from bringing the proprietary information or materials of third parties to us. We also require confidentiality agreements or material transfer agreements from third parties that receive our confidential information or materials.

For further details on the risks relating to our intellectual property, please see the risk factors under Item 1A of this report, including, but not limited to, the risk factors entitled “Our success depends substantially upon our ability to obtain and maintain intellectual property protection relating to our drug candidates and research technologies” and “If we are sued for infringing third-party intellectual property rights, it will be costly and time-consuming, and an unfavorable outcome would have a significant adverse effect on our business.”

Government Regulation

The FDA and comparable regulatory agencies in state and local jurisdictions and in foreign countries impose substantial requirements upon the clinical development, manufacture, marketing and distribution of drugs. These agencies and other federal, state and local entities regulate research and development activities and the testing, manufacture, quality control, labeling, storage, record keeping, approval, advertising and promotion of our drug candidates and drugs.

In the United States, the FDA regulates drugs under the Federal Food, Drug and Cosmetic Act and implementing regulations. The process required by the FDA before our drug candidates may be marketed in the United States generally involves the following:

- completion of extensive preclinical laboratory tests, preclinical animal studies and formulation studies, all performed in accordance with the FDA’s good laboratory practice regulations;
- submission to the FDA of an investigational new drug application (“IND”), which must become effective before clinical trials may begin;
- performance of adequate and well-controlled clinical trials to establish the safety and efficacy of the drug candidate for each proposed indication in accordance with good clinical practices;
- submission of a new drug application (“NDA”) to the FDA, which must usually be accompanied by payment of a substantial user fee;
- satisfactory completion of an FDA preapproval inspection of the manufacturing facilities at which the product is produced to assess compliance with current good manufacturing practice (“cGMP”) regulations and FDA audits of select clinical investigator sites to assess compliance with good clinical practices (“GCP”); and
- FDA review and approval of the NDA prior to any commercial marketing, sale or shipment of the drug.

Similar regulatory procedures generally apply in countries outside of the United States. This testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for our drug candidates will be granted on a timely basis, if at all.

Non-clinical tests include laboratory evaluation of product chemistry, formulation and stability, and studies to evaluate toxicity and pharmacokinetics in animals. The results of non-clinical tests, together with manufacturing information and analytical data, are submitted as part of an IND application to the FDA. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day period, raises concerns or

questions about the conduct of the proposed clinical trial, including concerns that human research subjects may be exposed to unreasonable health risks. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Our submission of an IND or a foreign equivalent, or those of our collaborators, may not result in authorization from the FDA or its foreign equivalent to commence a clinical trial. A separate submission to an existing IND must also be made for each successive clinical trial conducted during product development. Further, an independent institutional review board ("IRB") or its foreign equivalent for each medical center proposing to conduct the clinical trial must review and approve the plan for any clinical trial before it commences at that center and it must monitor the clinical trial until completed. The FDA, the IRB or their foreign equivalents, or the clinical trial sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk.

Clinical Trials. For purposes of an NDA or equivalent submission and approval, clinical trials are typically conducted in the following three sequential phases, which may overlap:

- Phase 1: Phase 1 trials include the initial introduction of a drug candidate into humans. These studies may be conducted in patients, but are usually conducted in healthy volunteer subjects. These studies are designed to determine the metabolic and pharmacologic actions of the drug candidate in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness. During Phase 1, sufficient information about the drug candidate's pharmacokinetics and pharmacological effects should be obtained to permit the design of well-controlled, scientifically valid, Phase 2 trials.

- Phase 2: Phase 2 trials include the early controlled clinical studies conducted to obtain some preliminary data on the effectiveness of the drug candidate for a particular indication or indications in patients with the disease or condition. This phase of testing also helps determine the common short-term side effects and risks associated with the drug candidate. These clinical trials are generally conducted in a limited patient population to identify possible adverse effects and safety risks, to make an initial determination of potential efficacy of the drug candidate for specific targeted indications and to determine dose tolerance and optimal dosage. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more expensive Phase 3 clinical trials. Phase 2a clinical trials generally are designed to study the pharmacokinetic or pharmacodynamic properties and to conduct a preliminary assessment of safety of the drug candidate over a measured dose response range. In some cases, a sponsor may decide to conduct a Phase 2b clinical trial, which is a second, typically larger, confirmatory Phase 2 trial that could, if positive and accepted by a regulatory authority, support approval of a drug candidate.
- Phase 3: If the Phase 2 clinical trials demonstrate that a dose range of the drug candidate is potentially effective and has an acceptable safety profile, Phase 3 clinical trials are then undertaken in large patient populations to further evaluate dosage, to provide substantial evidence of clinical efficacy and to further test for safety in an expanded and diverse patient population at multiple, geographically dispersed clinical trial sites. Phase 3 trials are also intended to provide an adequate basis for extrapolating the results to the general population and transmitting that information in the drug labeling. Phase 3 studies usually include several hundred to several thousand people, and are usually longer in duration than Phase 2 trials.

At any time during the conduct of a clinical trial, the FDA or a foreign equivalent can impose a clinical hold on the trial if it believes the trial is unsafe or that the protocol is clearly deficient in design in meeting its stated objectives, which requires the conduct of the trial to cease until the clinical hold is removed. In some cases, the FDA or foreign equivalent may condition approval of marketing approval for a drug candidate on the sponsor's agreement to conduct additional clinical trials to further assess the drug's safety and effectiveness after marketing approval, known as Phase 4 clinical trials.

The clinical trials we conduct for our drug candidates, both before and after approval, and the results of those trials, are generally required to be included in a clinical trials registry database that is available and accessible to the public via the internet. A failure by us to properly participate in the clinical trial database registry could subject us to significant civil monetary penalties.

Health care providers in the United States, including research institutions from which we or our partners obtain patient information, are subject to privacy rules under the Health Insurance Portability and Accountability Act of 1996 and state and local privacy laws. In the European Union, these entities are subject to the Directive 95/46-EC of the European Parliament on the protection of individuals with regard to the processing of personal data and individual European Union member states implementing additional legislation. The General Data Protection Regulation (EU) 2016/679 is a regulation in EU law on data protection and privacy for all individuals within the EU and the European Economic Area. Other countries have similar privacy legislation. We could face substantial penalties if we knowingly receive individually identifiable health information from a health care provider that has not satisfied the applicable privacy laws. In addition, certain privacy laws and genetic testing laws may apply directly to our operations and/or those of our partners and may impose restrictions on the use and dissemination of individuals' health information and use of biological samples.

New Drug/Marketing Approval Application. The results of drug candidate development, preclinical testing and clinical trials are submitted to the FDA as part of an NDA. The NDA also must contain extensive manufacturing information. In addition, the FDA may require that a proposed Risk Evaluation and Mitigation Strategy, also known as a REMS, be submitted as part of the NDA if the FDA determines that it is necessary to ensure that the benefits of the drug outweigh its risks. Similar, and in some cases additional, requirements apply in foreign jurisdictions for marketing approval applications for drugs in those jurisdictions. The FDA may refer the NDA to an advisory

committee for review, evaluation and recommendation as to whether the application should be approved. The FDA often, but not always, follows the advisory committee's recommendations. The FDA may deny approval of an NDA by issuing a complete response letter if the applicable regulatory criteria are not satisfied, or it may require additional clinical data, including data in a pediatric population, or an additional Phase 3 clinical trial or impose other conditions that must be met in order to secure final approval for an NDA.

Even if such data are submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. Data from clinical trials are not always conclusive and the FDA may interpret data differently than we or our partners do. Once issued, the FDA or foreign equivalent may withdraw a drug approval if ongoing regulatory requirements are not met or if safety problems occur after the drug reaches the market. In addition, the FDA or its foreign counterparts may require further testing, including Phase 4 clinical trials, and surveillance or restrictive distribution programs to monitor the effect of approved drugs which have been commercialized. The FDA and its foreign counterparts have the power to prevent or limit further marketing of a drug based on the results of these post-marketing programs. Drugs may be marketed only for the approved indications and in accordance with the provisions of the approved label. Further, if there are any modifications to a drug, including changes in indications, labeling or manufacturing processes or facilities, we may be required to submit and obtain prior FDA approval of a new NDA or NDA supplement, or the foreign equivalent, which may require us to develop additional data or conduct additional preclinical studies and clinical trials.

Satisfaction of FDA regulations and requirements or similar regulations and requirements of state, local and foreign regulatory agencies typically takes several years. The actual time required may vary substantially based upon the type, complexity and novelty of the drug candidate or disease. Typically, if a drug candidate is intended to treat a chronic disease, as is the case with some of our drug candidates, safety and efficacy data must be gathered over an extended period of time. Government regulation may delay or prevent marketing of drug candidates for a considerable period of time and impose costly procedures upon our activities. The FDA or any other regulatory agency may not grant approvals for new indications for our drug candidates on a timely basis, if at all. Even if a drug candidate receives regulatory approval, the approval may be significantly limited to specific disease states, patient populations and dosages or restrictive distribution programs. Further, even after regulatory approval is obtained, later discovery of previously unknown problems with a drug may result in restrictions on the drug or even complete withdrawal of the drug from the market. Delays in obtaining, or failures to obtain, regulatory approvals for any of our drug candidates would harm our business. In addition, we cannot predict what future U.S. or foreign governmental regulations may be implemented.

Orphan Drug Designation. Some jurisdictions, including the United States, may designate drugs for relatively small patient populations as orphan drugs. The FDA grants orphan drug designation to drugs intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States.

An FDA orphan drug designation does not shorten the duration of the regulatory review and approval process. If a drug candidate that has an orphan drug designation receives the first FDA marketing approval for the indication for which the designation was granted, then the approved drug is entitled to orphan drug exclusivity. This means that the FDA may not approve another company's application to market the same drug for the same indication for a period of seven years, except in certain circumstances, such as a showing of clinical superiority to the drug with orphan exclusivity or if the holder of the orphan drug designation cannot assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the designation was granted. Competitors may receive approval of different drugs or biologics for the indications for which the orphan drug has exclusivity.

Special Protocol Assessment. A sponsor may request a Special Protocol Assessment, or SPA, agreement with FDA on the Phase 3 clinical trial protocol design and analysis that will form the primary basis of an efficacy claim. Even if the FDA agrees to the design, execution and analyses proposed in protocols reviewed under the SPA process, the FDA may revoke or alter its agreement if public health concerns emerge that were unrecognized at the time of the SPA agreement, or a substantial scientific issue essential to determining safety or efficacy is identified after testing has begun. An SPA does not guarantee that an NDA will be approved.

Fast Track Designation. Fast track is a process designed by the FDA to facilitate the development and expedite the review of drugs to treat serious diseases and fill an unmet medical need. Although fast track designation does not affect the standards for approval, the benefits of this designation include scheduled meetings to seek FDA input into development plans, the option of submitting an NDA in sections rather than all components simultaneously, and the potential eligibility for priority review if supported by clinical data.

Other Regulatory Requirements. Any drugs manufactured or distributed by us or our partners pursuant to FDA approvals or their foreign counterparts are subject to continuing regulation by the applicable regulatory authority, including recordkeeping requirements and reporting of adverse experiences associated with the drug. Drug manufacturers and their subcontractors are required to register their establishments with the FDA and other applicable regulatory authorities, and are subject to periodic unannounced inspections by these regulatory authorities for compliance with ongoing regulatory requirements, including cGMPs, which impose certain procedural and documentation requirements upon us and our third-party manufacturers. Failure to comply with the statutory and regulatory requirements can subject a manufacturer to possible legal or regulatory action, such as warning letters,

suspension of manufacturing, seizure of product, injunctive action or possible civil penalties. We cannot be certain that we or our present or future third-party manufacturers or suppliers will be able to comply with the cGMP regulations and other ongoing FDA and other regulatory requirements. If our present or future third-party manufacturers or suppliers are not able to comply with these requirements, the FDA or its foreign counterparts may halt our or our partners' clinical trials, require us to recall a drug from distribution, or withdraw approval of the NDA for that drug.

For further details on the risks relating to government regulation of our business, please see the risk factors under Item 1A of this report, including, but not limited to, the risk factor entitled "The regulatory approval process is expensive, time-consuming and uncertain and may prevent our partners or us from obtaining approvals to commercialize some or all of our drug candidates."

Competition

We compete in the segments of the pharmaceutical, biotechnology and other related markets that address neuromuscular and cardiovascular diseases and other diseases relating to muscle dysfunction, each of which is highly competitive. We face significant competition from most pharmaceutical companies and biotechnology companies that are also researching and selling products designed to address cardiovascular diseases and diseases and medical conditions associated with skeletal muscle weakness and wasting. Many of our competitors have significantly greater financial, manufacturing, marketing and drug development resources than we do. Large pharmaceutical companies in particular have extensive experience in clinical testing and in obtaining regulatory approvals for drugs. These companies also have significantly greater research capabilities than we do. In addition, many universities

and private and public research institutes are active in research of neuromuscular and cardiovascular diseases and other diseases where there is muscle dysfunction, some in direct competition with us.

We believe that our ability to successfully compete will depend on, among other things:

- our drug candidates' efficacy, safety and tolerability;
- the speed and cost-effectiveness with which we develop our drug candidates;
- the selection of suitable indications for which to develop our drug candidates;
- the successful completion of clinical development and laboratory testing of our drug candidates;
- the timing and scope of any regulatory approvals we or our partners obtain for our drug candidates;
- our or our partners' ability to manufacture and sell commercial quantities of our approved drugs to meet market demand;
- acceptance of our drugs by physicians and other health care providers;
    - the willingness of third-party payors to provide reimbursement for the use of our drugs;
- our ability to protect our intellectual property and avoid infringing the intellectual property of others;
- the quality and breadth of our technology;
- our employees' skills and our ability to recruit and retain skilled employees;
    - our cash flows under existing and potential future arrangements with licensees, partners and other parties; and
- the availability of substantial capital resources to fund development and commercialization activities.

Our competitors may develop drug candidates and market drugs that are less expensive and more effective than our future drugs or that may render our drugs obsolete. Our current or future competitors may also commercialize competing drugs before we or our partners can launch any drugs developed from our drug candidates. These organizations also compete with us to attract qualified personnel and potential parties for acquisitions, joint ventures or other strategic alliances.

If omecamtiv mecarbil is approved for marketing by the FDA or other regulatory authorities for the treatment of heart failure with reduced ejection fraction, it would compete against other drugs used for the treatment of chronic heart failure. These include generic drugs, such as milrinone, dobutamine or digoxin and branded drugs such as Corlanor (ivabradine), and Entresto®. Omecamtiv mecarbil could also potentially compete against other novel drug candidates and therapies in development, such as those being developed by ARCA biopharma, Inc., Novartis, Bayer, Merck, Theravance Biopharma, Capricor, Cardiorentis AG, Ono Pharmaceutical Company, ARMGO Pharma, Inc., Bristol-Myers Squibb Company, Zensun Sci & Tech, Ltd., and Tenax Therapeutics (formerly known as Oxygen Biotherapeutics, Inc.). In addition, there are a number of medical devices both marketed and in development for the potential treatment of heart failure.

If reldesemtiv is approved by the FDA or other regulatory authorities for the treatment of ALS, it may then compete with other drugs used for the treatment of ALS including Radicava (edaravone) and potential new therapies for ALS that are currently being developed by companies such as Ionis Pharmaceuticals, Inc. (in collaboration with Biogen), Genervon Biopharmaceuticals, LLC, Orion Pharmaceuticals, Orphazyme, Eisai Co., Ltd., Genentech, Inc., BioElectron Technology Corporation, Q Therapeutics, AB Science, VM Biopharma, Mallinckrodt Pharmaceuticals, Chronos Therapeutics, Denali Therapeutics (in collaboration with Sanofi), and MediciNova, Inc. In addition, BrainStorm Cell Therapeutics and Neuralstem, Inc. are each conducting clinical development of stem cell therapies for the potential treatment of ALS. If reldesemtiv is approved by the FDA or other regulatory authorities for the potential treatment of SMA, potential competitors include Roche (in collaboration with PTC Therapeutics), AveXis, Inc. (a Novartis company), Biogen Inc. (in collaboration with Ionis Pharmaceuticals, Inc.), Novartis AG, and Bioblast Pharma Ltd. Drugs that could compete with reldesemtiv could also compete against tirasemtiv in ALS or other neuromuscular diseases, should the appropriate clinical trials be conducted. If reldesemtiv is approved by the FDA for

the potential treatment of non-neuromuscular indications associated with muscle weakness, potential competitors include Ligand Pharmaceuticals, Inc., GTx, Inc., Regeneron Pharmaceuticals, Inc. (in collaboration with Sanofi), Eli Lilly & Company, Acceleron Pharma, Stealth BioTherapeutics, Scholar Rock, Summit Therapeutics, Pfizer Inc., and Novartis (in collaboration with MorphoSys AG).

Employees

As of December 31, 2018, we had 130 full-time employees.

We have no collective bargaining agreements with our employees, and we have not experienced any work stoppages. We believe that our relations with our employees are good.

Investor Information

We file electronically with the SEC our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K pursuant to Section 13 or 15(d) of the Exchange Act. The SEC maintains an Internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. The address of that site is www.sec.gov.

You may obtain a free copy of our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K and amendments to those reports on the day of filing with the SEC on our website at www.cytokinetics.com or by contacting the Investor Relations Department at our corporate offices by calling 650-624-3060. The information found on our website is not part of this or any other report filed with or furnished to the SEC.

Item 1A. Risk Factors

In evaluating our business, you should carefully consider the following risks in addition to the other information in this report. Any of the following risks could materially and adversely affect our business, results of operations, financial condition or your investment in our securities, and many are beyond our control. The risks and uncertainties described below are not the only ones facing us. Additional risks and uncertainties not presently known to us, or that we currently see as immaterial, may also adversely affect our business.

Risks Related To Our Business

We have a history of significant losses and may not achieve or sustain profitability and, as a result, you may lose all or part of your investment.

We have generally incurred operating losses in each year since our inception in 1997, due to costs incurred in connection with our research and development activities and general and administrative costs associated with our operations. Our drug candidates are all in early through late-stage clinical testing, and we and our partners must conduct significant additional clinical trials before we and our partners can seek the regulatory approvals necessary to begin commercial sales of our drugs. We expect to incur increasing losses for at least several more years, as we continue our research activities and conduct development of, and seek regulatory approvals for, our drug candidates, and commercialize any approved drugs. If our drug candidates fail or do not gain regulatory approval, or if our drugs do not achieve market acceptance, we will not be profitable. If we fail to become and remain profitable, or if we are unable to fund our continuing losses, you could lose all or part of your investment.

We will need substantial additional capital in the future to sufficiently fund our operations.

We have consumed substantial amounts of capital to date, and our operating expenditures will increase over the next several years if we expand our research and development activities. We have funded our operations and capital expenditures with proceeds primarily from private and public sales of our equity securities, a royalty monetization agreement, strategic alliances, long-term debt, other financings, interest on investments and grants. We believe that our existing cash and cash equivalents, short-term investments and interest earned on investments should be sufficient to meet our projected operating requirements for at least the next 12 months. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect. Because of the numerous risks and uncertainties associated with the development of our drug candidates and other research and development activities, including risks and uncertainties that could impact the rate of progress of our development activities, we are unable to estimate with certainty the amounts of capital outlays and operating expenditures associated with these activities.

For the foreseeable future, our operations will require significant additional funding, in large part due to our research and development expenses and the absence of any revenues from product sales. For example, we will require significant additional funding to enable us to conduct further development of our product candidates. Until we can generate a sufficient amount of product revenue, we expect to raise future capital through strategic alliance and licensing arrangements, public or private equity offerings and debt financings. We do not currently have any commitments for future funding other than reimbursements, milestone and royalty payments that we may receive under our collaboration agreements with Amgen and Astellas. We may not receive any further funds under those

agreements. Our ability to raise funds may be adversely impacted by current economic conditions. As a result of these and other factors, we do not know whether additional financing will be available when needed, or that, if available, such financing would be on terms favorable to our stockholders or us.

To the extent that we raise additional funds through strategic alliances or licensing or other arrangements with third parties, we will likely have to relinquish valuable rights to our technologies, research programs or drug candidates, or grant licenses on terms that may not be favorable to us. To the extent that we raise additional funds by issuing equity securities, our stockholders will experience additional dilution and our share price may decline. To the extent that we raise additional funds through debt financing, the financing may involve covenants that restrict our business activities. In addition, funding from any of these sources, if needed, may not be available to us on favorable terms, or at all, or in accordance with our planned timelines.

If we cannot raise the funds we need to operate our business, we will need to delay or discontinue certain research and development activities, and our stock price may be negatively affected.

We are obligated to develop and maintain proper and effective internal control over financial reporting. In February 2019, our management identified a material weakness in our internal control over financial reporting. If we are unable to remediate the material weakness or other control deficiencies are identified, we may not be able to report our financial results accurately,

prevent fraud or file our periodic reports in a timely manner, which may adversely affect investor confidence in our company and, as a result, the value of our common stock.

We are required, pursuant to Section 404 of the Sarbanes-Oxley Act, to furnish a report by management on, among other things, the effectiveness of our internal control over financial reporting.

Complying with Section 404 requires a rigorous compliance program as well as adequate time and resources. We may not be able to complete our internal control evaluation, testing and any required remediation in a timely fashion. Additionally, if we identify one or more material weaknesses in our internal control over financial reporting, we will not be able to assert that our internal controls are effective. A material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of the company's annual or interim financial statements will not be prevented or detected on a timely basis. On February 27, 2019, our management concluded that our internal controls over financial reporting were ineffective as of December 31, 2018 due to the identification of a material weakness. As of December 31, 2018, we identified a material weakness related to the ineffective review and verification of internally prepared reports and analyses utilized in our financial statement closing process. The material weakness is related to employee turnover resulting in a temporary lack of resources in financial reporting roles with the appropriate skills to perform effective review during our financial statement close process. This material weakness did not result in the restatement of prior quarterly or annually filed financial statements. To remediate the material weakness described above, we are actively recruiting for open positions within the accounting department and will, as necessary, supplement any interim staffing needs with temporary resources. We will also continue to evaluate and improve our internal controls, processes and procedures in the financial statement close process.

We also previously concluded that our internal controls over financial reporting were not effective as of September 30, 2016, because a material weakness existed in our internal control over financial reporting related to research and development expenses associated with the review of clinical trial expenses incurred under our clinical research organization trial agreements, including in part, our review of information received from third-party service providers that is used in the operation of this control. We remediated this material weakness as of December 31, 2016.

We cannot be certain that these measures will successfully remediate the material weakness identified in connection with the audit of our financial statements for the year ended December 31, 2018 and that other material weaknesses and control deficiencies will not be discovered in the future. If our efforts are not successful or other material weaknesses are identified in the future or we are not able to comply with the requirements of Section 404 in a timely manner, our reported financial results could be materially misstated, we would receive an adverse opinion regarding our internal controls over financial reporting from our independent registered public accounting firm, and we could be subject to investigations or sanctions by regulatory authorities, which would require additional financial and management resources, and the value of our common stock could decline. In addition, because we concluded that our internal controls over financial reporting were not effective as of December 31, 2018 and as of September 30, 2016, and to the extent we identify future weaknesses or deficiencies, there could be material misstatements in our consolidated financial statements and we could fail to meet our financial reporting obligations. As a result, our ability to obtain additional financing, or obtain additional financing on favorable terms, could be materially and adversely affected which, in turn, could materially and adversely affect our business, our financial condition and the value of our common stock. If we are unable to assert that our internal control over financial reporting is effective in the future, or if our independent registered public accounting firm is unable to express an opinion or expresses an adverse opinion on the effectiveness of our internal controls in the future, investor confidence in the accuracy and completeness of our financial reports could be further eroded, which would have a material adverse effect on the price of our common stock.

Covenants in our Loan Agreement restrict our business and operations in many ways and if we do not effectively manage our covenants, our financial conditions and results of operations could be adversely affected. Our operations may not provide sufficient cash to meet the repayment obligations of our debt incurred under the Loan Agreement.

The Loan Agreement requires that we comply with certain covenants applicable to us, including among other things, covenants restricting dispositions, changes in business, management, ownership or business locations, mergers or acquisitions, indebtedness, encumbrances, distributions, investments, transactions with affiliates and subordinated debt, any of which could restrict our business and operations, particularly our ability to respond to changes in our business or to take specified actions to take advantage of certain business opportunities that may be presented to us. Our failure to comply with any of the covenants could result in a default under the Loan Agreement, which could permit the lenders to declare all or part of any outstanding borrowings to be immediately due and payable.

If we are unable to repay those amounts, the Lenders could proceed against the collateral granted to them to secure that debt, which would seriously harm our business. In addition, should we be unable to comply with these covenants or if we default on any portion of our outstanding borrowings, the lenders can also impose a 5.0% penalty.

We have never generated, and may never generate, revenues from commercial sales of our drugs and we will not have drugs to market for at least several years, if ever.

We currently have no drugs for sale and we cannot guarantee that we will ever develop or obtain approval to market any drugs. To receive marketing approval for any drug candidate, we must demonstrate that the drug candidate satisfies rigorous standards of safety and efficacy to the FDA in the United States and other regulatory authorities abroad. We and our partners will need to conduct significant additional research and preclinical and clinical testing before we or our partners can file applications with the FDA or other regulatory authorities for approval of any of our drug candidates. In addition, to compete effectively, our drugs must be easy to use, cost-effective, covered by insurance or government sponsored medical plans, and economical to manufacture on a commercial scale, compared to other therapies available for the treatment of the same conditions. We may not achieve any of these objectives. Currently, our drug candidates in clinical development include omecamtiv mecarbil for the potential treatment of heart failure and reldesemtiv for the potential treatment of SMA, ALS and potentially other neuromuscular and non-neuromuscular indications associated with muscle weakness. We cannot be certain that the clinical development of our current or any future drug candidates will be successful, that they will receive the regulatory approvals required to commercialize them, that they will ultimately be accepted by prescribers or reimbursed by insurers or that any of our other research programs will yield a drug candidate suitable for clinical testing or commercialization. Our commercial revenues, if any, will be derived from sales of drugs that we do not expect to be commercially marketed for at least several years, if at all. The development of any one or all of these drug candidates may be discontinued at any stage of our clinical trials programs and we may not generate revenue from any of these drug candidates.

Clinical trials may fail to demonstrate the desired safety and efficacy of our drug candidates, which could prevent or significantly delay completion of clinical development and regulatory approval.

Prior to receiving approval to commercialize any of our drug candidates, we or our partners must adequately demonstrate to the satisfaction of FDA and foreign regulatory authorities that the drug candidate is sufficiently safe and effective with substantial evidence from well-controlled clinical trials. We or our partners will need to demonstrate efficacy in clinical trials for the treatment of specific indications and monitor safety throughout the clinical development process and following approval. None of our drug candidates have yet met the safety and efficacy standards required for regulatory approval for commercialization and they may never do so. In addition, for each of our preclinical compounds, we or our partners must adequately demonstrate satisfactory chemistry, formulation, quality, stability and toxicity in order to submit an IND to the FDA, or an equivalent application in foreign jurisdictions, that would allow us to advance that compound into clinical trials. Furthermore, we or our partners may need to submit separate INDs (or foreign equivalent) to different divisions within the FDA (or foreign regulatory authorities) in order to pursue clinical trials in different therapeutic areas. Each new IND (or foreign equivalent) must be reviewed by the new regulatory division before the clinical trial under its jurisdiction can proceed, entailing all the risks of delay inherent to regulatory review. If our or our partners' current or future preclinical studies or clinical trials are unsuccessful, our business will be significantly harmed and our stock price could be negatively affected.

All of our drug candidates are prone to the risks of failure inherent in drug development. Preclinical studies may not yield results that would adequately support the filing of an IND (or a foreign equivalent) with respect to our potential drug candidates. Even if the results of preclinical studies for a drug candidate are sufficient to support such a filing, the results of preclinical studies do not necessarily predict the results of clinical trials. As an example, because the physiology of animal species used in preclinical studies may vary substantially from other animal species and from

humans, it may be difficult to assess with certainty whether a finding from a study in a particular animal species will result in similar findings in other animal species or in humans. For any of our drug candidates, the results from Phase 1 clinical trials in healthy volunteers and clinical results from Phase 1 and 2 trials in patients are not necessarily indicative of the results of later and larger clinical trials that are necessary to establish whether the drug candidate is safe and effective for the applicable indication. Likewise, interim results from a clinical trial may not be indicative of the final results from that trial, and results from early Phase 2 clinical trials may not be indicative of the results from later clinical trials. For example, early Phase 2 clinical trials of tirasemtiv in patients with ALS showed encouraging dose-related trends in measurements of the ALSFRS-R, a clinically validated instrument designed to measure disease progression and changes in functional status, for patients receiving tirasemtiv compared to those receiving placebo. However, BENEFIT-ALS, a Phase 2b clinical trial of tirasemtiv in patients with ALS, did not achieve its primary efficacy endpoint, the mean change from baseline in the ALSFRS-R for patients receiving tirasemtiv compared to those receiving placebo, and in November 2017, we announced that VITALITY-ALS did not achieve its primary endpoint or secondary endpoints. Following the results of VITALITY-ALS, we suspended development of tirasemtiv.

Moreover, the Phase 2 clinical trial of reldesemtiv in COPD and Phase 1b clinical trial of reldesemtiv in elderly subjects with limited mobility did not show efficacy, and there can be no assurance that reldesemtiv will demonstrate efficacy in other indications, regardless of the phase of development.

In addition, while the clinical trials of our drug candidates are designed based on the available relevant information, such information may not accurately predict what actually occurs during the course of the trial itself, which may have consequences for the conduct of an ongoing clinical trial or for the eventual results of that trial. For example, the number of patients planned to be enrolled in a placebo-controlled clinical trial is determined in part by estimates relating to expected treatment effect and variability about the

primary endpoint. These estimates are based upon earlier non-clinical and clinical studies of the drug candidate itself and clinical trials of other drugs thought to have similar effects in a similar patient population. If information gained during the conduct of the trial shows these estimates to be inaccurate, we may elect to adjust the enrollment accordingly, which may cause delays in completing the trial, additional expense or a statistical penalty to apply to the evaluation of the trial results.

Furthermore, in view of the uncertainties inherent in drug development, such clinical trials may not be designed with focus on indications, patient populations, dosing regimens, endpoints, safety, efficacy or pharmacokinetic parameters or other variables that will provide the necessary safety or efficacy data to support regulatory approval to commercialize the resulting drugs. For example, we believe that effects on respiratory function, including SVC, may be appropriate as a clinical endpoint for reldesemtiv; however, regulatory authorities may not accept these effects as a clinical endpoint to support registration of reldesemtiv for the treatment of ALS. Clinical trials of our drug candidates are designed based on guidance or advice from regulatory agencies, which is subject to change during the development of the drug candidate at any time. Such a change in a regulatory agency's guidance or advice may cause that agency to deem results from trials to be insufficient to support approval of the drug candidate and require further clinical trials of that drug candidate to be conducted. In addition, individual patient responses to the dose administered of a drug may vary in a manner that is difficult to predict. Also, the methods we select to assess particular safety, efficacy or pharmacokinetic parameters may not yield the same statistical precision in estimating our drug candidates' effects as may other methodologies. Even if we believe the data collected from clinical trials of our drug candidates are promising, these data may not be sufficient to support approval by the FDA or foreign regulatory authorities. Non-clinical and clinical data can be interpreted in different ways. Accordingly, the FDA or foreign regulatory authorities could interpret these data in different ways from us or our partners, which could delay, limit or prevent regulatory approval.

Furthermore, while planned interim analyses in clinical trials can enable early terminations for futility or for overwhelming efficacy, the timing, which can be based on accrual of events, enrollment or other factors, and the results of such analyses, is unpredictable. For example, in GALACTIC-HF, a Phase 3 clinical trial of omecamtiv mecarbil, we anticipate an interim analysis for futility in the first half of 2019 and another interim analysis for overwhelming efficacy in 2020, but the exact timing and outcome of such interim analyses are uncertain. Although our GALACTIC-HF trial is being conducted under an SPA agreement with FDA, there is no guarantee that either the trial will be successful, or even if successful, that FDA would approve any resulting NDA.

Administering any of our drug candidates or potential drug candidates may produce undesirable side effects, also known as adverse events. Toxicities and adverse events observed in preclinical studies for some compounds in a particular research and development program may also occur in preclinical studies or clinical trials of other compounds from the same program. Potential toxicity issues may arise from the effects of the active pharmaceutical ingredient itself or from impurities or degradants that are present in the active pharmaceutical ingredient or could form over time in the formulated drug candidate or the active pharmaceutical ingredient. These toxicities or adverse events could delay or prevent the filing of an IND (or a foreign equivalent) with respect to our drug candidates or potential drug candidates or cause us, our partners or the FDA or foreign regulatory authorities to modify, suspend or terminate clinical trials with respect to any drug candidate at any time during the development program. Further, the administration of two or more drugs contemporaneously can lead to interactions between them, and our drug candidates may interact with other drugs that trial subjects are taking. If the adverse events are severe or frequent enough to outweigh the potential efficacy of a drug candidate, the FDA or other regulatory authorities could deny approval of that drug candidate for any or all targeted indications. Even if one or more of our drug candidates were approved for sale as drugs, the occurrence of even a limited number of adverse events or toxicities when used in large populations may cause the FDA or foreign regulatory authorities to impose restrictions on, or stop, the further marketing of those drugs. Indications of potential adverse events or toxicities which do not seem significant during the course of clinical trials may later turn out to actually constitute serious adverse events or toxicities when a drug is used

in large populations or for extended periods of time.

We have observed certain adverse events in the clinical trials conducted with our drug candidates. For example, in clinical trials of omecamtiv mecarbil, adverse events of chest discomfort, palpitations, dizziness and feeling hot, increases in heart rate, declines in blood pressure, electrocardiographic changes consistent with acute myocardial ischemia and transient rises in the MB fraction of creatine kinase and cardiac troponins I and T, which are indicative of myocardial infarction were observed during treatment with omecamtiv mecarbil.

In addition, clinical trials of reldesemtiv and omecamtiv mecarbil enroll patients who typically suffer from serious diseases which put them at increased risk of death. These patients may die while receiving our drug candidates. In such circumstances, it may not be possible to exclude with certainty a causal relationship to our drug candidate, even though the responsible clinical investigator may view such an event as not study drug-related.

Any failure or significant delay in completing preclinical studies or clinical trials for our drug candidates, or in receiving and maintaining regulatory approval for the sale of any resulting drugs, may significantly harm our business and negatively affect our stock price.

The failure of a number of Phase 3 clinical trials evaluating other compounds as potential treatments for patients with ALS may suggest an increased risk that our clinical development program of reldesemtiv in patients with ALS will also fail.

In recent years, a number of Phase 3 clinical trials of potential treatments for ALS have failed to demonstrate the requisite efficacy for regulatory approval or for their continued development. These include our trial of tirasemtiv known as VITALITY-ALS, Biogen's trial of dexpramipexole, known as EMPOWER, the National Institute of Neurological Disorders and Stroke's trial of ceftriaxone, and Trophos SA's trial of olesoxime. Reldesemtiv, like these compounds, may fail in clinical development if it does not show a statistically significant level of clinical efficacy or if the adverse event profile is too great compared to it benefits. Further, even if we believe the data collected from the planned clinical development program of reldesemtiv are promising and should support approval, the FDA or other regulatory authorities may not deem these data to be sufficient to support approval.

Clinical trials are expensive, time-consuming and subject to delay.

Clinical trials are subject to rigorous regulatory requirements and are very expensive, difficult and time-consuming to design and implement. The length of time and number of trial sites and patients required for clinical trials vary substantially based on the type, complexity, novelty, intended use of the drug candidate and safety concerns. Clinical trials of our current drug candidates can each continue for several more years. However, the clinical trials for all or any of our drug candidates may take significantly longer to complete. The commencement and completion of our or our partners' clinical trials could be delayed or prevented by many factors, including, but not limited to:

- delays in obtaining, or inability to obtain, regulatory or other approvals to commence and conduct clinical trials in the manner we or our partners deem necessary for the appropriate and timely development of our drug candidates and commercialization of any resulting drugs;
- delays in identifying and reaching agreement, or inability to identify and reach agreement, on acceptable terms, with prospective clinical trial sites and other entities involved in the conduct of our or our partners' clinical trials;
- delays or additional costs in developing, or inability to develop, appropriate formulations of our drug candidates for clinical trial use;
- slower than expected rates of patient recruitment and enrollment;
- for those drug candidates that are the subject of a strategic alliance, delays in reaching agreement with our partner as to appropriate development strategies;
    - a regulatory authority may require changes to a protocol for a clinical trial that then may require approval from regulatory agencies in other jurisdictions where the trial is being conducted;
- an institutional review board ("IRB") or its foreign equivalent may require changes to a protocol that then require approval from regulatory agencies and other IRBs and their foreign equivalents, or regulatory authorities may require changes to a protocol that then require approval from the IRBs or their foreign equivalents;
- for clinical trials conducted in foreign countries, the time and resources required to identify, interpret and comply with foreign regulatory requirements or changes in those requirements, and political instability or natural disasters occurring in those countries;

- lack of effectiveness of our drug candidates during clinical trials;
- unforeseen safety issues;
- inadequate supply, or delays in the manufacture or supply, of clinical trial materials;
- uncertain dosing issues;
- failure by us, our partners, or clinical research organizations, investigators or site personnel engaged by us or our partners to comply with good clinical practices and other applicable laws and regulations, including those concerning informed consent;
- inability or unwillingness of investigators or their staffs to follow clinical protocols;
- failure by our clinical research organizations, clinical manufacturing organizations and other third parties supporting our or our partners' clinical trials to fulfill their obligations;
- inability to monitor patients adequately during or after treatment;

- introduction of new therapies or changes in standards of practice or regulatory guidance that render our drug candidates or their clinical trial endpoints obsolete; and
- results from non-clinical studies that may adversely impact the timing or further development of our drug candidates.

We do not know whether planned clinical trials will begin on time, or whether planned or currently ongoing clinical trials will need to be restructured or will be completed on schedule, if at all. Significant delays in clinical trials will impede our ability to commercialize our drug candidates and generate revenue and could significantly increase our development costs.

If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the trial until its conclusion. We may experience difficulties in patient enrollment in clinical trials for a variety of reasons. The enrollment of patients depends on many factors, including:

- the patient eligibility criteria defined in the protocol;
- the size of the patient population required for analysis of the trial's primary endpoints;
- the proximity of patients to study sites;
- the design of the trial;
- the ability to recruit clinical trial investigators with the appropriate competencies and experience;
- clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies or clinical trials, including any new drugs that may be approved for the indications we are investigating or clinical trial results;
- the ability to obtain and maintain patient consents; and
- the risk that patients enrolled in clinical trials will drop out of the trials before completion.

In addition, our and our partners' clinical trials will compete with other clinical trials for product candidates that are in the same therapeutic areas as our and our partners' product candidates, and this competition will reduce the number and types of patients available to us, because some patients who might have opted to enroll in our or our partners' trials may instead opt to enroll in a trial being conducted by one of our competitors. Since the number of qualified clinical investigators is limited, we expect to conduct some of our or our partners' clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials in such clinical trial site.

Delays in patient enrollment may result in increased costs or may affect the timing or outcome of the planned clinical trials, which could prevent completion of these trials and adversely affect our and our partners' ability to advance the development of product candidates.

We depend on Amgen for the conduct and funding of the development and commercialization of omecamtiv mecarbil.

Under our strategic alliance, Amgen holds an exclusive worldwide license to our drug candidate omecamtiv mecarbil. As a result, Amgen is responsible for the development and obtaining and maintaining regulatory approval of omecamtiv mecarbil for the potential treatment of heart failure worldwide.

Amgen is conducting GALACTIC-HF, a Phase 3 clinical trial of omecamtiv mecarbil. We do not control the development activities being conducted or that may be conducted in the future by Amgen, including, but not limited to, the timing of initiation, termination or completion of clinical trials, the analysis of data arising out of those clinical trials or the timing of release of data concerning those clinical trials, which may impact our ability to report on Amgen's results. Amgen may conduct these activities more slowly or in a different manner than we would if we

controlled the development of omecamtiv mecarbil. Amgen is responsible for submitting future applications to the FDA and other regulatory authorities for approval of omecamtiv mecarbil and will be the owner of marketing approvals issued by the FDA and other regulatory authorities for omecamtiv mecarbil, subject to Servier's exclusive rights for the commercialization of omecamtiv mecarbil in Europe, as well as the CIS, including Russia. If the FDA or other regulatory authorities approve omecamtiv mecarbil, Amgen will also be responsible for the marketing and sale of the resulting drug, subject to our right to co-promote omecamtiv mecarbil in North America in connection with the exercise of our option to co-fund Phase 3 development costs of omecamtiv mecarbil under the collaboration and subject to Servier's exclusive rights for the commercialization of omecamtiv mecarbil in Europe, as well as the CIS, including Russia. However, we cannot control whether Amgen will devote sufficient attention and resources to the development of omecamtiv mecarbil or will proceed in an expeditious manner, even with our exercise of our option and co-funding of the Phase 3 development program of omecamtiv mecarbil. Even if the FDA or other regulatory agencies approve omecamtiv mecarbil, Amgen or Servier may elect not to proceed with the commercialization of the resulting drug in one or more countries.

Disputes may arise between us and Amgen, which may delay or cause the termination of any clinical trials of omecamtiv mecarbil, result in significant litigation or cause Amgen to act in a manner that is not in our best interest. The costs associated with the continuing development of omecamtiv mecarbil may cause Amgen to reconsider the terms of its investment and seek to amend or terminate our collaboration agreement or to suspend the development of omecamtiv mecarbil. If development of omecamtiv mecarbil does not progress for these or any other reasons, we would not receive further milestone payments or royalties on product sales from Amgen with respect to omecamtiv mecarbil. If the results of one or more clinical trials with omecamtiv mecarbil do not meet Amgen's expectations at any time, Amgen may elect to terminate further development of omecamtiv mecarbil or certain of the potential clinical trials for omecamtiv mecarbil, even if the actual number of patients treated at that time is relatively small. In addition, Amgen generally has discretion to elect whether to pursue or abandon the development of omecamtiv mecarbil and may terminate our strategic alliance for any reason upon six months prior notice. With our consent, Amgen granted Servier an option to commercialize omecamtiv mecarbil in Europe and the CIS, including Russia, which Servier decided to exercise. In August 2016, we entered into a letter agreement with Amgen and Servier, which provides that if Amgen's rights to omecamtiv mecarbil are terminated with respect to the territory subject to Servier's sublicense, the sublicensed rights previously granted by Amgen to Servier with respect to omecamtiv mecarbil will remain in effect and become a direct license or sublicense of such rights by us to Servier, on substantially the same terms as those in the Option, License and Collaboration Agreement between Amgen and Servier. If Amgen abandons omecamtiv mecarbil, it would result in a delay in or could prevent us from commercializing omecamtiv mecarbil and would delay and could prevent us from obtaining revenues for this drug candidate. In addition, we would be required to provide Servier with a direct license or sublicense and the rights to commercialize omecamtiv mecarbil in Europe and the CIS, including Russia, on terms that were not negotiated by us. There can be no assurance that we would be able to negotiate and enter into a definitive agreement with Servier on terms favorable or acceptable to us, or at all.

If Amgen abandons development of omecamtiv mecarbil prior to regulatory approval or if it elects not to proceed with commercialization of the resulting drug following regulatory approval, we would have to seek a new partner for development or commercialization, curtail or abandon that development or commercialization, or undertake and fund the development of omecamtiv mecarbil or commercialization of the resulting drug ourselves. If we seek a new partner but are unable to do so on acceptable terms, or at all, or do not have sufficient funds to conduct the development or commercialization of omecamtiv mecarbil ourselves, we would have to curtail or abandon that development or commercialization, which could harm our business.

We depend on Astellas for the conduct and funding of the development and commercialization of reldesemtiv.

The primary objective of our strategic alliance with Astellas is to advance skeletal muscle activators including reldesemtiv as novel therapies for indications associated with muscle weakness.

Astellas has an exclusive license to co-develop and commercialize reldesemtiv for potential application in certain neuromuscular and non-neuromuscular indications worldwide, subject to certain Cytokinetics' development and commercialization rights. Under this strategic alliance, we have conducted a Phase 2 clinical trial of reldesemtiv in patients with SMA and Astellas has conducted a Phase 2 clinical trial of reldesemtiv in patients with COPD and a Phase 1b clinical trial of reldesemtiv in elderly subjects with limited mobility.

In addition, we are collaborating with Astellas to develop reldesemtiv in ALS. Astellas is primarily responsible for the development of reldesemtiv in ALS, and we are responsible for conducting FORTITUDE-ALS.

We do not control the development activities that may be conducted by Astellas, including, but not limited to, the timing of initiation, termination or completion of clinical trials, the analysis of data arising out of those clinical trials or the timing of release of data concerning those clinical trials, which may impact our ability to report on Astellas' results. Astellas may conduct these activities more slowly or in a different manner than we would. In general, Astellas

is responsible for submitting future applications to the FDA or other regulatory authorities for approval of reldesemtiv and will be the owner of any marketing approvals issued by the FDA or other regulatory authorities for reldesemtiv. If the FDA or other regulatory authorities approve reldesemtiv, Astellas will also be responsible for the marketing and sale of the resulting drug, subject to our right to co-promote the drug in the United States, Canada and, for neuromuscular indications, Europe. However, we cannot control whether Astellas will devote sufficient attention and resources to the development of reldesemtiv or will proceed in an expeditious manner. Even if the FDA or other regulatory agencies approve reldesemtiv, Astellas may elect not to proceed with the commercialization of the resulting drug in one or more countries.

If the results of one or more clinical trials with reldesemtiv, including the Phase 2 clinical trial of reldesemtiv in patients with SMA, do not meet Astellas' expectations at any time, Astellas may elect to terminate further development of reldesemtiv or certain of the potential clinical trials for reldesemtiv, even if the actual number of patients treated at that time is relatively small. In addition, Astellas generally has discretion to elect whether to pursue or abandon the development of reldesemtiv. Astellas may terminate our strategic alliance in whole or in part for any reason upon six months prior notice at any time following expiration of the strategic alliance's research term, which will expire December 31, 2019. If Astellas abandons reldesemtiv, it would result in a delay in or could prevent us from further developing or commercializing reldesemtiv and would delay and could prevent us from obtaining revenues for this drug candidate. Disputes may arise between us and Astellas, which may delay or cause the termination of any clinical trials of reldesemtiv, result in significant litigation or cause Astellas to act in a manner that is not in our best interest. If development of reldesemtiv does not progress for these or any other reasons, we would not receive further milestone payments or royalties on product sales from Astellas with respect to reldesemtiv. If Astellas abandons development of reldesemtiv prior to regulatory approval or if it

elects not to proceed with commercialization of the resulting drug following regulatory approval, we would have to seek a new partner for development or commercialization, curtail or abandon that development or commercialization, or undertake and fund the development of reldesemtiv or commercialization of the resulting drug ourselves. If we seek a new partner but are unable to do so on acceptable terms, or at all, or do not have sufficient funds to conduct the development or commercialization of reldesemtiv ourselves, we would have to curtail or abandon that development or commercialization, which could harm our business.

If we do not enter into strategic alliances for our unpartnered drug candidates or research and development programs or fail to successfully maintain our current or future strategic alliances, we may have to reduce, delay or discontinue our advancement of our drug candidates and programs or expand our research and development capabilities and increase our expenditures.

Drug development is complicated and expensive. We currently have limited financial and operational resources to carry out drug development. Our strategy for developing, manufacturing and commercializing our drug candidates currently requires us to enter into and successfully maintain strategic alliances with pharmaceutical companies or other industry participants to advance our programs and reduce our expenditures on each program. Accordingly, the success of our development activities depends in large part on our current and future strategic partners' performance, over which we have little or no control.

Our ability to commercialize drugs that we develop with our partners and that generate royalties from product sales depends on our partners' abilities to assist us in establishing the safety and efficacy of our drug candidates, obtaining and maintaining regulatory approvals and achieving market acceptance of the drugs once commercialized. Our partners may elect to delay or terminate development of one or more drug candidates, independently develop drugs that could compete with ours or fail to commit sufficient resources to the marketing and distribution of drugs developed through their strategic alliances with us. Our partners may not proceed with the development and commercialization of our drug candidates with the same degree of urgency as we would because of other priorities they face. In addition, new business combinations or changes in a partner's business strategy may adversely affect its willingness or ability to carry out its obligations under a strategic alliance.

If we are not able to successfully maintain our existing strategic alliances or establish and successfully maintain additional strategic alliances, we will have to limit the size or scope of, or delay or discontinue, one or more of our drug development programs or research programs, or undertake and fund these programs ourselves. Alternatively, if we elect to continue to conduct any of these drug development programs or research programs on our own, we will need to expand our capability to conduct clinical development by bringing additional skills, technical expertise and resources into our organization. This would require significant additional funding, which may not be available to us on acceptable terms, or at all.

To the extent we elect to fund the development of a drug candidate, or the commercialization of a drug at our expense, we will need substantial additional funding.

The discovery, development and commercialization of new drugs is costly. As a result, to the extent we elect to fund the development of a drug candidate or the commercialization of a drug, we will need to raise additional capital to:

- fund clinical trials and seek regulatory approvals;
- expand our development capabilities;
- engage third-party manufacturers for such drug candidate or drug;
- build or access commercialization capabilities;
- implement additional internal systems and infrastructure;
- maintain, defend and expand the scope of our intellectual property; and

- hire and support additional management and scientific personnel.

Our future funding requirements will depend on many factors, including, but not limited to:

- the rate of progress and costs of our or our partners' clinical trials and other research and development activities;
- the costs and timing of seeking and obtaining regulatory approvals;
- the costs associated with establishing manufacturing and commercialization capabilities;
- the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights;
- the costs of acquiring or investing in businesses, products and technologies;
- the effect of competing technological and market developments; and
- the status of, payment and other terms, and timing of any strategic alliance, licensing or other arrangements that we have entered into or may establish.

Until we can generate a sufficient amount of product revenue to finance our cash requirements, which we may never do, we expect to continue to finance our future cash needs primarily through strategic alliances and other financings. We cannot be certain that additional funding will be available on acceptable terms, or at all. If we are not able to secure additional funding when needed, we may have to delay, reduce the scope of or eliminate one or more of our clinical trials or research and development programs or future

commercialization initiatives.

We depend on contract research organizations ("CROs") to conduct our clinical trials and have limited control over their performance. If these CROs do not successfully carry out their contractual duties or meet expected deadlines, or if we lose any of our CROs, we may not be able to obtain regulatory approval for or commercialize our product candidates on a timely basis, if at all.

We have used and intend to continue to use a limited number of CROs within and outside of the United States to conduct clinical trials of our drug candidates and related activities. We do not have control over many aspects of our CROs' activities, and cannot fully control the amount, timing or quality of resources that they devote to our programs. CROs may not assign as high a priority to our programs or pursue them as diligently as we would if we were undertaking these programs ourselves. The activities conducted by our CROs therefore may not be completed on schedule or in a satisfactory manner. CROs may also give higher priority to relationships with our competitors and potential competitors than to their relationships with us. Outside of the United States, we are particularly dependent on our CROs' expertise in communicating with clinical trial sites and regulatory authorities and ensuring that our clinical trials and related activities and regulatory filings comply with applicable laws.

Our CROs' failure to carry out development activities on our behalf as agreed and in accordance with our and the FDA's or other regulatory agencies' requirements and applicable U.S. and foreign laws, or our failure to properly coordinate and manage these activities, could increase the cost of our operations and delay or prevent the development, approval and commercialization of our drug candidates. For example, in June 2013, we learned from our data management vendor for BENEFIT-ALS that a programming error in the electronic data capture system controlling study drug assignment caused 58 patients initially randomized to and treated with tirasemtiv to receive placebo instead at a certain trial visit and for the remainder of the trial. In order to maintain the originally intended statistical power of the trial, we amended the protocol to permit enrollment of approximately 680 patients, or 180 patients in addition to the 500 patients allowed under the existing protocol. This protocol amendment resulted in additional costs and delays in conducting BENEFIT-ALS. Further, for the quarter ended September 30, 2016, we determined that there was an error in the accounting for the recognition of clinical research and development expenses related to the information received from one of our CROs, which resulted in a restatement of our clinical research and development expenses, related clinical accrual accounts and related financial disclosures as of and for the three and nine month periods ended September 30, 2016. In addition, if a CRO fails to perform as agreed, our ability to collect damages may be contractually limited. If we fail to effectively manage the CROs carrying out the development of our drug candidates or if our CROs fail to perform as agreed, the commercialization of our drug candidates will be delayed or prevented. In many cases, our CROs have the right to terminate their agreements with us in the event of an uncured material breach. Identifying, qualifying and managing performance of third-party service providers can be difficult, time consuming and cause delays in our development programs. In addition, there is a natural transition period when a new CRO commences work and the new CRO may not provide the same type or level of services as the original provider. If any of our relationships with our third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs or to do so timely or on commercially reasonable terms.

We have no manufacturing capacity and depend on our strategic partners and contract manufacturers to produce our clinical trial materials, including our drug candidates, and anticipate continued reliance on contract manufacturers for the development and commercialization of our potential drugs.

We do not currently operate manufacturing facilities for clinical or commercial production of our drug candidates. We have limited experience in drug formulation and manufacturing, and we lack the resources and the capabilities to manufacture any of our drug candidates on a clinical or commercial scale. Amgen has assumed responsibility to conduct these activities for the ongoing development of omecamtiv mecarbil worldwide. Astellas has primary responsibility for the manufacturing for the ongoing development of reldesemtiv worldwide. We expect to rely on

contract manufacturers to supply all future drug candidates for which we conduct development, as well as other materials required to conduct our clinical trials. If any of our existing or future contract manufacturers fail to perform satisfactorily, it could delay development or regulatory approval of our drug candidates or commercialization of our drugs, producing additional losses and depriving us of potential product revenues. In addition, if a contract manufacturer fails to perform as agreed, our ability to collect damages may be contractually limited.

Our drug candidates require precise high-quality manufacturing. The failure to achieve and maintain high manufacturing standards, including failure to detect or control anticipated or unanticipated manufacturing errors or the frequent occurrence of such errors, could result in patient injury or death, discontinuance or delay of ongoing or planned clinical trials, delays or failures in product testing or delivery, cost overruns, product recalls or withdrawals and other problems that could seriously hurt our business. Contract drug manufacturers often encounter difficulties involving production yields, quality control and quality assurance and shortages of qualified personnel. These manufacturers are subject to stringent regulatory requirements, including the FDA's current good manufacturing practices regulations and similar foreign laws and standards. Each contract manufacturer must pass a pre-approval inspection before we can obtain marketing approval for any of our drug candidates and following approval will be subject to ongoing periodic unannounced inspections by the FDA, the U.S. Drug Enforcement Agency and other regulatory agencies, to ensure strict compliance with current good manufacturing practices and other applicable government regulations and corresponding foreign laws and standards. We seek to ensure that our contract manufacturers comply fully with all applicable regulations, laws and standards. However, we do not have control over our contract manufacturers' compliance with these regulations, laws and standards. If one of our contract manufacturers fails to pass its pre-approval inspection or maintain ongoing compliance at any time, the production of our

drug candidates could be interrupted, resulting in delays or discontinuance of our clinical trials, additional costs and potentially lost revenues. In addition, failure of any third-party manufacturers or us to comply with applicable regulations, including pre- or post-approval inspections and the current good manufacturing practice requirements of the FDA or other comparable regulatory agencies, could result in sanctions being imposed on us. These sanctions could include fines, injunctions, civil penalties, failure of regulatory authorities to grant marketing approval of our products, delay, suspension or withdrawal of approvals, license revocation, product seizures or recalls, operational restrictions and criminal prosecutions, any of which could significantly and adversely affect our business.

In addition, our existing and future contract manufacturers may not perform as agreed or may not remain in the contract manufacturing business for the time required to successfully produce, store and distribute our drug candidates. If a natural disaster, business failure, strike or other difficulty occurs, we may be unable to replace these contract manufacturers in a timely or cost-effective manner and the production of our drug candidates would be interrupted, resulting in delays, loss of customers and additional costs.

Switching manufacturers or manufacturing sites would be difficult and time-consuming because the number of potential manufacturers is limited. In addition, before a drug from any replacement manufacturer or manufacturing site can be commercialized, the FDA and, in some cases, foreign regulatory agencies, must approve that site. These approvals would require regulatory testing and compliance inspections. A new manufacturer or manufacturing site also would have to be educated in, or develop substantially equivalent processes for, production of our drugs and drug candidates. It may be difficult or impossible to transfer certain elements of a manufacturing process to a new manufacturer or for us to find a replacement manufacturer on acceptable terms quickly, or at all, either of which would delay or prevent our ability to develop drug candidates and commercialize any resulting drugs.

We may not be able to successfully manufacture our drug candidates in sufficient quality and quantity, which would delay or prevent us from developing our drug candidates and commercializing resulting approved drugs, if any.

To date, our drug candidates have been manufactured in quantities adequate for preclinical studies and early through late-stage clinical trials. In order to conduct large scale clinical trials for a drug candidate and for commercialization of the resulting drug if that drug candidate is approved for sale, we will need to manufacture some drug candidates in larger quantities. We may not be able to successfully repeat or increase the manufacturing capacity for any of our drug candidates, whether in collaboration with third-party manufacturers or on our own, in a timely or cost-effective manner or at all. If a contract manufacturer makes improvements in the manufacturing process for our drug candidates, we may not own, or may have to share, the intellectual property rights to those improvements. Significant changes or scale-up of manufacturing may require additional validation studies, which are costly and which regulatory authorities must review and approve. In addition, quality issues may arise during those changes or scale-up activities because of the inherent properties of a drug candidate itself or of a drug candidate in combination with other components added during the manufacturing and packaging process, or during shipping and storage of the finished product or active pharmaceutical ingredients. If we are unable to successfully manufacture of any of our drug candidates in sufficient quality and quantity, the development of that drug candidate and regulatory approval or commercial launch for any resulting drugs may be delayed or there may be a shortage in supply, which could significantly harm our business. In addition, data demonstrating the stability of both drug substance and drug product, using the commercial manufacturing process and at commercial scale, are required for marketing applications. Failure to produce drug substance and drug products in a timely manner and obtain stability data could result in delay of submission of marketing applications.

The mechanisms of action of our drug candidates are unproven, and we do not know whether we will be able to develop any drug of commercial value.

We have discovered and develop drug candidates that have what we believe are novel mechanisms of action directed against cytoskeletal targets. Because no currently-approved drugs appear to operate via the same biochemical mechanisms as our compounds, we cannot be certain that our drug candidates will result in commercially viable drugs that safely and effectively treat the indications for which we intend to develop them. The results we have seen for our compounds in preclinical models may not translate into similar results in humans, and results of early clinical trials in humans may not be predictive of the results of larger clinical trials that may later be conducted with our drug candidates. Even if we are successful in developing and receiving regulatory approval for a drug candidate for the treatment of a particular disease, we cannot be certain that it will be accepted by prescribers or be reimbursed by insurers or that we will also be able to develop and receive regulatory approval for that or other drug candidates for the treatment of other diseases. If we or our partners are unable to successfully develop and commercialize our drug candidates, our business will be materially harmed.

Our success depends substantially upon our ability to obtain and maintain intellectual property protection relating to our drug candidates, compounds and research technologies.

We own, co-own or hold exclusive licenses to a number of U.S. and foreign patents and patent applications directed to our drug candidates, compounds and research technologies. Our success depends on our ability to obtain patent protection both in the United States and in other countries for our drug candidates, their methods of manufacture and use, and our technologies. Our ability to protect our drug candidates, compounds and technologies from unauthorized or infringing use by third parties depends substantially on our ability to obtain and enforce our patents. If our issued patents and patent applications, if granted, do not adequately describe,

enable or otherwise provide coverage of our technologies and drug candidates, we or our licensees would not be able to exclude others from developing or commercializing these drug candidates. Furthermore, the degree of future protection of our proprietary rights is uncertain because legal means may not adequately protect our rights or permit us to gain or keep our competitive advantage. If we are unable to obtain and maintain sufficient intellectual property protection for our technologies and drug candidates, or if the scope of the intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize drug candidates similar or identical to ours, and our ability to successfully commercialize product candidates that we may pursue may be impaired.

Obtaining and enforcing biopharmaceutical patents is costly, time consuming and complex, and we may not be able to file and prosecute all necessary or desirable patent applications, or maintain, enforce and license any patents that may issue from such 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. We may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the rights to patents licensed to third parties. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

Due to evolving legal standards relating to the patentability, validity and enforceability of patents covering pharmaceutical inventions and the claim scope of these patents, our ability to enforce our existing patents and to obtain and enforce patents that may issue from any pending or future patent applications is uncertain and involves complex legal, scientific and factual questions. The standards which the U.S. Patent and Trademark Office and its foreign counterparts use to grant patents are not always applied predictably or uniformly and are subject to change. To date, no consistent policy has emerged regarding the breadth of claims allowed in biotechnology and pharmaceutical patents. Thus, we cannot be sure that any patents will issue from any pending or future patent applications owned by, co-owned by or licensed to us. Even if patents do issue, we cannot be sure that the claims of these patents will be held valid or enforceable by a court of law, will provide us with any significant protection against competitive products, or will afford us a commercial advantage over competitive products. In particular:

- we or our licensors might not have been the first to make the inventions covered by each of our pending patent applications or issued patents;
- we or our licensors might not have been the first to file patent applications for the inventions covered by our pending patent applications or issued patents;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- some or all of our or our licensors' pending patent applications may not result in issued patents or the claims that issue may be narrow in scope and not provide us with competitive advantages;
- our and our licensors' issued patents may not provide a basis for commercially viable drugs or therapies or may be challenged and invalidated by third parties;
- our or our licensors' patent applications or patents may be subject to interference, post-grant proceedings, derivation, reexamination, inter partes review, opposition or similar legal and administrative proceedings that may result in a reduction in their scope or their loss altogether;
- we may not develop additional proprietary technologies or drug candidates that are patentable; or
- the patents of others may prevent us or our partners from discovering, developing or commercializing our drug candidates.

We may not be able to protect our intellectual property rights throughout the world. Patent protection is afforded on a country-by-country basis. Filing, prosecuting and defending patents on our 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. Many companies have encountered significant difficulties in protecting and defending intellectual property rights in foreign jurisdictions. Some of our development efforts are performed in countries outside of the United States through third-party contractors. We may not be able to

effectively monitor and assess intellectual property developed by these contractors. We therefore may not be able to effectively protect this intellectual property and could lose potentially valuable intellectual property rights. In addition, the legal protection afforded to inventors and owners of intellectual property in countries outside of the United States may not be as protective of intellectual property rights as in the United States. Therefore, we may be unable to acquire and protect intellectual property developed by these contractors to the same extent as if these development activities were being conducted in the United States. If we encounter difficulties in protecting our intellectual property rights in foreign jurisdictions, our business prospects could be substantially harmed.

Patent terms may be inadequate to protect our competitive position on our technologies and drug candidates for an adequate amount of time. Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our technologies and drug candidates are obtained, once the patent life has expired, we may be open to competition from competitive products, including generics or biosimilars. Given the amount of time required for the development, testing and regulatory review of new drug candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned, co-owned and licensed patent

portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours or our partners.

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 and/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 and/or applications. Non-compliance could 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.

We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property. We rely on intellectual property assignment agreements with our corporate partners, employees, consultants, scientific advisors and other collaborators to grant us ownership of new intellectual property that is developed. These agreements may not result in the effective assignment to us of that intellectual property. As a result, our ownership of key intellectual property could be compromised.

We or our licensors may be subject to claims that former employees, collaborators, consultants or other third parties have an interest in our owned, co-owned or in-licensed patents, trade secrets, or other intellectual property as an inventor or co-inventor. For example, we or our licensors may have inventorship disputes arise from conflicting obligations of employees, collaborators, 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 our or our licensors' ownership of our owned, co-owned or in-licensed patents, trade secrets or other intellectual property. If we or our licensors 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, intellectual property that is important to our product candidates. 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. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

We are a party to license agreements and may need to obtain additional licenses from others to advance our research and development activities or allow the commercialization of our drug candidates and future drug candidates we may identify and pursue. If we fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties or these agreements are terminated or we otherwise experience disruptions to our business relationships with our licensors, we could lose intellectual property rights that are important to our business. Our licensors might conclude that we have materially breached our obligations under such license agreements and might therefore terminate, or seek to terminate, the license agreements, thereby removing or limiting our ability to develop and commercialize products and technology covered by these license agreements. If our license agreements are terminated, we may be required to cease our development and commercialization of our product candidates. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations and prospects. Moreover, disputes may arise regarding intellectual property subject to a licensing agreement. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the agreement, either of which could have a material adverse effect on our business, financial condition, results of operations and prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates. Any

of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations and prospects.

Changes in either the patent laws or their interpretation in the United States or other countries may diminish the value of our intellectual property or our ability to obtain patents. For example, the America Invents Act of 2011 may affect the scope, strength and enforceability of our patent rights in the United States or the nature of proceedings which may be brought by us related to our patent rights in the United States.

If one or more products resulting from our drug candidates is approved for sale by the FDA and we do not have adequate intellectual property protection for those products, competitors could duplicate them for approval and sale in the United States without repeating the extensive testing required of us or our partners to obtain FDA approval. Regardless of any patent protection, under current law, an application for a generic version of a new chemical entity cannot be approved until at least five years after the FDA has approved the original product. When that period expires, or if that period is altered, the FDA could approve a generic version of our product regardless of our patent protection. An applicant for a generic version of our product may only be required to conduct a relatively inexpensive study to show that its product is bioequivalent to our product, and may not have to repeat the lengthy and expensive clinical trials that we or our partners conducted to demonstrate that the product is safe and effective. In the absence of adequate patent protection for our products in other countries, competitors may similarly be able to obtain regulatory approval in those countries of generic versions of our products.

If we are unable to protect the confidentiality of our trade secrets, the value of our technology could be materially adversely affected and our business would be harmed.

We also rely on trade secrets to protect our technology, particularly where we believe patent protection is not appropriate or obtainable. However, trade secrets are often difficult to protect, especially outside of the United States. While we endeavor to use reasonable efforts to protect our trade secrets, our or our partners' employees, consultants, contractors or scientific and other advisors may unintentionally or willfully disclose our information to competitors. In addition, confidentiality agreements, if any, executed by those individuals may not be enforceable or provide meaningful protection for our trade secrets or other proprietary information in the event of unauthorized use or disclosure. We cannot be certain that such agreements have been entered into with all relevant parties, and we cannot be certain 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. Pursuing a claim that a third party had illegally obtained and was using our trade secrets would be expensive and time-consuming, and the outcome would be unpredictable. Even if we are able to maintain our trade secrets as confidential, if our competitors lawfully obtain or independently develop information equivalent or similar to our trade secrets, our business could be harmed.

If we are not able to defend the patent or trade secret protection position of our technologies and drug candidates, then we will not be able to exclude competitors from developing or marketing competing drugs, and we may not generate enough revenue from product sales to justify the cost of development of our drugs or to achieve or maintain profitability.

If we are sued for infringing third-party intellectual property rights, it will be costly and time-consuming, and an unfavorable outcome could have a significant adverse effect on our business.

Our ability to commercialize drugs depends on our ability to use, manufacture and sell those drugs without infringing the patents or other proprietary rights of third parties. Numerous U.S. and foreign issued patents and pending patent applications owned by third parties exist in the therapeutic areas in which we are developing drug candidates and seeking new potential drug candidates. In addition, because patent applications can take several years to issue, there may be currently pending applications, unknown to us, which could later result in issued patents that our activities with our drug candidates could infringe. There may also be existing patents, unknown to us, that our activities with our drug candidates could infringe.

Other future products of ours may be impacted by patents of companies engaged in competitive programs with significantly greater resources. Further development of these products could be impacted by these patents and result in significant legal fees.

If a third party claims that our actions infringe its patents or other proprietary rights, we could face a number of issues that could seriously harm our competitive position, including, but not limited to:

- infringement and other intellectual property claims that, even if meritless, can be costly and time-consuming to litigate, delay the regulatory approval process and divert management's attention from our core business operations;
- substantial damages for past infringement which we may have to pay if a court determines that our drugs or technologies infringe a third party's patent or other proprietary rights;
- a court prohibiting us from selling or licensing our drugs or technologies unless the holder licenses the patent or other proprietary rights to us, which it is not required to do; and
- if a license is available from a holder, we may have to pay substantial royalties or grant cross-licenses to our patents or other proprietary rights.

If any of these events occur, it could significantly harm our business and negatively affect our stock price.

We may undertake infringement or other legal proceedings against third parties, causing us to spend substantial resources on litigation and exposing our own intellectual property portfolio to challenge.

Third parties may infringe our patents. To prevent infringement or unauthorized use, we may need to file infringement suits, which are expensive and time-consuming. In an infringement proceeding, a court may decide that one or more of our patents is invalid, unenforceable, or both. In such case third parties may be able to use our technology without paying licensing fees or royalties. Even if the validity of our patents is upheld, a court may refuse to stop the other party from using the technology at issue on the ground that the other party's activities are not covered by our patents. Policing unauthorized use of our intellectual property is difficult, and we may not be able to prevent misappropriation of our proprietary rights, particularly in countries where the laws may not protect such rights as fully as in the United States. In addition, third parties may affirmatively challenge our rights to, or the scope or validity of, our patent rights.

The uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to conduct clinical trials, continue our research programs, license necessary technology from third parties, or enter into development partnerships that would help us bring our drug candidates or other product candidates that we may identify to market. 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 become involved in disputes with our strategic partners over intellectual property ownership, and publications by our research collaborators and clinical investigators could impair our ability to obtain patent protection or protect our proprietary information, either of which would have a significant impact on our business.

Inventions discovered under our current or future strategic alliance agreements may become jointly owned by our strategic partners and us in some cases, and the exclusive property of one of us in other cases. Under some circumstances, it may be difficult to determine who owns a particular invention or whether it is jointly owned, and disputes could arise regarding ownership or use of those inventions. These disputes could be costly and time-consuming, and an unfavorable outcome could have a significant adverse effect on our business if we were not able to protect or license rights to these inventions. In addition, our research collaborators and clinical investigators generally have contractual rights to publish data arising from their work. Publications by our research collaborators and clinical investigators relating to our research and development programs, either with or without our consent, could benefit our current or potential competitors and may impair our ability to obtain patent protection or protect our proprietary information, which could significantly harm our business.

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 we or our employees have wrongfully used or disclosed trade secrets of their former employers.

Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although no legal proceedings against us are currently pending, we may be subject to claims that these employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. If we fail in defending these claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. A loss of key research personnel or their work product could hamper or prevent our ability to develop and commercialize certain potential drugs, which could significantly harm our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and distract management.

Our competitors may develop drugs that are less expensive, safer or more effective than ours, which may diminish or eliminate the commercial success of any drugs that we may commercialize.

We compete with companies that have developed drugs or are developing drug candidates for cardiovascular diseases, diseases and conditions associated with muscle weakness or wasting and other diseases for which our drug candidates may be useful treatments. For example, if reldesemtiv is approved for marketing by the FDA or other regulatory authorities for the treatment of ALS, it will then compete with RADICAVA™ (edaravone), the first FDA approved drug for the treatment of ALS since riluzole in 1995, and may then compete with other potential new therapies for ALS that are currently being developed by companies including, but not limited to, Neuraltus Pharmaceuticals, Inc., Ionis Pharmaceuticals, Inc. (in collaboration with Biogen Inc.), AB Science, Mitsubishi Tanabe Pharma Corporation, Treeway, Genentech, Inc., and BrainStorm Cell Therapeutics. Also, if reldesemtiv is approved by the FDA or other regulatory authorities for the treatment of SMA, it will then compete with SPINRAZA® (nusinersen) and may then compete with other potential new therapies being developed by companies including, but not limited to, Roche (in collaboration with PTC Therapeutics) and AveXis, Inc. (a Novartis company). If reldesemtiv is approved by the FDA or other regulatory authorities for the treatment of non-neuromuscular indications associated with muscle weakness, it may then compete with other potential new therapies being developed by companies including, but not limited to, Regeneron Pharmaceuticals, Inc. (in collaboration with Sanofi), Eli Lilly and Company, Acceleron Pharma, Stealth Biotherapeutics, and Novartis (in collaboration with MorphoSys AG).

If omecamtiv mecarbil is approved for marketing by the FDA or other regulatory authorities for the treatment of heart failure, it would compete against other drugs used for the treatment of acute and chronic heart failure. These include generic drugs, such as milrinone, dobutamine or digoxin and branded drugs such as Natrecor® (nesiritide), Corlanor® (ivabradine), and Entresto® (sacubitril/valsartan). Omecamtiv mecarbil could also potentially compete against other novel drug candidates and therapies in development, such as those being developed by, but not limited to, Novartis, Bayer, Stealth Biotherapeutics, and MyoKardia. In addition, there are a number of medical devices both marketed and in development for the potential treatment of heart failure.

Our competitors may:

- develop drug candidates and market drugs that are less expensive or more effective than our future drugs;
- commercialize competing drugs before we or our partners can launch any drugs developed from our drug candidates;
- hold or obtain proprietary rights that could prevent us from commercializing our products;
- initiate or withstand substantial price competition more successfully than we can;
    - more successfully recruit skilled scientific workers and management from the limited pool of available talent;
- more effectively negotiate third-party licenses and strategic alliances;
- take advantage of acquisition or other opportunities more readily than we can;

- develop drug candidates and market drugs that increase the levels of safety or efficacy that our drug candidates will need to show in order to obtain regulatory approval; or
- introduce therapies or market drugs that render the market opportunity for our potential drugs obsolete.

We will compete for market share against large pharmaceutical and biotechnology companies and smaller companies that are collaborating with larger pharmaceutical companies, new companies, academic institutions, government agencies and other public and private research organizations. Many of these competitors, either alone or together with their partners, may develop new drug candidates that will compete with ours. Many of these competitors have larger research and development programs or substantially greater financial resources than we do. Our competitors may also have significantly greater experience in:

- developing drug candidates;
- undertaking preclinical testing and clinical trials;
- building relationships with key customers and opinion-leading physicians;
- obtaining and maintaining FDA and other regulatory approvals of drug candidates;
- formulating and manufacturing drugs; and
- launching, marketing and selling drugs.

If our competitors market drugs that are less expensive, safer or more efficacious than our potential drugs, or that reach the market sooner than our potential drugs, we may not achieve commercial success. In addition, the life sciences industry is characterized by rapid technological change. If we fail to stay at the forefront of technological change, we may be unable to compete effectively. Our competitors may render our technologies obsolete by improving existing technological approaches or developing new or different approaches, potentially eliminating the advantages in our drug discovery process that we believe we derive from our research approach and proprietary technologies.

We have been granted orphan designation in the U.S. for reldesemtiv; however, there can be no guarantee that we will receive orphan approval for reldesemtiv, nor that we will be able to prevent third parties from developing and commercializing products that are competitive to reldesemtiv.

We have been granted orphan drug designation in the U.S. by the FDA for reldesemtiv for the potential treatment of SMA. In the U.S., upon approval from the FDA of an NDA, products granted orphan drug designation are generally provided with seven years of marketing exclusivity in the U.S., meaning the FDA will generally not approve applications for other product candidates that contain the same active ingredient for the same orphan indication. Even if we are the first to obtain approval of an orphan product and are granted such exclusivity in the U.S., there are limited circumstances under which a later competitor product may be approved for the same indication during the seven-year period of marketing exclusivity, such as if the later product is shown to be clinically superior to our product or due to an inability to assure a sufficient quantity of the orphan drug.

Orphan medicinal product status in the Europe Union can provide up to 10 years of marketing exclusivity, meaning that another application for marketing authorization of a later similar medicinal product for the same therapeutic indication will generally not be approved in the European Union. Although we may have drug candidates that may obtain orphan drug exclusivity in Europe, the orphan approval and associated exclusivity period may be modified for several reasons, including a significant change to the orphan medicinal product designations or approval criteria after-market authorization of the orphan product (e.g., product profitability exceeds the criteria for orphan drug designation), problems with the production or supply of the orphan drug or a competitor drug, although similar, is safer, more effective or otherwise clinically superior than the initial orphan drug.

We are not guaranteed to maintain orphan status for reldesemtiv or to receive orphan status for reldesemtiv for any other indication or for any of our other drug candidates for any indication. If our drug candidates that are granted orphan status were to lose their status as orphan drugs or the marketing exclusivity provided for them in the U.S. or

the European Union, our business and results of operations could be materially adversely affected. While orphan status for any of our products, if granted or maintained, would provide market exclusivity in the U.S. and the European Union for the time periods specified above, we would not be able to exclude other companies from manufacturing and/or selling products using the same active ingredient for the same indication beyond the exclusivity period applicable to our product on the basis of orphan drug status. Moreover, we cannot guarantee that another company will not receive approval before we do of an orphan drug application in the U.S. or the European Union for a product candidate that has the same active ingredient or is a similar medicinal product for the same indication as any of our drug candidates for which we plan to file for orphan designation and status. If that were to happen, our orphan drug applications for our drug candidate for that indication may not be approved until the competing company's period of exclusivity has expired in the U.S. or the European Union, as applicable. Further, application of the orphan drug regulations in the U.S. and Europe is uncertain, and we cannot predict how the respective regulatory bodies will interpret and apply the regulations to our or our competitors' products.

Our failure to attract and retain skilled personnel could impair our drug development, commercialization and financial reporting activities.

Our business depends on the performance of our senior management and key scientific and technical personnel. The loss of the services of any member of our senior management or key scientific, technical or financial reporting staff may significantly delay or prevent the achievement of drug development and other business objectives by diverting management's attention to transition matters and identifying suitable replacements. For example, our management concluded that our internal controls over financial reporting were not effective as of December 31, 2018 because an unremediated material weakness existed in our internal control over financial reporting related to employee turnover resulting in a temporary lack of resources in financial reporting roles with the appropriate skills to perform effective review during our financial statement close process. We also rely on consultants and advisors to assist us in formulating our research and development strategy. All of our consultants and advisors are either self-employed or employed by other organizations, and they may have conflicts of interest or other commitments, such as consulting or advisory contracts with other organizations, that may affect their ability to contribute to us. In addition, if and as our business grows, we will need to recruit additional executive management and scientific, technical and financial reporting personnel. There is intense competition for skilled executives and employees with relevant scientific and technical expertise, and this competition is likely to continue. Our inability to attract and retain sufficient scientific, technical and managerial personnel could limit or delay our product development activities, which would adversely affect the development of our drug candidates and commercialization of our potential drugs and growth of our business.

Any future workforce and expense reductions may have an adverse impact on our internal programs and our ability to hire and retain skilled personnel.

Our future success will depend in large part upon our ability to attract and retain highly skilled personnel. In light of our continued need for funding and cost control, we may be required to implement future workforce and expense reductions, which could further limit our research and development activities. We may have difficulty retaining and attracting such personnel as a result of a perceived risk of future workforce reductions. In addition, the implementation of any additional workforce or expense reduction programs may divert the efforts of our management team and other key employees, which could adversely affect our business.

We may expand our development and clinical research capabilities and, as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We may have growth in our expenditures, the number of our employees and the scope of our operations, in particular with respect to those drug candidates that we elect to develop or commercialize independently or together with a partner. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited resources, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The physical expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

We currently have no sales or marketing capabilities and, if we are unable to enter into or maintain strategic alliances with marketing partners or to develop our own sales and marketing capabilities, we may not be successful in commercializing our potential drugs.

We currently have no sales, marketing or distribution capabilities. We plan to commercialize drugs that can be effectively marketed and sold in concentrated markets that do not require a large sales force to be competitive. To

achieve this goal, we will need to establish our own specialized sales force and marketing organization with technical expertise and supporting distribution capabilities. Developing such an organization is expensive and time-consuming and could delay a product launch. In addition, we may not be able to develop this capacity efficiently, cost-effectively or at all, which could make us unable to commercialize our drugs. If we determine not to market our drugs on our own, we will depend on strategic alliances with third parties, such as Amgen and Astellas, which have established distribution systems and direct sales forces to commercialize them. If we are unable to enter into such arrangements on acceptable terms, we may not be able to successfully commercialize these drugs. To the extent that we are not successful in commercializing any drugs ourselves or through a strategic alliance, our product revenues and business will suffer and our stock price would decrease.

Our internal computer systems, or those of our CROs, CMOs, supply chain partners, collaboration partners or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our drug development programs.

Despite the implementation of security measures, our internal computer systems and those of our third-party contract research organizations ("CROs"), CMOs, supply chain partners, collaboration partners and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our drug development programs. For example, the loss of clinical study data from completed or ongoing clinical studies for any of our drug candidates could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent

that any disruption or security breach were to result in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our operations could be compromised and the further development of our product candidates could be delayed.

Significant disruptions of information technology systems or breaches of data security could adversely affect our business.

Our business is increasingly dependent on complex and interdependent information technology systems, including internet-based systems, databases and programs, to support our business processes as well as internal and external communications. As use of information technology systems has increased, deliberate attacks and attempts to gain unauthorized access to computer systems and networks have increased in frequency and sophistication. Our information technology, systems and networks are potentially vulnerable to breakdown, malicious intrusion and computer viruses which may result in the impairment of production and key business processes or loss of data or information. We are also potentially vulnerable to data security breaches—whether by employees or others—which may expose sensitive data to unauthorized persons. We have in the past and may in the future be subject to security breaches. For example, in February 2018, we discovered that our e-mail server suffered unauthorized intrusions in which proprietary business information was accessed. Although we do not believe that we have experienced any material losses related to security breaches, including a recent cybersecurity incident, there can be no assurance that we will not suffer such losses in the future. Breaches and other inappropriate access can be difficult to detect and any delay in identifying them could increase their harm. While we have implemented security measures to protect our data security and information technology systems, such measures may not prevent such events. Any such breaches of security and inappropriate access could disrupt our operations, harm our reputation or otherwise have a material adverse effect on our business, financial condition and results of operations.

Our reported financial results may be adversely affected by changes in accounting principles generally accepted in the U.S.

We prepare our financial statements in conformity with accounting principles generally accepted in the U.S. These accounting principles are subject to interpretation by the Financial Accounting Standards Board (“FASB”) and the SEC. A change in these policies or interpretations could have a significant effect on our reported financial results, may retroactively affect previously reported results, could cause unexpected financial reporting fluctuations, and may require us to make costly changes to our operational processes and accounting systems.

Our revenue to date has been primarily derived from our research and license agreements, which can result in significant fluctuation in our revenue from period to period, and our past revenue is therefore not necessarily indicative of our future revenue.

Our revenue is primarily derived from our research and license agreements, from which we receive upfront fees, contract research payments, milestone and other contingent payments based on clinical progress, regulatory progress or net sales achievements and royalties. Significant variations in the timing of receipt of cash payments and our recognition of revenue can result from significant payments based on the execution of new research and license agreements, the timing of clinical outcomes, regulatory approval, commercial launch or the achievement of certain annual sales thresholds. The amount of our revenue derived from research and license agreements in any given period will depend on a number of unpredictable factors, including our ability to find and maintain suitable collaboration partners, the timing of the negotiation and conclusion of collaboration agreements with such partners, whether and when we or our collaboration partners achieve clinical, regulatory and sales milestones, the timing of regulatory approvals in one or more major markets, reimbursement levels by private and government payers, and the market introduction of new drugs or generic versions of the approved drug, as well as other factors. Our past revenue generated from these agreements is not necessarily indicative of our future revenue. If any of our existing or future

collaboration partners fails to develop, obtain regulatory approval for, manufacture or ultimately commercialize any product candidate under our collaboration agreement, our business, financial condition, and results of operations could be materially and adversely affected.

Indebtedness under our Loan Agreement bears interest at variable interest rates based on LIBOR. Changes in the method of determining LIBOR, or the replacement of LIBOR with an alternative reference rate, may adversely affect interest rates on our current or future indebtedness and may otherwise adversely affect our financial condition and results of operations.

In July 2017, the Financial Conduct Authority, the authority that regulates LIBOR, announced that it intended to stop compelling banks to submit rates for the calculation of LIBOR after 2021. The Alternative Reference Rates Committee ("ARRC") in the U.S. has proposed that the Secured Overnight Financing Rate ("SOFR") is the rate that represents best practice as the alternative to the U.S. dollar LIBOR for use in derivatives and other financial contracts that are currently indexed to LIBOR. ARRC has proposed a paced market transition plan to SOFR from U.S. dollar LIBOR and organizations are currently working on industry-wide and company-specific transition plans as relating to derivatives and cash markets exposed to U.S. dollar LIBOR. We have certain financial contracts, including the Loan Agreement, that are indexed to U.S. dollar LIBOR. Changes in the method of determining LIBOR, or the replacement of LIBOR with an alternative reference rate, may adversely affect interest rates on our current or future indebtedness. Any transition process may involve, among other things, increased volatility or illiquidity in markets for instruments that rely on LIBOR, reductions in the value of certain instruments or the effectiveness of related transactions such as hedges, increased borrowing costs, uncertainty under applicable documentation, or difficult and costly consent processes. We are monitoring this activity and evaluating the related risks, and any such effects of the transition away from LIBOR may result in increased expenses, may impair our ability to refinance our indebtedness or hedge our exposure to floating rate instruments, or may result in difficulties,

complications or delays in connection with future financing efforts, any of which could adversely affect our financial condition and results of operations.

Risks Related To Our Industry

The regulatory approval process is expensive, time-consuming and uncertain and may prevent our partners or us from obtaining approvals to commercialize some or all of our drug candidates.

The research, testing, manufacturing, selling and marketing of drugs are subject to extensive regulation by the FDA and other regulatory authorities in the United States and other countries, and regulations differ from country to country. Neither we nor our partners are permitted to market our potential drugs in the United States until we receive approval of a new drug application ("NDA") from the FDA. Neither we nor our partners have received NDA or other marketing approval for any of our drug candidates.

Obtaining NDA approval is a lengthy, expensive and uncertain process. In addition, failure to comply with FDA and other applicable foreign and U.S. regulatory requirements may subject us to administrative or judicially imposed sanctions. These include warning letters, civil and criminal penalties, injunctions, product seizure or detention, product recalls, total or partial suspension of production, and refusal to approve pending NDAs or supplements to approved NDAs.

Regulatory approval of an NDA or NDA supplement is never guaranteed, and the approval process typically takes several years and is extremely expensive. The FDA and foreign regulatory agencies also have substantial discretion in the drug approval process, and the guidance and advice issued by such agencies is subject to change at any time. Despite the time and efforts exerted, failure can occur at any stage, and we may encounter problems that cause us to abandon clinical trials or to repeat or perform additional preclinical testing and clinical trials. The number and focus of preclinical studies and clinical trials that will be required for approval by the FDA and foreign regulatory agencies varies depending on the drug candidate, the disease or condition that the drug candidate is designed to address, and the regulations applicable to any particular drug candidate. In addition, the FDA may require that a proposed Risk Evaluation and Mitigation Strategy ("REMS") be submitted as part of an NDA if the FDA determines that it is necessary to ensure that the benefits of the drug outweigh its risks. The FDA and foreign regulatory agencies can delay, limit or deny approval of a drug candidate for many reasons, including, but not limited to:

- they might determine that a drug candidate is not safe or effective;
- they might not find the data from non-clinical testing and clinical trials sufficient and could request that additional trials be performed;
- they might not approve our, our partner's or the contract manufacturer's processes or facilities; or
- they might change their approval policies or adopt new regulations.

Even if we receive regulatory approval to manufacture and sell a drug in a particular regulatory jurisdiction, other jurisdictions' regulatory authorities may not approve that drug for manufacture and sale. If we or our partners fail to receive and maintain regulatory approval for the sale of any drugs resulting from our drug candidates, it would significantly harm our business and negatively affect our stock price.

If we or our partners receive regulatory approval for our drug candidates, we or they will be subject to ongoing obligations to and continued regulatory review by the FDA and foreign regulatory agencies, and may be subject to additional post-marketing obligations, all of which may result in significant expense and limit commercialization of our potential drugs.

Any regulatory approvals that we or our partners receive for our drug candidates may be subject to limitations on the indicated uses for which the drug may be marketed or require potentially costly post-marketing follow-up studies or

compliance with a REMS. In addition, if the FDA or foreign regulatory agencies approves any of our drug candidates, the labeling, packaging, adverse event reporting, storage, advertising, promotion and record-keeping for the drug will be subject to extensive regulatory requirements. The subsequent discovery of previously unknown problems with the drug, including adverse events of unanticipated severity or frequency, or the discovery that adverse events or toxicities observed in preclinical research or clinical trials that were believed to be minor constitute much more serious problems, may result in restrictions on the marketing of the drug or withdrawal of the drug from the market.

The FDA and foreign regulatory agencies may change their policies and additional government regulations may be enacted that could prevent or delay regulatory approval of our drug candidates. We cannot predict the likelihood, nature or extent of adverse government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are not able to maintain regulatory compliance, we might not be permitted to market our drugs and our business would suffer.

If physicians and patients do not accept our drugs, we may be unable to generate significant revenue, if any.

Even if our drug candidates obtain regulatory approval, the resulting drugs, if any, may not gain market acceptance among physicians, healthcare payors, patients and the medical community. Even if the clinical safety and efficacy of drugs developed from our drug candidates are established for purposes of approval, physicians may elect not to recommend these drugs for a variety of reasons including, but not limited to:

- introduction of competitive drugs to the market;
- clinical safety and efficacy of alternative drugs or treatments;
- cost-effectiveness;
- availability of coverage and reimbursement from health maintenance organizations and other third-party payors;
- convenience and ease of administration;
- prevalence and severity of adverse events;
- other potential disadvantages relative to alternative treatment methods; or
- insufficient marketing and distribution support.

If our drugs fail to achieve market acceptance, we may not be able to generate significant revenue and our business would suffer.

Recently enacted and future legislation, including potentially unfavorable pricing regulations or other healthcare reform initiatives, may increase the difficulty and cost for us to obtain regulatory approval of and commercialize our product candidates and affect the prices we may obtain.

The regulations that govern, among other things, regulatory approvals, coverage, pricing and reimbursement for new drug products vary widely from country to country. In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay regulatory approval of our product candidates, restrict or regulate post-approval activities and affect our ability to successfully sell any product candidates for which we obtain regulatory approval. In particular, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively, the "ACA") was enacted, which substantially changes the way health care is financed by both governmental and private insurers, and significantly impacts the U.S. pharmaceutical industry. The ACA and its implementing regulations, among other things, addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for certain drugs and biologics, including our product candidates that are inhaled, infused, instilled, implanted or injected, increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program, extended the Medicaid Drug Rebate Program to utilization of prescriptions of individuals enrolled in Medicaid managed care organizations, subjected manufacturers to new annual fees and taxes for certain branded prescription drugs, provided incentives to programs that increase the federal government's comparative effectiveness research and established a new Medicare Part D coverage gap discount program.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by the U.S. Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect in April 2013, and, due to subsequent legislative amendments, will remain in effect through 2027 unless additional Congressional action is taken. In January 2013, the American Taxpayer Relief Act of 2012 was enacted which, among other things, further reduced Medicare payments to several providers, including hospitals and outpatient clinics, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Since its enactment, there have been judicial and Congressional challenges to numerous elements of the ACA, as well as efforts by both the executive and legislative branches of the federal government to repeal or replace certain aspects of the ACA. For example, the President signed Executive Orders designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. In addition, the U.S. Congress has considered legislation that would repeal or repeal and replace all or part of the ACA. While the U.S. Congress has not passed comprehensive repeal legislation, it has enacted laws that modify certain provisions of the ACA, such as removing penalties, starting January 1, 2019, for not complying with the ACA's individual mandate to carry health insurance, delaying the implementation of certain mandated fees, and increasing the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D. In December 2018, a Texas U.S. District Court Judge ruled that the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Cuts and Jobs Act of 2017, or the Tax Act. The Texas U.S. District Court Judge, as well as the presidential administration and the CMS, have stated that the ruling will have no immediate effect pending appeal of the decision, but it is unclear how this decision, subsequent appeals, and other efforts to repeal and replace the ACA will impact the ACA and our business. The U.S. Congress may consider and adopt other legislation to repeal and replace all or certain

elements of the ACA. Any other executive, legislative or judicial action to "repeal and replace" all or part of the ACA may have the effect of limiting the amounts that government agencies will pay for healthcare products and services, which could result in reduced demand for our products or additional pricing pressure, or may lead to significant deregulation, which could make the introduction of competing products and technologies much easier. Policy changes, including potential modification or repeal of all or parts of the ACA or the implementation of new health care legislation, could result in significant changes to the health care system which may adversely affect our business in unpredictable ways.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. We cannot predict the initiatives that may be adopted in the future. The continuing efforts of governments, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare, including by imposing price controls, may adversely affect the demand for our product candidates for which we obtain regulatory approval and our ability to set a price that we believe is fair for our products. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA or foreign regulations, guidance or interpretations will be changed, or what the impact of these changes on the regulatory approvals of our product candidates, if any, may be. In the United States, the European Union and other potentially significant markets for our product candidates, government authorities and third-party payors are increasingly attempting to limit or regulate the price of medical products and services, particularly for new and innovative products and therapies, which has resulted in lower average selling prices. For example, in the United States, there have been several recent Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. Additionally, in May 2018, the U.S. presidential administration laid out a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out of pocket costs of drug products paid by consumers. The U.S. Department of Health and Human Services ("HHS") has started the process of soliciting feedback on some of these measures and, at the same time, is immediately implementing others under its existing authority. In January 2019, the HHS Office of Inspector General proposed modifications to U.S. federal healthcare Anti-Kickback Statute safe harbors which, among other things, will affect rebates paid by manufacturers to Medicare Part D plans, the purpose of which is to further reduce the cost of drug products to consumers. Although some of these and other proposals may require authorization through additional legislation to become effective, members of Congress and the presidential administration have indicated that they will continue to seek new legislative or administrative measures to control drug costs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, to encourage importation from other countries and bulk purchasing. Furthermore, the increased emphasis on managed healthcare in the United States and on country and regional pricing and reimbursement controls in the European Union will put additional pressure on product pricing, reimbursement and usage, which may adversely affect our future product sales. These pressures can arise from rules and practices of managed care groups, judicial decisions and governmental laws and regulations related to Medicare, Medicaid and healthcare reform, pharmaceutical reimbursement policies and pricing in general.

In addition, there is significant uncertainty regarding the reimbursement status of newly approved healthcare products. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the cost-effectiveness of our products. If third-party payors do not consider our products to be cost-effective compared to other therapies, the payors may not cover our products after approved as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis.

We may be subject to costly product liability or other liability claims and may not be able to obtain adequate insurance.

The use of our drug candidates in clinical trials may result in adverse events. We cannot predict all the possible harms or adverse events that may result from our clinical trials. We currently maintain limited product liability insurance. We may not have sufficient resources to pay for any liabilities resulting from a personal injury or other claim excluded from, or beyond the limit of, our insurance coverage. Our insurance does not cover third-parties' negligence or malpractice, and our clinical investigators and sites may have inadequate insurance or none at all. In addition, in order to conduct clinical trials or otherwise carry out our business, we may have to contractually assume liabilities for which we may not be insured. If we are unable to look to our own insurance or a third-party's insurance to pay claims against us, we may have to pay any arising costs and damages ourselves, which may be substantial.

In addition, if we commercially launch drugs based on our drug candidates, we will face even greater exposure to product liability claims. This risk exists even with respect to those drugs that are approved for commercial sale by the FDA and foreign regulatory agencies and manufactured in licensed and regulated facilities. We intend to secure additional limited product liability insurance coverage for drugs that we commercialize, but may not be able to obtain such insurance on acceptable terms with adequate

coverage, or at reasonable costs. Even if we are ultimately successful in product liability litigation, the litigation would consume substantial amounts of our financial and managerial resources and may create adverse publicity, all of which would impair our ability to generate sales of the affected product and our other potential drugs. Moreover, product recalls may be issued at our discretion or at the direction of the FDA and foreign regulatory agencies, other governmental agencies or companies having regulatory control for drug sales. Product recalls are generally expensive and often have an adverse effect on the reputation of the drugs being recalled and of the drug's developer or manufacturer.

We may be required to indemnify third parties against damages and other liabilities arising out of our development, commercialization and other business activities, which could be costly and time-consuming and distract management. If third parties that have agreed to indemnify us against damages and other liabilities arising from their activities do not fulfill their obligations, then we may be held responsible for those damages and other liabilities.

Our relationships with customers, healthcare providers, clinical trial sites and professionals and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other laws and regulations. If we fail to comply with federal, state and foreign laws and regulations, including healthcare, privacy and data security laws and regulations, we could face criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of any drug candidates for which we may obtain marketing approval. Our arrangements with customers, healthcare providers and professionals and third-party payors may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we develop, and may market, sell and distribute, our products for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations, include, but are not limited to, the following:

- The federal healthcare anti-kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federally funded healthcare programs such as Medicare and Medicaid. This statute has been broadly interpreted to apply to manufacturer arrangements with prescribers, purchasers and formulary managers, among others. Several other countries, including the United Kingdom, have enacted similar anti-kickback, fraud and abuse, and healthcare laws and regulations.
- The federal False Claims Act imposes civil penalties, including civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. The government and qui tam relators have brought False Claims Act actions against pharmaceutical companies on the theory that their practices have caused false claims to be submitted to the government. There is also a separate false claims provision imposing criminal penalties.
- The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program. HIPAA also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information. HIPAA also imposes criminal liability for knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services.
- The federal Physician Payments Sunshine Act requires manufacturers of drugs, devices, biologics and medical supplies to report to the HHS information related to payments and other transfers of value made to or at the request

of covered recipients, such as physicians and teaching hospitals, and physician ownership and investment interests in such manufacturers. Payments made to physicians and research institutions for clinical trials are included within the ambit of this law.

- Analogous state laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, and some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. Exclusion, suspension and debarment from government funded healthcare programs would significantly impact our ability to commercialize, sell or distribute

any drug. If any of the physicians or other providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

The collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the European Union, including personal health data, is subject to the EU General Data Protection Regulation (the "GDPR"), which became effective in May 2018. The GDPR, which is wide-ranging in scope, imposes several requirements relating to the control over personal data by individuals to whom the personal data relates, the information provided to the individuals, the documentation we must maintain, the security and confidentiality of the personal data, data breach notification and the use of third-party processors in connection with the processing of personal data. The GDPR also imposes strict rules on the transfer of personal data out of the European Union, provides an enforcement authority and authorizes the imposition of large penalties for noncompliance, including the potential for fines of up to €20 million or 4% of the annual global revenues of the non-compliant company, whichever is greater. The GDPR has increased our responsibility and potential liability in relation to personal data that we process compared to prior European Union law, and we may be required to put in place additional mechanisms to ensure compliance with the GDPR, which could divert management's attention and increase our cost of doing business. However, despite our ongoing efforts to bring our practices into compliance with the GDPR, we may not be successful either due to various factors within our control or other factors outside our control. It is also possible that local data protection authorities may have different interpretations of the GDPR, leading to potential inconsistencies amongst various European Union Member States. Any failure or alleged failure (including as a result of deficiencies in our policies, procedures or measures relating to privacy, data security, marketing or communications) by us to comply with laws, regulations, policies, legal or contractual obligations, industry standards or regulatory guidance relating to privacy or data security, may result in governmental investigations and enforcement actions, litigation, fines and penalties or adverse publicity. In addition, new regulation, legislative actions or changes in interpretation of existing laws or regulations regarding data privacy and security (together with applicable industry standards) may increase our costs of doing business. We expect that there will continue to be new proposed laws, regulations and industry standards relating to privacy and data protection in the United States, the European Union and other jurisdictions, such as the California Consumer Privacy Act of 2018 that will go into effect beginning January 1, 2020, and we cannot determine the impact such future laws, regulations and standards will have on our business.

Comprehensive U.S. tax reform legislation could increase the tax burden on our orphan drug programs and adversely affect our business and financial condition.

The U.S. government enacted comprehensive tax legislation in 2017 (the "2017 Tax Act") that includes significant changes to the taxation of business entities. These changes include, among others, (i) a permanent reduction to the corporate income tax rate, (ii) a partial limitation on the deductibility of business interest expense and net operating loss carryforwards, (iii) a shift of the U.S. taxation of multinational corporations from a tax on worldwide income to a territorial system (along with certain rules designed to prevent erosion of the U.S. income tax base) and (iv) a one-time tax on accumulated offshore earnings held in cash and illiquid assets, with the latter taxed at a lower rate. Further, the comprehensive tax legislation, among other things, reduces the orphan drug tax credit from 50% to 25% of qualifying expenditures. When and if we become profitable, this reduction in tax credits may result in an increased federal income tax burden on our orphan drug programs as it may cause us to pay federal income taxes earlier under the revised tax law than under the prior law and, despite being partially off-set by a reduction in the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, may increase our total federal tax liability attributable to such programs.

Notwithstanding the reduction in the corporate income tax rate, the overall impact of this comprehensive tax legislation resulted in an overall reduction in our deferred tax assets, and our business and financial condition could still be adversely affected as additional guidance and regulations are issued with respect to the original tax law change.

In addition, it is uncertain if and to what extent various states will conform to this comprehensive tax legislation. The impact of this comprehensive tax legislation on holders of our common stock is also uncertain and could be adverse. Investors should consult with their legal and tax advisors with respect to this comprehensive tax legislation and the potential tax consequences of investing in or holding our common stock.

Our ability to use net operating loss carryforwards and tax credit carryforwards to offset future taxable income may be subject to certain limitations, and ownership changes may limit our ability to use our net operating losses and tax credits in the future.

Our ability to use our federal and state net operating loss carryforwards ("NOLs") to offset potential future taxable income and reduce related income taxes depends upon our generation of future taxable income. We cannot predict with certainty when, or whether, we will generate sufficient taxable income to use our NOLs.

Our federal NOLs generated prior to 2018 will continue to be governed by tax rules in effect prior to the 2017 Tax Act, with unused NOLs expiring 20 years after we report a tax loss. These NOLs could expire unused and be unavailable to offset future taxable income. We cannot predict if and to what extent various states will conform to the 2017 Tax Act.

In addition, generally, if one or more stockholders or groups of stockholders who owns at least 5% of stock increases its ownership by more than 50% over its lowest ownership percentage within a three-year testing period, an ownership change occurs (an "Ownership Change"). Our ability to utilize our NOLs and tax credit carryforwards to reduce taxes payable in a year we have taxable income may be limited if there has been an Ownership Change in our stock. Similar rules may apply under state tax laws. We may experience a Ownership Changes in the future as a result of future stock sales or other changes in the ownership of our stock, some of which are beyond our control and, as a result, NOLs generated in 2017 and before, may expire unused.

Any material limitation or expiration of our NOLs and tax credit carryforwards may harm our future net income by effectively increasing our future effective tax rate, which could result in a reduction in the market price of our common stock.

Responding to any claims relating to improper handling, storage or disposal of the hazardous chemicals and radioactive and biological materials we use in our business could be time-consuming and costly.

Our research and development processes involve the controlled use of hazardous materials, including chemicals and radioactive and biological materials. Our operations produce hazardous waste products. We cannot eliminate the risk of accidental contamination or discharge and any resultant injury from those materials. Federal, state and local laws and regulations govern the use, manufacture, storage, handling and disposal of hazardous materials. We may be sued for any injury or contamination that results from our or third parties' use of these materials. Compliance with environmental laws and regulations is expensive, and current or future environmental regulations may impair our research, development and production activities.

Our facilities in California are located near an earthquake fault, and an earthquake or other types of natural disasters, catastrophic events or resource shortages could disrupt our operations and adversely affect our results.

All our facilities and our important documents and records, such as hard and electronic copies of our laboratory books and records for our drug candidates and compounds and our electronic business records, are located in our corporate headquarters at a single location in South San Francisco, California near active earthquake zones. If a natural disaster, such as an earthquake, fire or flood, a catastrophic event such as a disease pandemic or terrorist attack, or a localized extended outage of critical utilities or transportation systems occurs, we could experience a significant business interruption. Our partners and other third parties on which we rely may also be subject to business interruptions from such events. In addition, California from time to time has experienced shortages of water, electric power and natural gas. Future shortages and conservation measures could disrupt our operations and cause expense, thus adversely affecting our business and financial results.

Risks Related to an Investment in Our Common Stock

We expect that our stock price will fluctuate significantly, and you may not be able to resell your shares at or at or above your investment price.

The stock market, particularly in recent years, has experienced significant volatility, particularly with respect to pharmaceutical, biotechnology and other life sciences company stocks, which often does not relate to the operating performance of the companies represented by the stock. Factors that could cause volatility in the market price of our common stock include, but are not limited to:

- announcements concerning any of the clinical trials for our drug candidates (including, but not limited to, the timing of initiation or completion of such trials and the results of such trials, and delays or discontinuations of such trials, including delays resulting from slower than expected or suspended patient enrollment or discontinuations resulting from a failure to meet pre-defined clinical end points);
- announcements concerning our strategic alliance with Amgen or Astellas or future strategic alliances;
- failure or delays in entering additional drug candidates into clinical trials;
- failure or discontinuation of any of our research programs;
- issuance of new or changed securities analysts' reports or recommendations;
- failure or delay in establishing new strategic alliances, or the terms of those alliances;
- market conditions in the pharmaceutical, biotechnology and other healthcare-related sectors;
- actual or anticipated fluctuations in our quarterly financial and operating results;

- developments or disputes concerning our intellectual property or other proprietary rights;
- introduction of technological innovations or new products by us or our competitors;
- issues in manufacturing, packaging, labeling and distribution of our drug candidates or drugs;
- market acceptance of our drugs;
- third-party healthcare coverage and reimbursement policies;
- FDA or other U.S. or foreign regulatory actions affecting us or our industry;
- litigation or public concern about the safety of our drug candidates or drugs;
- additions or departures of key personnel;
- substantial sales of our common stock by our existing stockholders, whether or not related to our performance;
- automated trading activity by algorithmic and high-frequency trading programs; and
- volatility in the stock prices of other companies in our industry or in the stock market generally.

These and other external factors may cause the market price and demand for our common stock to fluctuate substantially, which may limit or prevent investors from readily selling their shares of common stock and may otherwise negatively affect the liquidity of our common stock. In addition, when the market price of a stock has been volatile, holders of that stock have instituted securities class action litigation against the company that issued the stock. If any of our stockholders brought a lawsuit against us, we could incur substantial costs defending the lawsuit. Such a lawsuit could also divert our management's time and attention.

If securities or industry analysts publish inaccurate or unfavorable research about our business, our stock price and trading volume could decline.

The trading market for our common stock depends in part on the research and reports that securities or industry analysts publish about us or our business. If one or more of the analysts who covers us downgrades our stock or publishes inaccurate or unfavorable research about our business, our stock price may decline. If one or more of these analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline.

In addition, as required by the new revenue recognition standards under ASC 606, we disclose the aggregate unsatisfied amount of transaction price allocated to performance obligations as of the end of the reporting period. Market practices surrounding the calculation of this measure are still evolving. It is possible that analysts and investors could misinterpret our disclosure or that the terms of our research or license agreements or other circumstances could cause our methods for preparing this disclosure to differ significantly from others, which could lead to inaccurate or unfavorable forecasts by analysts and investors.

Regardless of accuracy, unfavorable interpretations of our financial information and other public disclosures could have a negative impact on our stock price. If our financial performance fails to meet analyst estimates, for any of the reasons discussed above or otherwise, or one or more of the analysts who cover us downgrade our common stock or change their opinion of our common stock, our stock price would likely decline.

If the ownership of our common stock continues to be highly concentrated, it may prevent you and other stockholders from influencing significant corporate decisions and may result in conflicts of interest that could cause our stock price to decline.

Our executive officers, directors and their affiliates beneficially own or control some of the outstanding shares of our common stock. Accordingly, these executive officers, directors and their affiliates, acting as a group, may have substantial influence over the outcome of corporate actions requiring stockholder approval, including the election of directors, any merger, consolidation or sale of all or substantially all our assets or any other significant corporate transactions. These stockholders may also delay or prevent a change of control of us, even if such a change of control would benefit our other stockholders. The significant concentration of stock ownership may adversely affect the trading price of our common stock due to investors' perception that conflicts of interest may exist or arise.

Volatility in the stock prices of other companies may contribute to volatility in our stock price.

The stock market in general, and the Nasdaq stock exchanges and the market for technology companies in particular, have experienced significant price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of those companies. Further, there has been particular volatility in the market prices of securities of early stage and clinical stage life sciences companies. These broad market and industry factors may seriously harm the market price of our common stock, regardless of our operating performance. In the past, following periods of volatility in the market price of a company's securities, securities class action litigation has often been instituted. A securities class action suit against us could result in substantial costs, potential liabilities and the

diversion of management's attention and resources, and could harm our reputation and business.

Our common stock is thinly traded and there may not be an active, liquid trading market for our common stock.

There is no guarantee that an active trading market for our common stock will be maintained on Nasdaq, or that the volume of trading will be sufficient to allow for timely trades. Investors may not be able to sell their shares quickly or at the latest market price if trading in our stock is not active or if trading volume is limited. In addition, if trading volume in our common stock is limited, trades of relatively small numbers of shares may have a disproportionate effect on the market price of our common stock.

Our stockholders will experience substantial additional dilution if outstanding equity awards are exercised or settled for common stock.

The exercise of stock options or settlement of equity awards for common stock would be substantially dilutive to the outstanding shares of common stock. Any dilution or potential dilution may cause our stockholders to sell their shares, which would contribute to a downward movement in the market price of our common stock.

Evolving regulation of corporate governance and public disclosure may result in additional expenses, use of resources and continuing uncertainty.

We regularly evaluate and monitor developments with respect to new and proposed laws, regulations and standards. For example, we spend significant financial and human resources to document and test the adequacy of our internal control over financial reporting to comply with the internal control requirements the Sarbanes-Oxley Act.

We intend to maintain high standards of corporate governance and public disclosure and to invest the resources necessary to comply with evolving laws, regulations and standards. This investment may result in increased general and administrative expenses and a diversion of management time and attention from revenue-generating activities to compliance activities.

Changing laws, regulations and standards relating to corporate governance and public disclosure create uncertainty for public companies. In many cases, changes lack specificity and compliance with these changes may evolve over time as new guidance is provided by regulatory and governing bodies. We cannot accurately predict or estimate the amount or timing of the additional effort or expense we may incur complying with changes in these laws, regulations and standards. Therefore, we can provide no assurance as to conclusions of management or by our independent registered public accounting firm with respect to the effectiveness of our internal control over financial reporting in the future. If our efforts to comply with new or changed laws, regulations and standards differ from the activities intended by regulatory or governing bodies, due to ambiguities related to practice or otherwise, regulatory authorities may initiate legal proceedings against us, which could be costly and time-consuming, and our reputation and business may be harmed.

We have never paid dividends on our capital stock, and we do not anticipate paying any cash dividends in the foreseeable future.

We have paid no cash dividends on any of our classes of capital stock to date and we currently intend to retain our future earnings, if any, to fund the development and growth of our businesses. In addition, the terms of existing or any future debts may preclude us from paying these dividends.

Item 1B. Unresolved Staff Comments
None.

Item 2. Properties
Our facilities consist of approximately 81,587 square feet of leased research and office space in South San Francisco, California. Our lease expires in June 2021. We believe that these facilities are suitable and adequate for our current needs.

Item 3. Legal Proceedings
We are not currently subject to any material legal proceedings.

Item 4. Mine Safety Disclosures
Not applicable.

PART II

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

Our common stock is listed on the Nasdaq Global Select Market under the symbol "CYTK." On March 5, 2019, the last reported sale price for our common stock was $6.50 per share. We currently expect to retain future earnings, if any, for use in the operation and expansion of our business and have not paid and do not in the foreseeable future anticipate paying any cash dividends. As of March 5, 2019, there were 52 holders of record of our common stock.

Equity Compensation Information

Information regarding our equity compensation plans and the securities authorized for issuance thereunder is set forth in Part III, Item 12.

Item 6. Selected Financial Data

(Not required)

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

This discussion and analysis should be read in conjunction with our financial statements and accompanying notes included elsewhere in this report. Operating results are not necessarily indicative of results that may occur in future periods.

Overview

We are a late-stage biopharmaceutical company focused on discovering, developing and commercializing first-in-class muscle activators and best-in-class muscle inhibitors as potential treatments for debilitating diseases in which muscle performance is compromised and/or declining. We have discovered and are developing muscle-directed investigational medicines that may potentially improve the healthspan of people with devastating cardiovascular and neuromuscular diseases of impaired muscle function. Our research and development activities relating to the biology of muscle function have evolved from our knowledge and expertise regarding the cytoskeleton, a complex biological infrastructure that plays a fundamental role within every human cell. As a leader in muscle biology and the mechanics of muscle performance, we are developing small molecule drug candidates specifically engineered to impact muscle function and contractility.

Our drug candidates currently in clinical development are: omecamtiv mecarbil, a novel cardiac myosin activator which we are developing for the potential treatment of heart failure, reldesemtiv, a novel fast skeletal muscle troponin activator ("FSTA") which we are developing for the potential treatment of amyotrophic lateral sclerosis ("ALS") and spinal muscular atrophy ("SMA"), CK-3773274 ("CK-274"), a novel cardiac myosin inhibitor, which we are developing for the potential treatment of hypertrophic cardiomyopathy ("HCM") and AMG 594, a novel cardiac troponin activator which is the subject of a Phase 1 clinical study.

Omecamtiv mecarbil is being evaluated for the potential treatment of heart failure under a strategic alliance with Amgen established in 2006 to discover, develop, and commercialize novel small molecule therapeutics designed to activate cardiac muscle contractility pursuant to the collaboration and option agreement dated December 29, 2006, as amended (the "Amgen Agreement"). Amgen, in collaboration with Cytokinetics, is conducting GALACTIC-HF (Global Approach to Lowering Adverse Cardiac Outcomes Through Improving Contractility in Heart Failure), a Phase 3 cardiovascular outcomes clinical trial of omecamtiv mecarbil in heart failure. In collaboration with Amgen, we are conducting METEORIC-HF (Multicenter Exercise Tolerance Evaluation of Omecamtiv Mecarbil Related to Increased Contractility in Heart Failure), a second Phase 3 clinical trial intended to evaluate its potential to increase exercise

performance.

Reldesemtiv selectively activates the fast skeletal muscle troponin complex in the sarcomere by increasing its sensitivity to calcium, leading to an increase in skeletal muscle contractility. Cytokinetics and Astellas are developing reldesemtiv under the Amended and Restated License and Collaboration Agreement dated December 22, 2014, as amended (the "Astellas Agreement"). Astellas holds an exclusive license to develop and commercialize reldesemtiv worldwide, subject to our development and commercialization participation rights. In collaboration with Astellas, we conducted a Phase 2 clinical trial of reldesemtiv in patients with SMA and we are conducting a Phase 2 clinical trial of reldesemtiv in patients with ALS, called FORTITUDE-ALS (Functional Outcomes in a Randomized Trial of Investigational Treatment with CK-2127107 to Understand Decline in Endpoints – in ALS). Astellas, in collaboration with us, conducted a Phase 2 clinical trial of reldesemtiv in patients with chronic obstructive pulmonary disease ("COPD") and a Phase 1b clinical trial of reldesemtiv in elderly subjects with limited mobility.

CK-274 is a novel, oral, small molecule cardiac myosin inhibitor that we discovered independent of our collaborations. CK-274 arose from an extensive chemical optimization program conducted with careful attention to therapeutic index and pharmacokinetic properties that may translate into best-in-class potential in clinical development. CK-274 was designed to reduce the hypercontractility that is associated with HCM. In preclinical models, CK-274 reduces myocardial contractility by binding directly to cardiac myosin at a distinct and selective allosteric binding site, thereby preventing myosin from entering a force producing state. CK-274 reduces the number of active actin-myosin cross bridges during each cardiac cycle and consequently reduces myocardial contractility. This

mechanism of action may be therapeutically effective in conditions characterized by excessive hypercontractility, such as HCM. We are conducting a Phase 1 double-blind, randomized, placebo-controlled, multi-part, single and multiple ascending dose clinical trial of CK-274 in healthy adult subjects.

AMG 594 was discovered under our joint research program with Amgen. In collaboration with Cytokinetics, Amgen is conducting a randomized, placebo-controlled, double-blind, single and multiple ascending dose, single-center Phase 1 study to assess the safety, tolerability, pharmacokinetics and pharmacodynamics of AMG 594 in healthy subjects.

Our research continues to drive innovation and leadership in muscle biology, evidenced by three new muscle biology directed compounds advancing from research to development in 2018. All of our drug candidates have arisen from our cytoskeletal research activities. Our focus on the biology of the cytoskeleton distinguishes us from other biopharmaceutical companies, and potentially positions us to discover and develop novel therapeutics that may be useful for the treatment of severe diseases and medical conditions. Each of our drug candidates has a novel mechanism of action compared to currently marketed drugs, which we believe validates our focus on the cytoskeleton as a productive area for drug discovery and development. We intend to leverage our experience in muscle contractility to expand our current pipeline and expect to identify additional potential drug candidates that may be suitable for clinical development.

Critical Accounting Polices and Significant Estimates

Our discussion and analysis of our financial condition and results of operations are based on our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities and expenses and related disclosure of contingent assets and liabilities. We review our estimates on an ongoing basis. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances. Actual results may differ from these estimates under different assumptions or conditions. While our significant accounting policies are described in more detail in the notes to our financial statements included in this Annual Report on Form 10-K, we believe the following accounting policies to be critical to the judgments and estimates used in the preparation of our financial statements.

Revenue Recognition

On January 1, 2018, we adopted Accounting Standards Codification 606, Revenue from Contracts with Customers (“ASC 606”), using the modified retrospective method. On January 1, 2018, for contracts within the scope of ASC 606, we recognized a contract asset or liability and reduced our accumulated deficit for the effect of adopting ASC 606 and did not revise our prior period financial statements. Pursuant to ASC 606, to recognize revenue from a contract with a customer, we:

(i) identify our contracts with our customers;

(ii) identify our distinct performance obligations in each contract;

(iii) determine the transaction price of each contract;

(iv) allocate the transaction price to the performance obligations; and

(v) recognize revenue as we satisfy our performance obligations.

At contract inception, we assess the goods or services promised within each contract and assess whether each promised good or service is distinct and determine those that are performance obligations. We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

Collaborative Arrangements

We enter into collaborative arrangements with partners that typically include payment to us for one of more of the following: (i) license fees; (ii) milestone payments related to the achievement of developmental, regulatory, or commercial goals; and (iii) royalties on net sales of licensed products. Each of these payments results in collaboration or other revenues. Where a portion of non-refundable up-front fees or other payments received are allocated to continuing performance obligations under the terms of a collaborative arrangement, they are recorded as deferred revenue and recognized as revenue when (or as) the underlying performance obligation is satisfied.

As part of the accounting for these arrangements, we must develop estimates and assumptions that require judgment to determine the underlying stand-alone selling price for each performance obligation which determines how the transaction price is allocated among the performance obligation. The stand-alone selling price may include such items as, forecasted revenues, development timelines, reimbursement rates for personnel costs, discount rates and probabilities of technical and regulatory success, to determine the transaction price to allocate to each performance obligation.

For our collaboration agreements that include more than one performance obligation, such as a license combined with a commitment to perform research and development services, we make judgments to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from non-refundable, up-front fees. We evaluate our progress each reporting period and, if necessary, adjust the measure of a performance obligation and related revenue recognition.

License Fees: If a license to our intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, we recognize revenues from non-refundable, up-front fees allocated to the license when the license is transferred to the licensee and the licensee is able to use and benefit from the license. For licenses that are bundled with other promises, we utilize judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from non-refundable, up-front license fees. We evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition.

Milestone Payments: We use judgement to determine whether a milestone is considered probable of being reached. Using the most likely amount method, we include the value of a milestone payment in the consideration for a contract at inception if we then conclude achieving the milestone is more likely than not. Otherwise, we exclude the value of a milestone payment from contract consideration at inception and recognize revenue for a milestone at a later date, when we judge that it is more likely than not that the milestone will be achieved. If we conclude it is probable that a significant revenue reversal would not occur, the associated milestone is included in the transaction price. We then allocate the transaction price to each performance obligation on a relative stand-alone selling price basis, for which we recognize revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, we re-evaluate the probability of achievement of such milestones and any related constraint, and if necessary, adjust our estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect license, collaboration and other revenues and earnings in the period of adjustment.

Royalties: For contracts that include sales-based royalties, we recognize revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied. To date, we have not recognized any royalty revenues resulting from contracts.

Research and Development Cost Reimbursements: Our Astellas and Amgen arrangements include promises of research and development services. We have determined that these services collectively are distinct from the licenses provided to Astellas and Amgen and as such, these promises are accounted for as a separate performance obligation recorded over time. We record revenue for these services as the performance obligations are satisfied, which we estimate using internal development costs incurred.

Accrued Research and Development Expenditures

A substantial portion of our preclinical studies and all of our clinical trials have been performed by third-party CROs and other vendors and our accruals for expenses for preclinical studies and clinical trials may be significant. For preclinical studies, the significant factors used in estimating accruals include the percentage of work completed to date and contract milestones achieved. For clinical trial expenses, the significant factors used in estimating accruals include the number of patients enrolled, duration of enrollment, milestones achieved and percentage of work completed to date. We monitor patient enrollment levels and related activities to the extent practicable through internal reviews, correspondence and status meetings with CROs, and review of contractual terms. We depend on the timeliness and accuracy of data provided by its CROs and other vendors to accrue expenses. If we receive and rely on incomplete or inaccurate data, accruals and expenses may be too high or too low at a given point in time and corresponding adjustments to accruals and expenses would be made in future periods when the actual expense becomes known.

Liability Related to Sale of Future Royalties

We treat the Liability related to sale of future royalties as a debt financing, to be amortized under the effective interest rate method over the life of the related royalty stream.

The Liability related to sale of future royalties and the debt amortization are based on our current estimates of future royalties expected to be paid over the life of the arrangement. We will periodically assess the expected royalty payments using a combination of internal projections and forecasts from external sources. To the extent our future estimates of future royalty payments are greater or less than its previous estimates or the estimated timing of such payments is materially different than its previous estimates, we will adjust the Liability related to sale of future royalties and prospectively recognize related non-cash interest expense.

Results of Operations

Revenues

Our revenues since inception were primarily from our strategic alliances and grants revenues. Under our agreements with Amgen and Astellas, we received payments including upfront license fees, reimbursements of internal costs of certain FTEs and costs to support research and development programs, and milestone payments. We have not generated any revenue from commercial product sales to date.

We may also be entitled to additional milestone payments and other contingent payments upon the occurrence of specific events. We expect that our revenue will continue to fluctuate in future periods.

	Years Ended December 31,		
	2018	2017	Increase (Decrease)
	(In millions)		
Research and development, grant and other revenues, net	$ 26.4	$ 4.6	$ 21.8
License revenues	5.1	8.8	(3.7)
Total revenues	$ 31.5	$ 13.4	$ 18.1

Our revenues in 2018 and 2017 were primarily from our strategic alliances with Astellas and Amgen. Research and development revenues from Astellas were $24.4 million in 2018, including $22.4 million for reimbursements and $2.0 million in a milestone payment for initiation of IND-enabling studies for CK-601. Research and development revenues from Astellas were $11.9 million in 2017 for reimbursements. Research and development revenues from Amgen were $1.9 million in 2018 for reimbursements and $12.3 million in 2017, consisting of $1.3 for reimbursements and $11.0 million in milestone payments. Research and development revenues from Amgen in 2017 was offset by $20.0 million for our payments to Amgen to co-fund the Phase 3 development program of omecamtiv mecarbil in exchange for an increased royalty upon potential commercialization. Research and development revenue included $0.2 million in 2018 for a milestone payment received under our agreement with MyoKardia, Inc. and $0.4 million in 2017 in grant revenue.

License revenue from Astellas was $5.1 million in 2018 and $8.8 million in 2017 and consisted of recognition of license fees for development of reldesemtiv. License revenue decreased in 2018 from 2017 primarily because of adopting ASC 606, Revenue from Contracts with Customers.

Research and development expenses

We incur research and development expenses associated with both partnered and our own research activities.

Research and development expenses related to any development we elect to fund consist primarily of employee compensation, supplies and materials, costs for consultants and contract research and manufacturing, facilities costs and depreciation of equipment.

Research and development expenses decreased to $89.1 million in 2018 from $90.3 million in 2017. Research and development expenses by program for 2018 and 2017 were:

	Years Ended December 31,		
	2018	2017	Increase (Decrease)
	(In millions)		
Cardiac muscle contractility	$ 19.0	$ 10.6	$ 8.4
Skeletal muscle contractility	50.9	75.4	(24.5)
All other research programs	19.2	4.3	14.9
Total research and development expenses	$ 89.1	$ 90.3	$ (1.2)

Research and development expenses decreased in 2018 compared to 2017 primarily due to suspending development of tirasemtiv in late 2017, offset in part by increased clinical development of reldesemtiv and omecamtiv mecarbil and development activities for CK-274.

Under our strategic alliance with Astellas, we expect to continue developing reldesemtiv to treat ALS and SMA, as well as CK-601, potentially to treat other diseases and medical conditions associated with muscle weakness or wasting. Under our strategic alliance with Amgen, we expect to continue the Phase 3 development of omecamtiv mecarbil for the potential treatment of heart failure. We expect to continue the development of CK-274 to assess the potential of CK 274 to improve exercise capacity and relieve symptoms in patients with hyperdynamic ventricular

contraction due to HCM.

Clinical development timelines, the likelihood of success and total completion costs vary significantly for each drug candidate and are difficult to estimate. We anticipate that we will determine on an ongoing basis which research and development programs to pursue and how much funding to direct to each program, taking into account the scientific and clinical success of each drug candidate. The lengthy process of seeking regulatory approvals and subsequent compliance with applicable regulations requires the expenditure of substantial resources. Any failure by us to obtain and maintain, or any delay in obtaining, regulatory approvals could cause our research and development expenditures to increase and, in turn, could have a material adverse effect on our results of operations.

General and administrative expenses

General and administrative expenses consist primarily of compensation for employees in executive and administrative functions, including, but not limited to, finance, human resources, legal, business and commercial development and strategic planning. Other significant costs include facilities costs, consulting costs and professional fees for accounting and legal services, including legal services associated with obtaining and maintaining patents and regulatory compliance.

General and administrative expenses decreased to $31.3 million in 2018 from $36.5 million in 2017, primarily due to lower commercial readiness activities after suspending development of tirasemtiv in late 2017.

We expect that general and administrative expenses will fluctuate in the future, depending in part on the timing of and investments in commercial readiness.

Interest expense

Interest expense in 2018 and 2017 consisted primarily of interest expense related to the Loan and Security Agreement, dated as of October 19, 2015 and amended on October 27, 2017 by and among the Company, Oxford Finance LLC and Silicon Valley Bank, as amended (the "Loan Agreement"). Interest expense increased in 2018 compared to 2017 primarily due to higher average loan balances outstanding in 2018 compared to 2017 as well as due to increases in prevailing interest rates.

Non-cash interest expense on Liability related to sale of future royalties

Non-cash interest expense related to Liability related to sale of future royalties in 2018 and 2017 results from accretion of the liability related to sale of future royalties. We anticipate that this non-cash interest expense will increase in the future primarily due to increased accretion over time.

Interest and Other Income, net

Interest and other income, net for 2018 and 2017 consisted primarily of interest income generated from our cash, cash equivalents and investments. Other income consisted of net gains on upon disposal of equipment.

Liquidity and Capital Resources

At December 31, 2018, our cash, cash equivalents and short-term investments totaled $198.7 million.

Sources and Uses of Cash

We have funded our operations and capital expenditures with proceeds primarily from private and public sales of our equity securities, a royalty monetization agreement, strategic alliances, long-term debt, other financings, interest on investments and grants. We have generated significant operating losses since our inception. Our expenditures are primarily related to research and development activities.

Net cash used in operating activities was $101.2 million for 2018 and was largely due to our net loss for 2018, offset by non-cash expenses included in net loss, as well as cash used to fund the Co-Invest Option for omecamtiv mecarbil. Net cash used in operating activities was $101.8 million for 2017 and was largely due to our net loss of $127.8 million less non-cash charges such as stock-based compensation expense and non-cash interest expense on liability related to sale of future royalties of $9.0 million and $14.0 million, respectively.

Net cash provided in investing activities of $5.1 million in 2018 was primarily due to maturities of investments of $246.2 million, offset in part by purchases of investments of $240.2 million and property and equipment of $0.9 million. Net cash used in investing activities of $65.8 million in 2017 was primarily due to purchases of investments of $240.4 million and property and equipment of $2.9 million, partially offset by maturities of investments of $177.5 million.

Net cash provided by financing activities of $13.1 million in 2018 was primarily due to proceeds from additional long-term debt of $10.0 million and net proceeds from issuance of our Common Stock. Net cash provided by financing activities was $225.9 million in 2017 was primarily due to net proceeds from issuance of our Common Stock and from the liability related to sales of future royalties.

In November 2017, we entered into a Controlled Equity Offering[SM] Sales Agreement (the "ATM Facility") with Cantor Fitzgerald & Co. ("Cantor") for the sale, in our sole discretion, of shares of our common stock, having an aggregate offering price of up to $75.0 million through Cantor, as our sales agent. As of December 31, 2018, we had not sold any shares of common stock under the ATM Facility.

In March 2019, we terminated the ATM Facility and entered into a new sales agreement (the "New ATM Facility") with Cantor, which provides for the sale, in our sole discretion, of shares of our common stock having an aggregate offering price of up to $35.0 million through Cantor, as our sales agent. The issuance and sale of these shares by us pursuant to the New ATM Facility are deemed "at the market" offerings and are registered under the Securities Act of 1933, as amended. We will pay a commission of up to 3.0% of gross sales proceeds of any common stock sold under the New ATM Facility.

In future periods, we expect to incur substantial costs as we continue to expand our research programs and related research and development activities. We expect to incur significant research and development expenses as we advance the research and development of compounds from our other muscle biology programs through research to candidate selection to clinical development.

Our future capital uses and requirements depend on numerous factors. These factors include, but are not limited to, the following:

- the initiation, progress, timing, scope and completion of preclinical research, non-clinical development, chemistry, manufacturing, and controls ("CMC"), and clinical trials for our drug candidates and other compounds;
- the time and costs involved in obtaining regulatory approvals;
- delays that may be caused by requirements of regulatory agencies;
- Amgen's decisions with regard to funding of development and commercialization of omecamtiv mecarbil or other compounds for the potential treatment of heart failure under the Amgen Agreement;
- Astellas' decisions with regard to funding of development and commercialization of reldesemtiv or other skeletal muscle activators under the Astellas Agreement;
- our level of funding for the development of current or future drug candidates;
- the number of drug candidates we pursue;
- the costs involved in filing and prosecuting patent applications and enforcing or defending patent claims;
- our ability to establish and maintain selected strategic alliances required for the development of drug candidates and commercialization of our potential drugs;
- our plans or ability to expand our drug development capabilities, including our capabilities to conduct clinical trials for our drug candidates;
- our plans or ability to engage third-party manufacturers for our drug candidates and potential drugs;
- our plans or ability to build or access sales and marketing capabilities and to achieve market acceptance for potential drugs;
- the expansion and advancement of our research programs;
- the hiring of additional employees and consultants;
- the expansion of our facilities;
- the acquisition of technologies, products and other business opportunities that require financial commitments; and
- our revenues, if any, from successful development of our drug candidates and commercialization of potential drugs.

We have incurred an accumulated deficit of $743.3 million since inception and there can be no assurance that we will attain profitability. We are subject to risks common to clinical-stage companies including, but not limited to, development of new drug candidates, dependence on key personnel, and the ability to obtain additional capital as needed to fund our future plans. Our liquidity will be impaired if sufficient additional capital is not available on terms acceptable to us, if at all. Until we achieve profitable operations, we intend to continue to fund operations through payments from strategic collaborations, additional sales of equity securities, grants and other financings. We have never generated revenues from commercial sales of our drugs and may not have drugs to market for at least several years, if ever. Our success is dependent on our ability to obtain additional capital by entering into new strategic collaborations and/or through financings, and ultimately on our and our collaborators' ability to successfully develop and market one or more of our drug candidates. We cannot be certain that sufficient funds will be available from such collaborators or financings when needed or on satisfactory terms. Additionally, there can be no assurance that any of drugs based on our drug candidates will be accepted in the marketplace or that any future products can be developed or manufactured at an acceptable cost. These factors could have a material adverse effect on our future financial results, financial position and cash flows.

Based on the current status of our development plans, we believe that our existing cash and cash equivalents, investments and interest earned on investments will be sufficient to meet our projected operating requirements for at least the next 12 months. If, at any time, our prospects for internally financing our research and development programs decline, we may decide to reduce research and development expenses by delaying, discontinuing or reducing our funding of development of one or more of our drug candidates or of other research and development programs. Alternatively, we might raise funds through strategic relationships, public or private financings or other arrangements. There can be no assurance that funding, if needed, will be available on attractive terms, or at all, or in accordance with our planned timelines. Furthermore, financing obtained through future strategic relationships may require us to forego

certain commercialization and other rights to our drug candidates. Similarly, any additional equity financing may be dilutive to stockholders and debt financing, if available, may involve restrictive covenants. Our failure to raise capital as and when needed could have a negative impact on our financial condition and our ability to pursue our business strategy.

Segment Information

We have one primary business activity and operate in one reportable segment.

Off-balance Sheet Arrangements

We are not party to any off-balance sheet arrangements that have, or are reasonably likely to have, a material current or future effect on our financial condition, revenues or expenses, results of operations, liquidity, capital expenditures or capital resources.

Recent Accounting Pronouncements

The information required by this item is included in Item 8, Note 1, Organization and Accounting Policies, in our Consolidated Financial Statements included in this Annual Report on Form 10 K.

Item 7A.Quantitative and Qualitative Disclosures About Market Risk

(Not Required)

Item 8. Financial Statements and Supplementary Data

CYTOKINETICS, INCORPORATED

INDEX TO FINANCIAL STATEMENTS

REPORT OF ERNST & YOUNG LLP, INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders

Cytokinetics, Incorporated

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheet of Cytokinetics, Incorporated (the "Company") as of December 31, 2018, the related consolidated statements of operations and comprehensive loss, stockholders' equity, and cash flows for the year then ended, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2018, and the results of its operations and its cash flows for the year then ended, in conformity with US generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2018, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 Framework) and our report dated March 6, 2019 expressed an adverse opinion thereon.

Adoption of ASU No. 2014-09

As discussed in Note 1 to the consolidated financial statements, the Company changed its method for recognizing revenue as a result of the adoption of Accounting Standards Update (ASU) No. 2014-09, Revenue from Contracts with Customers (Topic 606), using the modified retrospective method effective January 1, 2018.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the US federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audit included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to

those risks. Such procedures include examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audit also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audit provides a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2018.

Redwood City, California

March 6, 2019

REPORT OF PRICE WATERHOUSE COOPERS LLP, INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders of Cytokinetics, Incorporated:

Opinion on the Financial Statements

We have audited the consolidated balance sheet of Cytokinetics, Inc. and its subsidiary (the “Company”) as of December 31, 2017, and the related consolidated statements of operations and comprehensive (loss) income, stockholders’ equity and cash flows for the year ended December 31, 2017, including the related notes (collectively referred to as the “consolidated financial statements”). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2017, and the results of its operations and its cash flows for the year ended December 31, 2017 in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

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

We conducted our audit of these consolidated financial statements in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud.

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

/s/ PricewaterhouseCoopers LLP

San Jose, California

March 5, 2018

We served as the Company's auditor from 1999 to 2018.

CYTOKINETICS, INCORPORATED

CONSOLIDATED BALANCE SHEETS

	December 31,	
	2018	2017
	(In thousands, except share and per share data)	
ASSETS		
Current assets:		
Cash and cash equivalents	$42,256	$125,206
Short-term investments	156,475	143,685
Accounts receivable	2,231	1,112
Contract assets	4,554	—
Prepaid and other current assets	2,158	4,292
Total current assets	207,674	274,295
Long-term investments	—	16,518
Property and equipment, net	3,204	3,568
Other assets	300	429
Total assets	$211,178	$294,810
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$3,764	$5,253
Accrued liabilities	15,757	17,392
Deferred revenue, current	—	9,572
Current portion of long-term debt	2,607	—
Other current liabilities	66	227
Total current liabilities	22,194	32,444
Long-term debt	39,806	31,777
Liability related to the sale of future royalties, net	122,473	104,650
Deferred revenue, non-current	—	15,000
Other long-term liabilities	771	1,097
Total liabilities	185,244	184,968
Commitments and contingencies		
Stockholders' equity:		
Preferred stock, $0.001 par value:		
Authorized: 10,000,000 shares; Issued and outstanding: none	—	—
Common stock, $0.001 par value:		
Authorized: 163,000,000 shares		
Issued and outstanding: 54,717,906 shares at December 31, 2018		
and 53,960,832 shares at December 31, 2017	55	54
Additional paid-in capital	768,703	755,526
Accumulated other comprehensive income	500	343
Accumulated deficit	(743,324)	(646,081)

Total stockholders' equity	25,934	109,842
Total liabilities and stockholders' equity	$211,178	$294,810

The accompanying notes are an integral part of these consolidated financial statements.

CYTOKINETICS, INCORPORATED

CONSOLIDATED STATEMENT OF OPERATIONS AND COMPREHENSIVE LOSS

	Years Ended December 31,	
	2018	2017
	(In thousands, except per share data)	
Revenues:		
Research and development, grant and other revenues, net	$26,368	$4,569
License revenues	5,133	8,799
Total revenues	31,501	13,368
Operating expenses:		
Research and development	89,135	90,296
General and administrative	31,282	36,468
Total operating expenses	120,417	126,764
Operating loss	(88,916)	(113,396)
Interest expense	(3,797)	(3,016)
Non-cash interest expense on liability related to sale of future royalties	(17,767)	(13,980)
Interest and other income, net	4,191	2,602
Net loss	$(106,289)	$(127,790)
Net loss income per share — basic and diluted	$(1.95)	$(2.59)
Weighted-average number of shares used in computing net loss per share — basic and diluted	54,420	49,404
Other comprehensive loss:		
Unrealized gains on available-for-sale securities, net	157	206
Comprehensive loss	$(106,132)	$(127,584)

The accompanying notes are an integral part of these consolidated financial statements.

CYTOKINETICS, INCORPORATED

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY

	Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Income	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
	(In thousands)					
Balance, December 31, 2016	40,646,595	$ 41	$ 612,474	$ 137	$ (518,291)	$ 94,361
Exercise of stock options	264,164	—	1,918	—	—	1,918
Issuance under Employee Stock Purchase Plan	120,959	—	1,167	—	—	1,167
Vesting of restricted stock units, net of taxes withheld	128,711	—	(904)	—	—	(904)
Exercise of warrants	3,450,122	3	12,068	—	—	12,071
Issuance under secondary offering net of issuance costs	6,049,000	6	82,364	—	—	82,370
Issuance net of commission and issuance costs	2,425,625	3	29,852	—	—	29,855
Issuance pursuant to Royalty Purchase Agreement	875,656	1	7,559	—	—	7,560
Stock-based compensation	—	—	9,028	—	—	9,028
Other comprehensive loss	—	—	—	206	—	206
Net loss	—	—	—	—	(127,790)	(127,790)
Balance, December 31, 2017	53,960,832	54	755,526	343	(646,081)	109,842
Exercise of stock options	422,819	1	3,172	—	—	3,173
Issuance under Employee Stock Purchase Plan	144,822	—	928	—	—	928
Vesting of restricted stock units, net of taxes withheld	189,433	—	(866)	—	—	(866)
Issuance of warrants	—	—	182	—	—	182
Stock-based compensation	—	—	9,761	—	—	9,761
ASC 606 Adoption	—	—	—	—	9,046	9,046
Other comprehensive loss	—	—	—	157	—	157
Net loss	—	—	—	—	(106,289)	(106,289)
Balance, December 31, 2018	54,717,906	$ 55	$ 768,703	$ 500	$ (743,324)	$ 25,934

The accompanying notes are an integral part of these consolidated financial statements.

CYTOKINETICS, INCORPORATED

CONSOLIDATED STATEMENTS OF CASH FLOWS

	Years Ended December 31,	
	2018	2017
	(In thousands)	
Cash flows from operating activities:		
Net loss	$(106,289)	$(127,790)
Adjustments to reconcile net loss to net cash used in operating activities:		
Non-cash interest expense on liability related to sale of future royalties	17,767	14,028
Stock-based compensation	9,761	9,028
Depreciation and amortization of property and equipment	1,239	1,920
Interest receivable and amortization on investments	(1,677)	—
Net gain on disposal of equipment	—	(67)
Non-cash interest expense related to long-term debt	920	635
Changes in operating assets and liabilities:		
Accounts receivable	(1,119)	(1,088)
Contract assets	5,154	—
Prepaid and other assets	1,817	(2,161)
Accounts payable	(1,490)	1,457
Accrued and other liabilities	(2,063)	766
Contract liabilities	(18,750)	—
Deferred revenue	(6,485)	1,513
Net cash used in operating activities	(101,215)	(101,759)
Cash flows from investing activities:		
Purchases of investments	(240,224)	(240,413)
Sales and maturities of investments	246,232	177,462
Purchases of property and equipment	(889)	(2,877)
Sales of property and equipment	14	—
Net cash provided by (used in) investing activities	5,133	(65,828)
Cash flows from financing activities:		
Proceeds from public offerings of common stock, net of issuance costs	—	112,224
Proceeds from sale of future royalties, net of issuance costs	—	90,621
Proceeds from issuance of common stock related to sale of future royalties, net of issuance costs	—	7,560
Net proceeds from long-term debt, net of debt discount and issuance costs	9,898	1,261
Proceeds from stock based award activities and warrants, net	3,234	14,253
Net cash provided by financing activities	13,132	225,919
Net (decrease) increase in cash and cash equivalents	(82,950)	58,332
Cash and cash equivalents, beginning of period	125,206	66,874
Cash and cash equivalents, end of period	$42,256	$125,206
Supplemental disclosure of cash flow information		

Cash paid for interest	2,877	2,128
Cash paid for taxes	1	1

The accompanying notes are an integral part of these consolidated financial statements.

CYTOKINETICS, INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

Note 1 — Organization and Accounting Policies

Organization

Cytokinetics, Incorporated (the "Company", "we" or "our") was incorporated under the laws of the state of Delaware on August 5, 1997. We are a late-stage biopharmaceutical company focused on the discovery and development of novel small molecule therapeutics that modulate muscle function for the potential treatment of serious diseases and medical conditions.

Our financial statements contemplate the conduct of our operations in the normal course of business. We have incurred an accumulated deficit of $743.3 million since inception and there can be no assurance that we will attain profitability. We had a net loss of $106.3 million and net cash used in operations of $101.2 million for the year ended December 31, 2018. Cash, cash equivalents and investments increased to $198.7 million at December 31, 2018 from $285.4 million at December 31, 2017. We anticipate that we will have operating losses and net cash outflows in future periods.

We are subject to risks common to late-stage biopharmaceutical companies including, but not limited to, development of new drug candidates, dependence on key personnel, and the ability to obtain additional capital as needed to fund our future plans. Our liquidity will be impaired if sufficient additional capital is not available on terms acceptable to us. We have funded our operations and capital expenditures with proceeds primarily from private and public sales of our equity securities, a royalty monetization agreement, strategic alliances, long-term debt, other financings, interest on investments and grants. Until we achieve profitable operations, we intend to continue to fund operations through payments from strategic collaborations, additional sales of equity securities, grants and debt financings. We have never generated revenues from commercial sales of our drugs and may not have drugs to market for at least several years, if ever. Our success is dependent on our ability to enter into new strategic collaborations and/or raise additional capital and to successfully develop and market one or more of our drug candidates. As a result, we may choose to raise additional capital through equity or debt financings to continue to fund our operations in the future. We cannot be certain that sufficient funds will be available from such a financing or through a collaborator when required or on satisfactory terms. Additionally, there can be no assurance that our drug candidates will be accepted in the marketplace or that any future products can be developed or manufactured at an acceptable cost. These factors could have a material adverse effect on our future financial results, financial position and cash flows.

Based on the current status of our research and development plans, we believe that our existing cash, cash equivalents and investments will be sufficient to fund our cash requirements for at least the next 12 months after the issuance of the consolidated financial statements. If, at any time, our prospects for financing our research and development programs decline, we may decide to reduce research and development expenses by delaying, discontinuing or reducing our funding of one or more of our research or development programs. Alternatively, we might raise funds through strategic collaborations, public or private financings or other arrangements. Such funding, if needed, may not be available on favorable terms, or at all. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosures of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates.

Basis of Presentation

The consolidated financial statements include the accounts of Cytokinetics Incorporated and its wholly owned subsidiary and have been prepared in accordance with U.S. generally accepted accounting principles ("US GAAP"). Intercompany transactions and balances have been eliminated in consolidation.

Concentration of Credit Risk and Other Risks and Uncertainties

Financial instruments that potentially subject us to concentrations of risk consist principally of cash and cash equivalents, investments, long-term debt and accounts receivable.

Our cash, cash equivalents and investments are invested in deposits with two major financial institutions in the United States. Deposits in these banks may exceed the amount of insurance provided on such deposits.

Our exposure to credit risk associated with non-payment is limited to our strategic partners Amgen Inc. ("Amgen") and Astellas Pharma Inc. ("Astellas") and any material non-payment from our partners would result in a material breach of the agreements underlying our strategic partnerships.

CYTOKINETICS, INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

Drug candidates we develop may require approvals or clearances from the U.S. Food and Drug Administration ("FDA") or other regulatory agencies prior to commercial sales. There can be no assurance that our drug candidates will receive any of the required approvals or clearances. If we were to be denied approval, or clearance or any such approval or clearance was to be delayed, it would have a material adverse impact on us.

Cash and Cash Equivalents

We consider all highly liquid investments with a maturity of three months or less at the time of purchase to be cash equivalents.

Investments

Available-for-sale investments. Our investments consist of U.S. Treasury securities, agency bonds, commercial paper, corporate debt and money market funds. We designate all investments as available-for-sale and report them at fair value, based on quoted marked prices, with unrealized gains and losses recorded in accumulated other comprehensive loss. The cost of securities sold is based on the specific-identification method. Investments with original maturities greater than three months and remaining maturities of one year or less are classified as short-term investments. Investments with remaining maturities greater than one year are classified as long-term investments. The amortized cost of debt securities in this category is adjusted for amortization of premiums and accretion of discounts to maturity. Such amortization is included in interest income. Recognized gains and losses and declines in value judged to be other-than-temporary, if any, on available-for-sale securities are included in other income or expense. Interest and dividends on securities classified as available-for-sale are included in Interest and other, net.

Other-than-temporary impairment. All of our available-for-sale investments are subject to a periodic impairment review. We recognize an impairment charge when a decline in the fair value of investments below the cost basis is judged to be other-than-temporary. Factors we consider in assessing whether an other-than-temporary impairment has occurred include: the nature of the investment; whether the decline in fair value is attributable to specific adverse conditions affecting the investment; the financial condition of the investee; the severity and the duration of the impairment; and whether we have the intent and ability to hold the investment to maturity. When we determine that an other-than-temporary impairment has occurred, the investment is written down to its market value at the end of the period in which it is determined that an other-than-temporary decline has occurred.

Property and Equipment, net

Property and equipment are stated at cost less accumulated depreciation and are depreciated on a straight-line basis over the estimated useful lives of the related assets, which are generally three years for computer equipment and software, five years for laboratory equipment and office equipment, and seven years for furniture and fixtures. Amortization of leasehold improvements is computed using the straight-line method over the shorter of the remaining lease term or the estimated useful life of the related assets, typically ranging from three to seven years. Upon sale or retirement of assets, the costs and related accumulated depreciation and amortization are removed from the balance sheet and the resulting gain or loss is reflected in operations.

Impairment of Long-lived Assets

We review long-lived assets, including property and equipment, for impairment whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. Impairment is measured as the amount by which the carrying amount of a long-lived asset exceeds its fair value. We would recognize an impairment loss when estimated undiscounted future cash flows expected to result from the use of the asset and its eventual disposition are materially less than its carrying amount.

Revenue Recognition

On January 1, 2018, we adopted Accounting Standards Codification 606, Revenue from Contracts with Customers ("ASC 606"), using the modified retrospective method. On January 1, 2018, for contracts within the scope of ASC 606, we recognized a contract asset or liability and reduced our accumulated deficit for the effect of adopting ASC 606 and did not revise our prior period financial statements. Pursuant to ASC 606, to recognize revenue from a contract with a customer, we:

(i) identify our contracts with our customers;

(ii) identify our distinct performance obligations in each contract;

(iii) determine the transaction price of each contract;

(iv) allocate the transaction price to the performance obligations; and

(v) recognize revenue as we satisfy our performance obligations.

At contract inception, we assess the goods or services promised within each contract and assess whether each promised good or service is distinct and determine those that are performance obligations. We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

Collaborative Arrangements

CYTOKINETICS, INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

We enter into collaborative arrangements with partners that typically include payment to us for one of more of the following: (i) license fees; (ii) milestone payments related to the achievement of developmental, regulatory, or commercial goals; and (iii) royalties on net sales of licensed products. Each of these payments results in collaboration or other revenues. Where a portion of non-refundable up-front fees or other payments received are allocated to continuing performance obligations under the terms of a collaborative arrangement, they are recorded as deferred revenue and recognized as revenue when (or as) the underlying performance obligation is satisfied.

As part of the accounting for these arrangements, we must develop estimates and assumptions that require judgment to determine the underlying stand-alone selling price for each performance obligation which determines how the transaction price is allocated among the performance obligation. The stand-alone selling price may include such items as, forecasted revenues, development timelines, reimbursement rates for personnel costs, discount rates and probabilities of technical and regulatory success, to determine the transaction price to allocate to each performance obligation.

For our collaboration agreements that include more than one performance obligation, such as a license combined with a commitment to perform research and development services, we make judgments to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from non-refundable, up-front fees. We evaluate our progress each reporting period and, if necessary, adjust the measure of a performance obligation and related revenue recognition.

License Fees: If a license to our intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, we recognize revenues from non-refundable, up-front fees allocated to the license when the license is transferred to the licensee and the licensee is able to use and benefit from the license. For licenses that are bundled with other promises, we utilize judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from non-refundable, up-front license fees. We evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition.

Milestone Payments: We use judgement to determine whether a milestone is considered probable of being reached. Using the most likely amount method, we include the value of a milestone payment in the consideration for a contract at inception if we then conclude achieving the milestone is more likely than not. Otherwise, we exclude the value of a milestone payment from contract consideration at inception and recognize revenue for a milestone at a later date, when we judge that it is more likely than not that the milestone will be achieved. If we conclude it is probable that a significant revenue reversal would not occur, the associated milestone is included in the transaction price. We then allocate the transaction price to each performance obligation on a relative stand-alone selling price basis, for which we recognize revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, we re-evaluate the probability of achievement of such milestones and any related constraint, and if necessary, adjust our estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect license, collaboration and other revenues and earnings in the period of adjustment.

Royalties: For contracts that include sales-based royalties, we recognize revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been

satisfied. To date, we have not recognized any royalty revenues resulting from contracts.

Research and Development Cost Reimbursements: Our Astellas and Amgen arrangements include promises of research and development services. We have determined that these services collectively are distinct from the licenses provided to Astellas and Amgen and as such, these promises are accounted for as a separate performance obligation recorded over time. We record revenue for these services as the performance obligations are satisfied, which we estimate using internal development costs incurred.

CYTOKINETICS, INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

Accrued Research and Development Expenditures

A substantial portion of our preclinical studies and all of our clinical trials have been performed by third-party contract research organizations ("CROs") and other vendors and our accruals for expenses for preclinical studies and clinical trials may be significant. For preclinical studies, the significant factors used in estimating accruals include the percentage of work completed to date and contract milestones achieved. For clinical trial expenses, the significant factors used in estimating accruals include the number of patients enrolled, duration of enrollment, milestones achieved and percentage of work completed to date. We monitor patient enrollment levels and related activities to the extent practicable through internal reviews, correspondence and status meetings with CROs, and review of contractual terms. We depend on the timeliness and accuracy of data provided by its CROs and other vendors to accrue expenses. If we receive and rely on incomplete or inaccurate data, accruals and expenses may be too high or too low at a given point in time and corresponding adjustments to accruals and expenses would be made in future periods when the actual expense becomes known.

Research and Development Expenditures

Research and development costs are charged to operations as incurred. Research and development expenses consist primarily of clinical manufacturing costs, preclinical study expenses, consulting and other third-party costs, employee compensation, supplies and materials, allocation of overhead and occupancy costs, facilities costs and depreciation of equipment.

Income Taxes

We account for income taxes under the asset and liability method. Under this method, deferred tax assets and liabilities are determined based on the difference between the financial statement and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to affect taxable income. Valuation allowances are established when necessary to reduce deferred tax assets to the amounts expected to be realized.

We recognize uncertain tax positions taken or expected to be taken on a tax return. Tax positions are initially recognized when it is more likely than not that the position will be sustained upon examination by the tax authorities. Such tax positions are initially and subsequently measured as the largest amount of tax benefit that is more likely than not of being realized upon ultimate settlement with the tax authority assuming full knowledge of the position and relevant facts.

We recognize interest accrued related to unrecognized tax benefits and penalties as income tax expense.

Stock-Based Compensation

We maintain equity incentive plans under which incentive stock options may be granted to employees and nonqualified stock options, restricted stock awards, restricted stock units and stock appreciation rights may be granted to employees, directors, consultants and advisors. In addition, we maintain an employee stock purchase plan ("ESPP") under which employees may purchase shares of our common stock through payroll deductions.

Stock-based compensation expense related to stock options granted to employees and directors is recognized based on the grant date estimated fair values, net of an estimated forfeiture rate, using the Black Scholes option pricing model.

The value of the portion of the award that is ultimately expected to vest is recognized as expense ratably over the requisite service period. We estimate our forfeiture rate based on an analysis of our actual forfeitures and the experience of other companies in the same industry, and we will continue to evaluate the adequacy of the forfeiture rate assumption based on actual forfeitures, analysis of employee turnover and other related factors.

Stock-based compensation expense related to restricted stock units granted to employees is recognized based on the grant-date fair value of each award and recorded as expense over the vesting period using the straight-line method, net of estimated forfeitures.

Stock-based compensation expense related to the ESPP is recognized based on the fair value of each award estimated on the first day of the offering period using the Black Scholes option pricing model and recorded as expense over the service period using the straight-line method.

Amortization of Debt Discount and Issuance Costs

Debt discount and issuance costs, consisting of legal and other fees directly related to the debt, are offset against gross proceeds from the issuance of debt and are amortized to interest expense over the estimated life of the debt based on the effective interest method.

CYTOKINETICS, INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

Liability Related to Sale of Future Royalties

We treat the Liability related to sale of future royalties as a debt financing, to be amortized under the effective interest rate method over the life of the related royalty stream.

The Liability related to sale of future royalties and the debt amortization are based on our current estimates of future royalties expected to be paid over the life of the arrangement. We will periodically assess the expected royalty payments using a combination of internal projections and forecasts from external sources. To the extent our future estimates of future royalty payments are greater or less than its previous estimates or the estimated timing of such payments is materially different than its previous estimates, we will adjust the Liability related to sale of future royalties and prospectively recognize related non-cash interest expense.

Recent Accounting Pronouncements

In June 2016, the FASB issued ASU 2016-13, ‘Financial Instruments — Credit Losses — Measurement of Credit Losses on Financial Instruments. ASU 2016-13 changes the impairment model for most financial assets and certain other instruments. ASU 2016-13 is effective for annual and interim reporting periods beginning after December 15, 2019. We are in the process of evaluating the impact the adoption of this standard would have on our financial statements and disclosures.

In February 2016, the FASB issued ASU 2016-02, Leases (Topic 842). ASU 2016-02 requires management to record right-to-use asset and lease liability on the statement of financial position for operating leases. ASU 2016-02 is effective for annual and interim reporting periods beginning on or after December 15, 2018 and modified retrospective approach is required. We are in the process of evaluating the impact the adoption of this standard will have on its financial statements and disclosures and believe that adoption will be material to our balance sheet as a result of the recognition of a right-to-use asset and corresponding liability for our building leases but will not have a material impact on our results of operations.

In November 2018, the Financial Accounting Standards Board (“FASB”) issued ASU 2018-18, Collaborative Arrangements (Topic 808): Clarifying the Interaction between Topic 808 and Topic 606 (“ASU 2018-18”), which make targeted improvements to clarify the interaction between Topic 808, Collaborative Arrangements, and Topic 606, Revenue from Contracts with Customers. ASU 2018-18 is effective for fiscal years beginning after December 15, 2019, and interim periods within those fiscal years. Early adoption is permitted. We are currently evaluating the impact of adopting ASU 2018-18.

Note 2 — Net Loss Per Share

Basic net loss per share is computed by dividing net loss by the weighted average number of vested common shares outstanding during the period. Diluted net (loss) income per share is computed by giving effect to all potentially dilutive common shares, including outstanding stock options, unvested restricted stock, warrants, convertible preferred stock and shares issuable under our Employee Stock Purchase Plan (“ESPP”), by applying the treasury stock method.

The following instruments were excluded from the computation of diluted net loss per share for the periods presented because their effect would have been antidilutive (in thousands):

	December 31,	
	2018	2017
Options to purchase common stock	5,476	5,957
Warrants to purchase common stock	116	100
Restricted and Performance stock units	547	457
Shares issuable related to the ESPP	107	20
Total shares	6,246	6,534

CYTOKINETICS, INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

Note 3 – Revenue Recognition

We believe recognizing revenue as research and development services are performed provides a faithful depiction of the transfer of the services because completion of clinical programs results in data useful to determine satisfaction of our promise. We may fund research and development in advance of the performance of the services. When we complete our performance obligation, if we have received more than we incurred, we are obligated to return unused advance funding. We recognize these advance payments as deferred revenue until we perform the related services. As discussed in Note 1, prior period amounts continue to be reported in accordance with our historic accounting under previous revenue recognition guidance, ASC 605.

Our revenue for 2018 was affected by adopting ASC 606 as follows (in thousands):

	2018
Research and development revenue using guidance in effect prior to ASC 606	$18,672
Impact of adoption of ASC 606	7,696
Research and development revenue	$26,368
License revenue using guidance in effect prior to ASC 606	$(5,347)
Impact of adoption of ASC 606	10,480
License revenue	$5,133

The impact of adoption of ASC 606 on our net loss per share was as follows (in thousands):

	2018
Net loss per share using guidance in effect prior to ASC 606	$(2.28)
Impact of adoption of ASC 606	(0.33)
Net loss per share	$(1.95)

We recognized contract assets and contract liabilities for our Co-Invest Option from the Amgen Agreement, the 2014 Astellas Amendment and the 2016 Astellas Amendment, further described in Note 7. Research and Development Arrangements, below. In 2018, we completed our performance obligations for the Co-Invest Option and the 2014 Astellas Amendment. We expect to complete our performance obligations for the 2016 Astellas Amendment in 2019. Our contract assets and liabilities changed during the period, as follows (in thousands):

	2018
Contract liability from the Amgen Agreement for the Co-Invest Option	
Balance at beginning of period	$ 18,750
Payments made for the Co-Invest Option	(18,750)
Balance at end of period	$ —

Contract asset from the 2016 Astellas Amendment		
Balance at beginning of period	$	9,708
Services performed	$	11,713
Cash received for services	$	(16,867)
Balance at end of period	$	4,554
Contract liability from the 2014 Astellas Amendment		
Balance at beginning of period	$	6,288
Services performed		(6,288)
Balance at end of period	$	—

CYTOKINETICS, INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

Note 4 — Cash Equivalents and Investments

Cash Equivalents and Available for Sale Investments

The amortized cost and fair value of cash equivalents and available for sale investments at December 31, 2018 and 2017 were as follows (in thousands):

	December 31, 2018			
Cash and Investments available for sale	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Money market funds	$34,771	$ —	$ —	$34,771
U.S. Treasury securities	56,999	—	(41)	56,958
Agency bonds	61,792	1	(14)	61,779
Commercial paper	19,448	—	(13)	19,435
Corporate obligations	17,644	2	(8)	17,638
	$190,654	$ 3	$ (76)	$190,581

	December 31, 2017			
	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Cash equivalents —				
U. S. Treasury securities and money market funds	$111,501	$ —	$ —	$111,501
Short-term investments —				
U.S. Treasury securities and Agency bonds	$143,895	$ —	$ (210)	$143,685
Long-term investments — Equity				
and U.S. Treasury securities	$16,538	$ —	$ (20)	$16,518

As of December 31, 2018, none of the investments were other-than-temporarily impaired, no investment was in a continuous unrealized loss position for more than one year, unrealized losses were not due to change in credit risk and we believe investments with an unrealized loss would be held until maturity.

Note 5 — Fair Value Measurements

We value our financial assets and liabilities at fair value, defined as the price that would be received for assets when sold or paid to transfer a liability in an orderly transaction between market participants at the measurement date (exit price). We utilize market data or assumptions that we believe market participants would use in pricing the asset or liability, including assumptions about risk and the risks inherent in the inputs to the valuation technique. These inputs can be readily observable, market corroborated or generally unobservable.

We primarily apply the market approach for recurring fair value measurements and endeavors to utilize the best information reasonably available. Accordingly, we utilize valuation techniques that maximize the use of observable inputs and minimize the use of unobservable inputs to the extent possible and considers the security issuers' and the third-party insurers' credit risk in its assessment of fair value.

We classify the determined fair value based on the observability of those inputs. Fair value accounting guidance establishes a fair value hierarchy that prioritizes the inputs used to measure fair value. The hierarchy gives the highest priority to unadjusted quoted prices in active markets for identical assets or liabilities (Level 1 measurement) and the lowest priority to unobservable inputs (Level 3 measurement). The three defined levels of the fair value hierarchy are as follows:

Level 1 — Observable inputs, such as quoted prices in active markets for identical assets or liabilities;

Level 2 — Inputs, other than the quoted prices in active markets, that are observable either directly or through corroboration with observable market data; and

Level 3 — Unobservable inputs, for which there is little or no market data for the assets or liabilities, such as internally-developed valuation models.

CYTOKINETICS, INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

Financial assets measured at fair value on a recurring basis as of December 31, 2018 and 2017 are classified in the table below in one of the three categories described above (in thousands):

	December 31, 2018 Fair Value Measurements Using			Assets
	Level 1	Level 2	Level 3	At Fair Value
Assets:				
Money market funds	$34,771	$—	$ —	$ 34,771
U.S. Treasury securities	56,958	—	—	56,958
Agency bonds	—	61,779	—	61,779
Commercial paper	—	19,435	—	19,435
Corporate obligations	—	17,638	—	17,638
Total	$91,729	$98,852	$ —	$ 190,581

	December 31, 2017 Fair Value Measurements Using			Assets
	Level 1	Level 2	Level 3	At Fair Value
Assets:				
Money market funds	$51,001	$—	$ —	$ 51,001
U.S. Treasury securities	165,801	—	—	165,801
Agency bonds	—	54,329		54,329
Equity securities	573	—	—	573
	$217,375	$54,329	$ —	$ 271,704

Investments available for sale at December 31, 2018 excludes an investment in equity classified as a Level 1 investment in our short-term investments with a fair value and unrealized gain of $0.7 million. At December 31, 2018, there were no investments that had been in a continuous unrealized loss position for 12 months or longer.

The carrying amount of our accounts receivable and accounts payable approximates fair value due to the short-term nature of these instruments.

Fair value of financial liabilities:

As of December 31, 2018 and 2017, the fair value of the long-term debt, payable in installments through 2020, approximated its carrying value of $42.1 million and $31.8 million, respectively, because it is carried at a market observable interest rate, which is a Level 2 input.

As of December 31, 2018, the fair value of the Liability related to the sale of future royalties is based on our current estimates of future royalties expected to be paid to RPI Finance Trust (“RPI”), an entity related to Royalty Pharma, over the life of the arrangement, which are considered Level 3 inputs (See Note 9 – “Liability Related to Sale of Future Royalties”).

There were no transfers between Level 1, Level 2, and Level 3 during the periods presented.

Note 6 — Balance Sheet Components

Our property and equipment consisted of (in thousands):

	December 31,	
	2018	2017
Property and equipment, net:		
Laboratory equipment	$17,916	$17,100
Computer equipment and software	2,882	2,890
Office equipment, furniture and fixtures	1,137	1,137
Leasehold improvements	5,130	5,067
Total property and equipment	27,065	26,194
Less: Accumulated depreciation and amortization	(23,861)	(22,626)
	$3,204	$3,568

CYTOKINETICS, INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

Depreciation expense was $1.2 million for 2018 and $1.9 million for 2017.

Our accrued liabilities were (in thousands):

	December 31,	
	2018	2017
Accrued liabilities:		
Clinical and preclinical costs	$8,618	$8,370
Compensation related	6,118	6,261
Other accrued expenses	1,021	2,761
	$15,757	$17,392

We sponsor a 401(k) defined contribution plan covering all employees and contributed $0.5 million to this plan in both 2018 and 2017.

Note 7 — Research and Development Arrangements

Amgen Inc. (“Amgen”)

We and Amgen continue activities related to novel small molecule therapeutics, including omecamtiv mecarbil, that activate cardiac muscle contractility for potential applications in the treatment of heart failure under our collaboration and option agreement with Amgen dated December 29, 2006, as amended (the “Amgen Agreement”). We recognize research and development revenue for reimbursements from Amgen of both internal costs of certain FTEs and other costs related to the Amgen Agreement.

Under the Amgen Agreement, we are eligible to receive over $300.0 million in additional development milestone payments based on various clinical milestones, including the initiation of certain clinical studies, the submission of an application for marketing authorization for a drug candidate to certain regulatory authorities and the receipt of such approvals. Additionally, we are eligible to receive up to $300.0 million in commercial milestone payments provided certain sales targets are met. Due to the nature of drug development, including the inherent risk of development and approval of drug candidates by regulatory authorities, we cannot estimate if and when these milestone payments could be achieved or become due and, accordingly, we consider the milestone payments to be constrained and exclude the milestone payments from the transaction price.

We paid Amgen $18.8 million in 2018 and $20.0 million in 2017 and have exercised our option under the Amgen Agreement to co-invest $40.0 million in the Phase 3 development program of omecamtiv mecarbil in exchange for a total incremental royalty from Amgen of up to 4% on increasing worldwide sales of omecamtiv mecarbil outside Japan (the “Co-Invest Option”).

Adoption of ASC 606

We determined that the Amgen Agreement was within the scope of ASC 606. As of January 1, 2018, all the performance obligations under the Amgen Agreement were complete. On January 1, 2018, we recognized a contract liability for $18.8 million with a corresponding increase in accumulated deficit for the Co-Invest Option. We paid Amgen $18.8 million for the Co-Invest Option during 2018.

Research and development revenues from Amgen for December 31, 2018 and 2017 were as follows (in thousands):

	Years Ended December 31,	
	2018	2017
Reimbursements	$1,915	$1,279
Milestone fees	—	11,000
Co-Invest Option payments	—	(20,000)
	$1,915	$(7,721)

Co-Invest Option payments in 2017 reduced our revenues in that year (prior to adopting ASC 606). Milestone fees in 2017 of $11.0 million consisted of $10.0 million related to the start in Japan of GALACTIC-HF, the Phase 3 cardiovascular outcomes clinical trial of omecamtiv mecarbil and $1.0 million related to a next-generation cardiac muscle activator that was nominated as a development candidate by the Joint Research Committee. Accounts receivable due from Amgen was $1.9 million at December 31, 2018 and $1.0 million at December 31, 2017. Prior period amounts continue to be reported in accordance with our historic accounting under previous revenue recognition guidance, ASC 605. See note 3 “Revenue Recognition” above, for more information about the impact of the adoption on ASC 606.

Astellas Pharma Inc. (“Astellas”)

We and Astellas continue activities focused on the research, development, and commercialization of skeletal muscle activators, including reldesemtiv, as novel drug candidates for diseases and medical conditions associated with muscle weakness under the

CYTOKINETICS, INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

Amended and Restated License and Collaboration Agreement dated December 22, 2014, as amended (the "Astellas Agreement"). We recognize research and development revenue for reimbursements from Astellas of internal costs of both FTEs and other costs related to Astellas Agreement.

In 2014, we and Astellas amended and restated the license and collaboration agreement (the "2014 Astellas Amendment") and expanded the objective of the collaboration to include spinal muscular atrophy ("SMA") and potentially other neuromuscular indications for reldesemtiv and other fast skeletal muscle troponin activators ("FSTAs"); in connection therewith, Astellas paid us a $30.0 million non-refundable upfront license fee and a $15.0 million milestone payment. We determined at that time that the license for the expanded SMA rights did not have stand-alone value and the license and research and development services were a single unit of accounting and recognized revenue for these payments using the proportional performance model.

In 2016, we and Astellas amended the Astellas Agreement (the "2016 Astellas Amendment") to expand the collaboration to include the development of reldesemtiv for the potential treatment of amyotrophic lateral sclerosis ("ALS"), as well as the possible development in ALS of other FSTAs previously licensed by us to Astellas, and Astellas paid us a $35.0 million non-refundable upfront amendment fee and an accelerated $15.0 million milestone payment for the initiation of the first Phase 2 clinical trial of reldesemtiv in ALS that was otherwise provided for in the Astellas Agreement, as if such milestone had been achieved upon the execution of the 2016 Astellas Amendment, and committed research and development consideration of $44.2 million, for total consideration of $94.2 million. We allocated the consideration to the license and to the research and development services, and recognized license revenue and research and development revenue using the proportional performance model. In addition, Astellas paid us a $15.0 million non-refundable million fee for the option for a global collaboration for the development and commercialization of tirasemtiv, our first-generation FSTA (the "Option on Tirasemtiv").

Under the Astellas Agreement, additional research and early and late state development milestone payments for research and clinical milestones, including the initiation of certain clinical studies, the submission of an application for marketing authorization for a drug candidate to certain regulatory authorities and the commercial launch of collaboration products could total over $600.0 million and include up to $95.0 million relating to reldesemtiv in non-neuromuscular indications, and over $100.0 million related to reldesemtiv in each of SMA, ALS and other neuromuscular indications. Additionally, $200.0 million in commercial milestones could be received under the Astellas Agreement provided certain sales targets are met. We are eligible to receive up to $2.0 million in research milestone payments under the collaboration for each future potential drug candidate. Due to the nature of drug development, including the inherent risk of development and approval of drug candidates by regulatory authorities, it is not possible to estimate if and when these milestone payments could be achieved or become due, and accordingly, are constrained and not included in the transaction price.

In collaboration with Astellas, we are conducting a Phase 2 clinical trial of reldesemtiv in patients with ALS, called FORTITUDE-ALS (Functional Outcomes in a Randomized Trial of Investigational Treatment with CK-2127107 to Understand Decline in Endpoints – in ALS). We and Astellas share equally the costs of developing reldesemtiv in ALS for potential registration and marketing authorization in the U.S. and Europe, provided that (i) Astellas has agreed to solely fund Phase 2 development costs of reldesemtiv in ALS subject to a right to recoup our share of such costs plus a 100% premium by reducing future milestone and royalty payments to us and (ii) we may defer (but not eliminate) a portion of its co-funding obligation for development activities after Phase 2 for up to 18 months, subject to certain conditions.

Adoption of ASC 606

On January 1, 2018, in adopting ASC 606, we concluded: (i) that the original agreement with Astellas in 2013 was outside the scope of ASC 606, since all performance obligations thereunder were completed prior to entering into the 2014 Astellas Amendment and the 2014 Astellas Amendment was not an amendment of the original agreement, (ii) the 2014 Astellas Amendment is a separate agreement within the scope of ASC 606 with no effect on the ongoing accounting for the related license and research and development service deliverables and (iii) the 2016 Astellas Amendment is a separate agreement within the scope of ASC 606.

In adopting ASC 606 for the 2016 Amendment, we determined:

- Our performance obligations were the delivery of the license and performance of research and development services;
- The transaction price included the $65.0 million in non-refundable fees and $35.6 million in then-committed research and development fees;
- The consideration allocated to the license resulted in a contract asset of $16.7 million, with a corresponding decrease to accumulated deficit on January 1, 2018, and to be realized using the proportional performance model; and
- Research services we perform under the Astellas Agreement in 2018 and beyond are a separate contract.

The transaction price above was allocated to the license (approximately $83 million) and to the services (approximately $18 million) based on their respective stand-alone prices.

CYTOKINETICS, INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

License revenues and research and development revenues from Astellas for 2018 and 2017 were as follows (in thousands):

	Years Ended December 31,	
	2018	2017
License revenues	$5,133	$8,799
Reimbursements	22,253	11,934
Milestone fees	2,000	—
	$29,386	$20,733

Of the revenue recognized in 2018, $9.6 million was included in the contract liability at the end of 2017 as a result of adopting ASC 606. This revenue includes the cumulative effect of changes made during 2018 in the estimated costs of research and development services to be incurred to satisfy the related deliverable. Prior period amounts continue to be reported in accordance with our historic accounting under previous revenue recognition guidance, ASC 605. See note 3 “Revenue Recognition” above, for more information about the impact of the adoption on ASC 606.

In 2018, we completed all our deliverables for the 2014 Astellas Amendment and have recognized as revenue all the consideration under that agreement. We expect to complete all our deliverables for the 2016 Astellas Amendment in 2019.

We had accounts receivable from Astellas of $0.3 million at December 31, 2018 and none at December 31, 2017. Deferred revenue, current at December 31, 2017 of $9.6 million reflected the unrecognized portion of the license revenue and reimbursements and Deferred revenue, non-current at December 31, 2017 of $15.0 million reflected the Option on Tirasemtiv (prior to adopting ASC 606).

MyoKardia Inc. (“MyoKardia”)

In July 2018, we received $0.2 million for achievement of a clinical milestone pursuant to our collaboration agreement with MyoKardia.

Note 8 — Long-Term Debt

We have a loan and security agreement (the “Loan Agreement”) with Oxford Finance LLC (“Oxford”) and Silicon Valley Bank (“SVB”) (Oxford and SVB, collectively the “Lenders”) to fund our working capital and other general corporate needs. In October 2017, we entered into a Second Amendment to Loan and Security Agreement (the “Amended Loan Agreement”) with Oxford and SVB, drew $32.0 million and retired our then-outstanding debt of $30.0 million, and $0.5 million related to the accrued portion of the final payment fee under the Loan Agreement. In August 2018, following the satisfaction of certain conditions related to Phase 2 data for reldesemtiv in SMA specified in the Loan Agreement, we drew down an additional $10.0 million under the Amended Loan Agreement and the interest-only period was extended to December 1, 2019.

Long-term debt and unamortized debt discount balances are as follows (in thousands):

	December 31,	
	2018	2017
Notes payable, gross	$42,000	$32,000
Unamortized debt discount and interest payable	(135)	(325)
Accretion of final exit fee	548	102
Carrying value of notes payable	42,413	31,777
Less: Current portion of long-term debt	2,607	—
Long-term debt	$39,806	$31,777

Payments on Long-term debt will be interest only through November 2019, followed by 35 months of equal monthly payments of interest and principal. We are required to make a final payment upon loan maturity of 6.5% of the amounts advanced. The interest rate under the Amended Loan Agreement is the greater of (a) 8.05% or (b) the sum of 6.81% plus the 30-day U.S. LIBOR rate.

The Loan Agreement contains customary representations and warranties and customary affirmative and negative covenants applicable to us and includes customary events of default, including but not limited to the nonpayment of principal or interest, violations of covenants and material adverse changes. Upon an event of default, the Lenders may, among other things, accelerate the loans and foreclose on the collateral. Our obligations under the Amended Loan Agreement are secured by substantially all our current and future assets, other than our intellectual property.

CYTOKINETICS, INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

Future minimum payments under the Loan Agreement loan, as of December 31, 2018 are as follows (in thousands):

2019	$5,166
2020	17,636
2021	16,267
2022	15,237
Total minimum payments	54,306
Less: Interest and final payment	(12,306)
Notes payable, gross	$42,000

Note 9 - Liability Related to Sale of Future Royalties

In February 2017, we and Royalty Pharma Inc. (“RPI”) entered into a Royalty Purchase Agreement (the “Royalty Agreement”), under which we sold to RPI for $90.0 million a portion of our right to receive royalties on potential net sales of omecamtiv mecarbil (and potentially other compounds with the same mechanism of action) under the Amgen Agreement (the “Royalty Monetization”). The Royalty Monetization is non-refundable, even if omecamtiv mecarbil is never commercialized. We account for the Royalty Monetization as a liability primarily because we have significant continued involvement in generating the royalty stream under the Amgen Agreement. Concurrently, we entered into a Common Stock Purchase Agreement with RPI through which RPI purchased from us 875,656 shares of our common stock for $10.0 million (the “RPI Common Stock”).

We concluded that there are two units of accounting for the Royalty Monetization and the RPI Common Stock: (1) the Liability related to sale of future royalties and (2) the sale of the RPI Common Stock. We determined the fair value for the Liability related to sale of future royalties at the time of the Royalty Monetization to be $96.7 million, with an effective annual non-cash interest rate of 17% based on our estimate of the cash flows to be received over the life of the Royalty Agreement. We determined that the fair value of the RPI Common Stock was $8.1 million at the time we entered into the Royalty Agreement. We determined the fair value at $131.6 million at December 31, 2017 after considering the new statutory effective tax rate of 21% in 2018.

We allocated the consideration of $100.0 million and related transaction costs of $1.8 million on a relative fair value basis to the liability for $92.3 million and the common stock for $7.7 million. Through December 31, 2018, we accreted the Liability related to sale of future royalties using the interest method with an annual pre-tax interest rate of 17% and recognized non-cash interest expense on liability related to sale of future royalties of $17.8 million in 2018 and $14.0 million in 2017. Transaction costs are amortized to interest expense over the estimated term of the Royalty Agreement. Payments made to RPI pursuant to the Royalty Monetization, if any, would reduce this liability.

Note 10 — Commitments and Contingencies

Commitments - Operating Lease

We lease office space under a non-cancelable operating lease that expires in June 2021. The lease provides for rental payments on a graduated scale and our payment of certain operating expenses. We recognize rent expense on a straight-line basis over the lease period. Rent expense was $5.0 million in 2018, $3.6 million in 2017 and $3.4 million in 2016.

As of December 31, 2018, future minimum lease payments under noncancelable operating leases were $4.7 million in 2019, $4.8 million in 2020 and $2.5 million in 2021.

Contingencies

In the ordinary course of business, we may provide indemnifications of varying scope and terms to vendors, lessors, business partners and other parties with respect to certain matters, including, but not limited to, losses arising out of our breach of such agreements, services to be provided by or on behalf of us, or from intellectual property infringement claims made by third parties. In addition, we have indemnification agreements with our directors and certain of our officers and employees that will require us, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors, officers or employees. We maintain director and officer insurance, which may cover certain liabilities arising from our obligation to indemnify our directors and certain of our officers and employees, and former officers and directors in certain circumstances. We maintain product liability insurance and comprehensive general liability insurance, which may cover certain liabilities arising from our indemnification obligations. It is not possible to determine the maximum potential amount of exposure under these indemnification obligations due to the limited history of prior indemnification claims and the unique facts and circumstances involved in each particular indemnification obligation. Such indemnification obligations may not be subject to maximum loss clauses. We are not currently aware of any matters that could have a material adverse effect on our financial position, results of operations or cash flows.

CYTOKINETICS, INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

Note 11 — Stockholders' Equity

Equity Incentive Plan

Our amended and restated 2004 Equity Incentive Plan (the "2004 Plan") provides for us to grant incentive stock options, nonstatutory stock options, restricted stock, stock appreciation rights, restricted stock units, performance shares and performance units to employees, directors and consultants. We may grant options for terms of up to ten years at prices not lower than 100% of the fair market value of our common stock on the date of grant. Options granted to new employees generally vest 25% after one year and monthly thereafter over a period of four years. Options granted to existing employees generally vest monthly over a period of four years. As of December 31, 2018, we have 2.4 million shares of common stock reserved and available for issuance under the 2004 Plan.

Stock option activity in 2018 was as follows:

	Stock Options Outstanding	Weighted Average Exercise Price per Share	Weighted Average Remaining Contractual Life (in years)	Aggregate Intrinsic Value (in thousands)
Balance at December 31, 2017	5,957,458	$ 9.19		
Granted	1,804,047	8.04		
Exercised	(422,819)	7.51		
Forfeited	(884,649)	11.06		
Balance at December 31, 2018	6,454,037	$ 8.72	6.6	$ 412
Exercisable at December 31, 2018	4,461,463	$ 8.72	5.7	$ 411

We expect all outstanding options to vest. The intrinsic value of stock options exercised, calculated based on the difference between the market value at the date of exercise and the exercise price, was $0.7 million for 2018 and $1.8 million for 2017. The intrinsic value of stock options outstanding at December 31, 2017 was $4.3 million.

Restricted stock and Performance unit activity in 2018 was as follows:

	Number of Restricted Stock Units	Weighted Average Award Date Fair Value per Share
Balance at December 31, 2017	456,752	$ 9.08
Granted	466,500	$ 7.80

Released	(301,000	) $	8.29
Forfeited	(75,752	) $	8.29
Balance at December 31, 2018	546,500	$	8.53

Restricted stock units generally vest monthly over three to four years. For 2018, the fair value of restricted stock and performance units vested, calculated based on the units vested multiplied by the closing price of our common stock on the date of vesting, was $2.3 million.

During 2015, we granted 685,000 Performance Units with a grant date fair value of $7.00 per share. In 2017, performance criteria for 342,500 Performance Units were met, 171,250 of those units vested. In March 2018, the remaining 171,250 of these Performance Units vested. In 2017, the other 342,500 Performance Units granted in 2015 were forfeited when we determined that the performance criteria for those Performance Units would not be met.

Employee Stock Purchase Plan

Under our 2015 Employee Stock Purchase Plan (the “ESPP”), employees may purchase common stock up to a specified maximum amount at a price equal to 85% of the fair market value at certain plan-defined dates.

We issued 144,822 shares at an average price of $6.40 during 2018 and 120,959 shares at an average price of $9.65 in 2017 pursuant to the ESPP. At December 31, 2018, we have 253,617 shares of common stock reserved for issuance under the ESPP.

CYTOKINETICS, INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

Stock-Based Compensation Expense

We use the Black-Scholes option pricing model to determine the fair value of stock option grants to employees and directors and employee stock purchase plan shares. The fair value of share-based payments was estimated on the date of grant based on the following assumptions:

	Year Ended December 31, 2018		Year Ended December 31, 2017	
	Options	ESPP	Options	ESPP
Risk-free interest rate	2.3% to 3.0%	1.5% to 2.5%	2.2%	1.3%
Volatility	73% to 74%	73% to 74%	74%	74%
Expected term in years	6.5	0.5	6.5	0.5
Expected dividend yield	0%	0%	0%	0%

We use the U.S. Treasury zero-coupon issues with remaining terms similar to the expected terms of the options for the risk-free interest rate. We use our own volatility history based on its stock’s trading history and our own historical exercise and forfeiture activity to estimate expected term for option grants. We do not anticipate paying dividends in the foreseeable future and use an expected dividend yield of zero.

We reviewed the impact of estimating forfeitures on our stock-based compensation, determined the impact was immaterial and stopped estimating forfeitures in 2018. Prior to 2018, we estimated forfeitures at the time of grant and revised those estimates in subsequent periods if actual forfeitures differ from our estimates using historical forfeiture data and recorded stock-based compensation expense on those awards that were expected to vest.

We measure compensation expense for restricted stock units at fair value on the date of grant and recognizes the expense over the expected vesting period. We recognize stock-based compensation expense on a straight-line basis over the requisite service period, generally the vesting period of the award for share-based awards. Stock-based compensation expense for 2018 and 2017 was as follows (in thousands):

	Years Ended December 31,	
	2018	2017
Research and development	$5,101	$5,656
General and administrative	4,660	3,372
	$9,761	$9,028

Non-cash stock-based compensation expense for share-based awards to non-employees was $0.1 million in 2018 and $0.5 million in 2017.

As of December 31, 2018, we expect to recognize $13.8 million of unrecognized compensation cost related to unvested stock options over a weighted-average period of 2.4 years and $3.5 million of unrecognized compensation cost related to unvested restricted stock over a weighted-average period of 1.8 years.

Warrants

Pursuant to the Loan Agreement described in Note 8 “Long-Term Debt,” we issued warrants to purchase 65,189 shares of our common stock at an exercise price of $6.90 per share and additional warrants to purchase 68,285 shares of our common stock at an exercise price of $6.59 per share. In 2017, we issued 16,126 shares of common stock related to cashless exercises of some of these warrants. In August 2018, we issued 42,253 warrants with a weighted average of $7.10 per share. At December 31, 2018, 142,359 warrants with a weighted average exercise price of $6.85 per share were outstanding.

In June 2012, we issued warrants with expiration in June 2017 pursuant to public offerings of our securities in 2012. In 2017, we issued 3,450,122 shares of common stock for exercise of these warrants, respectively.

Controlled Equity Offering

During 2017, we issued 2,425,625 shares of common stock under a Controlled Equity Offering Sales Agreement, an at-the-market issuance sales agreement, for net proceeds of $29.9 million and completed the offering.

Note 12 — Income Taxes

We did not record an income tax provision in 2018 and 2017 because we had net taxable losses.

CYTOKINETICS, INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

The following reconciles the statutory federal income tax rate to our effective tax rate:

	Years Ended December 31,	
	2018	2017
Tax at federal statutory tax rate	21 %	34 %
Tax credits (net)	1 %	8 %
Federal statutory rate reduction	—	(51)%
Change in valuation allowance	(17)%	10 %
Stock-based compensation	(1)%	—
Other	(3)%	(1)%
Total	0 %	0 %

Our significant jurisdictions are the United States and California. We are subject to income tax examination for all fiscal years since inception. Income (loss) before taxes includes the following components (in thousands):

	Years Ended December 31,	
	2018	2017
United States	$(106,289)	$(127,235)
Foreign	—	(555)
Total	$(106,289)	$(127,790)

Deferred tax assets, net, reflecting the net tax effect of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes, were as follows (in thousands):

	As of December 31,	
	2018	2017
Deferred tax assets:		
Net operating loss carryforwards	$121,748	$98,630
Tax credits	64,797	64,185
Liability related to sale of future royalties	26,294	24,593
Reserves and accruals	5,772	10,524
Capitalized R&D	4,614	6,432
Depreciation and amortization	586	546
Total noncurrent deferred tax assets	223,811	204,910
Deferred tax liabilities:		
Accounting method change	(2,682)	—
Other	(20)	—
Total noncurrent deferred tax liabilities	(2,702)	—
Less: Valuation allowance	(221,109)	(204,910)
Net deferred tax assets	$—	$—

At December 31, 2018, federal NOL carryforwards were $490.1 million and apportioned state NOL carryforwards before federal benefits were $252.8 million. If not utilized, federal and state operating loss carryforwards incurred prior to 2018 will begin to expire in various amounts beginning 2022 and 2028, respectively.

At December 31, 2018, tax credits of $61.6 million and $15.0 million for federal and state income tax purposes, respectively consisted of Research and Development Credits and Orphan Drug Credits. If not utilized, the federal carryforwards will expire in various amounts beginning in 2021. California based credit carryforwards do not expire.

Realization of deferred tax assets is dependent upon future earnings, if any, the timing and amount of which are uncertain. Based upon the weight of available evidence, which includes our historical operating performance, reported cumulative net losses since inception, expected future losses, and difficulty in accurately forecasting our future results and an assessment of both positive and negative evidence when determining whether it is more likely than not that deferred tax assets are recoverable, we maintained a full valuation allowance on the net deferred tax assets as of December 31, 2018 and 2017. The valuation allowance increased by $16.2 million in 2018 and decreased by $11.7 million in 2017.

In general, under Section 382 of the Internal Revenue Code (“Section 382”), a corporation that undergoes an ‘ownership change’ is subject to limitations on its ability to utilize its pre-change net operating losses and tax credits to offset future taxable income. We do not believe it has experienced an ownership change since 2006 expect a portion of its NOLs and tax credits from prior to 2007 will be subject to limitations under Section 382.

CYTOKINETICS, INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

Activity related to our gross unrecognized tax benefits were (in thousands):

	Years Ended December 31,	
	2018	2017
Balance at the beginning of the year	$9,365	$7,565
Decrease related to prior year tax positions	-	-
Increase related to current year tax positions	110	1,800
Balance at the end of the year	$9,475	$9,365

We are subject to income tax examination for all fiscal years since inception. Included in the balance of unrecognized tax benefits as of December 31, 2018 and 2017 are $8.6 million and $8.1 million of tax benefits, respectively, that, if recognized, would result in adjustments to other tax accounts, primarily deferred taxes.

Tax Reform

The Tax Cuts and Jobs Act of 2017 (the “Tax Act”) made significant changes to the Internal Revenue Code. Changes include, but are not limited to, a corporate tax rate decrease from 34% to 21% (the “Rate Reduction”) effective for tax years beginning after December 31, 2017. We reduced deferred tax assets at December 31, 2017 for the effect of the Rate Reduction. The Rate Reduction did not impact our provision for income taxes for 2017 due to the full valuation allowance on deferred tax assets.

Due to the complexities of implementing the provisions of the Tax Act, the staff of the U.S. Securities and Exchange Commission issued Staff Accounting Bulletin 118 (“SAB 118”), which provides guidance on accounting for tax effects of the Tax Act and permits a measurement period not to exceed one year from the enactment date for companies to complete the required analyses and accounting. As permitted under SAB 118, the adjustments we recorded due to the Tax Act, including the remeasurement of deferred tax assets and liabilities and the transition tax, were based on reasonable estimates and were considered provisional during the year. In the fourth quarter of 2018, we completed our analysis to determine the effect of the Tax Act and recorded immaterial adjustments as of December 31, 2018. The Company has considered and completed all applicable elements of tax reform under the remeasurement period.

Note 14 — Interest and Other Income, Net

Interest and other income, net for the years ended December 31, 2018 and 2017 primarily consisted of interest income generated from our cash, cash equivalents and investments.

71

Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosure
None.

Item 9A. Controls and Procedures
Evaluation of Disclosure Controls and Procedures:

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our reports under the Securities Exchange Act of 1934, as amended, or the Exchange Act, is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms and that such information is accumulated and communicated to our management, including our Chief Executive Officer, Chief Financial Officer and Chief Accounting Officer, as appropriate, to allow for timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, we recognize that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives, and in reaching a reasonable level of assurance, we are required to apply our judgment in evaluating the cost-benefit relationship of possible controls and procedures.

As of December 31, 2018, the end of the period covered by this report, we carried out an evaluation, including our Chief Executive Officer, Chief Financial Officer and Chief Accounting Officer of the effectiveness of the design and operation of our disclosure controls and procedures. Based on the foregoing, our Chief Executive Officer, Chief Financial Officer and Chief Accounting Officer concluded that our disclosure controls and procedures were not effective as of December 31, 2018.

Management's Annual Report on Internal Control Over Financial Reporting:

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Exchange Act Rules 13a-15(f) and 15d-15(f). Under the supervision and with the participation of our management, including our Chief Executive Officer, Chief Financial Officer and Chief Accounting Officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting as of December 31, 2018 based on the framework in Internal Control — Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 Framework) (the COSO criteria). Based on the above evaluation, our management concluded that our internal control over financial reporting was ineffective as of December 31, 2018 due to the identification of a material weakness.

A material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of the company's annual or interim financial statements will not be prevented or detected on a timely basis.

As of December 31, 2018, we identified a material weakness related to the ineffective review and verification of internally prepared reports and analyses utilized in the financial closing process. The material weakness is related to employee turnover resulting in a temporary lack of resources in financial reporting roles with the appropriate skills to perform effective review during our financial statement close process.

This material weakness did not result in the restatement of prior quarterly or annually filed financial statements.

Remediation Plan

To remediate the material weakness described above, we are actively recruiting for open positions within the accounting department and will, as necessary, supplement any interim staffing needs with temporary resources. We will also continue to evaluate and improve our internal controls, processes and procedures in the financial statement

close process.

Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders

Cytokinetics, Incorporated

Opinion on Internal Control over Financial Reporting

We have audited Cytokinetics, Incorporated's internal control over financial reporting as of December 31, 2018, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). In our opinion, because of the effect of the material weakness described below on the achievement of the objectives of the control criteria, Cytokinetics, Incorporated (the "Company") has not maintained effective internal control over financial reporting as of December 31, 2018, based on the COSO criteria.

A material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of the company's annual or interim financial statements will not be prevented or detected on a timely basis. The following material weakness has been identified and included in management's assessment. Management has identified a material weakness in controls related to the company's financial statement close process.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the 2018 consolidated financial statements of the Company. This material weakness was considered in determining the nature, timing and extent of audit tests applied in our audit of the 2018 consolidated financial statements, and this report does not affect our report dated March 6, 2019 which expressed an unqualified opinion thereon.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects.

Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control Over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ Ernst & Young LLP

Redwood City, California

March 6, 2019

Item 9B. Other Information

On March 6, 2019, we entered into a Controlled Equity Offering℠ Sales Agreement (the "New ATM Facility"), with Cantor Fitzgerald & Co. ("Cantor"), under which we may offer and sell, from time to time at our sole discretion, shares of our common stock, par value $0.001 per share, or the Common Stock, having an aggregate offering price of up to $35.0 million through Cantor, as sales agent. In connection with the entry into the New ATM Facility, we terminated our prior sales agreement, dated November 3, 2017, with Cantor.

Cantor may sell the Common Stock by any method that is deemed to be an "at the market offering" as defined in Rule 415 of the Securities Act of 1933, as amended, including sales made directly on the Nasdaq Global Select Market or any other trading market for our common stock. Cantor will use commercially reasonable efforts to sell the Common Stock from time to time, based upon instructions from us (including any price, time or size limits or other customary parameters or conditions we may impose). We will pay Cantor a commission of up to 3.0% of the aggregate gross sales proceeds of any common stock sold through Cantor under the New ATM Facility, and also have provided Cantor with customary indemnification rights.

We are not obligated to make any sales of Common Stock under the New ATM Facility. The offering of shares of Common Stock pursuant to the New ATM Facility will terminate upon the termination of the New ATM Facility in accordance with its terms.

The foregoing description of the New ATM Facility is qualified in its entirety by reference to the New ATM Facility, a copy of which is attached hereto as Exhibit 1.1 and incorporated herein by reference.

The legal opinion of Cooley LLP relating to the shares of Common Stock being offered pursuant to the New ATM Facility is filed as Exhibit 5.1 to this Annual Report on Form 10-K.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

The information regarding our directors and executive officers, our director nominating process and our audit committee is incorporated by reference from our definitive Proxy Statement for our 2019 Annual Meeting of Stockholders, where it appears under the headings “Board of Directors” and “Executive Officers.”

Section 16(a) Beneficial Ownership Reporting Compliance

The information regarding our Section 16 beneficial ownership reporting compliance is incorporated by reference from our definitive Proxy Statement described above, where it appears under the headings “Section 16(a) Beneficial Ownership Reporting Compliance.”

Code of Ethics

We have adopted a Code of Ethics that applies to all our directors, officers and employees. We publicize the Code of Ethics through posting the policy on our website, www.cytokinetics.com. We will disclose on our website any waivers of, or amendments to, our Code of Ethics within four business days following the date of such amendment or waiver.

Item 11. Executive Compensation

The information required by this Item is incorporated by reference from our definitive Proxy Statement referred to in Item 10 above, where it appears under the headings “Executive Compensation” and “Compensation Committee Interlocks and Insider Participation.”

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

The information required by this item is incorporated by reference from the applicable information set forth in “Certain Relationships and Related Party Transactions” and “Corporate Governance” which will be included in our definitive Proxy Statement for our 2019 Annual Meeting of Stockholders to be filed with the SEC.

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

The information required by this Item is incorporated by reference from our definitive Proxy Statement referred to in Item 10 above where it appears under the headings “Certain Business Relationships and Related Party Transactions” and “Board of Directors.”

Item 14. Principal Accounting Fees and Services

The information required by this Item is incorporated by reference from our definitive Proxy Statement referred to in Item 10 above, where it appears under the heading “Principal Accountant Fees and Services.”

PART IV

Item 15. Exhibits and Financial Statement Schedules

(a) The following documents are filed as part of this Form 10-K:

(1) Financial Statements (included in Part II of this report):

Our Consolidated Financial Statements are listed in the “Index to Consolidated Financial Statements” under Part II. Item 8 of this Annual Report on Form 10 K. Consolidated Balance Sheets

(2) Financial Statement Schedules:

Financial statement schedules are omitted because the information is inapplicable or presented in the notes to the financial statements.

(3) Exhibits:

Item 16. Form 10-K Summary

None.

EXHIBIT INDEX

		Incorporated by Reference				
Exhibit No.	Exhibits	Form	File No.	Filing Date	Exh. No.	Filed Herewith
1.1	Controlled Equity Offering Sales Agreement, dated as of March 6, 2019, by and between the Company and Cantor Fitzgerald & Co.					X
3.1	Amended and Restated Certificate of Incorporation.	S-3	333-174869	June 13, 2011	3.1	
3.2	Certificate of Amendment of Amended and Restated Certificate of Incorporation.	10-Q	000-50633	August 4, 2011	3.2	
3.3	Certificate of Amendment of Amended and Restated Certificate of Incorporation.	8-K	000-50633	June 25, 2013	5.1	
3.4	Certificate of Amendment of Amended and Restated Certificate of Incorporation	8-K	000-50633	May 20, 2016	3.1	
3.5	Amended and Restated Bylaws.	S-1	333-112261	January 27, 2004	3.2	
4.1	Specimen Common Stock Certificate.	10-Q	000-50633	May 9, 2007	4.1	
4.2	Form of Warrant	10-Q	000-50633	August 6, 2012	4.6	

4.3	Form of Common Stock Warrant Issued Pursuant to that certain Loan and Security Agreement, dated as of October 19, 2015, by and among the Company, Oxford Finance LLC and Silicon Valley Bank	10-K	000-50633	March 3, 2016	4.6

Exhibit No.	Exhibits	Incorporated by Reference				Filed Herewith
		Form	File No.	Filing Date	Exh. No.	
5.1	Opinion of Cooley LLP					X
10.1+	Amended and Restated 2004 Equity Incentive Plan	10-Q	000-50633	August 5, 2015	10.2	
10.2+	2015 Employee Stock Purchase Plan	10-Q	000-50633	August 5, 2015	10.42	
10.3	Build-to-Suit Lease, dated May 27, 1997, by and between Britannia Pointe Grand Limited Partnership and Metaxen, LLC	S-1	333-112261	January 27, 2004	10.5	
10.4	First Amendment to Lease, dated April 13, 1998, by and between Britannia Pointe Grand Limited Partnership and Metaxen, LLC	S-1	333-112261	January 27, 2004	10.6	
10.5	Sublease Agreement, dated May 1, 1998, by and between the Company and Metaxen, LLC	S-1	333-112261	January 27, 2004	10.7	
10.6	Sublease Agreement, dated March 1, 1999, by and between Metaxen, LLC and Exelixis Pharmaceuticals, Inc.	S-1	333-112261	January 27, 2004	10.8	
10.7	Assignment and Assumption Agreement and Consent, dated July 11, 1999, by and among Exelixis Pharmaceuticals, Metaxen, LLC, Xenova Group PLC and Britannia Pointe Grande Limited Partnership	S-1	333-112261	January 27, 2004	10.9	
10.8	Second Amendment to Lease, dated July 11, 1999, by and between Britannia Pointe Grand Limited Partnership and Exelixis Pharmaceuticals, Inc.	S-1	333-112261	January 27, 2004	10.10	
10.9	First Amendment to Sublease Agreement, dated July 20, 1999, by and between the Company and Metaxen	S-1	333-112261	January 27, 2004	10.11	
10.10	Agreement and Consent, dated July 20, 1999, by and among Exelixis Pharmaceuticals, Inc., the Company and Britannia Pointe Grand Limited Partnership	S-1	333-112261	January 27, 2004	10.12	
10.11	Amendment to Agreement and Consent, dated July 31, 2000, by and between the Company, Exelixis, Inc., and Britannia Pointe Grande Limited Partnership	S-1	333-112261	January 27, 2004	10.13	

Exhibit No.	Exhibits	Incorporated by Reference				Filed Herewith
		Form	File No.	Filing Date	Exh. No.	
10.12	Assignment and Assumption of Lease, dated September 28, 2000, by and between the Company and Exelixis, Inc.	S-1	333-112261	January 27, 2004	10.14	
10.13	Sublease Agreement, dated September 28, 2000, by and between the Company and Exelixis, Inc.	S-1	333-112261	January 27, 2004	10.15	
10.14*	Collaboration and Option Agreement, dated as of December 29, 2006, by and between the Company and Amgen Inc.	10-K	000-50633	March 12, 2007	10.63	
10.15	Form of Indemnification Agreement between the Company and each of its directors and executive officers	10-Q	000-50633	August 5, 2008	10.1	
10.17+	Amended and Restated Executive Employment Agreement, dated May 21, 2007, by and between the Company and Robert Blum	10-Q	000-50633	August 5, 2008	10.69	
10.18+	Form of Executive Employment Agreement between the Company and its executive officers	10-Q	000-50633	August 5, 2008	10.68	
10.19*	Amendment No. 1, dated June 17, 2008, to the Collaboration and Option Agreement by and between the Company and Amgen Inc.	10-K	000-50633	March 12, 2009	10.62	
10.20*	Amendment No. 2, dated September 30, 2008, to the Collaboration and Option Agreement by and between the Company and Amgen Inc.	10-K	000-50633	March 12, 2009	10.63	
10.21*	Amendment No. 3, dated October 31, 2008, to the Collaboration and Option Agreement by and between the Company and Amgen Inc.	10-K	000-50633	March 12, 2009	10.65	
10.22*	Amendment No. 4, dated February 20, 2009, to the Collaboration and Option Agreement by and between the Company and Amgen Inc.	10-K	000-50633	March 12, 2009	10.67	
10.23+	Form of Amendment No. 1 to Amended and Restated Executive Employment Agreements	10-K	000-50633	March 12, 2009	10.68	

Exhibit No.	Exhibits	Incorporated by Reference				Filed Herewith
		Form	File No.	Filing Date	Exh. No.	
10.24	Third Amendment to Lease, dated December 10, 2010, by and between the Company and Britannia Pointe Grand Limited Partnership	10-K	000-50633	March 11, 2011	10.65	
10.25*	Amendment No. 5, dated November 1, 2010, to the Collaboration and Option Agreement by and between the Company and Amgen Inc.	10-K	000-50633	March 11, 2011	10.66	
10.26+	2015 Compensation Information for the Company's Named Executive Officers	8-K	000-50633	March 2, 2015	10.1	
10.27+	Form of Option Agreement	10-K	000-50633	March 15, 2013	10.46	
10.28+	Form of Restricted Stock Unit Award Agreement	10-K	000-50633	March 15, 2013	10.47	
10.29	Common Stock Purchase Agreement dated June 11, 2013, by and between the Company and Amgen Inc.	8-K	000-50633	June 12, 2013	10.48	
10.30*	Amendment No. 6, dated June 11, 2013, to the Collaboration and Option Agreement by and between the Company and Amgen Inc.	10-Q	000-50633	August 7, 2013	10.46	
10.31+	Form of Executive Employment Agreement between the Company and its executive officers	10-K	000-50633	March 7, 2014	10.39	
10.32	Common Stock Purchase Agreement by and between the Company and Astellas Pharma Inc. dated December 22, 2014	8-K	000-50633	December 23, 2014	10.46	
10.33*	Amended and Restated License and Collaboration Agreement, dated December 22, 2014, by and between the Company and Astellas Pharma Inc.	10-K	000-50633	March 6, 2015	10.40	
10.34*	Amendment No. 7, dated March 19, 2015, to the Collaboration and Option Agreement by and between the Company and Amgen Inc.	10-Q	000-50633	May 4, 2015	10.41	
10.35	Amendment to Collaboration Agreement: Joint Development Committee Membership	10-Q	000-50633	August 7, 2018	10.1	

Exhibit No.	Exhibits	Incorporated by Reference				Filed Herewith
		Form	File No.	Filing Date	Exh. No.	
10.36*	Loan and Security Agreement, dated as of October 19, 2015, by and among the Company, Oxford Finance LLC and Silicon Valley Bank	10-K	000-50633	March 3, 2016	10.40	
10.37	Fourth Amendment to Build to Suit Lease, dated March 1, 2016, by and between the Company and Britannia Pointe Grand Limited Partnership	10-Q	000-50633	May 5, 2016	10.41	
10.38*	Amendment to the Amended and Restated License and Collaboration Agreement between the Company and Astellas Pharma Inc., dated July 27, 2016	10-Q/A	000-50633	January 20, 2017	10.42	
10.39*	Letter of Agreement by and between the Company and Amgen Inc. and Les Laboratoires Servier and Institut de Recherches Internationales Servier, dated August 29, 2016	10-Q	000-50633	November 3, 2016	10.43	
10.40*	Royalty Purchase Agreement by and between the Company and RPI Finance Trust, dated February 1, 2017	10-K	000-50633	March 6, 2017	10.44	
10.41	Common Stock Purchase Agreement by and between the Company and RPI Finance Trust, dated February 1, 2017	10-K	000-50633	March 6, 2017	10.45	
10.42*	Amendment to Collaboration Agreement between the Company and Astellas Pharma Inc., dated April 11, 2017	10-Q	000-50633	August 4, 2017	10.1	
10.43	Amendment to the Amended and Restated 2004 Equity Incentive Plan	10-Q	000-50633	November 3, 2017	10.1	
10.44	Second Amendment to Loan and Security Agreement by and among the Company, Oxford Finance LLC and Silicon Valley Bank, dated as of October 27, 2017	10-K	000-50633	March 5, 2018	10.45	
10.45	Compensation Information for Named Executive Officers	8-K	000-50633	February 28, 2017	10.1	
10.46	Fifth Amendment to Lease, dated December 18, 2017, by and between the Company and Britannia Pointe Grand Limited Partnership	10-K	000-50633	March 5, 2018	10.47	

Exhibit No.	Exhibits	Incorporated by Reference				Filed Herewith
		Form	File No.	Filing Date	Exh. No.	
10.47*	Amendment to Collaboration Agreement between the Company and Astellas Pharma Inc., dated December 21, 2017	10-K	000-50633	March 5, 2018	10.48	
10.48	Amendment to Collaboration Agreement; Joint Development Committee Membership	10-Q	000-50633	August 7, 2018	10.1	
10.49**	Amendment No. 8, dated November 30, 2016, to the Collaboration and Option Agreement by and between the Company and Amgen Inc.					X
10.50	Amendment No. 9, dated February 6, 2019, to the Collaboration and Option Agreement by and between the Company and Amgen Inc.					X
23.1	Consent of Ernst & Young LLP, Independent registered public accounting firm					X
23.2	Consent of Pricewaterhouse Coopers LLP Independent registered public accounting firm					X
23.3	Consent of Cooley LLP (included in Exhibit 5.1)					X
24.1	Power of Attorney (included in the signature page to this report)					X
31.1	Certification of Principal Executive Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002					X
31.2	Certification of Principal Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002					X
31.3	Certification of Principal Accounting Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002					X
32.1	Certifications of the Principal Executive Officer, the Principal Financial Officer, and the Principal Accounting Officer pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 (18 U.S.C. Section 1350) (1)					X
101.INS	XBRL Instance Document					X
101.SCH	XBRL Taxonomy Extension Schema Document					X

81

Exhibit No.	Exhibits	Incorporated by Reference				Filed Herewith
		Form	File No.	Filing Date	Exh. No.	
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document					X
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document					X
101.LAB	XBRL Taxonomy Extension Label Linkbase Document					X
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document					X

*Portions of this Exhibit are subject to a confidential treatment order.
**Registrant has requested confidential treatment for portions of this Exhibit.
+Management contract or compensatory plan.
(1)This certification accompanies the Form 10-K to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of the Registrant under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-K), irrespective of any general incorporation language contained in such filing.

(b)Exhibits

The exhibits listed under Item 15(a)(3) hereof are filed as part of this Form 10-K, other than Exhibit 32.1 which shall be deemed furnished.

(c)Financial Statement Schedules

None — All financial statement schedules are omitted because the information is inapplicable or presented in the notes to the financial statements.

Item 16. Form 10-K Summary

None.

SIGNATURES

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

CYTOKINETICS, INCORPORATED

By: / S / ROBERT I. BLUM
Robert I. Blum

President, Chief Executive Officer and Director

Dated: March 6, 2019

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Robert I. Blum, Ching Jaw, and Peter S. Roddy, and each of them, his true and lawful attorneys-in-fact, each with full power of substitution, for him in any and all capacities, to sign any amendments to this Annual Report on Form 10-K and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, hereby ratifying and confirming all that each of said attorneys-in-fact or their substitute or substitutes may do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities and Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ ROBERT I. BLUM Robert I. Blum	President, Chief Executive Officer and Director (Principal Executive Officer)	March 6, 2019
/s/ CHING JAW Ching Jaw	Senior Vice President, Chief Financial Officer (Principal Financial Officer)	March 6, 2019
/s/ PETER S. RODDY Peter S. Roddy	Senior Vice President, Chief Accounting Officer (Principal Accounting Officer)	March 6, 2019
/s/ L. PATRICK GAGE, PHD. L. Patrick Gage, Ph.D.	Chairman of the Board of Directors	March 6, 2019
/s/ ROBERT CALIFF, M.D.	Director	March 6, 2019

Robert Califf, M.D.		
/s/ SANTO J. COSTA Santo J. Costa	Director	March 6, 2019
/s/ JOHN T. HENDERSON, M.B. CH.B. John T. Henderson, M.B. Ch.B.	Director	March 6, 2019
/s/ EDWARD KAYE, M.D. Edward Kaye, M.D.	Director	March 6, 2019
/s/ B. LYNNE PARSHALL, ESQ. B. Lynne Parshall, Esq.	Director	March 6, 2019
/s/ SANDFORD D. SMITH Sandford D. Smith	Director	March 6, 2019
/s/ WENDELL WIERENGA, PH.D. Wendell Wierenga, Ph.D.	Director	March 6, 2019