

**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, 2020

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

*(State or other jurisdiction of
incorporation or organization)*

**280 East Grand Avenue
South San Francisco, CA**

(Address of principal executive offices)

94-3291317

*(I.R.S. Employer
Identification No.)*

94080

(Zip Code)

(650) 624-3000

(Registrant's telephone number, including area code)

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

Trading symbol

CYTK

Name of each exchange on which registered

The Nasdaq Global Select Market

Title of each class

Common Stock, \$0.001 par value

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 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 has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C.7262(b)) by the registered public accounting firm that prepared or issued its audit report.

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

As of June 30, 2020, the last business day of the Registrant's most recently completed second fiscal quarter, the aggregate market value of common stock held by non-affiliates of the Registrant was approximately \$1,413.0 million (based on a closing price of \$23.57 per share as reported by the Nasdaq Global Select Market on June 30, 2020). For purposes of this calculation, shares of common stock beneficially owned by the Registrant's directors, officers and certain stockholders as of June 30, 2020 have been excluded in that such persons may be deemed affiliates. The determination of affiliate status is not necessarily a conclusive determination for other purposes. The Registrant has no non-voting common equity.

As of February 23, 2021, the number of shares outstanding of the Registrant's common stock, par value \$0.001 per share, was 71,110,576 shares.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's Proxy Statement for its 2021 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, 2020
INDEX

	<u>Page</u>
Forward Looking Statements Private Securities Litigation Reform act of 1995	3
Summary of Principal Risk Factors	5
<u>PART I</u>	
Item 1. Business	7
Item 1A. Risk Factors	27
Item 1B. Unresolved Staff Comments	63
Item 2. Properties	63
Item 3. Legal Proceedings	63
Item 4. Mine Safety Disclosures	63
<u>PART II</u>	
Item 5. Market for Registrant’s Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities	64
Item 6. Selected Financial Data	65
Item 7. Management’s Discussion and Analysis of Financial Condition and Results of Operations	66
Item 7A. Quantitative and Qualitative Disclosures About Market Risk	76
Item 8. Financial Statements and Supplementary Data	77
Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure	109
Item 9A. Controls and Procedures	109
Item 9B. Other Information	111
<u>PART III</u>	
Item 10. Directors, Executive Officers and Corporate Governance	112
Item 11. Executive Compensation	112
Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters	112
Item 13. Certain Relationships and Related Transactions, and Director Independence	112
Item 14. Principal Accounting Fees and Services	112
<u>PART IV</u>	
Item 15. Exhibits and Financial Statement Schedules	113
Exhibits	113
Item 16. Form 10-K Summary	118
Signatures	119

**FORWARD LOOKING STATEMENTS
PRIVATE SECURITIES LITIGATION REFORM ACT OF 1995**

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 for 2021;
- 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, 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 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 timing and likelihood of regulatory approval for omecantiv mecarbil or any of our other drug candidates;
- our expected roles in research, development or commercialization under our strategic alliances with Amgen Inc. (“Amgen”), Astellas Pharma Inc. (“Astellas”) and Ji Xing Pharmaceuticals Limited (“Ji Xing”);
- 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;
- our ability to continue to identify additional potential drug candidates that may be suitable for clinical development;
- market acceptance of our drugs;
- changes in third party healthcare coverage and reimbursement policies;
- 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, lease agreements, and revenue interest agreement and the convertible notes;
- potential competitors and competitive products;
- retaining key personnel and recruiting additional key personnel; the potential impact of recent accounting pronouncements on our financial position or results of operations; and
- the continuing impact of the COVID-19 pandemic on our research and development activities and business operations.

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

- Astellas' decisions with respect to the timing, design and conduct of research and development activities for those skeletal muscle activators subject to the License and Collaboration Agreement for Other Skeletal Sarcomere Activators, dated April 23, 2020 (the "Astellas OSSA Agreement"); and Ji Xing's decisions with respect to the timing, design and conduct of development and commercialization activities for CK-274 in the People's Republic of China (including the Hong Kong SAR and Macau SAR) (together "China") and Taiwan;
- our ability to complete the transition of the programs related to omecamtiv mecarbil and CK-136 (formerly known as AMG 594) from Amgen to us effectively or efficiently by May 20, 2021;
- our ability to receive funds under the Funding Agreement, dated July 14, 2020 (the "Funding Agreement") between us and RTW Royalty Holdings Designated Activity Company ("RTW Royalty Holdings"), which is subject to certain conditions;
- our ability to enroll patients in our clinical trials by any particular date, including our ability to complete enrollment in Cohort 2 of REDWOOD-HCM by the first quarter of 2021 and complete METEORIC-HF enrollment in the first half of 2021;
- our ability to complete our clinical trials by any particular date, including our ability to complete and publish the results of REDWOOD-HCM by mid-2021;
- 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, in the development, testing, manufacturing or commercialization of our drug candidates or slower than anticipated patient enrollment, in our or partners' clinical trials, or 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 U.S. Food and Drug Administration (the "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 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, reimbursement and favorable drug pricing 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 and performance of 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.

SUMMARY OF PRINCIPAL RISK FACTORS

This summary briefly states the principal risks and uncertainties facing our business that could affect our common stock, which are only a select portion of those risks. A more complete statement of those risks and uncertainties is set forth in the Section 1A “Risk Factors” of this report. This summary is qualified in its entirety by that more complete statement. You should carefully read the entire statement and “Risk Factors” when considering the risks and uncertainties as part of your evaluation of an investment in our common stock.

- ***Notwithstanding GALACTIC-HF having met its primary efficacy endpoint, there is no guarantee that the FDA or any other regulatory authority will approve omecamtiv mecarbil.***

GALACTIC-HF demonstrated a statistically significant effect of treatment with omecamtiv mecarbil to reduce risk of the primary composite endpoint of cardiovascular death or heart failure events (heart failure hospitalization and other urgent treatment for heart failure) compared to placebo in patients treated with standard of care (HR: 0.92; 95% CI: 0.86, 0.99, p=0.025). The trial results, however, showed that no secondary endpoints were met. In particular, no reduction in the secondary endpoint of time to cardiovascular death was observed, and the KCCQ total symptom score by randomization setting did not meet the significance threshold of P=0.002 based upon the multiplicity control testing procedure. No assurances can be given that the primary endpoint results of GALACTIC-HF alone will be deemed sufficiently safe or efficacious to warrant approval by the FDA or any other regulatory authority. Although supplemental analyses showed that omecamtiv mecarbil potentially has a greater treatment effect in certain subgroups of trial patients, no assurance can be given that the FDA or any other regulatory authority will consider any such subgroup analysis as the basis for an approval of omecamtiv mecarbil without requiring additional clinical trials.

- ***Clinical trials may fail to demonstrate the desired safety and efficacy of our drug candidates, including CK-274 and reldesemtiv, which could prevent or significantly delay completion of clinical development and regulatory approval.***

All of our drug candidates, including CK-274 and reldesemtiv, 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 investigational new drug application with the FDA (or a foreign equivalent) (“IND”) 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 subsequent clinical trials. 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 of a new drug application (or foreign equivalent) by the FDA or foreign regulatory authorities (“NDA”).

- ***The transition of responsibilities for manufacturing, development, regulatory, commercial planning and other activities related to omecamtiv mecarbil and CK-136 (formerly known as AMG 594) from Amgen to us may not be completed effectively or efficiently and could result in substantial delays to these programs and significant increased costs to us.***

No assurance can be made that Amgen will cooperate with us and take such actions required of Amgen under our agreement with Amgen to transition responsibilities for the manufacturing, development, regulatory, commercial planning and other activities related to omecamtiv mecarbil and/or CK-136 to us effectively or efficiently. No assurance can be made that we will have or be able to mobilize the capital, personnel, systems or other resources required to ensure our ability to meet our legal or regulatory responsibilities and obligations, to continue the development of the omecamtiv mecarbil and/or CK-136 programs, including the conduct of clinical trials of omecamtiv mecarbil and/or CK-136, without substantial delays to the timelines previously anticipated prior to Amgen’s decision to terminate our agreement or without significant costs as compared to our anticipated costs prior to Amgen’s decision to terminate our agreement, or to ensure commercial preparedness for a potential product launch of omecamtiv mecarbil.

- ***We currently have limited 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 omecamtiv mecarbil or our other drug candidates.***

To effectively commercialize our drugs, we will need to establish and/or expand our own specialized sales force and marketing organization with technical expertise and supporting manufacturing and distribution capabilities. Developing such an organization is expensive and time-consuming and could delay a product launch.

In relation to omecamtiv mecarbil specifically, prior to Amgen’s notification of its election to terminate the Amgen Agreement, we expected that, consistent with the terms of such agreement, Amgen would bear primary operational and financial responsibility for the sales, marketing, manufacturing and distribution activities related to the product launch and commercialization of omecamtiv mecarbil. As a result of the anticipated termination of the Amgen Agreement, we must now build and/or expand our capabilities without Amgen’s operational or financial support, which will result in significantly higher costs to us than what we had expected prior to Amgen’s notification of its election to terminate the Amgen Agreement, and we may never be able to successfully build and/or expand our commercialization capabilities to fully substitute the capabilities of Amgen of which we were reliant upon. Moreover, as a

result of Servier's notification of its election to terminate the Servier Agreement, we will need to seek a replacement partner in Europe with the expertise and resources to successfully launch and commercialize omecantiv mecarbil in Europe or to establish our own commercial capabilities in Europe at our own cost and effort.

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

- ***The commercial success of our products depends on the availability and sufficiency of third-party payor coverage and reimbursement.***

Patients in the United States and elsewhere generally rely on third-party payors to reimburse part or all of the costs associated with their prescription drugs. Accordingly, market acceptance of our products is dependent on the extent to which third-party coverage and reimbursement is available from government health administration authorities (including in connection with government healthcare programs, such as Medicare and Medicaid in the United States), private healthcare insurers and other healthcare funding organizations. Significant uncertainty exists as to the coverage and reimbursement status of any products for which we may obtain regulatory approval.

- ***We have a history of significant losses and may not achieve or sustain profitability and, as a result, you may lose part or all 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 drug candidates.

- ***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 or launch commercial products. 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, grant licenses on terms that may not be favorable to us. To the extent that we raise additional funds through debt financing, the financing may involve covenants that restrict our business activities. To the extent that we raise additional funds by issuing equity securities, our stockholders will experience additional dilution and our share price may decline.

- ***Our business is currently adversely affected and could be materially and adversely affected in the future by the effects of disease outbreaks, epidemics and pandemics, including the ongoing COVID 19 pandemic. The COVID-19 pandemic continues to adversely impact our business and could materially and adversely affect our operations, as well as the businesses or operations of our or our partners, manufacturers, CROs or other third parties with whom we or our partners conduct business.***

PART I

ITEM 1. BUSINESS

When used in this report, unless otherwise indicated, “Cytokinetics,” “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 next-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 health span 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 clinical-stage drug candidates are: omecamtiv mecarbil, a novel cardiac myosin activator, CK-136 (formerly known as AMG 594), a novel cardiac troponin activator, reldesemtiv, a novel fast skeletal muscle troponin activator (“FSTA”), CK-3773274 (“CK-274”), a novel cardiac myosin inhibitor, and CK-3772271 (“CK-271”), our second novel cardiac myosin inhibitor.

Omecamtiv mecarbil is being evaluated for the potential treatment of heart failure under a strategic alliance with Amgen 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, conducted GALACTIC-HF (**G**lobal **A**pproach to **L**owering **A**dverse **C**ardiac **O**utcomes **T**hrough **I**mproving **C**ontractility in **H**eart **F**ailure), a Phase 3 cardiovascular outcomes clinical trial of omecamtiv mecarbil in heart failure. In collaboration with Amgen, we are conducting METEORIC-HF (**M**ulticenter **E**xercise **T**olerance **E**valuation of **O**mecamtiv **M**ecarbil **R**elated to **I**ncreased **C**ontractility in **H**eart **F**ailure), a second Phase 3 clinical trial intended to evaluate its potential to increase exercise performance.

CK-136 (formerly known as AMG 594) was discovered under our joint research program with Amgen. In collaboration with Cytokinetics, Amgen conducted 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 CK-136 in healthy subjects.

CK-274 is a novel, oral, small molecule cardiac myosin inhibitor. CK-274 arose from an extensive chemical optimization program conducted with attention to therapeutic index and pharmacokinetic properties that may translate into next-in-class potential in clinical development. CK-274 was designed to reduce the hypercontractility that is associated with hypertrophic cardiomyopathy (“HCM”).

CK-274 is being evaluated in patients with symptomatic, obstructive HCM in REDWOOD-HCM (**R**andomized **E**valuation of **D**osing **W**ith **C**K-274 in **O**bststructive **O**utflow **D**isease in **H**CM), a Phase 2 multicenter, randomized, placebo-controlled, double-blind, dose-finding clinical trial of CK-274.

CK-271 is our second novel, oral, small molecule cardiac myosin inhibitor. CK-271 is an allosteric cardiac myosin inhibitor that produces reversible dose and plasma concentration-dependent reductions in cardiac contractility without affecting heart rate in preclinical models. CK-271 reduces compensatory cardiac hypertrophy and cardiac fibrosis in preclinical models of HCM and heart failure with preserved ejection fraction. CK-271 is the second cardiac myosin inhibitor arising from the Company’s extensive chemical optimization program conducted with careful attention to therapeutic index and pharmacokinetic properties and may be therapeutically effective by providing rapid relief of excessive hypercontractility such as HCM.

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 was developed under our joint development program with Astellas.

In collaboration with Astellas, we conducted a Phase 2 clinical trial of reldesemtiv in patients with spinal muscular atrophy (“SMA”) and a Phase 2 clinical trial of reldesemtiv in patients with amyotrophic lateral sclerosis (“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. COURAGE-ALS (Clinical Outcomes Using Reldesemtiv on ALSFRS-R in a Global Evaluation in ALS) is the planned Phase 3 clinical trial of reldesemtiv in patients with ALS.

Our research continues to drive innovation and leadership in muscle biology. 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 next-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 to improve patient healthspan, with the intent of establishing a fully-integrated biopharmaceutical company.

In 2020, we articulated our five-year strategic plan, Vision 2025: “Leading with Science, Delivering for Patients,” enabling Cytokinetics to become the leading muscle biology biopharmaceutical company that meaningfully improves the lives of patients with diseases of impaired muscle function through access to novel medicines arising from its research.

The key components of our five-year Corporate Strategy are:

- *Achieve regulatory approvals for at least two drugs arising from our pipeline.* We are committed to fueling a diverse and expansive pipeline of muscle-directed drug candidates advancing toward regulatory approval. 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 achieving regulatory success and deliver effective therapies to patients that can address the needs of people living with devastating diseases of muscle impairment. Pursuing a broad-based clinical development strategy may afford us the opportunity to not be reliant on the outcome of a singular clinical program or clinical trial result, thereby potentially mitigating the risk of clinical development and regulatory hurdles. We or our partners have been conducting extensive clinical trials for our most advanced drug candidates and we believe that three drug candidates are poised to achieve potential regulatory approval by 2025 and we strive to develop compelling scientific, clinical and value-driven rationales that may lead to regulatory approvals.
- *Build commercial capabilities to market and sell our medicines reflective of their innovation and value.* 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, physicians, patients and payors, including the principal drivers of clinical and economic burdens associated with these diseases. We have established alliances and collaborations with leading academic institutions and professional societies to analyze clinical and claims data to better understand the real-world burden of disease from a clinical and economic standpoint. We believe this approach may inform the value proposition that our potential first-in-class and next-in-class therapies may offer to various stakeholders within the healthcare ecosystem. Targeting unmet medical needs may provide us competitive advantages and support our development of a franchises in diseases involving muscle function. In the markets for our potential therapies, 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 build sales and marketing capabilities in North America and Europe with the goal of becoming a fully-integrated biopharmaceutical company.

- *Generate sustainable and growing revenues from product sales.* As we move toward becoming a fully integrated biopharmaceutical company, we expect to evolve our corporate development strategies to raise capital through a combination of strategic partnerships and equity capital financings to one that is sustained from product generated revenues that are expected to grow over time. We expect to successfully commercialize at least two of our drug candidates in the U.S. and Europe and achieve growing profitability. Through prudent investment spending fueled by commercial returns alongside other potential strategic partnerships and royalty monetization deals, we seek to provide investor returns while continuing to conduct proprietary research to support future commercial programs. Additionally, we strive to ensure sustainable growth of product sales and long-term profitability through lifecycle management strategies.
- *Double our development pipeline to include ten therapeutic programs.* We believe that our extensive understanding of muscle biology and our proprietary research activities should enable us to discover and potentially to develop additional muscle directed 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. 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. In 2020 we advanced five potential drug candidates through various stages of clinical development. Over the next five years, we will expand our research discovery platform beyond muscle contractility to support doubling our pipeline to ten therapeutic programs.
- *Expand our discovery platform to muscle energetics, growth and metabolism.* We expect that we may be able to leverage our expertise in muscle contractility to expand muscle biology research programs related to other areas of muscle function and which may extend to the potential treatment of other serious, yet adjacent, diseases and conditions. As most muscle-related diseases are accompanied by defects in metabolism or mitochondrial function, we also anticipate that treatments that modulate contractility could be additive with therapeutics that boost metabolic capacity. We can augment our industry-leading expertise in muscle contractility by building similar expertise in mitochondrial biology and technologies. Strategies toward enhancing our discovery platform into muscle energetics and metabolism include building human and capital resources for mitochondrial and metabolism research capabilities, expanding strategic academic partnerships, engaging the mitochondrial research community, engaging the mitochondrial disease advocacy community, and evaluating therapeutic and technology platforms for potential in-licensing.
- *Be the science-driven company people want to join and partner with.* We build our science around patients and their families through authentic and ongoing engagement and are committed to transforming patients' lives through our activities. Our goal is to provide employees with an opportunity to contribute to something bigger than any one of the individuals at the company. We believe that a commitment to a diverse, inclusive and respectful culture goes beyond what is "right" to do; it is foundational to building a successful, creative, and science driven company, and essential to develop a community of colleagues who are impassioned by our purpose to improve the lives of patients. As a patient-centric organization, we rely on an approach where clinical outcomes, patient experiences and patients' goals for care intersect. We value our partnerships with industry, professional societies, advocacy organizations, vendors and academic institutions and aim to solicit ongoing feedback to ensure interests are aligned and collaborations are successful

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 \$97.0 million for 2020, \$86.1 million for 2019 and \$89.1 million for 2018.

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.

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. Currently, Amgen has exclusive, worldwide rights to develop and commercialize omecamtiv mecarbil and related compounds subject to our specified development and commercial participation rights. Amgen also entered an alliance with Les Laboratoires Servier and Institut de Recherches Internationales Servier (“Servier”) for exclusive commercialization rights for omecamtiv mecarbil in Europe as well as the Commonwealth of Independent States (“CIS”), including Russia; Servier has contributed funding for development and provides strategic support to the program.

On October 8, 2020, we, Amgen and Servier announced topline results from GALACTIC-HF. The results of GALACTIC-HF show that treatment with omecamtiv mecarbil achieved the primary composite efficacy endpoint and demonstrated a statistically significant effect to reduce cardiovascular (“CV”) death or heart failure events (heart failure hospitalization and other urgent treatment for heart failure), compared to placebo in patients treated with standard of care (HR: 0.92; 95% CI: 0.86, 0.99, p-0.025). No reduction in the secondary endpoint of CV death was observed. Adverse events, including major ischemic cardiac events, were balanced between treatment arms.

On November 23, 2020, we announced that Amgen has elected to terminate the Amgen Agreement and thereby end its collaboration with Cytokinetics, effective May 20, 2021, and intends to transition development and commercialization rights for omecamtiv mecarbil and CK-136 (formerly known as AMG 594) to Cytokinetics.

On December 23, 2020, we announced that Amgen notified us that Servier elected to terminate the sublicense agreement between Amgen and Servier for the development and commercialization of omecamtiv mecarbil in Europe and the Commonwealth of Independent States, including Russia (the “Servier Agreement”). The termination is effective as of March 18, 2021, after which all development, commercialization and other rights with respect to omecamtiv mecarbil previously granted by Amgen to Servier will revert to Amgen. Given Servier’s notice to Amgen, all worldwide rights related to the development and commercialization of omecamtiv mecarbil will now return to Cytokinetics commensurate with the effective termination of the Amgen Agreement on May 20, 2021.

As a result of Amgen's and Servier's elections to terminate the Amgen Agreement and the Servier Agreement respectively, we will dedicate resources to ensure the transition of the programs related to omecamtiv mecarbil and CK-136 (formerly known as AMG 594) to us. In addition, we anticipate engaging with regulatory authorities in 2021 regarding the results of GALACTIC-HF with the objective to assess potential regulatory paths for an NDA submission for omecamtiv mecarbil and continuing our commercial planning activities. Finally, we plan to evaluate a wide range of corporate development strategies for potential co-development, co-commercialization and licensing deals in relation to omecamtiv mecarbil and our other drug candidates in order to mitigate the cost effects of the termination of the Amgen Agreement and Servier Agreement and enhance our commercial capabilities.

In February 2017, we entered into a Royalty Purchase Agreement (the "RPI Royalty Purchase Agreement") with RPI Finance Trust ("RPI"). Under the RPI Royalty Purchase Agreement, Cytokinetics sold a portion of its right to receive royalties from Amgen on future net sales of omecamtiv mecarbil and other compounds with the same mechanism of action as omecamtiv mecarbil that are subject to the Amgen Agreement (together the "Amgen Alliance Compounds") to RPI for a one-time payment of \$90 million. The RPI Royalty Purchase Agreement provides for the sale of a royalty to RPI of 4.5% on worldwide net sales of omecamtiv mecarbil and other Amgen Alliance Compounds, subject to a potential increase of up to an additional 1% under certain circumstances (delay in US marketing approval). The RPI Royalty Purchase Agreement further provides that in the event Amgen elects to terminate the Amgen Agreement, we are obliged to enter into an agreement with RPI to preserve RPI's rights under the RPI Royalty Purchase Agreement, which includes the payment by Cytokinetics of 4.5% of its worldwide net sales of omecamtiv mecarbil and other Amgen Alliance Compounds, subject to a potential increase of up to an additional 1% under certain circumstances (delay in US marketing approval).

Omecamtiv mecarbil

Our lead drug candidate from our cardiac contractility program is omecamtiv mecarbil, a novel cardiac myosin activator. We are developing omecamtiv mecarbil 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 clinical trials development program in patients with heart failure with reduced ejection fraction under our strategic alliance with Amgen.

Omecamtiv mecarbil: Clinical Development

GALACTIC-HF: GALACTIC-HF is a Phase 3 cardiovascular outcomes clinical trial of omecamtiv mecarbil which was 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 was conducted under a Special Protocol Assessment ("SPA") with the FDA. GALACTIC-HF completed enrollment in mid-2019, having enrolled 8,256 symptomatic chronic heart failure patients with reduced ejection fraction in over 1,000 sites in 35 countries who were either currently hospitalized for a primary reason of heart failure or had had a hospitalization or admission to an emergency room for heart failure within one year prior to screening. Patients were 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 time to all-cause death.

In February 2020, we announced the publication of a manuscript relating to the design of GALACTIC-HF in the *Journal of American College of Cardiology: Heart Failure (JACC: HF)*.

In March 2020, we announced that patient baseline characteristics and demographics from GALACTIC-HF were published during the Virtual American College of Cardiology 69th Annual Scientific Session together with the World Congress of Cardiology (ACC.20/WCC Virtual).

In May 2020, we announced that the FDA granted fast track designation for omecamtiv mecarbil for the potential treatment of chronic heart failure with reduced ejection fraction. Fast track designation may potentially expedite the review of a drug that is intended for the treatment of a serious or life-threatening disease or condition and demonstrates the potential to address an unmet medical need for such a disease or condition.

On October 2, 2020, we announced that a manuscript detailing the baseline characteristics from GALACTIC-HF was published in the *European Journal of Heart Failure*.

On October 5, 2020, we announced that new data were presented at the Heart Failure Society of America (HFSA) Virtual Annual Scientific Meeting 2020. The first presentation provided analyses of outcomes research in patients with heart failure with reduced ejection fraction whose characteristics were similar to those patients who met eligibility criteria for GALACTIC-HF. The second presentation provided post hoc analyses of effects of omecamtiv mecarbil on right ventricular function arising from COSMIC-HF.

On October 8, 2020 we announced the topline results from GALACTIC-HF and on November 13, 2020 we announced the primary results from GALACTIC-HF. The results of GALACTIC-HF show that after a median duration of follow-up of 21.8 months, the trial demonstrated a statistically significant effect of treatment with omecamtiv mecarbil to reduce risk of the primary composite endpoint of cardiovascular (“CV”) death or heart failure events (heart failure hospitalization and other urgent treatment for heart failure) compared to placebo in patients treated with standard of care. A first primary endpoint event occurred in 1,523 of 4,120 patients (37.0%) in the omecamtiv mecarbil group and in 1,607 of 4,112 patients (39.1%) in the placebo group (hazard ratio, 0.92; 95% confidence interval [CI] 0.86, 0.99; $p=0.025$). This effect was observed without evidence of an increase in the overall rates of myocardial ischemic events, ventricular arrhythmias or death from cardiovascular or all causes.

The statistically significant reduction in the composite of heart failure events or CV deaths, without significant imbalances in the overall incidence of adverse events across treatment arms, was observed in one of the broadest and most diverse range of patients enrolled in a contemporary heart failure trial. GALACTIC-HF included both inpatients and outpatients, and with a high representation of participants with moderate to severe heart failure symptoms as well as lower ejection fraction, systolic blood pressure and renal function.

No reduction in the secondary endpoint of time to CV death was observed. Death from cardiovascular causes occurred in 808 (19.6%) patients treated with omecamtiv mecarbil and 798 patients (19.4%) assigned to placebo (hazard ratio, 1.01; 95% CI, 0.92 to 1.11; $p=0.86$). The pre-specified analysis of change from baseline to week 24 in the KCCQ total symptom score by randomization setting (inpatient mean difference [95% CI]: 2.50 [0.54, 4.46], outpatient mean difference: -0.46 [-1.40, 0.48], joint $P = 0.028$) did not meet the significance threshold of $P=0.002$ based upon the multiplicity control testing procedure. No other secondary endpoints were met in accordance with the prespecified statistical analysis.

The effect of omecamtiv mecarbil was consistent across most prespecified subgroups and with a potentially greater treatment effect suggested in patients with a lower left ventricular ejection fraction (LVEF $\leq 28\%$, $n=4,000$, hazard ratio, 0.84; 95% CI 0.77, 0.92; interaction $p=0.003$). Omecamtiv mecarbil also significantly decreased NT-proBNP concentrations by 10% (95% CI 6-14%) at Week 24 compared to placebo.

The overall safety profile of omecamtiv mecarbil in GALACTIC-HF appeared to be consistent with data from previous trials. Adverse events and treatment discontinuation of study drug were balanced between the treatment arms. In general, the overall rates of myocardial ischemia, ventricular arrhythmias and death were similar between treatment and placebo groups. Additionally, there was no significant difference in the change in systolic blood pressure between baseline and at 24 or 48 weeks between the omecamtiv mecarbil and placebo groups. There was a small but significant decrease in heart rate in participants assigned to omecamtiv mecarbil compared to placebo at both timepoints. Median cardiac troponin I concentration increased 4 ng/L (95% CI 3-5; limit of detection, 6 ng/L) from baseline with omecamtiv mecarbil compared to placebo.

On December 7, 2020, we announced additional results from GALACTIC-HF. These results of GALACTIC-HF showed that the effect of omecamtiv mecarbil on the primary composite endpoint in GALACTIC-HF was consistent across most prespecified subgroups and with a potentially greater treatment effect suggested in patients with a lower left ventricular ejection fraction (LVEF $\leq 28\%$, $n=4,456$, hazard ratio, 0.84; 95% CI 0.77, 0.92; interaction $p=0.003$). Supplemental analyses of this lower ejection fraction subgroup in GALACTIC-HF showed that this potentially greater treatment effect in patients who received omecamtiv mecarbil was consistently observed in patients with characteristics that may indicate advanced heart failure status, such as being hospitalized within the last 3 months (HR 0.83, 95% CI 0.74 – 0.93, $p=0.001$), having New York Association Class III or IV heart failure (HR 0.80, 95% CI 0.71 – 0.90, $p<0.001$), higher N-terminal-pro brain natriuretic peptide levels (HR 0.77, 95% CI 0.69 – 0.87, $p<0.001$), and lower blood pressures (HR 0.81, 95% CI 0.70 – 0.92, $p=0.002$). The absolute risk reductions (ARR) ranged from 5.2% to 8.1% in these subgroups as compared to the ARR of 2.1% observed in the overall population.

Additionally, a supplemental analysis of the continuous relationship between ejection fraction and the hazard ratio for the primary composite endpoint in GALACTIC-HF suggested a potentially stronger treatment effect of omecamtiv mecarbil in patients with increasingly lower ejection fractions.

We are continuing to review prespecified analyses and supplemental analyses of results of GALACTIC-HF. In addition, we plan on engaging regulatory authorities in 2021 with the objective to assess potential regulatory paths and continuing our commercial planning activities. As a consequence of Amgen's election to terminate the Amgen Agreement, we are engaging with Amgen to transition development and commercialization activities with respect to omecamtiv mecarbil to us by May 20, 2021.

METEORIC-HF: In collaboration with Amgen, we are conducting METEORIC-HF, a second Phase 3 clinical trial intended to evaluate its potential to increase exercise performance. Patients are being randomized in a 2:1 fashion to omecamtiv mecarbil, which is started at 25 mg twice daily and titrated to 25, 37.5 or 50 mg twice daily based on the same pharmacokinetics-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. After temporarily suspending enrollment in METEORIC-HF due to the COVID-19 pandemic earlier this year, we resumed enrollment in June. We believe enrollment may be completed in the first half of 2021. After the effective termination of the Amgen Agreement, we will be solely responsible for the conduct of METEORIC-HF.

Omecamtiv mecarbil: Microgenics Immunoassay Development

Amgen and Microgenics Corporation ("Microgenics") are parties to that certain Collaborative Development and Commercialization Agreement, dated July 26, 2012 (as amended from time to time, the "Assay Agreement"), for the development of an antibody-based immunoassay (the "OM Assay") used for the in vitro measurement of concentrations of omecamtiv mecarbil in human blood and other bodily fluids, as well as related calibrator and controls, based on immunoassay technologies developed by Microgenics and its affiliates suitable for application on automated chemistry analyzers. The OM Assay is intended to ensure personalized dose optimization of omecamtiv mecarbil in patients being treated.

Following Amgen's notification of its decision to terminate the Amgen Agreement, we have commenced discussions with Microgenics related to the potential assignment of the Assay Agreement from Amgen to us and the continued development of the OM Assay and related regulatory filings and commercial planning activities by Microgenics such that the OM Assay may be approved by the FDA and other regulatory authorities and deployed for commercialization upon commercial launch of omecamtiv mecarbil.

CK-136 (formerly known as AMG 594)

CK-136 is a novel, selective, oral, small molecule cardiac troponin activator which was discovered under our joint research program with Amgen. In preclinical models, CK-136 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 March 2020, we announced that preclinical data were presented at the Keystone Symposium "Charting a New Course for Heart Failure: From Discovery to Data," demonstrating that CK-136 selectively increases calcium sensitivity of cardiac muscle fibers and increases cardiac contractility.

CK-136: Clinical Development

In collaboration with Cytokinetics, Amgen conducted 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 CK-136 in healthy subjects. As a consequence of Amgen's election to terminate the Amgen Agreement, we are engaging with Amgen to transition development activities with respect to CK-136 to us by May 20, 2021.

CK-274

CK-274 is a novel, oral, small molecule cardiac myosin inhibitor that our company scientists discovered. CK-274 arose from an extensive chemical optimization program conducted with attention to therapeutic index and pharmacokinetic properties that may translate into next-in-class potential in clinical development. CK-274 was purposely 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. The preclinical pharmacokinetics of CK-274 were characterized, evaluated and optimized for potential rapid onset, ease of titration and rapid symptom relief in the clinical setting. The initial focus of the development program for CK-274 will include an extensive characterization of its pharmacokinetics/pharmacodynamic (“PK/PD”) relationship as has been a hallmark of Cytokinetics’ industry-leading 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 conducted 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. In September 2019 we presented data from the Phase 1 study of CK-274 at the HFSA 23rd Annual Scientific Meeting in Philadelphia. The study met its primary and secondary objectives to assess the safety and tolerability of single and multiple oral doses of CK-274, describe the pharmacokinetics of CK-274 and its pharmacodynamic effects as measured by echocardiography, as well as to characterize the PK/PD relationship with regards to cardiac function. These data support the advancement of CK-274 into a Phase 2 clinical trial in patients with obstructive HCM (REDWOOD-HCM), which started in the first quarter of 2020 and will continue to be conducted in 2021.

In February 2020, we announced that preclinical data were presented at the Biophysical Society 64th Annual Meeting demonstrating that CK-274 has a distinct binding site on cardiac myosin, and selectively reduces cardiac myosin activity *in vitro*.

On October 27, 2020, we presented preclinical data at the American Association of Pharmaceutical Scientists (AAPS) 2020 PharmSci 360 showing that CK-274 demonstrated desirable pharmacokinetics *in vivo*, supporting the intended pharmacokinetic profile of once daily oral dosing and steady state plasma concentrations reached within two weeks of dosing onset in humans and steady state plasma concentrations achieved within two weeks of initiation of dosing.

On December 9, 2020, we announced that interim analysis of data from Cohort 1 of REDWOOD-HCM showed patients experienced substantial reductions in the average resting left ventricular outflow tract gradient (LVOT-G) as well as the post-Valsalva LVOT-G (defined as resting gradient <30 mmHg and post-Valsalva gradient <50 mmHg). These clinically relevant decreases in pressure gradients were achieved with only modest decreases in average left ventricular ejection fraction (LVEF); there were no dose interruptions due to LVEF falling below 50%, the prespecified safety threshold. Pharmacokinetic data were similar to those observed in Phase 1. In addition, the safety and tolerability data were supportive of continued dose escalation with no serious adverse events attributed to study treatment reported by the investigators.

Based on the interim analysis of data from Cohort 1 of REDWOOD-HCM, the steering committee and the data monitoring committee of REDWOOD-HCM recommended that the trial proceed to Cohort 2. Cohort 2 of REDWOOD-HCM is expected to enroll patients at centers in North America and Europe. Enrollment in Cohort 2 of REDWOOD-HCM is expected to complete in the first quarter of 2021 and full results from REDWOOD-HCM across both Cohort 1 and Cohort 2 are expected in mid-2021.

On January 11, 2021, we announced that the FDA granted orphan drug designation to CK-274 for the treatment of symptomatic HCM.

On January 13, 2021, we announced that the first patient had been dosed in Cohort 2 of REDWOOD-HCM, thereby earning a \$2.5 million milestone payment to us under our agreement with Ji Xing.

Ji Xing Strategic Alliance

On July 14, 2020, we entered into that certain License and Collaboration Agreement with Ji Xing (the “Ji Xing License Agreement”), pursuant to which we granted to Ji Xing an exclusive license to develop and commercialize CK-274 in China and Taiwan. Under the terms of the Ji Xing License Agreement, we received from Ji Xing an upfront payment of \$25.0 million. We may be eligible to receive from Ji Xing milestone payments totaling up to \$200.0 million for the achievement of certain development and commercial milestone events in connection to CK-274 in the field of obstructive hypertrophic cardiomyopathy, or oHCM, and/or non-obstructive hypertrophic cardiomyopathy, or nHCM, and other indications. In addition, Ji Xing will pay us tiered royalties in the low-to-high teens range on the net sales of CK-274 in China and Taiwan, subject to certain reductions for generic competition, patent expiration and payments for licenses to third party patents. The Ji Xing License Agreement, unless terminated earlier, will continue on a market-by-market basis until expiration of the relevant royalty term.

CK-271

In the first quarter of 2020, we submitted an IND for CK-271, a second cardiac myosin inhibitor, and we were notified by the FDA that the IND was accepted. One of the hallmarks of Cytokinetics’ research and development approach has been to advance multiple compounds to enable potential expansion of a drug development program into different indications and patient populations. On September 23, 2020, we announced that the first participants have been dosed in a Phase 1 placebo-controlled, single ascending dose clinical study of CK-271. The primary objective of this Phase 1 placebo-controlled, single ascending dose clinical study in healthy adults is to assess the safety and tolerability of CK-271. The secondary objective is to evaluate the pharmacokinetic profile of CK-271 following single oral ascending doses. The study design includes three cohorts, with 8 adults per cohort randomized (6:2) in a blinded fashion to CK-271 or placebo. Dose escalation decisions were made after review of the available safety, pharmacokinetic, and echocardiography data. In 2020, we completed our planned Phase 1, single-dose pharmacokinetic evaluation and tolerability assessments of CK-271 in healthy volunteers and determined it to be suitable for further development. We are evaluating its potential for its further development in connection with our plans to conduct a broad development program for our cardiac myosin inhibitor(s) in HCM and potentially other indications.

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).

Astellas Strategic Alliance

Our strategic alliance with Astellas to advance novel therapies for diseases and medical conditions associated with muscle impairment and weakness commenced in 2013 under the License and Collaboration Agreement, dated June 21, 2013 between the parties (the “Astellas Agreement”). Initially we 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, in 2014, 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.

On April 23, 2020, Cytokinetics and Astellas entered into two agreements, which, taken together, amend and restate our research, development and commercialization collaboration with Astellas under the Astellas Agreement, as set out below.

Cytokinetics and Astellas signed a Fast Skeletal Regulatory Activator Agreement dated April 23, 2020 (the “Astellas FSRA Agreement”). As a result of the FSRA Agreement, Cytokinetics will now have exclusive control and responsibility for Cytokinetics’ future development and commercialization of reldesemtiv, CK-601 and other fast skeletal regulatory activator (collectively “FSRA”) compounds and products, and accordingly, Astellas agreed to terminate its license to all FSRA compounds and related products. Under the Astellas FSRA Agreement, Astellas agreed to pay one-third of the out-of-pocket clinical development costs which may be incurred in connection with Cytokinetics’ potential Phase 3 clinical trial of reldesemtiv in ALS up to a maximum contribution by Astellas of \$12 million. In addition, Astellas agreed to non-cash contributions to Cytokinetics, which include the transfer of its existing inventories of active pharmaceutical ingredient of reldesemtiv and CK-601. Astellas also agreed to the continued conduct of ongoing stability studies pertaining to such existing inventories of active pharmaceutical ingredient, at Astellas’ cost. In exchange, Cytokinetics will pay Astellas a low- to mid- single digit royalty on sales of reldesemtiv in the United States, Canada, United Kingdom and the European Union until the later of (i) ten years following the first commercial sale of such product in a major market country, or (ii) December 31, 2034, subject to certain royalty reduction provisions. Cytokinetics would not owe Astellas royalties on sales of reldesemtiv in any other country, or on the sale of any FSRA compounds or related products other than reldesemtiv.

Cytokinetics and Astellas also signed the Astellas OSSA Agreement. The Astellas OSSA Agreement is an amendment and restatement of the Astellas Agreement and removes the FSRA compounds and related products from the collaboration.

Under the Astellas OSSA Agreement, Astellas extended the joint research program at Cytokinetics focused on the discovery of additional next-generation skeletal muscle activators (other than FSRAs) through December 31, 2020, with a minimum of fifteen (15) research FTE’s being supported by Astellas. The parties have subsequently agreed to extend this joint research program through March 31, 2021, with up to five (5) research FTE’s at Cytokinetics being supported by Astellas.

In addition, under the Astellas OSSA Agreement, Astellas has exclusive rights to co-develop and commercialize skeletal sarcomere activators (other than FSRA compounds and products) in all indications, subject to certain development and commercialization rights of Cytokinetics; Cytokinetics may co-promote and conduct certain commercial activities in the U.S., Canada and/or Europe under agreed scenarios. Astellas will be responsible for the costs associated with the development of all collaboration products under the Astellas OSSA Agreement, subject to Cytokinetics’ option to co-fund certain development costs as described below. Cytokinetics retains an option to conduct early-stage development for certain agreed indications at its initial expense, subject to reimbursement if development continues under the collaboration. Astellas will reimburse Cytokinetics for certain expenses associated with its co-promotion activities. The Astellas OSSA Agreement also provides for Cytokinetics to lead certain activities relating to the commercialization of collaboration products for neuromuscular indications in the U.S., Canada and Europe under particular scenarios.

If development candidates are identified and advance in clinical research, the Astellas OSSA Agreement contains provisions related to shared development roles between Cytokinetics and Astellas, and opportunities for Cytokinetics to co-invest and/or co-promote under certain conditions. In the case of molecules taken forward solely by Astellas, Cytokinetics would receive development and regulatory milestones of \$25 to \$35 million per product, up to \$250 million for all products, except under certain scenarios, commercial milestones of up to \$200 million, and royalties that range from a mid-single digit level to low double-digits. In the event of co-investment by Cytokinetics and approvals in certain indications, Cytokinetics would receive royalties ranging from mid-to-high double digits (not to exceed an incremental rate in the mid-twenties).

Astellas may terminate the Astellas OSSA Agreement as to any particular product or territory, or in its entirety, upon 180 days advance written notice following expiration of the research term.

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 granted reldesemtiv orphan drug designation for the potential treatment of SMA in 2017 and for the potential treatment of ALS in 2019. The European Medicines Agency (“EMA”) granted orphan medicinal product designation to reldesemtiv for the potential treatment of SMA in July 2019 and for the potential treatment of ALS in March 2020.

Reldesemtiv: Clinical Development

SMA: In 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. 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 in 2018 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, suggesting that as 6MWD increased, disease burden assessed by that domain of the SMA-HI was reduced.

In 2019, we announced that we received feedback from the FDA that the 6MWD 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.

In 2019, we announced that data from two preclinical studies of reldesemtiv showed that the addition of reldesemtiv to treatment with SMN upregulators (nusinersen and SMN-C1, an analogue to risdiplam) significantly increased muscle force in a mouse model of SMA.

ALS: In collaboration with Astellas, we conducted FORTITUDE-ALS. This trial enrolled 458 eligible ALS patients who were 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 was the change from baseline in the percent predicted slow vital capacity (“SVC”) at 12 weeks. Secondary endpoints included slope of the change from baseline in the mega-score of muscle strength measured by hand held dynamometry 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; and plasma concentrations of reldesemtiv at the sampled time points during the study. Exploratory endpoints measured included 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 the change from baseline in quality of life (as measured by the ALS Assessment Questionnaire-5) in patients on reldesemtiv.

In 2019, we announced that results of FORTITUDE-ALS. FORTITUDE-ALS did not achieve statistical significance for a pre-specified dose-response relationship in its primary endpoint of change from baseline in SVC after 12 weeks of dosing ($p=0.11$). Similar analyses of ALSFRS-R and slope of the Muscle Strength Mega-Score yielded p -values of 0.09 and 0.31, respectively. However, patients on all dose groups of reldesemtiv declined numerically less than patients on placebo for SVC and ALSFRS-R, with larger differences emerging over time.

While the dose-response analyses for the primary and secondary endpoints did not achieve statistical significance at the level of 0.05, in a post-hoc analysis pooling the doses together, patients who received reldesemtiv in FORTITUDE-ALS declined less than patients who received placebo. The trial showed numerical effects favoring reldesemtiv across dose levels and timepoints with clinically meaningful magnitudes of effect observed at 12 weeks for the primary and secondary endpoints. The differences between reldesemtiv and placebo in SVC and ALSFRS-R total score observed after 12 weeks of treatment were still evident at follow-up, four weeks after the last dose of study drug.

The incidence of early treatment discontinuations, serious adverse events and clinical adverse events in FORTITUDE-ALS were similar between placebo and active treatment arms. The most common clinical adverse effects in the trial included fatigue, nausea and headache. The leading cause for early termination from FORTITUDE-ALS for patients who received placebo was progressive disease; the leading cause for early termination for patients who received reldesemtiv was a decline in cystatin C based estimated glomerular filtration rate (“eGFR”), a measure of renal function. Elevations in transaminases and declines in cystatin C eGFR were dose-related.

In 2019, post-hoc analyses from FORTITUDE-ALS were presented. The analyses demonstrated that, in the combined middle and faster progressing tertiles of patients, the decline in the ALSFRS-R total score from baseline to week 12 in patients who received any dose of reldesemtiv was significantly smaller than the decline on placebo, while no significant difference between reldesemtiv and placebo was observed in slower progressing patients.

In 2019, we presented subgroup analyses of FORTITUDE-ALS showing that the effect of reldesemtiv on patients with ALS was similar whether or not patients were also receiving edaravone and/or riluzole.

On December 14, 2020, we announced that additional post-hoc analyses from FORTITUDE-ALS evaluating how baseline patient characteristics impacted the effect of treatment with reldesemtiv versus placebo. When patients were divided into faster, middle and slower progressing tertiles based on pre-study ALSFRS-R progression rates, the middle and fastest progressing tertiles of patients combined showed a 27% difference at 12 weeks between patients receiving reldesemtiv versus placebo (1.15 ALSFRS-R points, $p=0.011$), compared to 18% (0.4 points; $p=0.43$) in the slowest progressing tertile. In general, patients with a longer symptom duration were slower progressors; 59% of those with SD >24 months were in the slowest tertile. Most patients who were minimally affected with an ALSFRS-R ≥ 45 at baseline were also slow progressors. In comparing the treatment effect of slow progressing patients with symptoms ≤ 24 months and a baseline ALSFRS-R score of ≤ 44 to the original primary analysis population, the effect size and statistical significance increased, despite reducing the number of analyzed patients. In an analysis of the total study population ($n=458$), combining all patients who received reldesemtiv and comparing to those who received placebo, the change from baseline to week 12 in the ALSFRS-R total score showed a least square mean (LSM) difference of 0.87 ($p=0.013$). However, limiting the analysis population to patients with symptoms ≤ 24 months and a baseline ALSFRS-R score of ≤ 44 ($n=272$), the LSM difference was 1.84 ($p=0.0002$). Together, these post-hoc analyses indicate that the impact of treatment with reldesemtiv was more apparent in patients with faster pre-study rates of progression, which include patients with short symptom duration and lower baseline ALSFRS-R scores.

Also on December 14, 2020, we announced the design of COURAGE-ALS (Clinical Outcomes Using Reldesemtiv on ALSFRS-R in a Global Evaluation in ALS), the planned Phase 3 clinical trial of reldesemtiv in patients with ALS. COURAGE-ALS is expected to enroll approximately 555 patients with ALS. Patients will be randomized 2:1 to receive 300 mg of reldesemtiv or matching placebo dosed orally twice daily for 24 weeks, followed by a 24-week period in which all patients will receive 300 mg of reldesemtiv twice daily. Eligible patients will be within the first two years of their first symptom of muscle weakness, have a vital capacity of $\geq 65\%$ predicted, and a screening ALS Functional Rating Scale – Revised (ALSFRS-R) ≤ 44 . Patients currently taking stable doses of Radicava® (edaravone) and/or Rilutek® (riluzole) will be permitted and randomization stratified accordingly. The primary efficacy endpoint will be change from baseline to 24 weeks in ALSFRS-R. Secondary endpoints include combined assessment of ALSFRS-R total score; time to onset of respiratory insufficiency and survival time up to week 24 using a joint rank test; change from baseline to 24 weeks for vital capacity; ALSAQ-40; and bilateral handgrip strength. Two unblinded interim analyses by the Data Monitoring Committee are planned. The first will assess for futility, 12 weeks after approximately one-third or more of the planned sample size is randomized. A second interim analysis will also assess for futility, and there will be an option for a fixed increase in total enrollment if necessary to augment the statistical power of the trial. This Phase 3 clinical trial design builds on insights gained from FORTITUDE-ALS, the Phase 2 clinical trial of reldesemtiv in patients with ALS, further exploring the hypothesis that fast skeletal muscle activation with reldesemtiv may be an important therapeutic strategy in ALS.

Next Generation Fast Skeletal Muscle Troponin Activators

In 2018, we announced the advancement of CK-601, a next-generation FSTA, into IND-enabling studies, which triggered a \$2.0 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

Currently 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 are conducting preclinical research on other chemically and pharmacologically distinct skeletal sarcomere activators in our continued joint research program with Astellas, which was extended through March 31, 2021.

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.

Manufacturing Resources

Our drug candidates require precise high-quality manufacturing that is compliant with good manufacturing processes (or foreign equivalent) and other applicable laws. We have no manufacturing capabilities and rely on third party sources for the supply or sourcing of raw materials, the manufacture of active pharmaceutical ingredients and the manufacture and packaging of finished drug products for both clinical trial materials and commercial supply.

We have established relationships with leading contract manufacturers for the manufacture and supply of active pharmaceutical ingredients and finished drug product for use in our clinical trials. Clinical trial materials sourced from contract manufacturers generally have longer lead times than commercial product, have a higher cost per unit as a result of smaller batch sizes, and may be more difficult to manufacture to necessary specifications. As a result, we endeavor to seek contract manufacturers with proven manufacturing capabilities and quality standards whom we can rely on for timely supply.

In the event any of our drug candidates were to be approved for commercial marketing by the FDA or any other regulatory authorities, we would need to enter into contractual arrangements with contract manufacturers for the manufacture of active pharmaceutical ingredients and packaging of finished drug product for commercial use. Currently, we have no supply agreements for the commercial supply of active pharmaceutical ingredients or finished drug product.

Prior to Amgen's election to terminate the Amgen Agreement, we relied on Amgen for the supply of omecamtiv mecarbil for use in clinical trials of omecamtiv mecarbil, including the on-going Phase 3 clinical trial, METEORIC-HF. In furtherance to Amgen's transition obligations arising as a result of its election to terminate the Amgen Agreement, Amgen shall transfer to us certain requested quantities of the active pharmaceutical ingredient and finished drug product that we believe will be sufficient for use in METEORIC-HF. In addition, we are in discussions with Amgen and the contract manufacturers that Amgen has historically utilized for the manufacture and supply of omecamtiv mecarbil active pharmaceutical ingredient and finished drug product in view of enabling our ability to utilize such contract manufacturers and their existing manufacturing processes and capabilities for the potential manufacture and supply of omecamtiv mecarbil active pharmaceutical ingredient and finished drug product for commercial use.

We have contract manufacturing arrangements in place with leading contract manufacturers for the development and supply of CK-274 active pharmaceutical ingredient and finished drug product for use in our clinical trials, including REDWOOD-HCM.

Historically, we have relied on Astellas for the supply of reldesemtiv. As a result of our entry into the Astellas FSRA Agreement, we are in the process of completing the transfer of manufacture of reldesemtiv active pharmaceutical ingredient and finished drug product to leading contract manufacturers with whom we have existing supply agreements.

Intellectual Property Resources

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, 2020, we owned, co-owned or licensed 71 issued U.S. patents, over 550 issued patents in various foreign jurisdictions, and over 280 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, U.S. patents covering our skeletal muscle sarcomere activators including, but not limited to reldesemtiv, and a U.S. patent covering CK-274, which expire in 2027, 2031 and 2039, 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.

In relation to our collaborations, our partners may develop or have developed, solely or with us, intellectual property rights in connection with our drug candidates. Our collaboration agreements generally contain provisions regarding ownership, prosecution and maintenance, assignment and license rights to enable us to protect and benefit from intellectual property rights that are developed with or by our partners. For example, with respect to the Amgen Agreement, as a result of Amgen's election to terminate the Amgen Agreement, (i) licenses granted to Amgen under Cytokinetics controlled intellectual property under the Amgen Agreement shall terminate and all rights to exploit and practice such intellectual property rights shall revert to us, (ii) Amgen shall transfer and assign to us all rights in and to any trademarks specific to omecamtiv mecarbil and other compounds subject to the Amgen Agreement, (iii) Amgen shall grant to us an exclusive worldwide license to Amgen-controlled patent rights relating to omecamtiv mecarbil and other compounds subject to the Amgen Agreement and (iv) Amgen shall grant to us a non-exclusive worldwide license with respect to Amgen's trade secrets that were developed or utilized by Amgen in connection with omecamtiv mecarbil and other compounds subject to the Amgen Agreement solely to develop, manufacture and commercialize omecamtiv mecarbil and such other compounds.

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 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. 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. For example, an unknown third party has filed an opposition against a granted European patent relating to compositions of omeacamtiv mecarbil. Although we are defending the patent, we cannot be certain that the patent will be upheld as valid. If our European patent is invalidated, our intellectual property position in Europe could be weakened and it could have a negative impact 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. 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."

Compliance with 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 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 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.
- *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:* 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 (the "E.U."), 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 E.U. member states implementing additional legislation. The General Data Protection Regulation (E.U.) 2016/679 is a regulation in E.U. law on data protection and privacy for all individuals within the E.U. 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. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label may be subject to significant liability. However, physicians may, in their independent medical judgment, prescribe legally available products for off-label uses. The FDA does not regulate the behavior of physicians in their choice of treatments but the FDA does restrict manufacturer's communications on the subject of off-label use of their products. 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. 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.

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."

Other Healthcare Laws. We are currently or will in the future be subject to healthcare regulation and enforcement by the federal government and the states in which we will conduct our business once our product candidates are approved by the FDA and commercialized in the United States. In addition to the FDA's restrictions on marketing of pharmaceutical products, the U.S. healthcare laws and regulations that may affect our ability to operate include: the federal fraud and abuse laws, including the federal anti-kickback and false claims laws; federal data privacy and security laws; and federal transparency laws related to payments and/or other transfers of value made to physicians and other healthcare professionals and teaching hospitals. Many states have similar laws and regulations that may differ from each other and federal law in significant ways, thus complicating compliance efforts. For example, states have anti-kickback and false claims laws that may be broader in scope than analogous federal laws and may apply regardless of payer. In addition, state data privacy laws that protect the security of health information may differ from each other and may not be preempted by federal law. Moreover, several states have enacted legislation requiring pharmaceutical manufacturers to, among other things, establish marketing compliance programs, file periodic reports with the state, make periodic public disclosures on sales and marketing activities, report information related to drug pricing, require the registration of sales representatives, and prohibit certain other sales and marketing practices. If our operations are found to be in violation of these laws, we may be subject to significant civil, criminal, and administrative penalties, including, without limitation, damages, fines, imprisonment, exclusion from participation in government healthcare programs, additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Additionally, in the United States and some foreign jurisdictions there have been, and continue to be, several legislative and regulatory changes and proposed reforms of the healthcare system in an effort to contain costs, improve quality, and expand access to care. These reform initiatives may, among other things, result in modifications to the aforementioned laws and/or the implementation of new laws affecting the healthcare industry. Similarly, a significant trend in the healthcare industry is cost containment. Third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Our ability to commercialize any of our products successfully will depend in part on the extent to which coverage and adequate reimbursement for these products and will be available from third-party payors. Even if we obtain coverage for a given drug product, the associated reimbursement rate may not be adequate to cover our costs, including research, development, intellectual property, manufacture, sale and distribution expenses, or may require co-payments that patients find unacceptably high. Coverage and reimbursement policies for drug products can differ significantly from payor to payor as there is no uniform policy of coverage and reimbursement for drug products among third-party payors in the United States. There may be significant delays in obtaining coverage and reimbursement as the process of determining coverage and reimbursement is often time-consuming and costly.

Cytokinetics Human Capital

As of December 31, 2020, we had 184 employees and 51 consultants. 27 of those employees have more than 10 years tenure with us and 53 have over 5 years of service. In 2020 our turnover was 3.4%, which we believe is a lower attrition rate compared to the industry. Notwithstanding the historic low turnover in 2020, we routinely have lower attrition than our industry average.

We are committed to fostering and maintaining an environment that engenders collaboration and teamwork, respect, transparency and candor. Furthermore, we endeavor to provide our employees with the tools, training and resources they need to successfully grow their careers and experience development opportunities.

Our compensation and benefit programs are designed to enable us to attract and retain the best employees in a very competitive life science sector in a high cost of living geography of the Northern California Bay Area. We benchmark and survey the market to ensure we maintain competitive programs for our employees.

We have a rigorous annual goal setting and goal evaluation process under the supervision of our Board of Directors and senior management to assist our employees in understanding what is expected of them individually and as an organization.

In 2020 the Company implemented a formal Diversity & Inclusion program to, among other things, evaluate our recruiting and hiring practices and metrics.

We routinely survey our employees and transparently share the full results, take action on areas identified as needing improvement and look to augment those emphasized as important to our employees.

Our Compensation and Talent Committee of the Board of Directors reviews employee engagement, reward programs, human resource metrics, including attrition, retention and staffing on an on-going basis.

COVID-19 Business Update

We are continuing to closely monitor the impact of the global COVID-19 pandemic on our business and continue to take proactive efforts designed to protect the health and safety of our employees, patients, study investigators and clinical research staff, and to maintain business continuity. We believe that the measures we are implementing are appropriate and are helping to reduce the transmission of COVID-19, and we will continue to monitor and seek to comply with guidance from governmental authorities and adjust our activities as appropriate.

Based on guidance issued by federal, state and local authorities, we transitioned to a remote work model for a vast majority of our employees effective March 16, 2020, while maintaining certain essential in-person laboratory functions in order to advance key research and development initiatives, supported by the implementation of updated onsite procedures. We have since implemented a voluntary return to work for our employees subject to precautionary measures such as mandatory temperature checks for those employees that do work on site from time to time.

In the conduct of our business activities, we are also taking actions designed to protect the safety of patients and healthcare professionals. For patients already enrolled in our clinical trials, we and our partners are working closely with study investigators and clinical trial site staff to continue treatment in compliance with trial protocols and to uphold trial integrity, while working to observe government and institutional guidelines designed to safeguard the health and safety of patients and site staff.

After temporarily suspending enrollment in METEORIC-HF and REDWOOD-HCM due to the COVID-19 pandemic in the second quarter of 2020, we resumed enrollment in both trials by mid year 2020. We believe enrollment in METEORIC-HF may be completed in the first half of 2021. Enrollment in Cohort 2 of REDWOOD-HCM is expected to complete in the first quarter of 2021 and full results from REDWOOD-HCM across both Cohort 1 and Cohort 2 are expected in mid-2021.

While the potential economic impact brought by, and the duration of, the COVID-19 pandemic may be difficult to assess or predict, the pandemic could result in significant and prolonged disruption of global financial markets, reducing our ability to access capital, which could in the future negatively affect our liquidity. In addition, a recession or market correction resulting from the spread of COVID-19 could materially affect our business and the value of our common stock.

While we expect the COVID-19 pandemic to continue to affect our business operations, the extent of the impact on our clinical development and regulatory efforts and the value of and market for our common stock will depend on future developments that are highly uncertain and cannot be predicted with confidence at this time, such as the ultimate duration of the pandemic, travel restrictions, quarantines, social distancing and business closure requirements in the U.S. and in other countries, and the effectiveness of actions taken globally to contain and treat COVID-19. For additional information about risks and uncertainties related to the COVID-19 pandemic that may impact our business, our financial condition and our results of operations, see the section titled “Risk Factors” under Part I, Item 1A in this Annual Report on Form 10-K.

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 part or all 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 part or all 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, royalty monetization agreements, a revenue interest 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 through our Funding Agreement with RTW Royalty Holdings, and reimbursements, milestone and royalty payments that we may receive under our collaboration agreements with Amgen, Astellas and Ji Xing. 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.

For example, under the Funding Agreement, we have the right to exercise an option to receive up to \$90.0 million in cash upon initiation of a global registration program for CK-274 in each of oHCM and nHCM if certain conditions are met. No assurance can be given that any of such conditions will be fulfilled prior to expiration of our ability to exercise our option pursuant to the Funding Agreement, and all or part of the proceeds made available to us, may need to be utilized for the prepayment or repayment of other outstanding indebtedness at the time under our Loan and Security Agreement, dated as of May 17, 2019 (the "Term Loan Agreement") with Oxford Finance LLC ("Oxford"), as collateral agent, and Silicon Valley Bank and Oxford as lenders party thereto (the "Lenders"), pursuant to which the Lenders made available to us a \$45.0 million loan (the "Term Loan") or any other indebtedness we have outstanding at that time. Moreover, in the event we were to exercise our option pursuant to the Funding Agreement, we would be obligated to make royalty payments to RTW Royalty Holdings of up to 4% of our net sales of CK-274 in the United States, the European Union, Switzerland, the United Kingdom and certain other countries in Europe (collectively referred to as the "CK-274 Territory"), which may or may not be more favorable to us than prevailing interest rates at the time of exercising such option.

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, grant licenses on terms that may not be favorable to us, or, as in the case of the Funding Agreement, incur obligations to pay amounts based on future sales of our product candidate CK-274. 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.

Our business is currently adversely affected and could be materially and adversely affected in the future by the effects of disease outbreaks, epidemics and pandemics, including the ongoing COVID 19 pandemic. The COVID-19 pandemic continues to adversely impact our business and could materially and adversely affect our operations, as well as the businesses or operations of our or our partners, manufacturers, CROs or other third parties with whom we or our partners conduct business.

Disease outbreaks and epidemics in regions where we, our partners or other third parties on which we rely have manufacturing facilities, clinical trial sites or other important operations or pandemics such as the COVID-19 pandemic could adversely affect our business, including by causing significant disruptions in our operations and/or in the operations of third-party manufacturers and CROs upon whom we rely. For example, in March 2020, the World Health Organization declared the COVID-19 outbreak a pandemic, and the pandemic has presented a substantial public health and economic challenge around the world and is affecting employees, patients, communities and business operations, as well as the U.S. economy and financial markets. In this regard, the COVID-19 pandemic and government measures taken in response have had a significant impact, both direct and indirect, on business and commerce, as significant reductions in business-related activities have occurred, supply chains have been disrupted and manufacturing and clinical development activities have been curtailed or suspended.

Remote work policies, quarantines, shelter-in-place and similar governmental orders, shutdowns or other restrictions on the conduct of business operations related to the COVID-19 pandemic could materially and adversely affect our operations. Based on guidance issued by federal, state and local authorities, we have implemented a voluntary work-from-home policies for our employees. The effects of the safer community order and our work-from-home and voluntary work-on-site policies may negatively impact productivity, disrupt our, or our partners to which we rely, business and delay clinical programs and timelines, the magnitude of which will depend, in part, on the length and severity of the restrictions and other limitations on the ability to conduct business in the ordinary course. In connection with these measures, we may be subject to claims based upon, arising out of, or related to COVID-19 and our actions and responses thereto, including any determinations that we have made and may in the future make with respect to our onsite operations. These and similar, and perhaps more severe, disruptions in operations could negatively impact our business, operating results and financial condition.

In addition, our clinical trials or those conducted by our partners may continue to be adversely affected by the COVID-19 pandemic. For example, in 2020 we temporarily suspended enrollment in METEORIC-HF and REDWOOD-HCM due to the COVID-19 pandemic, although we have since resumed enrollment in both trials. Clinical site initiation, conduct, and patient enrollment has been and may continue to be delayed due to prioritization of medical resources toward the COVID-19 pandemic and restrictions on the ability to travel. It may not be possible to carry out some aspects of clinical trial protocols if quarantines or other restrictions impede patient movement or interrupt healthcare services. It may be necessary to suspend enrollment at some or all clinical trial sites to comply with shelter in place orders, and to reduce the risk to patients, their caretakers, and healthcare providers from contracting COVID-19. Patients may be forced to quarantine or comply with shelter-in-place orders or may refuse home healthcare visits, particularly in medically vulnerable patient populations. Similarly, principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19 but also may be pulled into clinical care and away from clinical research, may adversely impact our or our partner's clinical trial operations. Further, our clinical trial patients who contract COVID-19 may (i) experience unexpected adverse medical events that could be wrongfully attributable to our investigational drugs, and (ii) experience endpoint events because of COVID-19 that could confound the interpretation of data and results relating to our investigational drugs arising from our clinical trials. Other key clinical trial activities, such as clinical trial site data monitoring and site inspections, may also be adversely affected due to limitations on travel imposed or recommended by governmental authorities, which may impact the integrity of subject data and clinical study endpoints. Finally, disruptions in our supply chain due to loss of the ability of sites to dispense study drug, travel and import/export restrictions or lack of raw materials may result in an interruption, or delays in receiving, supplies of our drug candidates from our contract manufacturing organizations or study sites, which in turn may also adversely affect our clinical trials.

The spread of COVID-19, which has caused a broad impact globally, may materially affect us economically. While the potential economic impact brought by, and the duration of, COVID-19 may be difficult to assess or predict, a widespread pandemic could result in significant disruption of global financial markets, reducing our ability to access capital, which could in the future negatively affect our liquidity. In addition, a recession or market correction resulting from the spread of COVID-19 could materially affect our business and the value of our common stock.

The ultimate impact of the COVID-19 pandemic or a similar health epidemic is highly uncertain and subject to change. We do not yet know the full extent of potential delays or impacts on our business, our clinical trials, healthcare systems or the global economy as a whole. However, these effects could have a material impact on our operations, and we will continue to monitor the COVID-19 situation closely.

Our indebtedness and liabilities could limit the cash flow available for our operations, expose us to risks that could adversely affect our business, financial condition and results of operations and impair our ability to satisfy our obligations under the 2026 Notes and our Term Loan.

As of December 31, 2020, we had \$183.0 million aggregate principal amount of indebtedness, comprised of \$45.0 million under our Term Loan, on a senior secured basis, and \$138.0 million under our convertible senior notes due 2026, or the 2026 Notes. Additionally, we have the ability to exercise an option for up to \$90.0 million in cash under the Funding Agreement, which, if utilized, will result in additional payment obligations of up to 4% of our net sales of CK-274 in the CK-274 Territory. Finally, under our RPI Royalty Purchase Agreement, we will have a payment obligation of 4.5% on worldwide net sales of omecantiv mecarbil and other Amgen Alliance Compounds, subject to a potential increase of up to an additional 1% under certain circumstances (delay in US marketing approval). We may also incur additional indebtedness to meet future financing needs. Our indebtedness could have significant negative consequences for our security holders and our business, results of operations and financial condition by, among other things:

- increasing our vulnerability to adverse economic and industry conditions;
- limiting our ability to obtain additional financing;
- requiring the dedication of a substantial portion of our cash flow from operations to service our indebtedness, which will reduce the amount of cash available for other purposes;
- limiting our flexibility to plan for, or react to, changes in our business;
- diluting the interests of our existing stockholders as a result of issuing shares of our common stock upon conversion of the notes; and
- placing us at a possible competitive disadvantage with competitors that are less leveraged than us or have better access to capital.

Our business may not generate sufficient funds, and we may otherwise be unable to maintain sufficient cash reserves, to pay amounts due under our indebtedness, including the 2026 Notes, and our cash needs may increase in the future. In addition, any required repurchase of the 2026 Notes for cash as a result of a fundamental change would lower our current cash on hand such that we would not have those funds available for us in our business. Further any future indebtedness that we may incur may contain financial and other restrictive covenants that limit our ability to operate our business, raise capital or make payments under our other indebtedness. If we fail to comply with these covenants or to make payments under our indebtedness when due, then we would be in default under that indebtedness, which could, in turn, result in that and our other indebtedness becoming immediately payable in full.

Covenants in our Term Loan Agreement, the indenture related to the 2026 Notes and the Funding 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 Term Loan Agreement.

The Term Loan Agreement and the indenture related to the 2026 Notes 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. In addition, should we exercise our option pursuant to the Funding Agreement, such agreement contains certain covenants applicable to us, including among other things, development and commercialization diligence obligations in connection to CK-274, use of proceeds, reporting and encumbrances, which could also restrict our business and operations, particularly in connection to our development and commercialization of CK-274.

Our failure to comply with any of the covenants could result in a default under the Term Loan Agreement, the indenture related to the 2026 Notes, or the Funding Agreement which could permit the creditors to declare all or part of any outstanding borrowings or other payment obligations to be immediately due and payable and/or enforce any outstanding liens against our assets.

In addition, certain provisions in the 2026 Notes and the related indenture could make a third party attempt to acquire us more difficult or expensive. For example, if a takeover constitutes a fundamental change under our indenture, then noteholders will have the right to require us to repurchase their notes for cash. In addition, if a takeover constitutes a make-whole fundamental change under our indenture, then we may be required to temporarily increase the conversion rate. In either case, and in other cases, our obligations under the notes and the Indenture could increase the cost of acquiring us or otherwise discourage a third party from acquiring us or removing incumbent management, including in a transaction that noteholders or holders of our common stock may view as favorable.

If we are unable to repay those amounts, the relevant creditors could proceed against the collateral granted to them to secure that debt (if any), 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 in connection to the Term Loan can also impose a 5.0% penalty. In addition, the Term Loan has interest only payments through December 31, 2021.

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 clinical-stage drug candidates include omecamtiv mecarbil for the potential treatment of heart failure, reldesemtiv for the potential treatment of ALS and potentially other indications associated with muscle weakness, and CK-274 for the potential treatment of HCM and potentially other indications. 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, including CK-274 and reldesemtiv, 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, including CK-274 and reldesemtiv, 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 our first-generation FSTA, 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.

GALACTIC-HF was conducted under an SPA agreement with FDA. However, even where the FDA agrees to the design, execution and analysis proposed in protocols reviewed under the SPA process, the FDA may revoke or alter its agreement in certain circumstances, and the FDA retains significant latitude and discretion in interpreting the terms of the SPA agreement and the data and results from any study that is subject to the SPA agreement. The existence of an SPA agreement in respect of GALACTIC-HF or any other trial does not guarantee that FDA would approve any resulting NDA in respect of any product that is the subject of any clinical trial subject to an SPA agreement.

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 dexpropipexole, 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 its 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.

Notwithstanding GALACTIC-HF having met its primary efficacy endpoint, there is no guarantee that the FDA or any other regulatory authority will approve omecamtiv mecarbil.

In November 2020, we announced the primary results from GALACTIC-HF, the Phase 3 trial of omecamtiv mecarbil. The results of GALACTIC-HF show that after a median duration of follow-up of 21.8 months, the trial demonstrated a statistically significant effect of treatment with omecamtiv mecarbil to reduce risk of the primary composite endpoint of CV death or heart failure events (heart failure hospitalization and other urgent treatment for heart failure) compared to placebo in patients treated with standard of care (HR: 0.92; 95% CI: 0.86, 0.99, p=0.025). The trial results, however, showed that no secondary endpoints were met. In particular, no reduction in the secondary endpoint of time to CV death was observed, and the KCCQ total symptom score by randomization setting did not meet the significance threshold of P=0.002 based upon the multiplicity control testing procedure. No assurances can be given that the primary endpoint results of GALACTIC-HF alone will be deemed sufficiently safe or efficacious to warrant approval by the FDA or any other regulatory authority.

In December 2020, we announced that supplemental analyses of this lower ejection fraction subgroup in GALACTIC-HF showed that this potentially greater treatment effect in patients who received omecamtiv mecarbil was consistently observed in patients with characteristics that may indicate advanced heart failure status, such as being hospitalized within the last 3 months (HR 0.83, 95% CI 0.74 – 0.93, p=0.001), having New York Association Class III or IV heart failure (HR 0.80, 95% CI 0.71 – 0.90, p<0.001), higher N-terminal-pro brain natriuretic peptide levels (HR 0.77, 95% CI 0.69 – 0.87, p<0.001), and lower blood pressures (HR 0.81, 95% CI 0.70 – 0.92, p=0.002). The absolute risk reductions (ARR) ranged from 5.2% to 8.1% in these subgroups as compared to the ARR of 2.1% observed in the overall population. Although the supplemental analyses showed that omecamtiv mecarbil potentially has a greater treatment effect in these subgroups of trial patients, no assurance can be given that the FDA or any other regulatory authority will consider any such subgroup analysis as the basis for an approval of omecamtiv mecarbil without requiring additional clinical trials.

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.

The transition of responsibilities for manufacturing, development, regulatory, commercial planning and other activities related to omecamtiv mecarbil and CK-136 (formerly known as AMG 594) from Amgen to us may not be completed effectively or efficiently and could result in substantial delays to these programs and significant increased costs to us.

On November 23, 2020, we announced that Amgen elected to terminate the Amgen Agreement and thereby end its collaboration with Cytokinetics, effective May 20, 2021, and that it intends to transition development and commercialization rights for omecamtiv mecarbil and CK-136 to us. Pursuant to the terms of the Amgen Agreement, upon the effective date of Amgen's termination, research, development and commercialization rights for compounds, including omecamtiv mecarbil and CK-136, will transition to us. In addition, Amgen will have certain obligations set forth in the Amgen Agreement, including: cooperating with Cytokinetics and its designee(s) to facilitate a reasonably smooth, orderly and prompt transition of the programs, including transfer and assignment to us of specified regulatory filings, data and other information; if requested by us, transferring inventory of compounds to us at our expense; to the extent possible and requested by us, assigning relevant third-party manufacturing agreements to us; and granting to us exclusive and non-exclusive licenses to certain intellectual property rights.

No assurance can be made that Amgen will cooperate with us and take such actions required of Amgen under the Amgen Agreement to transition the omecamtiv mecarbil and/or CK-136 programs to us effectively or efficiently. Amgen may not dedicate sufficient resources to enable a prompt and efficient transition; it could reallocate and not make available to us key personnel who are aware of vital program information; it could provide information and take actions in an uncoordinated and inefficient manner that is difficult for our personnel to receive, understand and/or utilize; it could fail to identify program information that we are unaware of and thereby denying us the benefits of such information; it could immediately halt its regulatory interactions and other development activities and/or obstruct us from undertaking such regulatory interactions and other development activities prior to the effective date of termination of the Amgen Agreement; and it could take a narrow interpretation of its transition obligations under the Amgen Agreement and thereby denying us the ability to continue the development activities of omecamtiv mecarbil or CK-136 without duplicative work, all of which could result in substantial delays in the development and/or commercialization programs related to omecamtiv mecarbil and/or CK-136.

No assurance can be made that we will have the full benefit of all contracts between Amgen and various third parties under which such third parties may have provided Amgen with relevant services and/or materials (including drug product and drug substance) for the benefit of the omecamtiv mecarbil and/or CK-136 programs. Certain contracts may not be assignable to us without the cooperation and consent of third parties, and third parties may be unwilling to enter into replacement contracts with us on acceptable terms or at all. In such cases, we would be forced to seek alternative third party service providers and/or CMOs, potentially leading to substantial delays in the omecamtiv mecarbil and/or CK-136 programs and significant costs to us.

No assurance can be made that Amgen will not develop products, or enable its partners to develop products, that compete with omecamtiv mecarbil and/or CK-136 and use the information and experience gained in developing omecamtiv mecarbil and/or CK-136 to its or its partners' competitive advantage, thereby substantially diminishing the commercial prospects for omecamtiv mecarbil and/or CK-136.

Finally, no assurance can be made that we will have or be able to mobilize the capital, personnel, systems or other recourses required by the effective termination of the Amgen Agreement to ensure our ability to meet our legal or regulatory responsibilities and obligations, to continue the development of the omecamtiv mecarbil and/or CK-136 programs, including the design and conduct of clinical trials of omecamtiv mecarbil and/or CK-136, without substantial delays to the timelines previously anticipated prior to Amgen's decision to terminate the Amgen Agreement or without significant costs as compared to our anticipated costs prior to Amgen's decision to terminate the Amgen Agreement, or to ensure commercial preparedness for a potential product launch of omecamtiv mecarbil. In such cases, 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 CK-136 or commercialization of the resulting drugs 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 of omecamtiv mecarbil and/or CK-136, which could harm our business.

The transition of omecamtiv mecarbil from Servier to Amgen may not be completed effectively or efficiently and could result in substantial delays to the omecamtiv mecarbil development program in Europe and significant increased costs to us.

On December 23, 2020, we announced that Amgen notified us that Servier elected to terminate the Servier Agreement. The termination of the Servier Agreement is effective as of March 18, 2021, after which all development, commercialization and other rights with respect to omecamtiv mecarbil previously granted by Amgen to Servier will revert to Amgen. Given Servier's notice to Amgen to terminate the Servier Agreement and given Amgen's decision to terminate the Amgen Agreement, all worldwide rights related to the development and commercialization of omecamtiv mecarbil will now return to Cytokinetics commensurate with the effective termination of the Amgen Agreement on May 20, 2021.

As we are not a party to the Servier Agreement, we are wholly dependent on Amgen and Servier to ensure that all development and pre-commercial activities of Servier in Europe and the Commonwealth of Independent States, including Russia, are properly transitioned to Amgen, so as to enable Amgen to facilitate a reasonably smooth, orderly and prompt transition of the programs in such territories to us.

The failure to successfully develop, validate and obtain regulatory clearance or approval of the OM Assay by Microgenics could harm our development and commercialization strategy for omecamtiv mecarbil.

An important element of our development and commercialization strategy for omecamtiv mecarbil is the development of the OM Assay used for the in vitro measurement of concentrations of omecamtiv mecarbil in human blood and other bodily fluids, which is intended to ensure personalized dose optimization of omecamtiv mecarbil. The Assay Agreement is not assignable without the consent of Microgenics, and although we have commenced discussions with Microgenics in connection with the potential assignment of the Assay Agreement from Amgen to us and the continued development of the OM Assay by Microgenics such that the OM Assay may be approved by the FDA and other regulatory authorities and ready for commercialization upon commercial launch of omecamtiv mecarbil, there is no guarantee that Microgenics will agree to such assignment or that we will be able to conclude an agreement with Microgenics on terms that are favorable to us.

The development of the OM Assay for novel therapeutic such as omecamtiv mecarbil can be complex from an operational and regulatory perspective because of the need for both the drug and the diagnostic to receive regulatory clearance or approval. Should the regulatory clearance or approval process for the OM Assay be delayed, it could impact our ability to successfully commercialize omecamtiv mecarbil. Moreover, the OM Assay may not be readily or economically available in all territories where omecamtiv mecarbil could ultimately be commercialized.

We will depend on Ji Xing for the development and commercialization of CK-274 in China and Taiwan.

Under the terms of the Ji Xing License Agreement, Ji Xing will be responsible for the development and commercialization of CK-274 in China and Taiwan. The timing and amount of any milestone and royalty payments we may receive under the Ji Xing License Agreement will depend in part on the efforts and successful commercialization of CK-274 by Ji Xing. We do not control the individual efforts of Ji Xing, and any failure by Ji Xing to devote sufficient time and effort to the development and commercialization of CK-274 or to meet its obligations to us, including for future milestone and royalty payments; or to adequately deploy business continuity plans in the event of a crisis, or to satisfactorily resolve significant disagreements with us could each have an adverse impact on our financial results and operations. We will also depend on Ji Xing to comply with all applicable laws relative to the development and commercialization of CK-274 in China and Taiwan. If Ji Xing were to violate, or was alleged to have violated, any laws or regulations during the performance of its obligations for us, it is possible that we could suffer financial and reputational harm or other negative outcomes, including possible legal consequences.

Any termination, breach or expiration of the Ji Xing License Agreement could have a material adverse effect on our financial position by reducing or eliminating the potential for us to receive milestones and royalties. In such an event, we may be required to devote additional efforts and to incur additional costs associated with pursuing the development and commercialization of CK-274 in China and Taiwan. Alternatively, we may attempt to identify and transact with a new sub-licensee, but there can be no assurance that we would be able to identify a suitable sub-licensee or transact on terms that are favorable to us.

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 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 our Phase 2b clinical trial of tirasemtiv in patients with ALS, 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 had assumed responsibility to conduct these activities for the ongoing development of omecamtiv mecarbil worldwide. Now that Amgen has elected to terminate the Amgen Agreement, we will need to engage with Amgen's existing contract manufacturers for the manufacture and packaging of omecamtiv mecarbil, and if we are unable to enter into new agreements on acceptable terms therewith, we may need to transfer the manufacturing to new contract manufacturers and incur delays and incur additional costs in doing so.

Prior to entry into the Astellas FSRA Agreement, Astellas had primary responsibility for the manufacturing for the ongoing development of reldesemtiv worldwide. Now that we have assumed responsibility for the ongoing development of reldesemtiv worldwide, we will need to effect a transfer of manufacturing of reldesemtiv to one or more contract manufacturers and to rely on such contract manufacturers for future supply.

Under the Ji Xing License Agreement, we have committed to providing Ji Xing with supply of CK-274 for development and commercialization of CK-274 in China and Taiwan, which we will have to source from our contract manufacturers. 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, and to fulfil our obligations under the Ji Xing License Agreement.

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, and also lead to our breach of the Ji Xing License Agreement, giving rise to the ability to terminate such agreement and other adverse consequences as stipulated in the Ji Xing License Agreement. 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.

Moreover, in the event any of our competitors were to develop their own drug candidates that have a similar mechanism of action to any of our drug candidates and compounds, any efficacy or safety concerns identified during the development of such similar drug candidates may have an adverse impact on the development of our own drug candidates. For example, if a competitors' drug candidate having a similar mechanism of action as any of our own drug candidates is shown in clinical trials to give rise to serious safety concerns or have poor efficacy when administered to the target patient population, the FDA or other regulatory bodies may subject our drug candidates to increased scrutiny, leading to additional delays in development and potentially decreasing the chance of ultimate approval of our own drug candidates.

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, our licensors 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 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 Corlanor® (ivabradine), Entresto® (sacubitril/valsartan) and Verquvo® (vericiguat). 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 AG, Merck & Co., Inc., Bayer AG, AstraZeneca PLC and Bristol-Myers Squibb Company. Omecamtiv mecarbil may also compete with currently approved drugs, such as in the SGLT2 class, that may expand their labels to include treatment of patients with heart failure, including Forxiga® (dapagliflozin), Invokana® (canagliflozin), and Jardiance® (empagliflozin). 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 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, AB Science, Alexion Pharmaceuticals, Amylyx Pharmaceuticals Inc, BrainStorm Cell Therapeutics, Medicinova, Inc., Mitsubishi Tanabe Pharma Corporation, Orphazyme, and Revasio Corporation. Also, if reldesemtiv is approved by the FDA or other regulatory authorities for the treatment of SMA, it may be used in combination with or compete with SPINRAZA® (nusinersen), Zolgensma® (onasemnogene abeparvovec-xioi) and/or Evrysdi™ (risdiplam) or any other potential new therapies being developed by companies including, but not limited to, F. Hoffman-La Roche Ltd. (in collaboration with PTC Therapeutics, Inc.). 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, Stealth BioTherapeutics, and Novartis (in collaboration with MorphoSys AG).

If CK-274 is approved for marketing by the FDA or other regulatory authorities for the treatment of HCM, it may compete with mavacamten, a drug candidate being developed by Bristol-Myers Squibb Company.

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 by the FDA and EMA for reldesemtiv for the potential treatment of SMA and ALS and orphan designation by the FDA for CK-274 for the potential treatment of symptomatic HCM; however, there can be no guarantee that we will receive orphan approval for reldesemtiv or CK-274, nor that we will be able to prevent third parties from developing and commercializing products that are competitive to reldesemtiv or CK-274.

We have been granted orphan drug designation in the U.S. by the FDA for reldesemtiv for the potential treatment of SMA and the potential treatment of ALS and for CK-274 for the potential treatment of symptomatic HCM. 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.

EMA has granted orphan medicinal product designation to reldesemtiv for the potential treatment of SMA and the potential treatment of ALS. Orphan medicinal product status in the E.U. 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 E.U. 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 CK-274 or to receive orphan status for reldesemtiv or CK-274 for any other indication or for any of our other drug candidates for any indication. We are not guaranteed to be granted orphan designation in the E.U. for CK-274 by the EMA. 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 E.U., 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 E.U. 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 E.U. 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 E.U., 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.

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 limited 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 omecamtiv mecarbil or our other potential drugs.

We currently have limited 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 and/or expand 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 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.

In relation to omecamtiv mecarbil specifically, prior to Amgen's notification of its election to terminate the Amgen Agreement, we expected that, consistent with the terms of such agreement, Amgen would bear primary operational and financial responsibility for the sales, marketing, manufacturing and distribution activities related to the product launch and commercialization of omecamtiv mecarbil. As a result of the anticipated termination of the Amgen Agreement, we must now build and/or expand our capabilities without Amgen's operational or financial support, which will result in significantly higher costs to us than what we had expected prior to Amgen's notification of its election to terminate the Amgen Agreement, and we may never be able to successfully build and/or expand our commercialization capabilities to fully substitute the capabilities of Amgen of which we were reliant upon. Moreover, as a result of Servier's notification of its election to terminate the Servier Agreement, we will need to seek a replacement partner in Europe with the expertise and resources to successfully launch and commercialize omecamtiv mecarbil in Europe or to establish our own commercial capabilities in Europe at our own cost and effort.

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 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. In addition, in December 2019, one of our employee’s email account suffered an unauthorized intrusion, leading to the submission and inadvertent payment of a fraudulent invoice in the amount of approximately one hundred thousand dollars. In December 2019, our IT systems were exposed to a ransomware attack, which partially impaired certain IT systems for a short period of time. Finally, in September 2020, one of our employees’ email account suffered unauthorized access as result of a phishing incident, but the Company believes no sensitive information was accessed. Although we do not believe that we have experienced any material losses related to security breaches, including in three recent email “phishing” incidents or the ransomware attack, 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 measures to protect our data security and information technology systems, such measures may not prevent these 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 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 Term 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 Term 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.

Conversion of our outstanding 2026 Notes may result in the dilution of existing stockholders, create downward pressure on the price of our common stock, and restrict our ability to take advantage of future opportunities.

The 2026 Notes may be converted into cash and shares of our common stock (subject to our right or obligation to pay cash in lieu of all or a portion of such shares). If shares of our common stock are issued to the holders of the 2026 Notes upon conversion, there will be dilution to our stockholders’ equity and the market price of our shares may decrease due to the additional selling pressure in the market. Any downward pressure on the price of our common stock caused by the sale or potential sale of shares issuable upon conversion of the 2026 Notes could also encourage short sales by third parties, creating additional selling pressure on our stock. The existence of the 2026 Notes and the obligations that we incurred by issuing them may restrict our ability to take advantage of certain future opportunities, such as engaging in future debt or equity financing activities.

The accounting method for the 2026 Notes could adversely affect our reported financial condition and results.

The accounting method for reflecting the 2026 Notes on our balance sheet, accruing interest expense for the notes and reflecting the underlying shares of our common stock in our reported diluted earnings per share may adversely affect our reported earnings and financial condition.

Under applicable accounting principles, the initial liability carrying amount of the 2026 Notes will be the fair value of a similar debt instrument that does not have a conversion feature, valued using our cost of capital for straight, unconvertible debt. We currently reflect the difference between the net proceeds from the sale of the 2026 Notes and the initial carrying amount as a debt discount for accounting purposes, which is amortized into interest expense over the term of the 2026 Notes. As a result of this amortization, the interest expense recognized for the 2026 Notes for accounting purposes is greater than the cash interest payments we will pay on the 2026 Notes, which results in lower reported net income. The lower reported income resulting from this accounting treatment could depress the trading price of our common stock and the 2026 Notes.

In addition, under certain circumstances we may be eligible to use the treasury stock method to reflect the shares underlying the 2026 Notes in our diluted earnings per share. Under this method, if the conversion value of the 2026 Notes exceeds their principal amount for a reporting period, then we will calculate our diluted earnings per share assuming that all the 2026 Notes were converted and that we issued shares of our common stock to settle the excess. However, if reflecting the 2026 Notes in diluted earnings per share in this manner is anti-dilutive, or if the conversion value of the 2026 Notes does not exceed their principal amount for a reporting period, then the shares underlying the 2026 Notes will not be reflected in our diluted earnings per share. In addition, if accounting standards change in the future and we are not permitted to use the treasury stock method, then our diluted earnings per share may decline. For example, in July 2019, the Financial Accounting Standards Board published an exposure draft proposing to amend these accounting standards to eliminate the treasury stock method for convertible instruments and instead require application of the “if-converted” method. Under that method, if it is adopted, diluted earnings per share would generally be calculated assuming that all the 2026 Notes were converted solely into shares of common stock at the beginning of the reporting period, unless the result would be anti-dilutive. The application of the if-converted method may reduce our reported diluted earnings per share.

Furthermore, if any of the conditions to the convertibility of the notes is satisfied, then we may be required under applicable accounting standards to reclassify the liability carrying value of the 2026 Notes as a current, rather than a long-term, liability. This reclassification could be required even if no noteholders convert their 2026 Notes and could materially reduce our reported working capital.

The capped call transactions may affect the value of the 2026 Notes and our common stock.

In connection with the issuance of the 2026 Notes, we entered into certain capped call transactions (the “Capped Call Transactions”) with the capped call counterparty. The Capped Call Transactions are generally expected to reduce the potential dilution as a result of conversion of the 2026 Notes and/or offset any cash payments we are required to make in excess of the principal amount of converted notes, as the case may be, with such reduction and/or offset subject to a cap.

In connection with establishing its initial hedge of the Capped Call Transactions, the capped call counterparty or its affiliates purchased shares of our common stock and/or entered into various derivative transactions with respect to our common stock. This activity could have increased (or reduced the size of any decrease in) the market price of our common stock or the 2026 Notes at that time.

In addition, the capped call counterparty or its affiliates may modify their hedge positions by entering into or unwinding various derivatives with respect to our common stock and/or purchasing or selling our common stock or other securities of ours in secondary market transactions (and are likely to do so on each exercise date of the Capped Call Transactions, which are expected to occur during the 60 trading day period beginning on the 61st scheduled trading day prior to the maturity date of the 2026 Notes, or following any termination of any portion of the Capped Call Transaction in connection with any repurchase, redemption or early conversion of the 2026 Notes). This activity could also cause or avoid an increase or a decrease in the market price of our common stock or the 2026 Notes.

We are subject to counterparty risk with respect to the Capped Call Transactions.

The capped call counterparty to the agreement related to the Capped Call Transactions (the “Capped Call Agreements”) is a financial institution, and we will be subject to the risk that the capped call counterparty may default or otherwise fail to perform, or may exercise certain rights to terminate, its obligations under the Capped Call Agreements. Our exposure to the credit risk of the capped call counterparty will not be secured by any collateral. If the capped call counterparty becomes subject to insolvency proceedings, we will become an unsecured creditor in those proceedings with a claim equal to our exposure at the time under such transaction. Our exposure will depend on many factors but, generally, our exposure will increase if the market price or the volatility of our common stock increases. In addition, upon a default or other failure to perform, or a termination of obligations, under the Capped Call Agreements by the capped call counterparty, we may suffer adverse tax consequences and more dilution than we currently anticipate with respect to our common stock. We can provide no assurances as to the financial stability or viability of the capped call counterparty.

We may not be able to complete our relocation to our new facility as scheduled prior to expiry of the lease to our existing facility.

On July 24, 2019, we entered into a lease agreement with KR Oyster Point 1, LLC (the “Kilroy”), a subsidiary of Kilroy Realty Corporation, relating to the lease of approximately 234,892 square feet of office and laboratory space at a facility (currently under construction) located in South San Francisco, California (the “New Facility”). Kilroy is expected to deliver possession of the New Facility in the fourth quarter of 2021, while the lease (the “Current Lease”) to our existing facility at 280 E Grand Avenue, South San Francisco (the “Old Facility”) expires on June 30, 2021. In the event that the New Facility is not delivered to us in sufficient time to allow us to move our operations to the New Facility as anticipated, whether as a result of potential construction delays attributable to the COVID 19 pandemic or otherwise, we may be required to holdover the Old Facility past expiry of its term, leading to: (i) additional costs (including holdover rent at 150% of our current rent); (ii) liability under our indemnification obligations owed to our current landlord under the Current Lease; and (iii) disruption to our business.

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.

The commercial success of our products depends on the availability and sufficiency of third-party payor coverage and reimbursement.

Patients in the United States and elsewhere generally rely on third-party payors to reimburse part or all of the costs associated with their prescription drugs. Accordingly, market acceptance of our products is dependent on the extent to which third-party coverage and reimbursement is available from government health administration authorities (including in connection with government healthcare programs, such as Medicare and Medicaid in the United States), private healthcare insurers and other healthcare funding organizations. Significant uncertainty exists as to the coverage and reimbursement status of any products for which we may obtain regulatory approval. Even if we obtain coverage for a given drug product, the associated reimbursement rate may not be adequate to cover our costs, including research, development, intellectual property, manufacture, sale and distribution expenses, or may require co-payments that patients find unacceptably high.

Coverage and reimbursement policies for drug products can differ significantly from payor to payor as there is no uniform policy of coverage and reimbursement for drug products among third-party payors in the United States. There may be significant delays in obtaining coverage and reimbursement as the process of determining coverage and reimbursement is often time-consuming and costly which will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage or adequate reimbursement will be obtained. It is difficult to predict at this time what third-party will decide with respect to coverage and reimbursement for our products.

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 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 expect that increased emphasis on cost containment measures in the United States by third-party payors to continue and will place pressure on pharmaceutical pricing and coverage. Coverage policies and third-party reimbursement rates may change at any time. Therefore, even if favorable coverage and reimbursement status is attained for one or more drug products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future. If we are unable to obtain and maintain sufficient third-party coverage and adequate reimbursement for our products, the commercial success of our drug products may be greatly hindered and our financial condition and results of operations may be materially and adversely affected.

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 2030, except for a temporary suspension from May 1, 2020 through March 31, 2021 due to the COVID-19 pandemic, 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 the Trump administration to repeal or replace certain aspects of the ACA. For example, former President Trump 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, eliminating 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 (the "Tax Act"). Additionally, on December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the ACA are invalid as well. The U.S. Supreme Court is currently reviewing this case, although it is unclear when a decision will be made. It is also unclear how such litigation 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. 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, particularly in light of the new Presidential administration. 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 E.U. 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. At the federal level, the Trump administration's budget proposal for fiscal year 2021 includes a \$135 billion allowance to support legislative proposals seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients, and increase patient access to lower-cost generic and biosimilar drugs. On March 10, 2020, the Trump administration sent "principles" for drug pricing to Congress, calling for legislation that would, among other things, cap Medicare Part D beneficiary out-of-pocket pharmacy expenses, provide an option to cap Medicare Part D beneficiary monthly out-of-pocket expenses and place limits on pharmaceutical price increases. Additionally, in May 2018, the Trump administration previously laid out a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contained 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. On July 24, 2020 and September 13, 2020, the Trump administration announced several executive orders relating to prescription drug pricing that seek to implement several of the administration's proposals. As a result, several federal agencies have issued regulations to address these initiatives. For example, on November 2020, the Centers for Medicare & Medicaid Services issued an interim rule implementing President Trump's Most Favored Nation executive order, which would tie Medicare Part B payments for certain physician-administered drugs to the lowest price paid in other economically advanced countries, effective January 1, 2021. On December 28, 2020, the United States District Court in Northern California issued a nationwide preliminary injunction against implementation of the interim final rule. Although some of these and other measures may require additional authorization to become effective, it is unclear whether the Biden administration will work to reverse these measures or pursue similar policy initiatives. 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 E.U. 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.

We cannot predict the likelihood, nature, or extent of health reform initiatives that may arise from future legislation or administrative action, particularly as a result of the new Biden presidential administration. Furthermore, it is possible that additional governmental action is taken in respect to the COVID-19 pandemic.

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, including 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 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 laws, including the False Claims Act, which can be enforced through whistleblower or qui tam actions, imposes penalties 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.
- 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 physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) 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. Beginning January 1, 2022, applicable manufacturers will also be required to report information regarding payments and other transfers of value provided during the previous year to physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified nurse anesthetists, and certified nurse-midwives.

- 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 and state and local laws that require the registration of sales representatives.

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.

European data collection is governed by restrictive regulations governing the collection, use, processing and cross-border transfer of personal information.

We may collect, process, use or transfer personal information from individuals located in the EU in connection with our business, including in connection with conducting clinical trials in the EU. Additionally, if any of our product candidates are approved, we may seek to commercialize those products in the EU. The collection and use of personal health data in the EU are governed by the provisions of the General Data Protection Regulation ((EU) 2016/679) ("GDPR"). This legislation imposes requirements relating to having legal bases for processing personal information relating to identifiable individuals and transferring such information outside of the European Economic Area, including to the United States, providing details to those individuals regarding the processing of their personal information, keeping personal information secure, having data processing agreements with third parties who process personal information, responding to individuals' requests to exercise their rights in respect of their personal information, reporting security breaches involving personal data to the competent national data protection authority and affected individuals, appointing data protection officers, conducting data protection impact assessments and record-keeping. The GDPR imposes additional responsibilities and liabilities in relation to personal data that we process and we may be required to put in place additional mechanisms ensuring compliance with the new data protection rules. Failure to comply with the requirements of the GDPR and related national data protection laws of the member states of the EU may result in substantial fines, other administrative penalties and civil claims being brought against us, which could have a material adverse effect on our business, financial condition and results of operations.

European data protection laws, including the GDPR, generally restrict the transfer of personal information from Europe, including the European Economic Area, United Kingdom and Switzerland, to the United States and most other countries unless the parties to the transfer have implemented specific safeguards to protect the transferred personal information. One of the primary safeguards allowing United States companies to import personal information from Europe has been certification to the EU-U.S. Privacy Shield and Swiss-U.S. Privacy Shield frameworks administered by the United States Department of Commerce. However, the Court of Justice of the EU recently invalidated the EU-U.S. Privacy Shield. The same decision also raised questions about whether one of the primary alternatives to the EU-U.S. Privacy Shield, namely, the European Commission's Standard Contractual Clauses, can lawfully be used for personal information transfers from Europe to the United States or most other countries. At present, there are few, if any, viable alternatives to the EU-U.S. Privacy Shield and the Standard Contractual Clauses. Although we rely primarily on individuals' explicit consent to transfer their personal information from Europe to the United States and other countries, in certain cases we have relied or may rely on the Standard Contractual Clauses. Authorities in the United Kingdom and Switzerland, whose data protection laws are similar to those of the EU, may similarly invalidate use of the EU-U.S. Privacy Shield and Swiss-U.S. Privacy Shield, respectively, as mechanisms for lawful personal information transfers from those countries to the United States. As such, if we are unable to rely on explicit consent to transfer individuals' personal information from Europe, which can be revoked, or implement another valid compliance solution, we will face increased exposure to substantial fines under European data protection laws as well as injunctions against processing personal information from Europe. Inability to import personal information from the European Economic Area, United Kingdom or Switzerland may also restrict our clinical trial activities in Europe; limit our ability to collaborate with CROs, service providers, contractors and other companies subject to European data protection laws; and require us to increase our data processing capabilities in Europe at significant expense. Additionally, other countries outside of Europe have enacted or are considering enacting similar cross-border data transfer restrictions and laws requiring local data residency, which could increase the cost and complexity of delivering our services and operating our business.

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.

Generic Risk Factors

We are obligated to develop and maintain proper and effective internal control over financial reporting. In the future, we may not complete our execution of our internal control over financial reporting in a timely manner, or these internal controls may not be determined to be effective, which may result in additional material misstatements in our consolidated financial statements and 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. As of December 31, 2019, we have remediated the material weakness related to our internal controls over financial reporting that were determined to be ineffective as of December 31, 2018. 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 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. During 2019, management conducted a remediation plan to address its material weakness, which included increasing the quality and level of resources with the accounting department and other enhancements and design improvements to our processes to improve the level of review of financial information.

Even though we remediated this material weakness as of December 31, 2019, we cannot be certain 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. 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.

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 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 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 in taxable years beginning prior to 2018 will continue to be governed by tax rules in effect prior to the 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 Tax Act, as modified by additional tax legislation enacted in 2020.

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 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 taxable years beginning 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.

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

In 2017, the U.S. government enacted the Tax Act that includes significant changes to the taxation of business entities, which was modified by additional federal tax legislation in 2020. 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, and states may enact suspensions or limitations on the use of net operating losses and tax credits (including, without limitation, California legislation enacted in 2020 that suspends the use of California NOLs and limits the use of certain California tax credits for certain periods). 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 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.

We expect that our stock price will fluctuate significantly, and you may not be able to resell your shares 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 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;
- volatility in the stock prices of other companies in our industry or in the stock market generally; and
- other factors described in this "Risk Factors" section.

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 revenue recognition standard, 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 not heavily 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.

A rating agency may not rate the notes or may assign a rating that is lower than expected.

We do not intend to seek to have the 2026 Notes rated by any rating agency. However, if one or more rating agencies rates the notes and assigns a rating that is lower than the rating that investors expect, or reduces their rating in the future, then the trading price of our common stock and the 2026 Notes could significantly decline.

In addition, market perceptions of our creditworthiness will directly affect the trading price of our common stock and the 2026 Notes. Accordingly, if a ratings agency rates any of our indebtedness in the future or downgrades or withdraws the rating, or puts us on credit watch, then the trading price of our common stock and the 2026 Notes will likely decline.

Provisions in our charter documents and under Delaware law could discourage a takeover that stockholders may consider favorable and may lead to entrenchment of management.

Our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions also could limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- establish a classified board of directors with three-year staggered terms, which may delay the ability of stockholders to change the membership of a majority of our board of directors;
- eliminate cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates;
- establish the exclusive right of our board of directors to elect a director to fill a vacancy created by the expansion of the board of directors or the resignation, death or removal of a director, which prevents stockholders from being able to fill vacancies on our board of directors;
- prohibit removal of directors without cause;

- authorize our board of directors to issue preferred stock and to determine the price and other terms of those shares, including preferences and voting rights, without stockholder approval, which could be used to significantly dilute the ownership of a hostile acquirer;
- authorize our board of directors to alter our bylaws without obtaining stockholder approval;
- require the approval of at least two-thirds of the shares entitled to vote at an election of directors to adopt, amend or repeal our bylaws or repeal the provisions of our amended and restated certificate of incorporation regarding the election and removal of directors;
- prohibit stockholder action by written consent, which forces stockholder action to be taken at an annual or special meeting of our stockholders;
- require that a special meeting of stockholders be called only by the chairman of the board of directors, the chief executive officer, the president or the board of directors, which may delay the ability of our stockholders to force consideration of a proposal or to take action, including the removal of directors; and
- provide for advance notice procedures that stockholders must comply with in order to nominate candidates to our board of directors or to propose matters to be acted upon at a stockholders' meeting, which may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of us.

We are also subject to the anti-takeover provisions contained in Section 203 of the Delaware General Corporation Law. Under Section 203, a corporation may not, in general, engage in a business combination with any holder of 15% or more of its capital stock unless the holder has held the stock for three years or, among other exceptions, the board of directors has approved the transaction. These provisions could discourage potential acquisition proposals and could delay or prevent a change in control transaction. They could also have the effect of discouraging others from making tender offers for our common stock, including transactions that may be in your best interests. These provisions may also prevent changes in our management or limit the price that investors are willing to pay for our stock.

Claims for indemnification by our directors and officers may reduce our available funds to satisfy successful third-party claims against us and may reduce the amount of money available to us.

Our amended and restated certificate of incorporation and amended and restated bylaws provide that we will indemnify our directors and officers, in each case to the fullest extent permitted by Delaware law.

In addition, as permitted by Section 145 of the Delaware General Corporation Law, our amended and restated bylaws and our indemnification agreements that we have entered into with our directors and officers provide that:

- we will indemnify our directors and officers for serving us in those capacities or for serving other business enterprises at our request, to the fullest extent permitted by Delaware law. Delaware law provides that a corporation may indemnify such person if such person acted in good faith and in a manner such person reasonably believed to be in or not opposed to the best interests of the registrant and, with respect to any criminal proceeding, had no reasonable cause to believe such person's conduct was unlawful;
- we may, in our discretion, indemnify employees and agents in those circumstances where indemnification is permitted by applicable law;
- we are required to advance expenses, as incurred, to our directors and officers in connection with defending a proceeding, except that such directors or officers shall undertake to repay such advances if it is ultimately determined that such person is not entitled to indemnification;
- we will not be obligated pursuant to our amended and restated bylaws to indemnify a person with respect to proceedings initiated by that person against us or our other indemnitees, except with respect to proceedings authorized by our board of directors or brought to enforce a right to indemnification;
- the rights conferred in our amended and restated bylaws are not exclusive, and we are authorized to enter into indemnification agreements with our directors, officers, employees and agents and to obtain insurance to indemnify such persons; and
- we may not retroactively amend our amended and restated bylaw provisions to reduce our indemnification obligations to directors, officers, employees and agents.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

Our facilities consist of 81,587 square feet of leased office and laboratory space in South San Francisco, California. Our current lease expires in June 2021. In July 2019, we amended the lease agreement for an additional 9,350 square feet within the same office location (the “Expansion Lease”). The Expansion Lease has an initial term of 39 months and commenced in January 2020.

In July 2019, we entered into a lease agreement for 234,892 square feet of office and laboratory space at a facility in South San Francisco (the “Oyster Point Lease”). The Oyster Point Lease has an initial term of 12 years and is expected to commence in the third quarter of 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

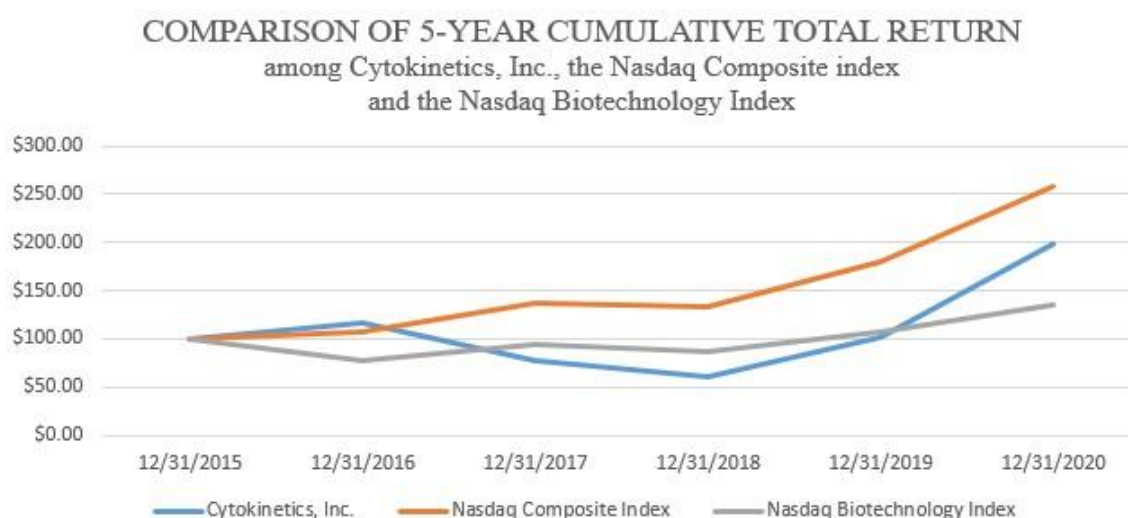
ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES**Market information for common stock**

Our common stock is listed on the Nasdaq Global Select Market under the symbol "CYTK." On February 23, 2021, the last reported sale price for our common stock was \$20.26 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.

Performance Graph

The comparisons in the table below are required by the SEC and are not intended to forecast or be indicative of possible future performance of our common stock. This graph shall not be deemed "soliciting material" or be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended ("Exchange Act"), or otherwise subject to the liabilities under that Section, and shall not be deemed to be incorporated by reference into any of our filings under the Securities Act, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing, except to the extent we specifically incorporate it by reference into such filing.

The following graph compares cumulative total return of our common stock with the cumulative total return of (i) The NASDAQ Composite Index, and (ii) The NASDAQ Biotechnology Index. The graph assumes (a) \$100 was invested on December 31, 2015 in each of our common stock, the stocks comprising the NASDAQ Composite Index and the stocks comprising the NASDAQ Biotechnology Index, and (b) the reinvestment of dividends into shares of common stock; however, no dividends have been declared on our common stock to date.



\$100 investment in stock or index	12/31/2015	12/31/2016	12/31/2017	12/31/2018	12/31/2019	12/31/2020
Cytokinetics, Inc.	\$ 100.00	\$ 116.16	\$ 77.92	\$ 60.42	\$ 101.43	\$ 198.66
Nasdaq Composite Index	\$ 100.00	\$ 107.50	\$ 137.86	\$ 132.51	\$ 179.19	\$ 257.38
Nasdaq Biotechnology Index	\$ 100.00	\$ 78.32	\$ 94.81	\$ 85.97	\$ 106.95	\$ 134.42

Holders of Record

As of February 23, 2021, we had 49 holders of record of common stock. The number of holders of record is based upon the actual number of holders registered as of such date and does not include holders of shares in "street name" or persons, partnerships, associates, corporations or other entities in security position listings maintained by depositories.

Dividends

We have never declared or paid, and do not anticipate declaring or paying in the foreseeable future, any cash dividends on our capital stock. Any future determination to declare cash dividends will be made at the discretion of our board of directors, subject to applicable laws, and will depend on our financial condition, results of operations, capital requirements, general business conditions and other factors that our board of directors may deem relevant.

Equity Compensation Information

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

Unregistered Sales of Equity Securities

None.

Issuer Purchases of Equity Securities

None.

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 next-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 health span 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 clinical-stage drug candidates are: omecamtiv mecarbil, a novel cardiac myosin activator, CK-136 (formerly known as AMG 594), a novel cardiac troponin activator, reldeesemtiv, a novel fast skeletal muscle troponin activator, CK-274, a novel cardiac myosin inhibitor, and CK-3772271 ("CK-271"), our second novel cardiac myosin inhibitor.

For further information regarding our business, refer to Part I, Item 1 (Business) of this Annual Report on Form 10-K.

Critical Accounting Policies 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

We recognize revenue when we transfer promised goods or services to customers in an amount that reflects the consideration for those goods or services. 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 agreements 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 to be recognized over time. We recognize 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 our 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 to RPI

We treat our liability to RPI related to sale of future royalties under the RPI Royalty Purchase Agreement as a debt financing, to be amortized under the effective interest rate method over the life of the related royalty stream.

Our liability to RPI related to sale of future royalties under the RPI Royalty Purchase Agreement (the “RPI Liability”) and related amortization are based on our current estimates of future royalties expected to be paid over the life of the arrangement. Concurrently with our entry into the RPI Royalty Purchase Agreement, we entered into a common stock purchase agreement with RPI. We allocated the consideration and issuance costs on a relative fair value basis to the RPI Liability and the common stock.

The RPI Royalty Purchase Agreement further provides that in the event Amgen elects to terminate the Amgen Agreement, we are obliged to enter into an agreement with RPI to preserve RPI’s rights under the RPI Royalty Purchase Agreement, which includes the payment by Cytokinetics of 4.5% of its worldwide net sales of omecamtiv mecarbil and other compounds with the same mechanism of action as omecamtiv mecarbil that are subject to the Amgen Agreement (together the “Amgen Alliance Compounds”), subject to a potential increase of up to an additional 1% under certain circumstances (delay in US marketing approval). Our obligation to enter into a new agreement with RPI does not impact our accounting treatment of the RPI Liability or our estimates.

The RPI Liability will be recognized using significant unobservable inputs. These inputs are derived using internal management estimates developed based on third party data and reflect management’s judgements, current market conditions surrounding competing products, and forecasts. The significant unobservable inputs include the estimated patient population, estimated selling price, estimated peak sales and sales ramp, the expected term of the royalty stream, timing of the expected launch and its impact on the royalty rate. A significant change in unobservable inputs could result in a material increase or decrease to the effective interest rate of the RPI Liability.

We will periodically assess the amount and timing of 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 previous estimates or the estimated timing of such payments is materially different than previous estimates, we will adjust the amortization of the RPI Liability related to sale of future royalties and prospectively recognize the related non-cash interest expense. We have updated the analysis to include the data released on October 8, 2020 relating to GALACTIC-HF. Our estimates regarding the amount and timing of future royalty payments have not changed as a result of Amgen’s election to terminate the Amgen Agreement or Servier’s election to terminate the Servier Agreement.

Results of Operations

A discussion of our results of operations for the year ended December 31, 2018 can be found in Item 7. Management’s Discussion and Analysis of Financial Condition and Results of Operations in our 2019 Annual Report.

Revenues

Our revenues since inception were primarily from our strategic alliances. 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.

License revenues for 2020 were the result of a series of transactions we entered into with RTW Royalty Holdings and Ji Xing related to Cytokinetics’ proprietary small molecule cardiac myosin inhibitor product referred to as CK-274 and other assets (together, the “RTW Transactions”).

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,			Change	
	2020	2019	2018	2020-2019	2019-2018
	(In millions)				
Research and development revenues	\$ 16.5	\$ 26.9	\$ 26.4	\$ (10.4)	\$ 0.5
License revenues	36.5	—	5.1	36.5	(5.1)
Milestone revenues	2.8	—	—	2.8	—
Total revenues	\$ 55.8	\$ 26.9	\$ 31.5	\$ 28.9	\$ (4.6)

Research and development revenues in 2020 and 2019 were primarily from our strategic alliances with Astellas and Amgen.

Research and development revenues from Astellas were \$6.6 million and \$13.1 million in 2020 and 2019, respectively, for reimbursements.

Research and development revenues from Amgen were \$10.0 million and \$13.8 million in 2020 and 2019, respectively, for reimbursements.

License revenues for 2020 was \$36.5 million and consisted of the residual allocation of consideration from the RTW Transactions.

Milestone revenues for 2020 were \$2.8 million and consisted primarily of the milestone earned from Ji Xing for the first patient dosed in Cohort 2 of REDWOOD-HCM.

We do expect future revenues from Amgen to decline due to the termination of the Amgen Agreement effective May 20, 2021.

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 increased to \$97.0 million in 2020 from \$86.1 million in 2019 primarily due to higher expenses for METEORIC-HF, for our cardiac myosin inhibitor program, and for reldesemtiv related to COURAGE-ALS offset by decreased spending for the Phase 2 clinical trial of reldesemtiv (FORTITUDE-ALS) which was completed in 2019.

Research and development expenses by program for 2020, 2019 and 2018 were:

	Years Ended December 31,			Change	
	2020	2019	2018	2020-2019	2019-2018
	(In millions)				
Cardiac muscle contractility	\$ 53.0	\$ 45.8	\$ 19.0	\$ 7.2	\$ 26.8
Skeletal muscle contractility	17.1	14.6	50.9	2.5	(36.3)
All other research programs	26.9	25.7	19.2	1.2	6.5
Total research and development expenses	<u>\$ 97.0</u>	<u>\$ 86.1</u>	<u>\$ 89.1</u>	<u>\$ 10.9</u>	<u>\$ (3.0)</u>

We may continue to develop reldesemtiv to treat ALS and SMA. Under the Astellas FSRA Agreement, Astellas has agreed to pay one-third of the out-of-pocket clinical development costs which may be incurred in connection with Cytokinetics' potential Phase 3 clinical trial of reldesemtiv in ALS up to a maximum contribution by Astellas of \$12 million. On December 14, 2020, we announced the design of COURAGE-ALS (Clinical Outcomes Using Reldesemtiv on ALSFRS-R in a Global Evaluation in ALS), the planned Phase 3 clinical trial of reldesemtiv in patients with ALS. In addition, Astellas agreed to non-cash contributions to Cytokinetics, which include the transfer of its existing inventories of active pharmaceutical ingredient of reldesemtiv and CK-601. Astellas has also agreed to the continued conduct of ongoing stability studies pertaining to such existing inventories of active pharmaceutical ingredient, at its cost.

Under our strategic alliance with Amgen, Amgen is responsible for the development of omecamtiv mecarbil until the effective termination of the Amgen Agreement (expected May 20, 2021). Following the effective termination of the Amgen Agreement, we expect to continue the Phase 3 development of omecamtiv mecarbil for the potential treatment of heart failure, at our own cost. 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. Under our strategic alliance with Ji Xing, Ji Xing is responsible for the development of CK-274 in China and Taiwan, and we may be entitled to receive milestone payments upon the achievement of certain development and commercial milestones.

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 potential 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 increased to \$52.8 million in 2020 from \$39.6 million in 2019, primarily due to an increase in personnel related costs including stock-based compensation and higher outside service spend.

General and administrative expenses by program for 2020, 2019 and 2018 were:

	Years Ended December 31,			Change	
	2020	2019	2018	2020-2019	2019-2018
	(In millions)				
Total general and administrative expenses	\$ 52.8	\$ 39.6	\$ 31.3	\$ 13.2	\$ 8.3

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 for 2020, 2019 and 2018 were:

	Years Ended December 31,			Change	
	2020	2019	2018	2020-2019	2019-2018
	(In millions)				
Term loan	\$ 4.9	\$ 5.2	\$ 3.8	\$ (0.3)	\$ 1.4
Convertible notes	10.8	1.4	—	9.4	1.4
Warrants	0.2	—	—	0.2	—
Other	0.1	—	—	0.1	—
Total interest expense	\$ 16.0	\$ 6.6	\$ 3.8	\$ 9.4	\$ 2.8

Interest expense in 2020 and 2019 consists of interest expense related to the Term Loan Agreement and respective warrants by and among the Company, Oxford and Silicon Valley Bank and interest expense related to the 2026 Notes. Approximately half of the 2026 Notes' interest expense is due to the amortization of the discount associated with the equity component of the 2026 Notes.

Interest expense increased in 2020 compared to 2019 primarily due to the convertible notes that were issued in November 2019 and offset by the decline in the term loan interest rate year over year.

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

Non-cash interest expense related to the RPI Liability related to sale of future royalties in 2020, 2019 and 2018 results from accretion of the liability related to sale of future royalties. This non-cash interest expense will continue to increase until omecamtiv mecarbil is commercialized and we start paying royalties to RPI in excess of the interest being accreted.

The RPI Royalty Purchase Agreement provides that in the event Amgen elects to terminate the Amgen Agreement, we are obliged to enter into an agreement with RPI to preserve RPI's rights under the RPI Royalty Purchase Agreement, which includes the payment by Cytokinetics of 4.5% of its worldwide net sales of omecamtiv mecarbil and other Amgen Alliance Compounds, subject to a potential increase of up to an additional 1% under certain circumstances (delay in US marketing approval). Our obligation to enter into a new agreement with RPI does not impact our accounting treatment of the RPI Liability or our estimates.

Interest and Other Income, net

Interest and other income, net for 2020, 2019 and 2018 consisted primarily of interest income generated from our cash, cash equivalents and investments.

We divested an equity investment in fiscal 2020 (classified as a Level 1 investment in our short-term investments) with a fair value of \$3.0 million for the year ended December 31, 2020, which resulted in an increase in interest income of \$2.6 million in 2020. In 2019, this equity investment resulted in a \$0.3 million increase in interest income.

Liquidity and Capital Resources

Our cash, cash equivalents and investments and a summary of our borrowings and working capital is summarized as follows:

	December 31, 2020	December 31, 2019
	(In millions)	
Financial assets:		
Cash and cash equivalents	\$ 83.0	\$ 36.4
Short-term investments	381.1	188.7
Total cash, cash equivalents and marketable securities	<u>\$ 464.1</u>	<u>\$ 225.1</u>
Borrowings:		
Term loan, net	\$ 46.2	\$ 45.1
Convertible notes, net	89.5	84.2
Total borrowings	<u>\$ 135.7</u>	<u>\$ 129.3</u>
Working capital:		
Current assets	\$ 474.2	\$ 233.8
Current liabilities	31.2	26.0
Working capital	<u>\$ 443.0</u>	<u>\$ 207.8</u>

The following table shows a summary of our cash flows for the periods set forth below:

	Years Ended December 31,		
	2020	2019	2018
	(In millions)		
Net cash provided by (used in) operating activities	\$ 8.9	\$ (90.9)	\$ (101.2)
Net cash (used in) provided by investing activities	(196.5)	(74.7)	5.1
Net cash provided by financing activities	234.1	159.8	13.1
	<u>\$ 46.5</u>	<u>\$ (5.8)</u>	<u>\$ (83.0)</u>

Sources and Uses of Cash in 2020

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 and interest on investments. We have generated significant operating losses since our inception. Our expenditures are primarily related to research and development activities.

Net cash provided by operating activities was \$8.9 million for 2020 which include a net loss of \$127.3 million largely due to ongoing research and development activities, and general and administrative expenses to support those activities. Net loss for 2020 included, among other items: non-cash stock-based compensation, non-cash interest expense related to sale of future royalties and non-cash interest expense related to debt. The net loss was offset by \$87.0 million in deferred revenues with respect to an agreement to sell to RTW Royalty Holdings our interest in certain future royalties on net sales of products containing the compound mavacamten that is being developed by Bristol-Myers Squibb Company. These funds were collected in 2020.

Net cash used in investing activities was \$196.5 million in 2020 and was primarily due to purchases of investments offset by proceeds from maturity of investments. Cash purchases of property plant and equipment was also included for \$11.1 million which will be primarily be utilized in our new building.

Net cash provided by financing activities was \$234.1 million in 2020 and was primarily due to \$188.9 million proceeds related to issuance of common stock in an underwritten public offering, proceeds from RTW private placement, stock based activities, and claims settlement with certain institutional investors that were beneficial owners of our common stock related to the disgorgement of short swing profits pursuant to Section 16(b) of the Exchange Act.

Public Offering of Common Stock

In July 2020, we closed an underwritten public offering of 8.4 million shares of our common stock at a public offering price per share of \$24.00, which included the exercise in full by the underwriters of their option to purchase up to 1,093,750 shares of our common stock at the same price. The gross proceeds were \$201.3 million and net proceeds were approximately \$188.9 million, after deducting underwriting discounts, commissions and offering costs.

RTW Transactions

On July 14, 2020, we entered into the RTW Transactions with RTW Royalty Holdings and Ji Xing. The RTW Transactions include entering into a licensing and collaboration agreement with Ji Xing, the sale of Cytokinetics common stock to the RTW Investors (as defined below), an agreement to sell to RTW Royalty Holdings our interest in certain future royalties on net sales of products containing the compound mavacamten that is being developed by Bristol-Myers Squibb Company (formerly by MyoKardia, Inc.) and the ability for the Company to obtain additional funding in the future from RTW Royalty Holdings, upon the achievement of certain clinical trial milestones, in exchange for future royalty payments as further discussed below. As a result, we have or expect to receive a combination of committed capital, funding and sale proceeds from the RTW Investors, RTW Royalty Holdings and Ji Xing.

On July 14, 2020, we entered into Common Stock Purchase Agreements (each, a “CSPA”) with each of RTW Master Fund, Ltd., RTW Innovation Master Fund, Ltd. and RTW Venture Fund Limited (collectively, the “RTW Investors”). The CSPAs provide for the sale and issuance of an aggregate of 2.0 million shares of common stock of Cytokinetics (the “Shares”) at a price per share of \$25.00 and an aggregate purchase price of \$50.0 million. The closing occurred on July 14, 2020. The RTW Investors have agreed to certain trading and other restrictions with respect to the Shares, including a restriction on sales or other transfers of the Shares, subject to certain exceptions, for a period of two years from the closing date, which period will be extended if certain conditions are met.

As of December 31, 2020, we have received \$25.0 million related to the licensing and collaboration agreement with Ji Xing, \$50.0 million associated with the sale of Cytokinetics common stock to the RTW Investors and \$85.0 million associated with the agreement to sell RTW Royalty Holdings our interest in certain future royalties on net sales of products containing the compound mavacamten that is being developed by Bristol-Myers Squibb Company (formerly by MyoKardia Inc.).

Funding Agreement

We entered into a Funding Agreement (the “Funding Agreement”) with RTW Royalty Holdings. Pursuant to the Funding Agreement, RTW Royalty Holdings has committed to provide up to \$90.0 million (the “Funding Commitment”), to fund our development and commercialization of CK-274 in nHCM and oHCM. Half of the Funding Commitment will be available, at our option, if certain clinical trial milestones of CK-274 for oHCM are achieved by January 14, 2023, and the remaining \$45.0 million of the Funding Commitment will be available, at our option, if certain clinical trial milestones of CK-274 for nHCM are achieved by January 14, 2024. If we develop CK-274 in another indication, we will negotiate an additional funding commitment from RTW to fund our development and commercialization of CK-274 in such other indication (other than oHCM or nHCM).

In exchange for the Funding Commitment and upon receipt of such funding from RTW Royalty Holdings, we have agreed to make payments to RTW Royalty Holdings equal to 2%, if RTW Royalty Holdings funds \$45.0 million of the Funding Commitment, or 4%, if RTW Royalty Holdings funds the full \$90.0 million of the Funding Commitment, in each case in respect of net sales of CK-274 by us and any of our licensees in the CK-274 Territory. In addition, should we exercise our option draw borrowings pursuant to the Funding Agreement, such agreement contains certain covenants applicable to us, including, among other things, development and commercialization diligence obligations in connection to the CK-274 Territory, use of proceeds, reporting and encumbrances. There are no performance obligations related to the Funding Agreement, as access to the Funding Commitment is at the option of the Company and based upon the achievement of certain development milestones.

The Funding Agreement contains customary conditions to disbursement, which may include the consent of our senior secured lenders, Oxford and SVB, at the time of disbursement. On July 16, 2020, we entered into an amendment to the Term Loan Agreement, as defined in Financial Statement Note 6 – Debt, which permits, subject to entry into an intercreditor agreement between Oxford and RTW Royalty Holdings in form.

Sources and Uses of Cash in 2019

At December 31, 2019, our cash, cash equivalents and short-term investments totaled \$225.1 million.

Net cash used in operating activities was \$90.9 million for 2019 and was largely due to our net loss for 2019, offset by non-cash expenses included in net loss.

Net cash used in investing activities was \$74.7 million in 2019 and was primarily due to purchases of investments of \$277.9 million, offset by sales and maturities of investments of \$205.8 million.

Net cash provided by financing activities was \$159.8 million in 2019 and was primarily due to proceeds from public offerings of common stock of \$36.2 million under the facility discussed below, proceeds from the convertible notes of \$133.9 million as discussed below, offset by the purchase of the capped call options related to the convertible notes of \$13.4 million as discussed below.

On November 13, 2019, the Company issued \$138.0 million aggregate principal amount of 4.0% convertible senior notes due 2026 (the “2026 Notes”). The 2026 Notes are unsecured obligations and bear interest at an annual rate of 4.0% per year, payable semi-annually on May 15 and December 15 of each year, beginning May 15, 2020. The 2026 Notes are governed by an indenture between the Company and U.S. Bank National Association, as trustee. The 2026 Notes will mature on November 15, 2026, unless earlier repurchased or redeemed by the Company or converted at the option of the holders. The Company may redeem the 2026 Notes prior to the maturity date but is not required to and no sinking fund is provided for the 2026 Notes. The 2026 Notes may be converted, under certain circumstances as described below, based on an initial conversion rate of 94.7811 shares of common stock per \$1,000 principal amount (which represents an initial conversion price of \$10.55 per share). The conversion rate for the 2026 Notes will be subject to adjustment upon the occurrence of certain specified events. In addition, upon the occurrence of a make-whole fundamental change (as defined in the indenture), the Company will, in certain circumstances, increase the conversion rate by a number of additional shares for a holder that elects to convert its notes in connection with such make-whole fundamental change. The Company received approximately \$133.9 million in net proceeds, after deducting the initial purchasers’ discount, from the issuance of the 2026 Notes.

In connection with the offering of the 2026 Notes, the Company entered into privately-negotiated capped call transactions with one of the underwriters in the offering or its affiliate. The Company used approximately \$13.4 million of the net proceeds from the offering of the 2026 Notes to pay the cost of the capped call transactions. The capped call transactions are expected generally to reduce potential dilution to the Company’s common stock upon any conversion of the 2026 Notes and/or offset any cash payments the Company is required to make in excess of the principal amount of converted 2026 Notes, as the case may be, in the event that the market value per share of the Company’s common stock, as measured under the terms of the capped call transactions at the time of exercise, is greater than the strike price of the capped call transactions (which initially corresponds to the initial conversion price of the 2026 Notes, and is subject to certain adjustments), with such reduction and/or offset subject to a cap initially equal to approximately \$14.07 (which represents a premium of approximately 70% over the last reported sale price of the Company’s common stock on November 7, 2019), subject to certain adjustments. The capped call transactions are separate transactions, entered into by the Company and are not part of the terms of the 2026 Notes.

In 2019, we terminated the original Controlled Equity OfferingSM 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 and we 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 \$85.0 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 pay a commission of up to 3.0% of gross sales proceeds of any common stock sold under the New ATM Facility. In 2019, we issued 3,984,849 shares of common stock for net proceeds of \$36.2 million under the New ATM Facility.

Future Sources and Uses of Cash

In 2021, in addition to the costs and expenses of our research and development activities, we expect to incur an increase in costs and expenses as compared to previous annual periods as a result of advancement of our pipeline, and our commercial planning activities in view of the potential commercial launch of omecamtiv mecarbil in the U.S. and potentially elsewhere. Such costs and expenses are likely to include an increase in headcount, particularly in our sales and marketing functions, and the procurement of omecamtiv mecarbil drug product for commercial launch. These costs and expenses will be greater than what they would have been had Amgen not elected to terminate the Amgen Agreement and Servier not elected to terminate the Servier Agreement. We may explore potential strategic transactions and/or structured financing transactions to finance the increase costs and expenses. We will also incur expenses in connection to our relocation from our Old Facilities to our New Facilities during the fourth quarter of 2021, including holdover rent payable to our current landlord.

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. We may also incur significant sales and marketing expenses if and when one or more of our molecules receive regulatory approvals.

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;
- the jurisdictions in which we are granted regulatory approvals and thus are able to successfully launch our products for commercial sale;
- delays that may be caused by requirements of regulatory agencies;
- our level of funding for the development of current or future drug candidates;
- the number of drug candidates we pursue and the stage of development that they are in;
- 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 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.

On November 23, 2020, we announced that Amgen has elected to terminate the Amgen Agreement and thereby end its collaboration with Cytokinetics, effective May 20, 2021, and intends to transition development and commercialization rights for omecamtiv mecarbil and CK-136 (formerly known as AMG 594) to Cytokinetics.

On December 23, 2020, we announced that Amgen notified us that Servier elected to terminate the Servier Agreement. The termination is effective as of March 18, 2021, after which all development, commercialization and other rights with respect to omecamtiv mecarbil previously granted by Amgen to Servier will revert to Amgen. Given Servier’s notice to Amgen, all worldwide rights related to the development and commercialization of omecamtiv mecarbil will now return to Cytokinetics commensurate with the effective termination of the Amgen Agreement on May 20, 2021.

As a result of Amgen’s and Servier’s elections to terminate the Amgen Agreement and the Servier Agreement respectively, we will dedicate resources to ensure the transition of the programs related to omecamtiv mecarbil and CK-136 (formerly known as AMG 594) to us. In addition, we anticipate engaging with regulatory authorities in 2021 regarding the results of GALACTIC-HF with the objective to assess potential regulatory paths for an NDA submission for omecamtiv mecarbil and continuing our commercial planning activities. Finally, we plan to evaluate a wide range of corporate development strategies for potential co-development, co-commercialization and licensing deals in relation to omecamtiv mecarbil and our other drug candidates in order to mitigate the cost effects of the termination of the Amgen Agreement and Servier Agreement and enhance our commercial capabilities. These cost effects of termination include forfeiture of potential milestone payments from Amgen to us, as well as additional costs to us relating to clinical studies, regulatory filing, and commercialization of omecamtiv mecarbil.

The RPI Royalty Purchase Agreement provides that in the event Amgen elects to terminate the Amgen Agreement, we are obliged to enter into an agreement with RPI to preserve RPI’s rights under the RPI Royalty Purchase Agreement, which includes the payment by Cytokinetics of 4.5% of its worldwide net sales of omecamtiv mecarbil and other Amgen Alliance Compounds, subject to a potential increase of up to an additional 1% under certain circumstances (delay in US marketing approval). Our obligation to enter into a new agreement with RPI does not impact our accounting treatment of the RPI Liability or our estimates.

Future uses of cash also include capital purchases of equipment and tenant improvements to build out the Oyster Point Lease totaling approximately \$35.0 million. We intend to occupy the Oyster Point building late 2021.

We have incurred an accumulated deficit of \$992.3 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 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.

Contractual Obligations and Other Commitments

The following table summarizes our contractual obligations as of December 31, 2020:

	Payment Due by Period				
	Total	Less than One Year	1-3 Years	3-5 Years	More than 5 Years
	(In millions)				
Operating lease obligations(1)	\$ 221.1	\$ 4.6	\$ 28.9	\$ 33.9	\$ 153.7
Long-term debt obligations(2)	57.1	3.7	53.4	—	—
Convertible notes(3)	33.0	5.5	11.0	11.0	5.5
Purchase obligations(4)	3.7	3.2	0.5	—	—
Total contractual obligations	\$ 314.9	\$ 17.0	\$ 93.8	\$ 44.9	\$ 159.2

(1) Represents undiscounted future non-cancellable lease payments for our operating leases.

(2) Represents future minimum payments for our term loan, including interest payable and final payment.

(3) Represents interest payable for our convertible notes.

(4) Represents payments for materials and software licenses that are firm commitments.

The above table does not include \$43.8 million of cancellable purchase orders for the construction of the Oyster Point Lease.

The above table does not include the RPI Liability payments due to the uncertain nature and timing.

The obligations in the above table are as of December 31, 2020. We expect the amount of these obligations to change materially over time as new contracts are initiated and existing contracts are completed, terminated, or modified.

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

We are exposed to market risks in the ordinary course of our business. These risks primarily include risk related to interest rate sensitivities.

Interest Rate Risk

We are exposed to market risk related to changes in interest rates. As of December 31, 2020, we had cash and short-term investments of \$464.1 million, which consisted of consist of U.S. Treasury securities, agency bonds, commercial paper, corporate debt and money market fund. To reduce the volatility relating to these exposures, we have put investment and risk management policies and procedures in place. The primary objective of our investment activities is to preserve capital to fund our operations. We do not enter into investments for trading or speculative purposes and have not used any derivative financial instruments to manage our interest rate risk exposure. Our investments are subject to interest rate risk and could fall in value if market interest rates increase. A hypothetical 10% relative change in interest rates during any of the periods presented would not have had a material impact on our consolidated financial statements.

Foreign Currency Risk

The majority of our transactions occur in U.S. dollars. However, we do have certain transactions that are denominated in currencies other than the U.S. dollar, primarily Euro and GBP and we therefore are subject to foreign currency exchange risk. The fluctuation in the value of the U.S. dollar against other currencies affects the reported amounts of expenses, assets and liabilities primarily associated with a limited number of operating activities. Foreign currency transaction gains and losses have not been material to our financial statements for the year ended December 31, 2020. A 10% increase or decrease in current exchange rates would not have a material effect on our financial results.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

	Page
Report of Independent Registered Public Accounting Firm	78
Consolidated Balance Sheets	81
Consolidated Statements of Operations and Comprehensive Loss	82
Consolidated Statements of Stockholders' Equity (Deficit)	83
Consolidated Statements of Cash Flows	84
Notes to Consolidated Financial Statements	85

REPORT OF 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 sheets of Cytokinetics, Incorporated (the “Company”) as of December 31, 2020 and 2019, the related consolidated statements of operations and comprehensive loss, stockholders’ equity (deficit), and cash flows, for each of the three years in the period ended December 31, 2020, 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, 2020 and 2019, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2020, in conformity with U.S. 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, 2020, 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 February 26, 2021 expressed an unqualified opinion thereon.

Basis for Opinion

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

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matters

The critical audit matters communicated below are matters arising from the current period audit of the financial statements that were communicated or required to be communicated to the audit committee and that: (1) relate to accounts or disclosures that are material to the financial statements and (2) involved especially challenging, subjective or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matters below, providing separate opinions on the critical audit matters or on the accounts or disclosures to which they relate.

Estimates Related to the Sale of Future Royalties

Description of the Matter

As described in Note 7 to the consolidated financial statements, the Company has entered into agreements with counterparties to monetize future royalty payments that the Company is entitled to receive upon commercialization of certain products that were previously licensed to others. Cash is received upon execution of such royalty monetization agreements, which are then accounted for as either a liability if the Company has significant continuing involvement in the related royalty stream or as deferred revenue if there is no significant continuing involvement. Regardless of whether there is significant continuing involvement, the Company is required to estimate the amount and timing of future royalty payments to be received from licensors and paid to the counterparties of the royalty monetization agreements. The Company periodically assesses the amount and timing of expected royalty payments using a combination of internal projections and forecasts from external sources.

There are a number of factors that could materially affect the amount and timing of royalty payments, most of which are not within the Company's control and management's estimates of the amount and timing of royalty payments to be received require the use of significant unobservable inputs. These inputs are derived using internal management estimates developed based on third party data and reflect management's judgements, current market conditions surrounding competing products, and forecasts. The significant unobservable inputs can include, to the extent applicable, estimates of patient populations, selling price, peak sales and sales ramp, the expected term of the related royalty streams, the timing of expected product launch and its impact on royalty rates, as well as the overall probability of clinical success and regulatory approval. A significant change in unobservable inputs could result in a material increase or decrease to the amount and timing of future cash flows. The Company recognized non-cash interest expense on the liability related to the sale of future royalties of \$22.7 million for the year ended December 31, 2020 and the liability related to the sale of future royalties, net was \$166.1 million as of December 31, 2020. During 2020, the Company also recognized \$87.0 million of deferred revenue related to the sale of a royalty stream to a third party as discussed in Note 3.

Auditing management's estimates of future royalty payments was especially challenging due to the significant judgment used by management in estimating the amount and timing of future royalty payments, which required the use of subjective inputs.

How We Addressed the Matter in Our Audit

We obtained an understanding, evaluated the design, and tested the operating effectiveness of controls over the Company's processes for estimating the amount and timing of future royalty payments.

Our audit procedures included, among others, testing management's process for estimating the amount and timing of future royalty payments and evaluating the reasonableness of significant assumptions used by management when developing the estimate of expected future royalties to be paid, including estimates of patient populations, selling price, peak sales and sales ramp, the expected term of the related royalty streams, the timing of expected product launch and its impact on royalty rates, as well as the overall probability of clinical success and regulatory approval. Evaluating the reasonableness of management's assumptions included, among others, consideration of (i) relevant industry forecasts, (ii) consistency with external market research and industry data, and (iii) whether the assumptions were consistent with evidence obtained in other areas of the audit.

Revenue from Collaborative and Licensing Arrangements

Description of the Matter

As described in Note 3, collaboration arrangements may include multiple elements such as license fees, milestone payments, royalties, and research and development cost reimbursement. Further, collaborations may include the delivery of various goods or services to the collaboration partner such as licenses to intellectual property or research and development services. The Company recognized \$36.5 million as license revenue during 2020 under the agreement with Ji Xing Pharmaceuticals Limited (the “Ji Xing License Agreement”).

Auditing the Company’s accounting for revenues from this collaboration arrangement was especially challenging due to the complex and highly judgmental nature of evaluating the terms of the related agreements, identifying performance obligations, and determining and allocating the transaction price to the performance obligations.

How We Addressed the Matter in Our Audit

We obtained an understanding, evaluated the design, and tested the operating effectiveness of controls over the Company’s processes for assessing the accounting treatment of any new collaboration agreements or modifications to existing collaboration agreements, including assessing the identification of and effort to satisfy performance obligations.

To test the accounting for revenue from the Ji Xing License Agreement, we tested and evaluated, among other things, the performance obligation identified, the estimates and assumptions used to determine the transaction price, and the allocation of the transaction price to the performance obligation. We also assessed whether the accounting conclusions for the Ji Xing License Agreement were appropriate.

/s/ Ernst & Young LLP

We have served as the Company’s auditor since 2018.
Redwood City, California
February 26, 2021

CYTOKINETICS, INCORPORATED
CONSOLIDATED BALANCE SHEETS
(in thousands, except share and per share data)

	December 31,	
	2020	2019
ASSETS		
Current assets:		
Cash and cash equivalents	\$ 82,985	\$ 36,433
Short-term investments	381,075	188,679
Accounts receivable	4,420	5,163
Prepaid expenses and other current assets	5,741	3,477
Total current assets	474,221	233,752
Long-term investments	36,954	42,650
Property and equipment, net	13,346	4,530
Operating lease right-of-use assets and other assets	9,282	8,882
Total assets	\$ 533,803	\$ 289,814
LIABILITIES AND STOCKHOLDERS' EQUITY (DEFICIT)		
Current liabilities:		
Accounts payable	\$ 8,050	\$ 8,160
Accrued liabilities	19,315	12,123
Short-term lease liability	2,785	4,616
Other current liabilities	1,049	1,124
Total current liabilities	31,199	26,023
Term loan, net	46,209	45,052
Convertible notes, net	89,504	84,205
Liability related to the sale of future royalties, net	166,068	143,276
Long-term deferred revenue	87,000	—
Long-term lease and other non-current liabilities	440	2,195
Total liabilities	420,420	300,751
Commitments and contingencies		
Stockholders' equity (deficit):		
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: 71,015,183 shares at December 31, 2020 and 59,172,124 shares at December 31, 2019	70	59
Additional paid-in capital	1,105,470	853,341
Accumulated other comprehensive income	149	679
Accumulated deficit	(992,306)	(865,016)
Total stockholders' equity (deficit)	113,383	(10,937)
Total liabilities and stockholders' equity (deficit)	\$ 533,803	\$ 289,814

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

CYTOKINETICS, INCORPORATED
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(in thousands, except per share data)

	Years Ended December 31,		
	2020	2019	2018
Revenues:			
Research and development revenues	\$ 16,527	\$ 26,868	\$ 26,368
License revenues	36,501	—	5,133
Milestone revenues	2,800	—	—
Total revenues	55,828	26,868	31,501
Operating expenses:			
Research and development	96,951	86,125	89,135
General and administrative	52,820	39,610	31,282
Total operating expenses	149,771	125,735	120,417
Operating loss	(93,943)	(98,867)	(88,916)
Interest expense	(15,963)	(6,623)	(3,797)
Non-cash interest expense on liability related to sale of future royalties	(22,713)	(20,737)	(17,767)
Interest and other income, net	5,329	4,535	4,191
Net loss	<u>\$ (127,290)</u>	<u>\$ (121,692)</u>	<u>\$ (106,289)</u>
Net loss per share — basic and diluted	<u>\$ (1.97)</u>	<u>\$ (2.11)</u>	<u>\$ (1.95)</u>
Weighted-average number of shares used in computing net loss per share — basic and diluted	<u>64,524</u>	<u>57,575</u>	<u>54,420</u>
Other comprehensive loss:			
Unrealized (losses) gains on available-for-sale securities, net	(530)	179	157
Comprehensive loss	<u>\$ (127,820)</u>	<u>\$ (121,513)</u>	<u>\$ (106,132)</u>

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

CYTOKINETICS, INCORPORATED
CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY (DEFICIT)

(in thousands, except shares)

	Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Income	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount				
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
Exercise of stock options	131,909	—	1,017	—	—	1,017
Issuance of common stock under at-the-market offering, net of issuance costs	3,984,849	4	36,210	—	—	36,214
Issuance under Employee Stock Purchase Plan	172,113	—	1,108	—	—	1,108
Vesting of restricted stock units, net of taxes withheld	165,347	—	(732)	—	—	(732)
Issuance of warrants	—	—	185	—	—	185
Equity component of convertible notes	—	—	49,477	—	—	49,477
Capped call options associated with convertible notes	—	—	(13,386)	—	—	(13,386)
Stock-based compensation	—	—	10,759	—	—	10,759
Other comprehensive loss	—	—	—	179	—	179
Net loss	—	—	—	—	(121,692)	(121,692)
Balance, December 31, 2019	59,172,124	59	853,341	679	(865,016)	(10,937)
Exercise of stock options	943,505	1	7,610	—	—	7,611
Exercise of warrants	104,890	—	—	—	—	—
Claims settlement under Section 16(b)	—	—	2,151	—	—	2,151
Underwritten public offering of common stock, net of discounts, commissions and offering cost	8,385,417	8	188,875	—	—	188,883
Issuance of common stock upon private placement	2,000,000	2	36,435	—	—	36,437
Issuance under Employee Stock Purchase Plan	134,684	—	1,509	—	—	1,509
Vesting of restricted stock units, net of taxes withheld	274,563	—	(2,255)	—	—	(2,255)
Issuance of warrants	—	—	184	—	—	184
Stock-based compensation	—	—	17,620	—	—	17,620
Other comprehensive loss	—	—	—	(530)	—	(530)
Net loss	—	—	—	—	(127,290)	(127,290)
Balance, December 31, 2020	<u>71,015,183</u>	<u>\$ 70</u>	<u>\$ 1,105,470</u>	<u>\$ 149</u>	<u>\$ (992,306)</u>	<u>\$ 113,383</u>

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

CYTOKINETICS, INCORPORATED
CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)

	Years Ended December 31,		
	2020	2019	2018
Cash flows from operating activities:			
Net loss	\$ (127,290)	\$ (121,692)	\$ (106,289)
Adjustments to reconcile net loss to net cash provided by (used in) operating activities:			
Non-cash interest expense on liability related to sale of future royalties	22,792	20,737	17,767
Non-cash stock-based compensation expense	17,620	10,759	9,761
Depreciation and amortization of property and equipment	1,831	1,293	1,239
Gain on investment, net	(573)	—	—
Interest receivable and amortization on investments	(1,194)	(2,587)	(1,677)
Non-cash interest expense related to debt	6,640	919	920
Changes in operating assets and liabilities:			
Accounts receivable	743	(2,932)	(1,119)
Contract assets	—	4,554	5,154
Prepaid and other current assets	(2,183)	(3,862)	1,817
Operating lease right-of-use assets and other assets	1,242	3,552	—
Accounts payable	(110)	4,396	(1,490)
Accrued and other liabilities	7,117	(2,168)	(2,063)
Contract liabilities	—	—	(18,750)
Operating lease liabilities	(4,692)	(3,876)	—
Deferred revenue	87,000	—	(6,485)
Net cash provided by (used in) operating activities	8,943	(90,907)	(101,215)
Cash flows from investing activities:			
Purchases of investments	(435,825)	(277,883)	(240,224)
Maturities of investments	247,301	202,599	246,232
Sales of investments	3,061	3,196	—
Purchases of property and equipment	(11,052)	(2,619)	(889)
Sales of property and equipment	—	—	14
Net cash (used in) provided by investing activities	(196,515)	(74,707)	5,133
Cash flows from financing activities:			
Proceeds from public offerings of common stock, net of discounts, commissions and offering cost	188,883	—	—
Proceeds from private placement, net	36,225	—	—
Proceeds from issuance under Employee Stock Purchase Plan	1,509	—	—
Proceeds from stock-based award activities, net	5,356	1,393	3,234
Claims settlement under Section 16(b)	2,151	—	—
Net proceeds from long-term debt, net of debt discount and issuance costs	—	1,710	9,898
Net proceeds from convertible notes, net of debt discount and issuance costs	—	133,860	—
Issuance of common stock under at-the-market offering, net of issuance costs	—	36,214	—
Purchase of capped call options associated with convertible notes	—	(13,386)	—
Net cash provided by financing activities	234,124	159,791	13,132
Net increase (decrease) in cash and cash equivalents	46,552	(5,823)	(82,950)
Cash and cash equivalents, beginning of period	36,433	42,256	125,206
Cash and cash equivalents, end of period	\$ 82,985	\$ 36,433	\$ 42,256
Supplemental cash flow disclosures:			
Cash paid for interest	9,620	4,059	2,877
Right-of-use assets recognized in exchange for lease obligations	1,106	10,687	—

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 \$992.3 million since inception and there can be no assurance that we will attain profitability. We had a net loss of \$127.3 million and net cash provided by operations of \$8.9 million for the year ended December 31, 2020. Cash, cash equivalents and investments increased to \$501.0 million as of December 31, 2020 from \$267.8 million as of December 31, 2019. 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. To date, we have funded operations primarily through sales of our common stock, contract payments under our collaboration agreements, sale of future royalties, debt financing arrangements, government grants and interest income. 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 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. Certain prior period amounts have been reclassified to conform the prior period presentation to the current year.

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, 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.

CYTOKINETICS, INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

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

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 market prices, with unrealized gains and losses recorded in accumulated other comprehensive income and 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 and other income, net. Recognized gains and losses and declines in value judged to be other-than-temporary, if any, on available-for-sale securities are included in Interest and other income, net. Interest and dividends on securities classified as available-for-sale are included in Interest and other income, net.

All of our available-for-sale investments are subject to a periodic impairment review. If an impairment is the result of a credit loss, we recognize an allowance for credit losses (“ACL”). ACL’s reflect management’s current estimate of credit losses that are expected to occur over the remaining life of a financial asset. 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.

CYTOKINETICS, INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

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.

Leases

We adopted Accounting Standards Update No. 2016-02, *Leases* (“Topic 842”) on January 1, 2019 using the modified retrospective approach. In adopting Topic 842, we recognized a right-of-use asset and a short-term and long-term lease liability on our consolidated balance sheets for our existing facilities leases with Britannia Pointe Grand Limited Partnership (the “Britannia Leases”). The right-of-use asset is based on the liability adjusted for any prepaid or deferred rent. We determined the lease term at the commencement date by considering whether renewal options and termination options are reasonably assured of exercise. In determining the present value of lease payments, we estimated our incremental borrowing rate based on information available when we adopted Topic 842. We base the Britannia Leases liability on the present value of remaining lease payments over the remaining terms of the Britannia Leases, using an estimated rate of interest that we would pay to borrow equivalent funds on a collateralized basis at the lease commencement date. We evaluated our other contracts and determined that, except for the Britannia Leases, none of our contracts contained a lease as defined in Topic 842.

We elected the package of practical expedients permitted under the transition guidance within Topic 842, which among other things, allowed us to carry forward the historical lease classification of those leases in place as of January 1, 2019. We also elected to exclude from our consolidated balance sheets recognition of leases having a term of 12 months or less (short-term leases) and elected to not separate lease components and non-lease components for Britannia Leases.

We recorded a lease liability of \$10.7 million and a corresponding right-of-use asset of \$9.6 million upon adoption of the new lease standard on January 1, 2019.

We recognize rent expense for operating leases on a straight-line basis over the lease term in operating expenses on the consolidated statements of operations.

Prior period amounts continue to be reported in accordance with our historic accounting under previous lease guidance, ASC 840, Leases (“Topic 840”).

Revenue Recognition

We recognize revenue when we transfer promised goods or services to customers in an amount that reflects the consideration for those goods or services. 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; (iii) royalties on net sales of licensed products; and (iv) research and development cost reimbursements. 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.

CYTOKINETICS, INCORPORATED**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)**

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 obligations. 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 judgment 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 probable 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 joint programs with Astellas under that certain License and Collaboration Agreement for Other Skeletal Sarcomere Activators, dated April 23, 2020, as amended (the “Astellas OSSA Agreement”), and with Amgen under that certain Collaboration and Option Agreement, dated December 29, 2006, as amended (the “Amgen Agreement”), include promises of research and development services. We have determined that these services collectively are distinct from the licenses provided to Astellas and Amgen under such agreements, and as such, these promises are accounted for as a separate performance obligation recorded over time. We recognize revenue for these services as the performance obligations are satisfied, which we estimate using internal research and 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 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 our 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.

CYTOKINETICS, INCORPORATED**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)*****Liability Related to Sale of Future Royalties***

We treat our liability to RPI Finance Trust (“RPI”) related to sale of future royalties under that certain Royalty Purchase Agreement, dated February 1, 2017 (the “RPI Royalty Purchase Agreement”) pursuant to which we sold a portion of our right to receive royalties from Amgen on potential net sales of omecamtiv mecarbil as a debt financing, to be amortized under the effective interest rate method over the life of the related royalty stream.

Our liability to RPI related to sale of future royalties under the RPI Royalty Purchase Agreement (the “RPI Liability”) and related amortization are based on our current estimates of future royalties expected to be paid over the life of the arrangement. Concurrently with our entry into the RPI Royalty Purchase Agreement, we entered into a common stock purchase agreement with RPI. We allocated the consideration and issuance costs on a relative fair value basis to the RPI Liability and the common stock.

The RPI Royalty Purchase Agreement further provides that in the event Amgen elects to terminate the Amgen Agreement, we are obliged to enter into an agreement with RPI to preserve RPI’s rights under the RPI Royalty Purchase Agreement, which includes the payment by Cytokinetics of 4.5% of its worldwide net sales of omecamtiv mecarbil and other compounds with the same mechanism of action as omecamtiv mecarbil that are subject to the Amgen Agreement (together the “Amgen Alliance Compounds”), subject to a potential increase of up to an additional 1% under certain circumstances (delay in US marketing approval). Our obligation to enter into a new agreement with RPI does not impact our accounting treatment of the RPI Liability or our estimates.

The RPI Liability will be recognized using significant unobservable inputs. These inputs are derived using internal management estimates developed based on third party data and reflect management’s judgements, current market conditions surrounding competing products, and forecasts. The significant unobservable inputs include the estimated patient population, estimated selling price, estimated peak sales and sales ramp, the expected term of the royalty stream, timing of the expected launch and its impact on the royalty rate. A significant change in unobservable inputs could result in a material increase or decrease to the effective interest rate of the RPI Liability.

We will periodically assess the amount and timing of 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 previous estimates or the estimated timing of such payments is materially different than previous estimates, we will adjust the amortization of the RPI Liability related to sale of future royalties and prospectively recognize the related non-cash interest expense. We have updated the analysis to include the data released on October 8, 2020 relating to GALACTIC-HF. Our estimates regarding the amount and timing of future royalty payments have not changed as a result of Amgen’s election to terminate the Amgen Agreement or Servier’s election to terminate the sublicense agreement (the “Servier Agreement”) between Amgen and Les Laboratoires Servier and Institut de Recherches Internationales Servier (“Servier”) respectively.

We account for the RPI Liability, as a liability primarily because we have significant continuing involvement in generating the royalty stream. If and when omecamtiv mecarbil is commercialized and royalties become due, we will recognize the portion of royalties paid to RPI as a decrease to the RPI Liability and a corresponding reduction in cash.

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.

CYTOKINETICS, INCORPORATED**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)**

In December 2019, the FASB issued ASU 2019-12, *Simplifying the Accounting for Income Taxes* (“ASU 2019-12”), as part of its Simplification Initiative to reduce the cost and complexity in accounting for income taxes. ASU 2019-12 removes certain exceptions related to the approach for intraperiod tax allocation, the methodology for calculating income taxes in an interim period and the recognition of deferred tax liabilities for outside basis differences. ASU 2019-12 also amends other aspects of Topic 740, *Income Taxes*, to help simplify and promote consistent application of US GAAP. The guidance is effective for interim and annual periods beginning after December 15, 2020, with early adoption permitted. We early adopted ASU 2019-12 in 2019 and it did not have a material impact on the Consolidated Financial Statements.

The only aspect of ASU 2019-12 that had a material impact on our consolidated financial statements was the removal of the exception related to intraperiod tax allocation. Starting in 2019, we followed the general intraperiod allocation of tax expense. We have a loss from continuing operations and subsequent to the adoption of ASU 2019-12, we determined the amount attributable to continuing operations without regard to the tax effect of other items. We prospectively applied the ASU 2019-12 amendment related to intraperiod tax allocation.

Had the Company not adopted ASU 2019-12, upon issuance of the convertible notes in 2019 (see Note 6 – Debt) a \$12.0 million deferred tax benefit would have been recognized along with corresponding decreases to net loss and accumulated deficit. The Company had no intraperiod tax allocation items in prior years.

Due to our net loss position, the income tax benefit generated without the adoption of ASU 2019-12 was a non-cash benefit. The adoption of ASU 2019-12 did not impact our cash flows.

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 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.

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 ratable method.

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 as well as the discount created by the bifurcation of the equity component and the debt component of the convertible senior notes due 2026 (the “2026 Notes”), 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.

Recent Accounting Standards

In June 2016, the Financial Accounting Standards Board (“FASB”) issued ASU 2016-13, *Financial Instruments — Credit Losses — Measurement of Credit Losses on Financial Instruments* (“ASU 2016-13”), which requires that financial assets measured at amortized cost be presented at the net amount expected to be collected. The measurement of expected credit losses is based on historical experience, current conditions, and reasonable and supportable forecasts that affect collectability. ASU 2016-13 also eliminates the concept of “other-than-temporary” impairment when evaluating available-for-sale debt securities and instead focuses on determining whether any impairment is a result of a credit loss or other factors. An entity will recognize an allowance for credit losses on available-for-sale debt securities rather than an other-than-temporary impairment that reduces the cost basis of the investment. ASU 2016-13 is effective for annual and interim reporting periods beginning after December 15, 2019. We adopted ASU 2016-13 as of January 1, 2020 and the adoption did not have a material impact on the Consolidated Financial Statements.

CYTOKINETICS, INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

In August 2018, the FASB issued ASU 2018-15, *Intangibles-Goodwill and Other-Internal-Use Software (Subtopic 350-40): Customer's Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement That Is a Service Contract*, which expands the scope of costs associated with cloud computing arrangements that must be capitalized. Under the new guidance, costs associated with implementing a cloud computing arrangement that is a service contract must be capitalized and expensed over the term of the hosting arrangement. This guidance should be applied either retrospectively or prospectively to all implementation costs incurred after the date of adoption. We adopted ASU 2018-15 on January 1, 2020 and the adoption did not have a material impact on the Consolidated Financial Statements.

In November 2018, the FASB issued ASU 2018-18, *Collaborative Arrangements (Topic 808): Clarifying the Interaction between Topic 808 and Topic 606, Revenue from Contracts with Customers*, ("ASU 2018-18"), which makes 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. We adopted ASU 2018-18 on January 1, 2020 and the adoption did not have a material impact on the Consolidated Financial Statements.

In November 2019, the FASB issued ASU 2019-08, *Compensation-Stock Compensation (Topic 718) and Revenue from Contracts with Customers (Topic 606): Codification Improvements-Share-Based Consideration Payable to a Customer*, which requires that an entity measure and classify share-based payment awards granted to a customer by applying the guidance in Topic 718. The amount recorded as a reduction of the transaction price is required to be measured on the basis of the grant-date fair value of the share-based payment award. We have adopted ASU 2019-08 as of January 1, 2020 and the adoption did not have any impact on the Consolidated Financial Statements.

In March 2020, the FASB issued ASU 2020-04, *Reference Rate Reform (Topic 848): Facilitation of the Effects of Reference Rate Reform on Financial Reporting* ("ASU 2020-04"). ASU 2020-04 provides optional guidance for a limited period of time to ease the potential burden associated with the expected market transition from the London Inter-Bank Offer Rate ("LIBOR") to alternative reference rates. Companies can apply ASU 2020-04 immediately, however the guidance will only be available until December 31, 2022. The Company's term loan utilizes LIBOR as the reference rate and we are currently evaluating the impact that adopting this new accounting standard will have on our Consolidated Financial Statements and related disclosures.

In August 2020, the FASB issued ASU 2020-06, *Debt-Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging-Contracts in Entity's Own Equity (Subtopic 815-40): Accounting for Convertible Instruments and Contracts in an Entity's Own Equity* ("ASU 2020-06"). ASU 2020-06 amends the guidance on convertible instruments and the derivatives scope exception for contracts in an entity's own equity, and also improves and amends the related earnings per share guidance. ASU 2020-06 will be effective for annual reporting periods after December 15, 2021 and interim periods within those annual periods and early adoption is permitted. We are currently evaluating the impact that adopting this new accounting standard will have on our Consolidated Financial Statements and related disclosures.

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 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 ESPP, during the period using the treasury stock method and convertible notes using the if-converted 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):

	Years Ended December 31,		
	2020	2019	2018
Options to purchase common stock	8,510	7,759	5,476
Warrants to purchase common stock	48	165	116
Restricted stock and performance units	1,117	839	547
Shares issuable related to the ESPP	12	27	107
Shares issuable upon conversion of convertible notes	16,675	16,675	—
Total shares	26,362	25,465	6,246

CYTOKINETICS, INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

Note 3 — Research and Development Arrangements

Our contract assets changed during the period, as follows (in thousands):

	December 31,		
	2020	2019	2018
Contract asset from the 2016 Astellas Amendment			
Balance at beginning of period	\$ —	\$ 4,554	\$ 9,708
Services performed	—	—	11,713
Cash received for services	—	(4,554)	(16,867)
Balance at end of period	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 4,554</u>

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 the Amgen Agreement.

On November 23, 2020, we announced that Amgen has elected to terminate the Amgen Agreement and thereby end its collaboration with Cytokinetics, effective May 20, 2021, and Amgen intends to transition development and commercialization rights for omecamtiv mecarbil and CK-136 (formerly known as AMG 594) to Cytokinetics.

On December 23, 2020, we announced that Amgen notified us that Servier elected to terminate the Servier Agreement. The termination is effective as of March 18, 2021, after which all development, commercialization and other rights with respect to omecamtiv mecarbil previously granted by Amgen to Servier will revert to Amgen.

Omecamtiv mecarbil is an investigational cardiac myosin activator, developed for the potential treatment of heart failure with reduced ejection fraction (“HFrEF”), and was recently studied in GALACTIC-HF (Global Approach to Lowering Adverse Cardiac Outcomes Through Improving Contractility in Heart Failure), a positive Phase 3 cardiovascular outcomes clinical trial, and is the subject of an ongoing Phase 3 clinical trial, METEORIC-HF (Multicenter Exercise Tolerance Evaluation of Omecamtiv Mecarbil Related to Increased Contractility in Heart Failure), a Phase 3 clinical trial intended to evaluate the potential of omecamtiv mecarbil to increase exercise performance. CK-136, a novel mechanism cardiac troponin activator, was recently studied in a Phase 1 clinical study.

We recognize research and development revenue for reimbursements from Amgen of both internal costs of certain full-time employee equivalents and other costs related to the Amgen Agreement, which will terminate effective as of May 20, 2021. Research and development revenue from Amgen of \$10.0 million in 2020, \$13.8 million in 2019 and \$1.9 million in 2018 consists of reimbursement of costs we incurred related to METEORIC-HF.

We had accounts receivable of \$1.7 million from Amgen as of December 31, 2020 and \$3.3 million as of December 31, 2019.

Astellas

Our strategic alliance with Astellas to advance novel therapies for diseases and medical conditions associated with muscle impairment and weakness commenced in 2013 under the License and Collaboration Agreement, dated June 21, 2013 between the parties (the “Astellas Agreement”).

In 2014, we and Astellas amended and restated the Astellas 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”). License revenues in 2018 related to our performance obligations under the 2014 Astellas Amendment. In 2018, we completed all our deliverables for the 2014 Astellas Amendment.

CYTOKINETICS, INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

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.

On April 23, 2020, we and Astellas entered into the two agreements referenced below which, taken together, amend and restate the Company’s research, development and commercialization collaboration with Astellas under the Astellas Agreement.

Fast Skeletal Regulatory Activator Agreement

The Company and Astellas entered into that certain Fast Skeletal Regulatory Activator Agreement, dated April 23, 2020 (the “Astellas FSRA Agreement”). As a result of the Astellas FSRA Agreement, the Company will now have exclusive control and responsibility for the Company’s future development and commercialization of reldesemtiv, CK-601 and other fast skeletal regulatory activator (collectively “FSRA”) compounds and products, and accordingly, Astellas has agreed to terminate its license to all FSRA compounds and related products.

Under the Astellas FSRA Agreement, Astellas has agreed to pay one-third of the out-of-pocket clinical development costs which may be incurred in connection with the Company’s potential Phase 3 clinical trial of reldesemtiv in ALS, up to a maximum contribution by Astellas of \$12 million. In addition, Astellas has agreed to non-cash contributions to the Company, which include the transfer of its existing inventories of active pharmaceutical ingredient of reldesemtiv and CK-601. Astellas has also agreed to the continued conduct of ongoing stability studies pertaining to such existing inventories of active pharmaceutical ingredient, at Astellas’ cost. In exchange, the Company will pay Astellas a low- to mid- single digit royalty on sales of reldesemtiv in the United States, Canada, United Kingdom and the European Union until the later of (i) ten years following the first commercial sale of such product in a major market country, or (ii) December 31, 2034, subject to certain royalty reduction provisions. The Company would not owe Astellas royalties on sales of reldesemtiv in any other country, or on the sale of any FSRA compounds or related products other than reldesemtiv.

License and Collaboration Agreement for Other Skeletal Sarcomere Activators

Under the Astellas OSSA Agreement, we are eligible to receive additional research and early and late stage 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, which could total up to \$250.0 million, except under certain scenarios. Additionally, \$200.0 million in commercial milestones could be received under the Astellas OSSA Agreement provided certain sales targets are met. We are eligible to receive \$1.0 million in research milestone payments under this 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.

We continue to recognize research revenue for reimbursements from Astellas of internal costs of certain full-time employee equivalents, supporting collaborative research and development programs, and of other costs related to those programs.

License revenues and research and development revenues from Astellas for 2020, 2019 and 2018 were as follows (in thousands):

	Years Ended December 31,		
	2020	2019	2018
License revenues	\$ —	\$ —	\$ 5,133
Reimbursements	6,555	13,106	22,253
Milestone fees	—	—	2,000
	<u>\$ 6,555</u>	<u>\$ 13,106</u>	<u>\$ 29,386</u>

We had accounts receivable from Astellas of \$2.7 million as of December 31, 2020 and \$1.9 million as of December 31, 2019.

CYTOKINETICS, INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

RTW Transactions

On July 14, 2020, we entered into a series of transactions as described below with RTW Royalty Holdings Designated Activity Company (“RTW Royalty Holdings”) and Ji Xing, related to Cytokinetics’ proprietary small molecule cardiac myosin inhibitor product referred to as CK-3773274 (“CK-274”), a novel cardiac myosin inhibitor, and other assets (together, the “RTW Transactions”). The RTW Transactions include entering into a licensing and collaboration agreement with Ji Xing, the sale of Cytokinetics common stock to the RTW Investors (as defined below), an agreement to sell to RTW Royalty Holdings our interest in certain future royalties on net sales of products containing the compound mavacamten that is being developed by Bristol-Myers Squibb Company (formerly by MyoKardia, Inc.), and the ability for the Company to obtain additional funding in the future from RTW Royalty Holdings, upon the achievement of certain clinical trial milestones, in exchange for future royalty payments as further discussed below. As a result, we have or expect to receive a combination of committed capital, funding and sale proceeds from the RTW Investors, RTW Royalty Holdings and Ji Xing.

The RTW Transactions were entered into with parties that are affiliated and in contemplation of one another and, accordingly, we have assessed the accounting for these transactions in the aggregate. We concluded that there were three units of accounting in the RTW Transactions as further described below. The Company allocated the total consideration in accordance with ASC 820, *Fair Value Measurement*, and ASC 606, *Revenue from Contracts with Customers*, as follows (in thousands):

	Allocated Consideration	
Units of Accounting:		
License and collaboration (residual)	\$	36,501
Royalty (fair value)		87,000
Common stock (fair value)		36,499
Total consideration	\$	<u>160,000</u>

License and Collaboration Agreement

We entered into a License and Collaboration Agreement (the “Ji Xing License Agreement”) with Ji Xing, pursuant to which we granted to Ji Xing an exclusive license to develop and commercialize CK-274 in People’s Republic of China (including the Hong Kong SAR and Macau SAR) (together “China”) and Taiwan. Under the terms of the Ji Xing License Agreement, we received from Ji Xing a nonrefundable upfront payment of \$25.0 million. We may be eligible to receive from Ji Xing milestone payments totaling up to \$200.0 million for the achievement of certain development and commercial milestone events in connection to CK-274 in the field of obstructive hypertrophic cardiomyopathy (“oHCM”) and/or non-obstructive hypertrophic cardiomyopathy (“nHCM”) and other indications. In addition, Ji Xing will pay us tiered royalties in the low-to-high teens range on the net sales of the products containing CK-274 in China and Taiwan, subject to certain reductions for generic competition, patent expiration and payments for licenses to third party patents.

Ji Xing will be responsible for the development and commercialization of CK-274 at its own cost and is required to use diligent efforts to develop and commercialize CK-274 in China and Taiwan. The development of CK-274 will be initially focused on hypertrophic cardiomyopathy, and Ji Xing will have the opportunity to participate in Cytokinetics’ global pivotal clinical trials of CK-274. Cytokinetics or a designated supplier will supply CK-274 to Ji Xing either as a finished product or as an active pharmaceutical ingredient.

The Ji Xing License Agreement, unless terminated earlier, will continue on a market-by-market basis until expiration of the relevant royalty term. Ji Xing has the right to terminate the Ji Xing License Agreement for convenience. Each party may terminate the Ji Xing License Agreement for the other party’s uncured material breach, insolvency, or failure to perform due to extended force majeure events. Cytokinetics may also terminate the Ji Xing License Agreement if Ji Xing challenges Cytokinetics’ patents or undergoes certain change of control transactions. Rights granted to Ji Xing in relation to CK-274 will revert to Cytokinetics upon termination, and, under certain circumstances, subject to a low single digit royalty payment by the Company to Ji Xing on the net sales of the products containing the compound CK-274 in China and Taiwan.

CYTOKINETICS, INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

License revenues and milestone revenues for 2020, 2019 and 2018 were as follows (in thousands):

	Years Ended December 31,		
	2020	2019	2018
License revenues	\$ 36,501	\$ —	\$ —
Milestone revenues	2,500	—	-
	<u>\$ 39,001</u>	<u>\$ —</u>	<u>\$ —</u>

We assessed this arrangement in accordance with ASC 606 and concluded that there is one performance obligation relating to the license of functional intellectual property. The performance obligation was satisfied, and we recognized the residual allocation of arrangement consideration as revenue of \$36.5 million for 2020. Due to the nature of development, including the inherent risk of development and approval by regulatory authorities, we are unable to estimate if and when the development milestone payments could be achieved or become due and, accordingly, we consider the milestone payments to be fully constrained and exclude the milestone payments from the initial transaction price.

The consideration related to sales-based milestone payments, including royalties, will be recognized when the related sales occur under the sales- and usage-based royalty exception as these amounts have been determined to relate predominantly to the license.

We re-evaluate the probability of achievement of development milestones and any related constraints each reporting period. We will include consideration, without constraint, in the transaction price to the extent it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur.

We earned a \$2.5 million milestone from Ji Xing as of December 31, 2020 for the first patient dosed in Cohort 2 of REDWOOD-HCM (Randomized Evaluation of Dosing With CK-274 in Obstructive Outflow Disease in HCM). We determined recognition of the milestone during 2020 based on clinical trial progress. Our determination that we expected to earn the \$2.5 million milestone resulted in a change in the overall transaction price of the collaboration agreement, as it was probable that a significant reversal of cumulative revenue would not occur. A corresponding contract asset was recorded in other current assets in our consolidated balance sheet as of December 31, 2020.

Royalty Purchase Agreement

We entered into a Royalty Purchase Agreement (the “RTW Royalty Purchase Agreement”) with RTW Royalty Holdings, pursuant to which we sold our right to receive certain payments on the net sales of products containing the compound mavacamten, a cardiac myosin inhibitor (the “Mavacamten Royalty”), under the Research Collaboration Agreement, dated August 24, 2012, between us and MyoKardia, Inc. to RTW Royalty Holdings for a one-time payment of \$85.0 million. The RTW Royalty Purchase Agreement transaction closed on November 13, 2020.

We accounted for the sale of our rights to the Mavacamten Royalty as deferred revenue under ASC 470, Debt, since the arrangement is a sale of our future right to receive royalties and not a sale of the underlying patents or related intangibles. Further, we do not have any significant continuing involvement in the further development, commercialization or sale of mavacamten, the one-time payment is not required to be paid back to RTW Royalty Holdings, the investor’s return is not limited and will be driven by net sales, and RTW Royalty Holdings does not have any recourse to the Company’s assets.

The allocation of the consideration for the RTW Transactions resulted in \$87.0 million being allocated to the RTW Royalty Purchase Agreement representing its fair value. The fair value was determined using an income approach method based on management’s estimates of the discounted cash flows to be received over the term of the related royalty agreement, which are Level 3 fair value inputs. Management’s estimates included significant unobservable inputs. These inputs are derived using internal management estimates developed based on third party data and reflect management’s judgements, current market conditions surrounding competing products, and forecasts. The significant unobservable inputs include the estimated patient population, estimated selling price, estimated peak sales and sales ramp, the expected term of the royalty stream, and timing of the expected launch. The \$87.0 million recorded as deferred revenue will be amortized using the units-of-revenue method.

CYTOKINETICS, INCORPORATED**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)**

We will recognize revenue related to the sale of the Mavacamten Royalty using the units-of-revenue method. Under the units-of-revenue method, the revenue to be recognized for a period is calculated by computing a ratio of the Mavacamten Royalty paid to RTW Royalty Holdings for a given period to the total payments expected to be made to RTW Royalty Holdings over the term of the agreement, and then applying that ratio to the period's cash payment. We will record any adjustments due to changes in the underlying royalties on a cumulative catch-up basis.

Common Stock Purchase Agreement

On July 14, 2020, we entered into Common Stock Purchase Agreements (each, a "CSPA") with each of RTW Master Fund, Ltd., RTW Innovation Master Fund, Ltd. and RTW Venture Fund Limited (collectively, the "RTW Investors"). The CSPAs provided for the sale and issuance of an aggregate of 2.0 million shares of common stock of Cytokinetics (the "Shares") at a price per share of \$25.00 and an aggregate purchase price of \$50.0 million. The closing occurred on July 14, 2020. The RTW Investors have agreed to certain trading and other restrictions with respect to the Shares, including a restriction on sales or other transfers of the Shares, subject to certain exceptions, for a period of two years from the closing date, which period will be extended if certain conditions are met. The restrictions resulted in a premium paid by RTW investors of \$13.5 million which represents the excess amount paid over the fair value of the Shares. The premium was determined by analyzing the holding period discount applied to the 30-day average stock price as of July 14, 2020, which is a Level 2 fair value inputs. The cash received less the calculated premium is the \$36.5 million fair value of the common stock recorded.

Funding Agreement

We entered into a Funding Agreement (the "Funding Agreement") with RTW Royalty Holdings. Pursuant to the Funding Agreement, RTW Royalty Holdings has committed to provide up to \$90.0 million (the "Funding Commitment") to fund our development and commercialization of CK-274 in nHCM and oHCM. Half of the Funding Commitment will be available, at our option, if certain clinical trial milestones of CK-274 for oHCM are achieved by January 14, 2023, and the remaining \$45.0 million of the Funding Commitment will be available, at our option, if certain clinical trial milestones of CK-274 for nHCM are achieved by January 14, 2024. If we develop CK-274 in another indication, we will negotiate an additional funding commitment from RTW to fund our development and commercialization of CK-274 in such other indication (other than oHCM or nHCM).

In exchange for the Funding Commitment and upon receipt of such funding from RTW Royalty Holdings, we have agreed to make payments to RTW Royalty Holdings equal to 2%, if RTW Royalty Holdings funds \$45.0 million of the Funding Commitment, or 4%, if RTW Royalty Holdings funds the full \$90.0 million of the Funding Commitment, in each case in respect of net sales of CK-274 by us and any of our licensees in the United States, the European Union, Switzerland, the United Kingdom and certain other countries in Europe (collectively referred to as the "CK-274 Territory"). In addition, should we exercise our option draw borrowings pursuant to the Funding Agreement, such agreement contains certain covenants applicable to us, including, among other things, development and commercialization diligence obligations in connection to the CK-274 Territory, use of proceeds, reporting and encumbrances. There are no performance obligations related to the Funding Agreement, as access to the Funding Commitment is at the option of the Company and based upon the achievement of certain development milestones.

The Funding Agreement contains customary conditions to disbursement, which may include the consent of our Lenders at the time of disbursement. On July 16, 2020, we entered into an amendment to the Term Loan Agreement, which permits, subject to entry into an intercreditor agreement between Oxford (as security agent for the Lenders) and RTW Royalty Holdings in form and substance reasonably satisfactory to the Lenders and RTW Royalty Holdings, the draw of funding under the Funding Agreement and the grant of a security interest to RTW Royalty Holdings in the intellectual property located in the United States and accounts receivable related to CK-274 thereunder.

The Company granted RTW Royalty Holdings a security interest in all of its rights, title and interest in, to certain intellectual property, accounts receivable and any proceeds from such collateral. The security interest will automatically terminate when total net payments made to RTW Royalty Holdings exceed a certain agreed threshold.

Note 4 — 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.

CYTOKINETICS, INCORPORATED
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

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

We classify fair value based on the observability of those inputs using a 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):

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.

Fair Value of Financial Assets

The follow tables set forth the fair value of our financial assets, which consists of cash equivalents and investments classified as available-for-sale securities, that were measured on a recurring basis (in thousands):

December 31, 2020

	Fair Value Hierarchy Level	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Money market funds	Level 1	\$ 80,050	\$ —	\$ —	\$ 80,050
U.S. Treasury securities	Level 1	274,407	147	(8)	274,546
Agency bonds	Level 2	51,581	15	(3)	51,593
Commercial paper	Level 2	49,500	3	(1)	49,502
Corporate obligations	Level 2	42,392	7	(11)	42,388
		<u>\$ 497,930</u>	<u>\$ 172</u>	<u>\$ (23)</u>	<u>\$ 498,079</u>

December 31, 2019

	Fair Value Hierarchy Level	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Money market funds	Level 1	\$ 31,535	\$ —	\$ —	\$ 31,535
U.S. Treasury securities	Level 1	134,845	72	(1)	134,916
Agency bonds	Level 2	47,024	23	(9)	47,038
Commercial paper	Level 2	10,435	4	—	10,439
Corporate obligations	Level 2	40,426	24	(7)	40,443
		<u>\$ 264,265</u>	<u>\$ 123</u>	<u>\$ (17)</u>	<u>\$ 264,371</u>

Interest income was \$5.3 million and \$4.5 million in 2020 and 2019, respectively.

Investments available for sale exclude an investment in equity classified as a Level 1 investment in our short-term investments with a fair value of \$1.0 million and an unrealized gain of \$0.3 million at December 31, 2019. As of December 31, 2020, the Level 1 investment had been divested. Unrealized losses were not due to changes in credit risk and we believe investments with an unrealized loss would be held until maturity.

No credit losses on debt securities were recognized in either 2020 or 2019. In its evaluation to determine expected credit losses, management considered all available historical and current information, expectations of future economic conditions, the type of security, the credit rating of the security, and the size of the loss position, as well as other relevant information. The Company does not intend to sell, and is unlikely to be required to sell, any of these available-for-sale investments before their effective maturity or market price recovery.

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

CYTOKINETICS, INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

Fair value of financial liabilities:

As of December 31, 2020 and 2019, the fair value of our term loan approximated its carrying value of \$46.2 million and \$45.1 million, respectively, because it is carried at a market observable interest rate, which is a Level 2 input (see Note 6 – Debt).

As of December 31, 2020, the estimated fair value of our convertible notes was \$638.7 million and was based upon observable, Level 2 inputs, including pricing information from recent trades of the convertible notes (see Note 6 – Debt).

As of December 31, 2020 and 2019, the fair value of the RPI Liability related to the sale of future royalties is based on our current estimates of future royalties expected to be paid to RPI, over the life of the arrangement, which are considered Level 3 inputs (see Note 7 – Liability Related to Sale of Future Royalties).

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

Note 5 — Balance Sheet Components

Our property and equipment consisted of (in thousands):

	December 31,	
	2020	2019
Property and equipment, net:		
Laboratory equipment	\$ 18,160	\$ 18,741
Computer equipment and software	2,940	2,940
Office equipment, furniture and fixtures	1,885	1,823
Leasehold improvements	5,872	5,221
Construction in progress	9,130	—
Total property and equipment	37,987	28,725
Less: Accumulated depreciation and amortization	(24,641)	(24,195)
	<u>\$ 13,346</u>	<u>\$ 4,530</u>

Depreciation expense was \$1.8 million for 2020 and \$1.3 million for 2019.

Our accrued liabilities were (in thousands):

	December 31,	
	2020	2019
Accrued liabilities:		
Clinical and preclinical costs	\$ 6,124	\$ 2,215
Compensation related	11,787	8,343
Other accrued expenses	1,404	1,565
Total accrued liabilities	<u>\$ 19,315</u>	<u>\$ 12,123</u>

CYTOKINETICS, INCORPORATED**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)**

We sponsor a 401(k) defined contribution plan covering all employees and contributed \$0.9 million and \$0.6 million to this plan in 2020 and 2019, respectively.

Note 6 — Debt***Term Loan***

Prior to May 17, 2019 we maintained a loan and security agreement dated as of October 19, 2015, as amended (the “Original Loan Agreement”) with the Lenders to fund our working capital and other general corporate needs.

On May 17, 2019, we entered into a new loan and security agreement (the “Term Loan Agreement”) with the Lenders for \$45.0 million (the “Term Loan”) and terminated the Original Loan Agreement. The proceeds of the Term Loan were used in part to repay in full all of the outstanding term loans under the Original Loan Agreement in an aggregate principal amount of \$42.0 million. On November 6, 2019 and November 7, 2019, the Company entered into a First Amendment and a Second Amendment to the Term Loan Agreement. The Term Loan Agreement, as amended, permits the issuance of the Convertible Notes and Capped Call Transactions discussed below. On July 16, 2020, the Company and the Lenders entered into the Third Amendment to the Term Loan Agreement, which amended the Term Loan Agreement to permit (i) the sale of the Mavacamten Royalty under the RTW Royalty Purchase Agreement and (ii) subject to entry into an intercreditor agreement between Oxford (as security agent for the Lenders) and RTW Royalty Holdings in form and substance reasonably satisfactory to the Lenders and RTW Royalty Holdings, permits the draw of funding under the Funding Agreement and the grant of a security interest to RTW Royalty Holdings in the intellectual property located in the United States and accounts receivable related to CK-274.

The Term Loan was accounted for as a debt modification in a non-troubled debt restructuring based on a comparison of the present value of the cash flows under the terms of the debt immediately before and after the effective date of the Term Loan, which resulted in a change of less than 10%. As a result, issuance costs paid to the lender in connection with the Term Loan were recorded as a reduction of the carrying amount of the debt liability and were not significant. Unamortized issuance costs as of the date of the modification were amortized to interest expense over the repayment term of Term Loan.

Both borrowings under the Original Loan Agreement and Term Loan bear interest at an annual rate equal to the greater of (a) 8.05% or (b) the sum of 6.81% plus the 30-day U.S. LIBOR rate. The borrowing under the Original Loan Agreement was repayable in monthly interest-only payments through November 2019 followed by 35 months of monthly payments of interest and principal. The borrowing under the Term Loan is repayable in monthly interest-only payments through December 31, 2020. The interest-only period was automatically extended until July 1, 2021 as a result of the Company’s initiation of a Phase 2 trial for CK-274 in cardiomyopathy and has been extended through December 31, 2021 as a result of the achievement of positive results in GALACTIC-HF, the trial of omecamtiv mecarbil in chronic heart failure as announced on October 8, 2020. The ultimate interest-only period will be followed by equal monthly payments of principal and interest to the maturity date in December 2023. The ultimate interest-only period will be followed by equal monthly payments of principal and interest to the maturity date in December 2023. We are required to make a final payment upon loan maturity of 6.00% of the notes payable, which we accrete over the life of the Term Loan. Our obligations under the Term Loan Agreement are secured by substantially all our current and future assets, other than our intellectual property.

Interest expense for the Term Loan was \$4.9 million, \$5.2 million and \$3.8 million for 2020, 2019 and 2018 respectively. As of December 31, 2020, the interest rate applicable to borrowings under the Term Loan was 8.05%.

The Term 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 Term Loan Agreement are secured by substantially all our current and future assets, other than our intellectual property. If the Term Loan becomes subject to mandatory prepayment under these provisions, we are subject to certain prepayment premiums of 3.00% in the first year, 2.00% in the second year and 1.00% in the third year and thereafter. We determined that these contingent prepayment provisions were an embedded component that qualified as a derivative which should be bifurcated from the Term Loan and accounted for separately from the host contract. As of December 31, 2020, the fair value of this embedded derivative was immaterial.

CYTOKINETICS, INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

Future minimum payments under the Term Loan Agreement are (in thousands):

Years ending December 31:

2021	3,673
2022	25,330
2023	28,079
Future minimum payments	57,082
Less: Interest and final payment	(12,082)
Term Loan, gross	<u>\$ 45,000</u>

Convertible Notes

On November 13, 2019, the Company issued \$138.0 million aggregate principal amount of 4.0% convertible senior notes due 2026 (the “2026 Notes”). The 2026 Notes are unsecured obligations and bear interest at an annual rate of 4.0% per year, payable semi-annually on May 15 and December 15 of each year, beginning May 15, 2020. The 2026 Notes are governed by an indenture between the Company and U.S. Bank National Association, as trustee. The 2026 Notes will mature on November 15, 2026, unless earlier repurchased or redeemed by the Company or converted at the option of the holders. The Company may redeem the 2026 Notes prior to the maturity date but is not required to and no sinking fund is provided for the 2026 Notes. The 2026 Notes may be converted, under certain circumstances as described below, based on an initial conversion rate of 94.7811 shares of common stock per \$1,000 principal amount (which represents an initial conversion price of \$10.55 per share). The conversion rate for the 2026 Notes will be subject to adjustment upon the occurrence of certain specified events. In addition, upon the occurrence of a make-whole fundamental change (as defined in the indenture), the Company will, in certain circumstances, increase the conversion rate by a number of additional shares for a holder that elects to convert its notes in connection with such make-whole fundamental change. The Company received approximately \$133.9 million in net proceeds, after deducting the initial purchasers’ discount, from the issuance of the 2026 Notes.

The 2026 Notes may be converted at the option of the holder under any of the following circumstances: (1) during any calendar quarter commencing after the calendar quarter ending on March 31, 2020 (and only during such calendar quarter), if the last reported sale price of the Company’s common stock for at least 20 trading days (whether or not consecutive) during a period of 30 consecutive trading days ending on, and including, the last trading day of the immediately preceding calendar quarter exceeds 127.5% of the last reported sale price of the Company’s common stock on November 7, 2019; (2) during the 5 consecutive business days immediately after any 10 consecutive trading day period (such 10 consecutive trading day period, the “measurement period”) if the trading price per \$1,000 principal amount of 2026 Notes for each trading day of the measurement period was less than 98% of the product of the last reported sale price per share of the Company’s common stock on such trading day and the conversion rate on such trading day; (3) upon the occurrence of certain corporate events or distributions on the Company’s common stock; (4) if the Company calls the 2026 Notes for redemption; and (5) at any time from, and including, July 15, 2026 until the close of business on the scheduled trading day immediately before the maturity date, November 15, 2026. The Company will settle conversions by paying or delivering, as applicable, cash, shares of the Company’s common stock, or a combination of cash and shares of the Company’s common stock, at the Company’s election, based on the applicable conversion rate.

The 2026 Notes will be redeemable, in whole or in part, at the Company’s option at any time, and from time to time, on or after November 20, 2023 and, in the case of any partial redemption, on or before the 60th scheduled trading day before the maturity date, at a cash redemption price equal to the principal amount of the 2026 Notes to be redeemed, plus accrued and unpaid interest, if any, to, but excluding, the redemption date but only if the last reported sale price per share of the Company’s common stock exceeds 130% of the conversion price on (1) each of at least 20 trading days, whether or not consecutive, during the 30 consecutive trading days ending on, and including, the trading day immediately before the date the Company sends the related redemption notice; and (2) the trading day immediately before the date the Company sends such notice. If a “fundamental change” (as defined in the indenture) occurs, then, subject to certain exceptions, holders may require the Company to repurchase their 2026 Notes at a cash repurchase price equal to the principal amount of the 2026 Notes to be repurchased, plus accrued and unpaid interest, if any, to, but excluding, the fundamental change repurchase date.

CYTOKINETICS, INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

In accounting for the issuance of the 2026 Notes, the Company separated the 2026 Notes into liability and equity components. The carrying amount of the liability component of approximately \$84.2 million was calculated by using a discount rate of 12.0%, which was estimated to be the Company's borrowing rate on the date of the issuance of the notes for a similar debt instrument without the conversion feature. The carrying amount of the equity component of approximately \$49.5 million, representing the conversion option, was determined by deducting the fair value of the liability component from the par value of the 2026 Notes. The equity component of the 2026 Notes is included in additional paid-in capital in the consolidated balance sheets and is not remeasured as long as it continues to meet the conditions for equity classification. The difference between the principal amount of the 2026 Notes and the liability component (the "debt discount") is amortized to interest expense using the effective interest method over the term of the 2026 Notes.

Debt issuance costs for the issuance of the 2026 Notes were approximately \$5.0 million, consisting of initial purchasers' discount and other issuance costs. In accounting for the transaction costs, the Company allocated the total amount incurred to the liability and equity components using the same proportions as the proceeds from the 2026 Notes. Transaction costs attributable to the liability component were approximately \$3.1 million, were recorded as debt issuance cost (presented as contra debt in the consolidated balance sheet) and are being amortized to interest expense over the term of the 2026 Notes. The transaction costs attributable to the equity component were approximately \$1.9 million and were netted with the equity component in stockholders' equity. As of December 31, 2020, the unamortized debt issuance cost for the 2026 Notes was \$2.8 million.

The following table presents the total amount of interest cost recognized relating to the 2026 Notes for 2020 and 2019 (in thousands):

	Years Ended December 31,	
	2020	2019
Contractual interest expense	\$ 5,520	\$ 721
Accretion of debt discount	5,246	673
Accretion of debt issuance costs	52	6
Total interest costs recognized	\$ 10,818	\$ 1,400

The effective interest rate on the liability component of the 2026 Notes was 12.5% for the year ended December 31, 2020, which remains unchanged from the date of issuance. The remaining unamortized debt discount was \$45.7 million as of December 31, 2020 and will be amortized over approximately 6.0 years.

Capped Call Transactions

In connection with the offering of the 2026 Notes, the Company entered into privately-negotiated capped call transactions with one of the underwriters in the offering or its affiliate. The Company used approximately \$13.4 million of the net proceeds from the offering of the 2026 Notes to pay the cost of the capped call transactions. The capped call transactions are expected generally to reduce potential dilution to the Company's common stock upon any conversion of the 2026 Notes and/or offset any cash payments the Company is required to make in excess of the principal amount of converted 2026 Notes, as the case may be, in the event that the market value per share of the Company's common stock, as measured under the terms of the capped call transactions at the time of exercise, is greater than the strike price of the capped call transactions (which initially corresponds to the initial conversion price of the 2026 Notes, and is subject to certain adjustments), with such reduction and/or offset subject to a cap initially equal to approximately \$14.07 per share (which represents a premium of approximately 70% over the last reported sale price of the Company's common stock on November 7, 2019), subject to certain adjustments. The capped call transactions are separate transactions, entered into by the Company and are not part of the terms of the 2026 Notes.

Given that the transactions meet certain accounting criteria, the convertible note capped call transactions are recorded in stockholders' equity, and they are not accounted for as derivatives and are not remeasured each reporting period. As of December 31, 2020, the Company had not purchased any shares under the convertible note capped call transactions.

Note 7 — Liability Related to Sale of Future Royalties to RPI

In February 2017, we entered into the RPI Royalty Purchase Agreement with RPI under which we sold a portion of our right to receive royalties on potential net sales of omeamtiv mecarbil (and potentially other compounds with the same mechanism of action) under the Amgen Agreement to RPI for a payment of \$90.0 million, which is non-refundable even if omeamtiv mecarbil is never commercialized. Concurrently, we entered into a common stock purchase agreement with RPI through which RPI purchased 875,656

CYTOKINETICS, INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

shares of the Company's common stock for \$10.0 million. We allocated the consideration and issuance costs on a relative fair value basis to the RPI Liability and the common stock, which resulted in the RPI Liability being initially recognized at \$92.3 million.

The RPI Royalty Purchase Agreement further provides that in the event Amgen elects to terminate the Amgen Agreement, we are obliged to enter into an agreement with RPI to preserve RPI's rights under the RPI Royalty Purchase Agreement, which includes the payment by Cytokinetics of 4.5% of its worldwide net sales of omecamtiv mecarbil and other Amgen Alliance Compounds, subject to a potential increase of up to an additional 1% under certain circumstances (delay in US marketing approval). Our obligation to enter into a new agreement with RPI does not impact our accounting treatment of the RPI Liability or our estimates.

We account for the RPI Liability as a liability primarily because we have significant continuing involvement in generating the royalty stream. If and when omecamtiv mecarbil is commercialized and royalties become payable, we will recognize the portion of royalties paid to RPI as a decrease to the RPI Liability with a corresponding reduction in cash.

The carrying amount of the RPI Liability is based on our estimate of the future royalties to be paid to RPI over the life of the arrangement as discounted using an imputed rate of interest. The excess of future estimated royalty payments over the \$92.3 million of allocated proceeds, less issuance costs, is recognized as non-cash interest expense using the effective interest method. The imputed rate of interest on the unamortized portion of the RPI Liability was approximately 15% as of December 31, 2020 and 17% as of December 31, 2019.

We periodically assess the amount and timing of expected royalty payments using a combination of internal projections and forecasts from external sources. To the extent such payments are greater or less than our initial estimates or the timing of such payments is materially different than its original estimates, we will prospectively adjust the amortization of the RPI Liability and the effective interest rate.

There are a number of factors that could materially affect the amount and timing of royalty payments, most of which are not within our control. The RPI Liability is recognized using significant unobservable inputs. These inputs are derived using internal management estimates developed based on third party data, including data historically provided by Amgen, and reflect management's judgements, current market conditions surrounding competing products, and forecasts. The significant unobservable inputs include the estimated patient population, estimated selling price, estimated peak sales and sales ramp, the expected term of the royalty stream, timing of the expected launch and its impact on the royalty rate as well as the overall probability of a success. A significant change in unobservable inputs could result in a material increase or decrease to the effective interest rate of the RPI Liability.

We have updated the analysis to include the data released on October 8, 2020 relating to GALACTIC-HF. Our estimates regarding the amount and timing of future royalty payments have not changed as a result of Amgen's election to terminate the Amgen Agreement or Servier's election to terminate the Servier Agreement.

Changes to the RPI Liability related to the sale of future royalties are as follows (in thousands):

	2020		2019	
Beginning balance, January 1	\$	143,276	\$	122,473
Interest accretion		22,713		20,737
Amortization of issuance costs		79		66
Ending balance, December 31	\$	<u>166,068</u>	\$	<u>143,276</u>

Note 8 — Stockholders' Equity**Common Stock Purchase Agreements**

On July 14, 2020, we entered into a CSPA with each of the RTW Investors. The CSPAs provide for the sale and issuance of an aggregate of 2.0 million shares of common stock of Cytokinetics (the "Shares") at a price per share of \$25.00 and an aggregate purchase price of \$50.0 million (see Note 3 – Research and Development Arrangements). The cash adjusted for the calculated premium is the \$36.5 million fair value of the common stock recorded.

CYTOKINETICS, INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

Public Offering of Common Stock

In July 2020, we closed an underwritten public offering of 8.4 million shares of our common stock at a public offering price per share of \$24.00, which included the exercise in full by the underwriters of their option to purchase up to 1,093,750 shares of our common stock at the same price. The gross proceeds were \$201.3 million and net proceeds were approximately \$188.9 million, after deducting underwriting discounts, commissions and offering costs.

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, 2020, we have 2.6 million shares of common stock reserved and available for issuance under the 2004 Plan.

In May 2019, the Company’s stockholders approved an amendment to the Amended and the 2004 Plan to increase the number of authorized shares reserved for issuance under the 2004 Plan by 4.1 million shares. In May 2020, the Company’s board of directors approved an amendment to the 2004 Plan to increase the number of authorized shares reserved for issuance under the 2004 Plan by 0.8 million shares for inducement grants to new employees. We started granting inducement grants in September 2020. As of December 31, 2020, an insignificant number of stock options were granted and 2.6 million authorized shares were available for grant under the 2004 Plan.

Stock option activity in 2020 was as follows:

	Stock Options Outstanding	Weighted Average Exercise Price per Share	Weighted Average Remaining Contractual Life (in years)	Aggregate Intrinsic Value (in millions)
Balance at December 31, 2018	6,454,037	\$ 8.72		
Granted	1,785,673	8.41		
Exercised	(126,793)	7.78		
Forfeited	(353,905)	10.44		
Balance at December 31, 2019	7,759,012	\$ 8.59		
Granted	1,944,562	15.59		
Exercised	(967,571)	8.27		
Forfeited	(234,054)	16.06		
Balance at December 31, 2020	8,501,949	\$ 10.02	6.6	\$ 91.9
Exercisable at December 31, 2020	5,704,396	\$ 8.91	5.6	\$ 67.8

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 \$14.0 million for 2020, \$0.5 million for 2019 and \$0.7 million for 2018. The intrinsic value of stock options outstanding at December 31, 2020 was \$91.9 million.

CYTOKINETICS, INCORPORATED
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

Restricted stock unit (“RSU”) activity in 2020 was as follows:

	Number of Restricted Stock Units	Weighted Average Award Date Fair Value per Share
Balance at December 31, 2018	546,500	\$ 8.53
Granted	607,150	7.14
Released	(266,500)	8.84
Forfeited	(48,075)	7.34
Balance at December 31, 2019	839,075	\$ 7.49
Granted	731,225	14.40
Released	(435,450)	7.72
Forfeited	(18,208)	10.37
Balance at December 31, 2020	1,116,642	\$ 11.88

RSUs generally vest annually over two to three years. For 2020, the fair value of RSUs vested, calculated based on the units vested multiplied by the closing price of our common stock on the date of vesting, was \$6.1 million.

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. In May 2020, the Company’s stockholders approved an amendment to the ESPP to increase the number of common stock shares reserved for issuance under the ESPP by 0.5 million shares.

We issued 11,565 shares at an average price of \$14.64 per share during 2020, 172,113 shares at an average price of \$6.43 per share in 2019, and 144,822 shares at an average price of \$6.40 per share in 2018 pursuant to the ESPP. At December 31, 2020, we have 446,820 shares of common stock reserved for issuance under the ESPP.

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, 2020		Year Ended December 31, 2019		Year Ended December 31, 2018	
	Options	ESPP	Options	ESPP	Options	ESPP
Risk-free interest rate	0.42% to 1.8%	0.11% to 1.8%	1.6% to 3.0%	1.8% to 2.4%	2.3% to 3.0%	1.5% to 2.5%
Volatility	74% to 75%	74% to 75%	73% to 76%	73% to 76%	73% to 74%	73% to 74%
Expected term in years	6.5 to 6.6	0.5	6.5	0.6	6.5	0.5
Expected dividend yield	0%	0%	0%	0%	0%	0%

We use 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 do not estimate forfeitures in our stock-based compensation.

We measure compensation expense for restricted stock units at fair value on the date of grant and recognize the expense over the expected vesting period. We recognize stock-based compensation expense on a ratable basis over the requisite service period, generally the vesting period of the award for share-based awards.

CYTOKINETICS, INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

Stock-based compensation expense for 2020 and 2019 was as follows (in thousands):

	Years Ended December 31,		
	2020	2019	2018
Research and development	\$ 6,949	\$ 4,260	\$ 5,101
General and administrative	10,671	6,499	4,660
	<u>\$ 17,620</u>	<u>\$ 10,759</u>	<u>\$ 9,761</u>

Stock-based compensation expense for share-based awards to non-employees was \$0.2 million in 2020, \$0.2 million in 2019 and \$0.1 million in 2018.

As of December 31, 2020, we expect to recognize \$22.2 million of unrecognized compensation cost related to unvested stock options over a weighted-average period of 2.5 years and \$7.9 million of unrecognized compensation cost related to unvested restricted stock over a weighted-average period of 1.7 years.

Warrants

Pursuant to the Term Loan agreement described in Note 6 - Debt, we issued a warrant with an exercise price of \$9.76 per share to purchase 23,065 shares of our common stock in 2019. The warrant was fully exercisable and expires in May 2029. As of December 31, 2019, warrants to purchase 165,424 shares of our common stock with a weighted average exercise price of \$7.25 per share were outstanding. All outstanding warrants are fully exercisable and expire ten years after issuance.

During the first quarter of 2020, in connection with the Term Loan Agreement further described in Note 6 - Debt, we issued a warrant with an exercise price of \$10.42 per share to purchase 21,595 shares of our common stock. The warrant was issued in connection with achieving the interest-only extension milestone 1 in the Term Loan Agreement. The warrant was fully exercisable and expires in January 2030. The \$0.2 million fair value of the warrant related to the Term Loan was recorded as interest expense in the period.

In July 2020, OTA LLC, an assignee of Oxford, exercised 51,214 warrants with a strike price of \$6.59 per share, 48,892 warrants with a strike price of \$6.903 per share, and 25,352 warrants with a strike price of \$7.10 per share and elected the cashless settlement method. Accordingly, in July 2020, we issued to OTA LLC a total of 95,932 shares of our common stock.

In October 2020, OTA LLC exercised 13,839 warrants with a strike price of \$9.755 per share and elected cashless settlement method. Accordingly, in October 2020, we issued OTA LLC a total of 8,958 shares of our common stock.

As of December 31, 2020, we had outstanding warrants issued pursuant to the Original Loan Agreement and Term Loan Agreement with a weighted average exercise price of \$9.12 per share to purchase 47,722 shares of our common stock.

Committed Equity Offering

In 2019, we terminated our original Controlled Equity OfferingSM 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 and we 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 \$85.0 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 pay a commission of up to 3.0% of gross sales proceeds of any common stock sold under the New ATM Facility. As of 2019, we issued 3,984,849 shares of common stock for net proceeds of \$36.2 million under the New ATM Facility.

Claims Settlement

In the first quarter of 2020, we received \$2.2 million from a claims settlement with certain institutional investors that were beneficial owners of our common stock related to the disgorgement of short swing profits pursuant to Section 16(b) of the Securities Exchange Act of 1934, as amended. This settlement was recognized in equity as additional paid-in capital.

CYTOKINETICS, INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

Note 9 — Commitments and Contingencies**Leases**

Our lease for 280 and 256 East Grand Avenue, South San Francisco, California for our existing facilities expires in 2021 and includes rental payments on a graduated scale and payment of certain operating expenses. As of December 31, 2020, the remaining lease term is 0.5 years and the discount rate used to determine the related operating lease liability was 9.0%.

In July 2019, we amended the lease agreement in connection with our leasing of additional premises at 250 East Grand Avenue, South San Francisco, California (the “Expansion Lease”) for 9,530 square feet of office space. The Expansion Lease has an initial term of 39 months, and commenced in January 2020. As of December 31, 2020, the remaining lease term of the Expansion Lease is 2.3 years and the discount rate used to determine the related operating lease liability was 11.5%.

In July 2019, we entered into a lease agreement for approximately 234,892 square feet of office and laboratory space at a facility located in South San Francisco, California (the “Oyster Point Lease”). The Oyster Point Lease has an initial term of twelve years, and is expected to commence in September 2021 and we have two consecutive five-year options to extend the lease. Subject to rent abatement for the first two months of the Oyster Point Lease, we will be required to pay \$5.45 per square foot for 159,891 square feet for the first twelve months of the lease term, which will increase at a rate of 3.5% per year. After the first twelve months of the Oyster Point Lease, rent will be payable on the entire leased square footage. We paid fifty percent of the security deposit amount on December 31, 2019 and the remaining fifty percent was paid in December 2020. The landlord will provide a tenant improvement allowance of \$35.3 million for costs relating to the initial design and construction of the improvements. We will pay certain operating costs of the facility and have certain rights to sublease under the related lease agreement. The total commitment of undiscounted lease payments for the Oyster Point Lease was \$217.7 million at December 31, 2020.

While we had \$9.1 million in construction in progress related to the Oyster Point Lease as of December 31, 2020, the Company has not recognized a right-of-use asset or aggregate lease liability as of December 31, 2020 for the Oyster Point Lease as the underlying assets were unavailable to use by the Company at any time in the period ended December 31, 2020.

The undiscounted future non-cancellable lease payments under the lease agreements as of December 31, 2020 is as follows (in thousands):

Years ending December 31:	
2021	\$ 4,616
2022	12,694
2023	16,194
2024	16,648
2025	17,231
Thereafter	153,689
Total undiscounted future lease payments	221,072
Less: Undiscounted lease payments related to Oyster Point Lease	(217,667)
Less: Present value adjustments	(180)
Total lease liability	\$ 3,225

As of December 31, 2020, future minimum lease payments under noncancelable operating leases were \$4.6 million in 2021, \$12.7 million in 2022 and \$16.2 million in 2023.

Cash paid for amounts included in the measurement of lease liabilities for the years ended December 31, 2020 and 2019 was \$6.7 million and \$5.0 million, respectively, and was included in net cash provided by operating activities in our consolidated statements of cash flows.

Rent expenses were \$5.7 million, \$5.1 million and \$5.0 million for 2020, 2019 and 2018, respectively.

CYTOKINETICS, INCORPORATED
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)
Note 10 — Income Taxes

We did not record an income tax provision in 2020, 2019 and 2018 because we had net taxable losses. Our significant jurisdictions are the United States and California.

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

	Years Ended December 31,		
	2020	2019	2018
Tax at federal statutory tax rate	21%	21%	21%
State tax, net of federal benefits	1%	3%	0%
Change in state effected rates	(2)%	4%	(4)%
Tax credits, net	3%	3%	1%
Change in valuation allowance	(23)%	(30)%	(17)%
Stock-based compensation	1%	(1)%	(1)%
Other	(1)%	0%	0%
Total	<u>0%</u>	<u>(0)%</u>	<u>(0)%</u>

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,	
	2020	2019
Deferred tax assets:		
Net operating loss carryforwards	\$ 162,514	\$ 143,228
Tax credits	71,976	67,892
Liability related to sale of future royalties	36,989	35,213
Reserves and accruals	10,876	8,690
Capitalized R&D	2,370	3,949
Long-term lease liability	718	1,674
Depreciation and amortization	746	722
Other	—	58
Total noncurrent deferred tax assets	<u>286,189</u>	<u>261,426</u>
Deferred tax liabilities:		
Accounting method change	(927)	(2,047)
Operating lease right-of-use assets	(651)	(1,484)
Convertible notes	(9,832)	(12,011)
Total noncurrent deferred tax liabilities	<u>(11,410)</u>	<u>(15,542)</u>
Less: Valuation allowance	(274,779)	(245,884)
Net deferred tax assets	<u>\$ —</u>	<u>\$ —</u>

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, 2020 and 2019. The valuation allowance increased by \$28.9 million in 2020 and increased by \$24.8 million in 2019.

At December 31, 2020 federal NOL carryforwards were \$662.9 million and apportioned state NOL carryforwards before federal benefits were \$317.0 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, 2020, tax credits of \$68.4 million and \$16.6 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.

CYTOKINETICS, INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

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, however, a portion of its NOLs and tax credits prior to 2007 will be subject to limitations under Section 382.

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

	Years Ended December 31,		
	2020	2019	2018
Balance at the beginning of the year	\$ 9,922	\$ 9,475	\$ 9,365
Decrease related to prior year tax positions	(3)	—	—
Increase related to current year tax positions	603	447	110
Balance at the end of the year	\$ 10,522	\$ 9,922	\$ 9,475

We are subject to income tax examination for all fiscal years with unutilized NOLs and tax credit carryforwards. Included in the balance of unrecognized tax benefits as of December 31, 2020, 2019 and 2018 are \$9.6 million, \$9.1 million and \$8.6 million of tax benefits, respectively, that, if recognized, would result in adjustments to other tax accounts, primarily deferred taxes.

On March 27, 2020, the Coronavirus Aid, Relief, and Economic Security (CARES) Act was signed into law making several changes to the Internal Revenue Code. We continue to evaluate the impact of the Employee Retention Credit and will consider future guidance from the IRS to determine any potential benefit given our specific facts and circumstances. The tax law changes in the CARES Act did not have a material impact on the Company's income tax provision.

Note 11 — Subsequent Events

In January 2021, we entered into a Second Amendment to the Oyster Point Lease. The Second Amendment increases the tenant improvement allowance by \$8.2 million, to cover the construction obligations of the improvements on the Oyster Point Lease. In addition, subject to rent abatement for the two months commencing in October 2021, the base rent for the initial lease term will be increased by \$0.1 million per month, commencing in September 2021, to repay the additional tenant improvement allowance to the landlord with interest at a rate of 8%. We will pay certain operating costs of the facility under the amended agreement.

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 required by Rule 13a-15(b) under the Exchange Act, our management, under the supervision and with the participation of our principal executive officer and principal financial officer, has evaluated the effectiveness of the design and operation of our disclosure controls and procedures (as such term is defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) as of December 31, 2020. Based on such evaluation, our principal executive officer and principal financial officer have concluded that, as of December 31, 2020, our disclosure controls and procedures were effective at the reasonable assurance level.

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, 2020 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 effective as of December 31, 2020.

Our independent registered public accounting firm, Ernst & Young LLP, has audited the financial statements included in this Annual Report and has issued a report on the effectiveness of our internal control over financial reporting. The report of Ernst & Young LLP is included below.

Changes in Internal Control over Financial Reporting

There were no other changes in our internal controls over financial reporting identified in connection with the evaluation required by Rules 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the fiscal quarter ended December 31, 2020 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

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, 2020, 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, Cytokinetics, Incorporated (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2020, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the 2020 consolidated financial statements of the Company and our report dated February 26, 2021 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 Annual 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
February 26, 2021

ITEM 9B. OTHER INFORMATION

None.

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 2020 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 for our 2020 Annual Meeting of Stockholders, where it appears under the heading “Executive Compensation.”

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 our definitive Proxy Statement for our 2020 Annual Meeting of Stockholders, where it appears under the headings “Certain Business Relationships and Related Party Transactions” and “Corporate Governance.”

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 for our 2020 Annual Meeting of Stockholders, 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 for our 2020 Annual Meeting of Stockholders, where it appears under the headings “Independent Registered Public Accounting Firm Services and Fees.”

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:

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.

(2) Financial Statement Schedules:

Financial statement schedules have been omitted in this report because they are not applicable, not required under the instructions, or the information requested is set forth in the consolidated financial statements or related notes thereto.

b) Exhibits:

EXHIBIT INDEX

Exhibit No.	Exhibits	Incorporated by Reference			Exh. No.	Filed Herewith
		Form	File No.	Filing Date		
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	
4.4	Form of Warrant Issuable to Oxford Finance LLC	10-Q	000-50633	August 9, 2019	4.2	
4.5	Form of Warrant Issuable to Silicon Valley Bank	10-Q	000-50633	August 9, 2019	4.3	
4.6	Base Indenture, dated November 13, 2019, between the Company and U.S. Bank National Association, as Trustee	8-K	000-50633	November 13, 2019	4.1	
4.7	First Supplemental Indenture, dated November 13, 2019, between the Company and U.S. Bank National Association, as Trustee (including the form of 4.00% Convertible Senior Note due 2026)	8-K	000-50633	November 13, 2019	4.2	

[Table of Contents](#)

Exhibit No.	Exhibits	Incorporated by Reference			Exh. No.	Filed Herewith
		Form	File No.	Filing Date		
4.8	Description of Securities	10-K	000-50633	March 4, 2020	4.8	
10.1+	Amended and Restated 2004 Equity Incentive Plan	S-8	333-238786	May 29, 2020	99.1	
10.2+	Amended and Restated 2015 Employee Stock Purchase Plan	DEF 14A	000-50633	March 26, 2020	Appendix A	
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	
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	

[Table of Contents](#)

Exhibit No.	Exhibits	Incorporated by Reference			Exh. No.	Filed Herewith
		Form	File No.	Filing Date		
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*	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	
10.19*	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	
10.20*	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	
10.21*	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	
10.22+	Form of Amendment No. 1 to Amended and Restated Executive Employment Agreements	10-K	000-50633	March 12, 2009	10.68	
10.23	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	
10.24*	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+	Form of Option Agreement	10-K	000-50633	March 15, 2013	10.46	
10.27+	Form of Restricted Stock Unit Award Agreement	10-K	000-50633	March 15, 2013	10.47	
10.29*	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	
10.30+	Form of Executive Employment Agreement between the Company and its executive officers	10-K	000-50633	March 7, 2014	10.39	
10.33*	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	
10.34	Amendment to Collaboration Agreement: Joint Development Committee Membership	10-Q	000-50633	August 7, 2018	10.1	

[Table of Contents](#)

Exhibit No.	Exhibits	Incorporated by Reference			Exh. No.	Filed Herewith
		Form	File No.	Filing Date		
10.36	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	
10.37#	Fast Skeletal Regulatory Activator Agreement, dated April 23, 2020, by and between the Company and Astellas Pharma Inc.	10-Q	000-50633	August 7, 2020	10.3	
10.38#	License and Collaboration Agreement for Other Skeletal Sarcomere Activators, dated April 23, 2020, by and between the Company and Astellas Pharma Inc.	10-Q	000-50633	August 7, 2020	10.4	
10.43	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	
10.44	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	
10.47*	Amendment No. 8, dated November 30, 2016, to the Collaboration and Option Agreement by and between the Company and Amgen Inc.	10-K	000-50633	March 7, 2019	10.49	
10.48	Amendment No. 9, dated February 6, 2019, to the Collaboration and Option Agreement by and between the Company and Amgen Inc.	10-K	000-50633	March 7, 2019	10.50	
10.49	Loan and Security Agreement, dated as of May 17, 2019, by and among the Company, Oxford Finance LLC and Silicon Valley Bank	10-Q	000-50633	August 9, 2019	10.1	
10.50	Seventh Amendment to Lease, dated July 11, 2019, by and between the Company and Britannia Pointe Grand Limited Partnership	10-Q	000-50633	November 1, 2019	10.51	
10.51	Lease, dated July 24, 2019, by and between the Company and KR Oyster Point 1, LLC	10-Q	000-50633	November 1, 2019	10.52	
10.52#	First Amendment to Loan and Security Agreement, dated as of November 6, 2019, by and among the Company, Oxford Finance LLC and Silicon Valley Bank	8-K	000-50633	November 13, 2019	10.1	
10.53#	Second Amendment to Loan and Security Agreement, dated as of November 7, 2019, by and among the Company, Oxford Finance LLC and Silicon Valley Bank	8-K	000-50633	November 13, 2019	10.2	

[Table of Contents](#)

Exhibit No.	Exhibits	Incorporated by Reference			Exh. No.	Filed Herewith
		Form	File No.	Filing Date		
10.54†	Third Amendment to Loan and Security Agreement, dated July 16, 2020, by and among the Company, Oxford Finance LLC and Silicon Valley Bank	10-Q	000-50633	November 6, 2020	10.5	
10.55#†	License and Collaboration Agreement, dated July 14, 2020, by and between the Company and Ji Xing Pharmaceuticals Limited	10-Q	000-50633	November 6, 2020	10.1	
10.56#†	Funding Agreement, dated July 14, 2020, by and between the Company and RTW Royalty Holdings Designated Activity Company (f/k/a/ Dolya Holdco 19 Designated Activity Company)	10-Q	000-50633	November 6, 2020	10.2	
10.57#†	Royalty Purchase Agreement, dated July 14, 2020, by and between the Company and RTW Royalty Holdings Designated Activity Company (f/k/a/ Dolya Holdco 19 Designated Activity Company)	10-Q	000-50633	November 6, 2020	10.3	
10.58#	Form of Common Stock Purchase Agreement, dated July 14, 2020	10-Q	000-50633	November 6, 2020	10.4	
10.59	First Amendment to Lease, dated May 12, 2020, by and between the Company and KR Oyster Point 1, LLC					X
10.60	Second Amendment to Lease, dated January 26, 2021, by and between the Company and KR Oyster Point 1, LLC					X
10.61#	Letter Agreement, dated December 23, 2020, by and between Company and Astellas amending the License and Collaboration Agreement for Other Skeletal Sarcomere Activators, dated April 23, 2020, by and between the Company and Astellas Pharma Inc.					X
23.1	Consent of independent registered public accounting firm					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

Exhibit No.	Exhibits	Incorporated by Reference			Exh. No.	Filed Herewith
		Form	File No.	Filing Date		
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	Inline XBRL Instance Document (the Instance Document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document)					X
101.SCH	Inline XBRL Taxonomy Extension Schema Document					X
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document					X
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document					X
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document					X
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document					X
104	Cover Page Interactive Data File (formatted as Inline XBRL in Exhibit 101)					X

* Portions of this Exhibit are subject to a confidential treatment order.

Portions of this Exhibit have been omitted as being immaterial and would be competitively harmful if publicly disclosed

+ Schedules have been omitted pursuant to Item 601(a)(5) of Regulation S-K and will be furnished on a supplemental basis to the Securities and Exchange Commission upon request

+ 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: February 26, 2021

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Robert I. Blum, Ching Jaw, Mark A. Schlossberg and Robert Wong, 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)	February 26, 2021
/s/ CHING W. JAW Ching W. Jaw	Senior Vice President, Chief Financial Officer (Principal Financial Officer)	February 26, 2021
/s/ ROBERT C. WONG Robert C. Wong	Vice President, Chief Accounting Officer (Principal Accounting Officer)	February 26, 2021
/s/ L. PATRICK GAGE, PH.D. L. Patrick Gage, Ph.D.	Chairman of the Board of Directors	February 26, 2021
/s/ ROBERT M. CALIFF, M.D. Robert M. Califf, M.D.	Director	February 26, 2021
/s/ SANTO J. COSTA Santo J. Costa	Director	February 26, 2021
/s/ JOHN T. HENDERSON, M.B. CH.B. John T. Henderson, M.B. Ch.B.	Director	February 26, 2021
/s/ EDWARD M. KAYE, M.D. Edward M. Kaye, M.D.	Director	February 26, 2021
/s/ B. LYNNE PARSHALL, Esq. B. Lynne Parshall, Esq.	Director	February 26, 2021
/s/ SANDFORD D. SMITH Sandford D. Smith	Director	February 26, 2021
/s/ WENDELL WIERENGA, PH.D. Wendell Wierenga, Ph.D.	Director	February 26, 2021
/s/ NANCY J. WYSENSKI Nancy J. Wysenski	Director	February 26, 2021
/s/ MUNA BHANJI Muna Bhanji	Director	February 26, 2021

FIRST AMENDMENT TO LEASE

This FIRST AMENDMENT TO LEASE ("**First Amendment**") is made and entered into as of May 12, 2020, by and between KR OYSTER POINT I, LLC, a Delaware limited liability company ("**Landlord**"), and CYTOKINETICS, INCORPORATED, a Delaware corporation ("**Tenant**").

RECITALS:

- A. Landlord and Tenant are parties to the Lease dated July 24, 2019 (the "**Lease**"), whereby Tenant leases certain space (the "**Premises**") within Building 3 in Phase 1 of that certain project commonly known as "**Kilroy Oyster Point**" and more particularly described in the Lease.
- B. Landlord and Tenant desire to amend the Lease on the terms and conditions set forth in this First Amendment.

AGREEMENT:

NOW, THEREFORE, in consideration of the foregoing recitals and the mutual covenants contained herein, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the parties hereto hereby agree as follows:

1. **Capitalized Terms.** All capitalized terms when used herein shall have the same meaning as is given such terms in the Lease unless expressly superseded by the terms of this First Amendment.
 2. **Construction of the Auditorium; Auditorium Allowance.** Notwithstanding any contrary provision contained in the Lease, including, without limitation, Section 1.1.1.1 of the Lease, Landlord and Tenant agree that Landlord shall not be obligated to construct the Auditorium as part of its construction of the Base, Shell and Core, and instead, Tenant shall construct the Auditorium as part of the Improvements (the "**Auditorium Work**"). Notwithstanding any contrary provision contained in the Lease, in addition to the Improvement Allowance, Tenant shall also be entitled to the following one-time improvement allowance in the amount of One Million Two Hundred Seventy Thousand Five Hundred Seventy-Five and 00/100 Dollars (\$1,270,575.00) (the "**Auditorium Allowance**") for the costs relating to the performance of the Auditorium Work. In no event shall Landlord make disbursements from the Auditorium Allowance for costs which are unrelated to the Auditorium Work nor for any Auditorium Work in a total amount which exceeds the Auditorium Allowance. The procedure for disbursement of the Auditorium Allowance shall be the same as the procedure to disburse the Improvement Allowance, and shall be subject to the Allowance Deadline.
 3. **Tenant Requested Changes to Base Building Plans.** Notwithstanding anything to the contrary set forth in the Lease or the Work Letter attached thereto, Tenant shall have the right to request additional changes to the Base Building Plans in writing and Landlord shall not unreasonably withhold its consent to such changes; provided that, (i) such modifications are minor
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and do not adversely affect the quality of the Base, Shell and Core, (ii) such modifications are consistent with the base building components of Comparable Buildings, (iii) such changes do not adversely affect the Gold LEED certification for the Base, Shell and Core, (iv) such changes do not materially reduce the RSF of the Building, (v) such changes will not adversely affect Landlord's ability to receive a temporary certificate of occupancy (including a fully signed off job card) from the City (as applicable, a "**TCO**") for Building 3 or any other portion of the Project, (f) such changes will not delay the construction schedule for Phase 1 or Landlord's ability to obtain a TCO for Building 3 or any other portion of the Project, and (vi) such changes comply with Applicable Laws ("**Tenant Requested Changes**"). Landlord has retained Hathaway Dinwiddie as the general contractor for the Base, Shell and Core ("**Landlord's GC**"). Landlord has conceptually approved the construction, by Landlord, of the certain Tenant Requested Changes, set forth on Exhibit A attached hereto, and designated certain such Tenant Requested Changes as Specialty Alterations that Tenant will be required to remove and restore pursuant to Section 8.5 of the Lease, as modified by Section 4 below.

3.1. **TRC Construction Drawings**. Prior to commencing to construct any Tenant Requested Change, Landlord shall cause Landlord's architect and engineers to cooperate with Tenant (and Tenant shall cooperate with Landlord's architect and engineers) to prepare all plans and specifications relating to the Tenant Requested Change, and Landlord's architect shall compile a fully coordinated set of architectural, structural, mechanical, electrical and plumbing working drawings and specifications in a form which is complete to allow subcontractors to bid on the work and to obtain all applicable permits (collectively, the "**TRC Construction Drawings**") and shall submit the same to Tenant for Tenant's approval. Tenant shall advise Landlord within five (5) business days after Tenant's receipt of the TRC Construction Drawings of whether Tenant approves or disapproves the TRC Construction Drawings. If Tenant fails to respond within such five (5) business day period, then Landlord shall deliver a second notice to Tenant requesting Tenant's approval of the TRC Construction Drawings (which second notice shall include a copy of such TRC Construction Drawings), and if Tenant fails to respond within three (3) business days following Tenant's receipt of such second notice then Tenant shall be deemed to have elected not to proceed with the applicable Tenant Requested Change. If Tenant disapproves all or any portion of the TRC Construction Drawings, Tenant shall provide reasons for such disapproval, Landlord shall cause the applicable TRC Construction Drawings to be revised to address Tenant's concerns. If Tenant determines not to proceed with any of the Tenant Requested Changes, thereafter within ten (10) days of request (including a reasonably detailed invoice therefor), Tenant shall reimburse Landlord for any soft and hard costs incurred by Landlord relating to the Tenant Requested Changes which costs shall be deducted from the undisbursed and unallocated Improvement Allowance.

3.2. **Approved Tenant Change; Scheduling; Cost Estimate**. After finalization of the TRC Construction Documents, Landlord shall deliver to Tenant written notice (a "**Tenant Change Estimate Notice**") of (i) the anticipated schedule and timing for performing the Tenant Requested Change, including the anticipated days to design and construct the applicable Tenant Requested Change (the "**TRC Construction Schedule**") and (ii) the estimate of the costs that will be incurred to implement the proposed Tenant Requested Change. After receipt of a Tenant Change Estimate Notice, Tenant shall advise Landlord within five (5) days of receipt whether Tenant irrevocably approves the proposed Tenant Requested Change (hereinafter referred to as an "**Approved Tenant Change**"), and then the Approved Tenant Change shall be constructed

by Landlord and the cost of each Approved Tenant Change shall be deducted from the Improvement Allowance (or if no Improvement Allowance funds are available, paid by Tenant within thirty (30) days after receipt of an invoice). If Tenant fails to respond to a Tenant Change Estimate Notice within such five (5) business day period, then Landlord shall deliver a second notice to Tenant requesting Tenant's approval of the Tenant Change Estimate Notice (which second notice shall include a copy of such Tenant Change Estimate Notice), and if Tenant fails to respond within three (3) business days following Tenant's receipt of such second notice then Tenant shall be deemed to have elected not to proceed with the applicable Tenant Requested Change. All Approved Tenant Changes shall be constructed as part of the Base, Shell and Core, and shall be at Tenant's sole cost and expense or deducted from the Allowance, including a Landlord supervision fee equal to three percent (3%) of the other costs of constructing the Approved Tenant Change. The TRC Construction Schedule will set forth anticipated timing for completion of the Tenant Requested Change, and may be adjusted by mutual agreement of the parties, by field conditions, by Force Majeure, or as otherwise requested or required by Tenant. Any delay in the construction of the Base, Shell and Core resulting from any Tenant Requested Change (whether or not such Tenant Requested Change ultimately becomes an Approved Tenant Change) shall be a Tenant Delay.

4. **Landlord's Property.** Notwithstanding any contrary provision contained in the Lease, effective as of the date of this First Amendment, Section 8.5 of the Lease is hereby deleted and replaced with the following:

"Landlord's Property. Tenant may remove any Alterations, Improvements, fixtures, affixed equipment and/or appurtenances from the Premises which Tenant can reasonably demonstrate were not paid for with the Improvement Allowance or other funds provided by Landlord, and may remove all items constituting Tenant's intellectual property or trade secrets that are not affixed to the Premises, provided that Tenant repairs any damage to the Premises caused by such removal. Furthermore, Landlord may, by written notice to Tenant at the time of Landlord's consent to any Alterations, Improvements or Tenant Requested Changes that constitute Specialty Alterations, require Tenant, at Tenant's expense, to remove any Specialty Alterations, and to repair any damage to the Premises and Project caused by such removal. **"Specialty Alterations"** means any Alterations or Improvements which are not typical tenant improvements for the Permitted Use and any Tenant Requested Changes. In addition to removing any Specialty Alterations designated by Landlord for removal as set forth above, in all cases Tenant shall be required to remove, and to restore the Premises or Project, as applicable, to their previous condition, the following: (a) any Cafeteria, kitchens, showers, restrooms, washrooms or similar facilities in the Premises that are not part of the Base Building, (b) any private/internal stairways in the Premises, as opposed to fire stairs (and Tenant shall be required to demolish and "cap" any such private/internal stairways at the expiration or earlier termination of this Lease), (c) any other items, improvements or fixtures which Tenant is expressly required to remove pursuant to the terms of this Lease, (d) any improvements or signage incorporating Tenant's name or logo, (e) safes and vaults, (f) raised flooring, and (g) any alteration, improvement or equipment not complying with Applicable Laws as of the date such Alteration or Improvement was made to the Premises (or subsequently modified by Tenant). If Tenant fails to complete such removal and/or to repair any damage caused by the removal of anything required to be removed under this section, then Landlord may do so and may charge the cost thereof to Tenant."

5. **Depiction of Parking Facilities.** Notwithstanding any contrary provision contained in the Lease, effective as of the date of this First Amendment, **Exhibit A-3** attached to the Lease is hereby deleted and replaced with **Exhibit B** attached hereto.

6. **No Broker.** Landlord and Tenant hereby warrant to each other that they have had no dealings with any real estate broker or agent in connection with the negotiation of this First Amendment, and that they know of no other real estate broker or agent who is entitled to a commission in connection with this First Amendment. Each party agrees to indemnify and defend the other party against and hold the other party harmless from and against any and all claims, demands, losses, liabilities, lawsuits, judgments, and costs and expenses (including, without limitation, reasonable attorneys' fees) with respect to any leasing commission or equivalent compensation alleged to be owing on account of the indemnifying party's dealings with any real estate broker or agent through, or under the indemnifying party. The terms of this **Section 6** shall survive the expiration or earlier termination of the term of the Lease, as hereby amended.

7. **Certified Access Specialist.** For purposes of Section 1938 of the California Civil Code, Landlord hereby discloses to Tenant, and Tenant hereby acknowledges, that the Premises have not undergone inspection by a Certified Access Specialist (CASp). As required by Section 1938(e) of the California Civil Code, Landlord hereby states as follows: "A Certified Access Specialist (CASp) can inspect the subject premises and determine whether the subject premises comply with all of the applicable construction-related accessibility standards under state law. Although state law does not require a CASp inspection of the subject premises, the commercial property owner or lessor may not prohibit the lessee or tenant from obtaining a CASp inspection of the subject premises for the occupancy or potential occupancy of the lessee or tenant, if requested by the lessee or tenant. The parties shall mutually agree on the arrangements for the time and manner of the CASp inspection, the payment of the fee for the CASp inspection, and the cost of making any repairs necessary to correct violations of construction-related accessibility standards within the premises." In furtherance of the foregoing, Landlord and Tenant hereby agree as follows: (a) any CASp inspection requested by Tenant shall be conducted, at Tenant's sole cost and expense, by a CASp designated by Landlord, subject to Landlord's reasonable rules and requirements; (b) Tenant, at its sole cost and expense, shall be responsible for making any improvements or repairs within the Premises to correct violations of construction-related accessibility standards; and (c) if anything done by or for Tenant in its use or occupancy of the Premises shall require any improvements or repairs to the Building or Project (outside the Premises) to correct violations of construction-related accessibility standards, then Tenant shall reimburse Landlord upon demand, as Additional Rent, for the cost to Landlord of performing such improvements or repairs.

8. **Prohibited Persons; Foreign Corrupt Practices Act and Anti-Money Laundering.** Neither Tenant nor any of its affiliates, nor any of their respective members, partners or other equity holders, and none of their respective officers, directors or managers is, nor prior to or during the Lease Term, will they become a person or entity with whom U.S. persons or entities are restricted from doing business under (a) the Patriot Act (as defined below), (b) any other requirements contained in the rules and regulations of the Office of Foreign Assets Control, Department of the Treasury ("**OFAC**") (including any "blocked" person or entity listed in the Annex to Executive Order Nos. 12947, 13099 and 13224 and any modifications thereto or thereof or any other person or entity named on OFAC's Specially Designated Blocked Persons List) or (c)

any other U.S. statute, Executive Order (including the September 24, 2001, Executive Order Blocking Property and Prohibiting Transactions with Persons Who Commit, Threaten to Commit or Support Terrorism) or other governmental action (collectively, "**Prohibited Persons**"). Prior to and during the Lease Term, Tenant, and to Tenant's knowledge, its employees and any person acting on its behalf have at all times fully complied with, and are currently in full compliance with, the Foreign Corrupt Practices Act of 1977 and any other applicable anti-bribery or anti-corruption laws. Tenant is not entering into this First Amendment, directly or indirectly, in violation of any laws relating to drug trafficking, money laundering or predicate crimes to money laundering. Notwithstanding anything contained herein to the contrary, for the purposes of this Section 8 the phrase "Tenant nor any of its affiliates, nor any of their respective members, partners or other equity holders" and all similar such phrases shall not include any holder of a direct or indirect interest in a publicly traded company whose shares are listed and traded on a United States national stock exchange. Neither Landlord nor any of its affiliates, nor any of their respective members, partners or other equity holders, and none of their respective officers, directors or managers is, nor prior to or during the Term, will they become Prohibited Persons. Prior to and during the Term, Landlord, and to Landlord's knowledge, its employees and any person acting on its behalf have at all times fully complied with, and are currently in full compliance with, the Foreign Corrupt Practices Act of 1977 and any other applicable anti-bribery or anti-corruption laws. Landlord is not entering into this First Amendment, directly or indirectly, in violation of any laws relating to drug trafficking, money laundering or predicate crimes to money laundering. Notwithstanding anything contained herein to the contrary, for the purposes of this Section 8 the phrase "Landlord nor any of its affiliates, nor any of their respective members, partners or other equity holders" and all similar such phrases shall not include (i) any holder of a direct or indirect interest in a publicly traded company whose shares are listed and traded on a United States national stock exchange or (ii) any limited partner, unit holder or shareholder owning an interest of five percent (5%) or less in Kilroy Realty, L.P. or Kilroy Realty Corporation. As used herein, "**Patriot Act**" shall mean the USA Patriot Act of 2001, 107 Public Law 56 (October 26, 2001) and all other statutes, orders, rules and regulations of the U.S. government and its various executive departments, agencies and offices interpreting and implementing the Patriot Act.

9. **Signatures.** The parties hereto consent and agree that this First Amendment may be signed and/or transmitted by facsimile, e-mail of a .pdf document or using electronic signature technology (e.g., via DocuSign or similar electronic signature technology), and that such signed electronic record shall be valid and as effective to bind the party so signing as a paper copy bearing such party's handwritten signature. The parties further consent and agree that (1) to the extent a party signs this First Amendment using electronic signature technology, by clicking "SIGN", such party is signing this First Amendment electronically, and (2) the electronic signatures appearing on this First Amendment shall be treated, for purposes of validity, enforceability and admissibility, the same as handwritten signatures.

10. **No Further Modification.** Except as set forth in this First Amendment, all of the terms and provisions of the Lease shall apply with respect to the Expansion Premises and shall remain unmodified and in full force and effect.

IN WITNESS WHEREOF, this First Amendment has been executed as of the day and year first above written.

"LANDLORD"

KILROY OYSTER POINT I, LLC,
a Delaware limited liability company

By: Kilroy Realty, L.P.,
a Delaware limited partnership
its Sole Member

By: Kilroy Realty Corporation,
a Maryland corporation
Its General Partner

By: /s/ Tyler Rose
Name: Tyler Rose
Its: EVP and CFO

By: /s/ Jeff Hawken
Name: Jeff Hawken
Its: COO

"TENANT"

CYTOKINETICS, INCORPORATED,
a Delaware corporation

By: /s/ Robert Blum
Name: Robert Blum
Its: President & CEO

By: _____
Name: _____
Its: _____

EXHIBIT A

PRE-APPROVED TENANT REQUESTED CHANGES

Item	Specialty Alteration	Additional Information
Slab-on-Grade Changes to accommodate Improvements	No	As outlined in HDCCO PCOR 1046 R1
Building 3 and Building 2 Concourse, convert roll up door to double glass (match exterior)	Yes, removal and restoration required	DGA Sketch title B3 & B2 Door Alternative dated 1/20/2020
Shift Doors and drains @elevator lobbies, L2-7 for (gender neutral restrooms to be constructed as part of Improvements)	Yes, removal and restoration required	DGS Sketch titled Proposed Elevator Lobby dated 1/16/2020, DGA ASR 2.10.20 HDCCO PCOR 1053

EXHIBIT B

OYSTER POINT

DEPICTION OF PARKING FACILITIES



SECOND AMENDMENT TO LEASE

This SECOND AMENDMENT TO LEASE ("**Second Amendment**") is made and entered into as of January 26, 2021, by and between KR OYSTER POINT I, LLC, a Delaware limited liability company ("**Landlord**"), and CYTOKINETICS INCORPORATED, a Delaware corporation ("**Tenant**").

R E C I T A L S :

A. Landlord and Tenant are parties to the Lease dated July 24, 2019 (the "**Original Lease**"), as amended by that certain First Amendment to Lease dated May 12, 2020 (the "**First Amendment**", together with the Original Lease, the "**Lease**") whereby Tenant leases certain space (the "**Premises**") within Building 3 in Phase 1 of that certain project commonly known as "**Kilroy Oyster Point**" and more particularly described in the Lease.

B. Landlord and Tenant desire to amend the Lease on the terms and conditions set forth in this Second Amendment.

A G R E E M E N T :

NOW, THEREFORE, in consideration of the foregoing recitals and the mutual covenants contained herein, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the parties hereto hereby agree as follows:

1. **Capitalized Terms.** All capitalized terms when used herein shall have the same meaning as is given such terms in the Lease unless expressly superseded by the terms of this Second Amendment.

2. **Additional Allowance.** Pursuant to Section 2 of the First Amendment, Tenant has been granted the "Auditorium Allowance" (as that term is defined in the First Amendment). Separate and in addition to such Auditorium Allowance, pursuant to Section 2.1 of the Work Letter, Tenant has elected to use the entire Additional Allowance in the amount of Eight Million Two Hundred Twenty-One Thousand Two Hundred Twenty and 00/100 Dollars (\$8,221,220.00) (i.e., Thirty-Five Dollars (\$35.00) per rentable square foot of the Premises). Accordingly, Tenant's Base Rent for the initial Lease Term shall be increased by Eighty-Eight Thousand Nine Hundred Ninety and 81/100 (\$88,990.81) per month (the "**Additional Allowance Payments**") commencing on October 1, 2021, in order to repay the Additional Allowance to Landlord with interest at a rate of eight percent (8%). In no event shall Landlord be obligated to pay a total amount which exceeds the Additional Allowance, and Tenant shall have no further right to any unused portion of the Additional Allowance as of the Allowance Deadline (as that term is defined in Section 2.1 of the Work Letter). The Additional Allowance shall be disbursed pursuant to Section 2.2 of the Work Letter.

3. **Base Rent.** Effective as of the date of this Second Amendment, in lieu of the Base Rent chart set forth in Section 4 of the Summary, Tenant shall pay Base Rent in accordance with the following schedule, and otherwise in accordance with the Lease:

<u>Period During Lease Term</u>	<u>Monthly Installment of Base Rent under the Original Lease</u>	<u>Increase to Monthly Installment of Base Rent for the Additional Allowance</u>	<u>Total Monthly Installment of Base Rent</u>
*September 21, 2021 – September 30, 2022	\$871,405.95**	\$88,990.81***	\$960,396.76
October 1, 2022 – September 30, 2023	\$1,324,967.05	\$88,990.81	\$1,413,957.86
October 1, 2023 – September 30, 2024	\$1,371,340.90	\$88,990.81	\$1,460,331.71
October 1, 2024 – September 30, 2025	\$1,419,337.83	\$88,990.81	\$1,508,328.64
October 1, 2025 – September 30, 2026	\$1,469,014.65	\$88,990.81	\$1,558,005.46
October 1, 2026 – September 30, 2027	\$1,520,430.16	\$88,990.81	\$1,609,420.97
October 1, 2027 – September 30, 2028	\$1,573,645.22	\$88,990.81	\$1,662,636.03
October 1, 2028 – September 30, 2029	\$1,628,722.80	\$88,990.81	\$1,717,713.61
October 1, 2029 – September 30, 2030	\$1,685,728.10	\$88,990.81	\$1,774,718.91
October 1, 2030 – September 30, 2031	\$1,744,728.58	\$88,990.81	\$1,833,719.39
October 1, 2031 – September 30, 2032	\$1,805,794.08	\$88,990.81	\$1,894,784.89
October 1, 2032 – September 30, 2033	\$1,868,996.87	\$88,990.81	\$1,957,987.68

* The Base Rent for the period commencing on September 21, 2021 and continuing through and including September 30, 2022 is calculated based on 159,891 rentable square feet in the Premises, notwithstanding that Tenant is leasing the entire Premises (consisting

of 234,892 rentable square feet); provided, however, that Tenant shall pay Tenant's Share of Operating Expenses and Tax Expenses and all other Additional Rent based on 234,892 rentable square feet in the Premises for the entire Lease Term.

** The portion of the monthly installment of Base Rent that is attributable to the Monthly Installment of Base Rent under the Original Lease (as shown in the second column of the above schedule) shall be abated for the two (2) month period commencing on October 1, 2021 and continuing through and including November 30, 2021. For the avoidance of doubt, Tenant shall remain obligated to pay the Additional Allowance Payments coming due during such two (2)-month period, and the same shall not be abated.

*** Tenant shall begin paying the Additional Allowance Payments commencing on October 1, 2021.

4. **First Amendment Allowance.** Notwithstanding any contrary provision contained in the Lease, including, without limitation, Section 2 of the First Amendment, the Auditorium Allowance shall be treated as part of the Improvement Allowance, and such allowance may be used towards costs relating to any Improvement Allowance Items.

5. **Tenant's Contractor.** Notwithstanding the Work Letter, Tenant has elected to complete construction of the Improvements in phases, with the first phase consisting of the floors one (1) through five (5) of the Building ("**Phase 1**") and the second phase consisting of floors six (6) and seven (7) of the Building ("**Phase 2**"). Pursuant to Section 4.1.1 of the Work Letter, Tenant has retained Hathaway Dinwiddie ("**Hathaway**") as its Contractor for construction of Phase 1. Notwithstanding the foregoing or any contrary term contained in the Lease, for construction of Phase 2, Tenant may retain a Contractor, other than Hathaway, which Contractor shall be designated by Tenant and approved by Landlord, such approval not to be unreasonably withheld, conditioned or delayed. However, Improvement Allowance Items shall only include items that relate to the Phase 1 construction, and Landlord shall disburse the Improvement Allowance, Auditorium Allowance, and Additional Allowance funds (and any corresponding Final Retention) solely with respect to the Phase 1 construction, and shall treat such disbursement as a separate construction project, including requiring Tenant to provide all documentation referenced in Section 2.2.2.2 of the Work Letter pertaining to completion of construction, notwithstanding that only Phase 1, and not Phase 2, will be complete at such time. Tenant agrees to diligently pursue completion of construction of Phase 1.

6. **IDF Room.** As part of the Improvements, Tenant shall install an IT Rack for certain components of the Building Systems ("**Base Building IDF Room Equipment**") within the level 7 IDF room (the "**IDF Room**") of the Building. Once installed, Tenant may not modify or remove the Base Building IDF Room Equipment. Tenant, at Tenant's cost, as part of the Improvements, may elect to install additional Tenant equipment within the IDF Room ("**Tenant's IDF Room Equipment**"). Tenant's IDF Room Equipment may not interfere with the Base Building IDF Room Equipment, and Landlord may require Tenant to reasonably modify or remove Tenant's IDF Room Equipment in the event of any interference. In order to provide cooling for the Base Building IDF Room Equipment, Tenant shall install a cooling system serving the IDF Room, as an additional component of the Building Systems ("**IDF Cooling Equipment**"), which is anticipated to have sufficient capacity to also serve Tenant's IDF Room

Equipment. Tenant, at Tenant's cost, shall be responsible for maintaining, repairing, and replacing the Base Building IDF Room Equipment, Tenant's IDF Room Equipment and the IDF Cooling Equipment as part of Tenant's obligations set forth in Article 7 of the Original Lease, and the Base Building IDF Room Equipment and IDF Cooling Equipment are part of the Building Systems for such purposes. In consideration of Tenant installing the Base Building IDF Room Equipment and the IDF Cooling Equipment, the Improvement Allowance shall be increased by an amount equal to Twenty-Five Thousand Seven Hundred Fourteen and No/100 Dollars (\$25,714.00).

7. **No Broker.** Landlord and Tenant hereby warrant to each other that they have had no dealings with any real estate broker or agent in connection with the negotiation of this Second Amendment, and that they know of no other real estate broker or agent who is entitled to a commission in connection with this Second Amendment. Each party agrees to indemnify and defend the other party against and hold the other party harmless from and against any and all claims, demands, losses, liabilities, lawsuits, judgments, and costs and expenses (including, without limitation, reasonable attorneys' fees) with respect to any leasing commission or equivalent compensation alleged to be owing on account of the indemnifying party's dealings with any real estate broker or agent through, or under the indemnifying party. The terms of this Section 7 shall survive the expiration or earlier termination of the term of the Lease, as hereby amended.

8. **Signatures.** The parties hereto consent and agree that this Second Amendment may be signed and/or transmitted by facsimile, e-mail of a .pdf document or using electronic signature technology (e.g., via DocuSign or similar electronic signature technology), and that such signed electronic record shall be valid and as effective to bind the party so signing as a paper copy bearing such party's handwritten signature. The parties further consent and agree that (1) to the extent a party signs this Second Amendment using electronic signature technology, by clicking "SIGN", such party is signing this Second Amendment electronically, and (2) the electronic signatures appearing on this Second Amendment shall be treated, for purposes of validity, enforceability and admissibility, the same as handwritten signatures.

9. **No Further Modification.** Except as set forth in this Second Amendment, all of the terms and provisions of the Lease shall apply with respect to the Expansion Premises and shall remain unmodified and in full force and effect.

[Signatures follow on next page]

IN WITNESS WHEREOF, this Second Amendment has been executed as of the day and year first above written.

"LANDLORD"

KILROY OYSTER POINT I, LLC,
a Delaware limited liability company

By: Kilroy Realty, L.P.,
a Delaware limited partnership
its Sole Member

By: Kilroy Realty Corporation,
a Maryland corporation
Its General Partner

By: /s/ Matt Griffin
Name: Matt Griffin
Title: SVP, Northern California

By: /s/ Robert Paratte
Name: Robert Paratte
Title: EVP, Leasing and Business
Development

"TENANT"

CYTOKINETICS, INCORPORATED,
a Delaware corporation

By: /s/ Robert Blum
Name: Robert Blum
Title: President & CEO

[*] – CERTAIN INFORMATION IN THIS DOCUMENT HAS BEEN EXCLUDED PURSUANT TO REGULATION S-K, ITEM 601(B)(10). SUCH EXCLUDED INFORMATION IS NOT MATERIAL AND WOULD LIKELY CAUSE COMPETITIVE HARM TO THE REGISTRANT IF PUBLICLY DISCLOSED.

December 23, 2020

Robert I. Blum
President and Chief Executive Officer
Cytokinetics, Incorporated
280 East Grand Avenue
South San Francisco, CA 94080
USA

RE: Amendment to Collaboration Agreement; Extension of Research Term

Dear Mr. Blum:

As you know, Astellas Pharma Inc. (“**Astellas**”) and Cytokinetics, Inc. (“**Cytokinetics**”) are parties to that certain License and Collaboration Agreement for Other Skeletal Sarcomere Activators dated April 23, 2020 (the “**Collaboration Agreement**”), which sets forth the terms and conditions under which the Parties agreed to continue their collaboration with respect to the Other Skeletal Sarcomere Activators. Capitalized terms used in this letter and not otherwise defined shall have the meaning ascribed to them in the Collaboration Agreement. The Parties hereby agree to extend the Research Term as follows, effective as of the date first set forth above:

1. In accordance with the second sentence of Section 5.2 of the Collaboration Agreement, the Parties hereby agree to extend the Research Term until March 31, 2021. Therefore, Section 5.2 of the Collaboration Agreement is hereby amended to replace the phrase “December 31, 2020” in the first sentence of such section with the phrase “March 31, 2021.”
 2. For the continued performance by Cytokinetics of Research activities under the Research Plan during the extended period of January 1, 2021 to March 31, 2021 (“**Extended Period**”), the Parties agree and confirm that the Research Budget will include up to five (5) Cytokinetics FTEs that Astellas will support for the Extended Period. Therefore, the third sentence of Section 5.3 of the Collaboration Agreement is hereby deleted and replaced with the following: “The Research Plan shall also set forth the detailed budget for such Research activities, including a minimum of fifteen (15) Cytokinetics FTEs that Astellas shall support annually through December 31, 2020 and up to five (5) Cytokinetics FTEs that Astellas shall support for the quarterly period commencing January 1, 2021 and ending on March 31, 2021 (the “**Cytokinetics Research FTEs**”), the
-

number of Astellas FTEs committed by Astellas during the Research Term and outsourced costs (the “**Research Budget**”).”

3. The FTE Rate applicable during the Extended Period shall be [*] for the Extended Period adjusted in accordance with Section 1.46 of the Collaboration Agreement.
4. For the avoidance of doubt, the reimbursement of Cytokinetics Research FTEs shall be made in accordance with Section 11.2 of the Collaboration Agreement and in accordance with Section 5.6 of the Collaboration Agreement, Astellas shall not be responsible for reimbursement of any costs for Cytokinetics Research FTEs in excess of the Research Budget as amended hereby.
5. Except as agreed or amended hereby, all other terms of the Collaboration Agreement shall remain in full force and effect.
6. This letter agreement shall be governed by and construed in accordance with the laws of the State of New York without reference to any rules of conflict of laws. Section 17.6(a) of the Collaboration Agreement shall apply to this letter agreement *mutatis mutandis*.

If the foregoing is acceptable to and agreed by Cytokinetics, please so indicate by having an authorized representative of Cytokinetics sign this letter in the appropriate signature line below, and return such signed copy to Shih-Chien Wang, Alliance Management Group, Business Development, at your earliest convenience. If you have any questions or comments, please do not hesitate to contact Shih-Chien at +81-3-3244-5257 or by e-mail at shihchien.wang@astellas.com.

Sincerely,

/s/Akihiko Iwai, Ph.D.
President, Drug Discovery Research
Astellas Pharma Inc.

Agreed and accepted:

Cytokinetics, Incorporated

By: /s/ Robert I. Blum
Name: Robert I. Blum
Title: President and Chief Executive Officer
Date: 1/14/21

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

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

- 1) Registration Statements (Form S-3 Nos. 333-215147, 333-221350, 333-231348 and 333-234537) of Cytokinetics, Incorporated, and
- 2) Registration Statements (Form S-8 Nos. 333-115146, 333-125973, 333-133323, 333-136524, 333-140963, 333-149713, 333-152850, 333-161116, 333-168520, 333-176089, 333-183091, 333-190458, 333-206101, 333-221348, 333-236889 and 333-238786) pertaining to the Amended and Restated 2004 Equity Incentive Plan of Cytokinetics, Incorporated;

of our reports dated February 26, 2021, with respect to the consolidated financial statements of Cytokinetics, Incorporated and the effectiveness of internal control over financial reporting of Cytokinetics, Incorporated included in this Annual Report (Form 10-K) of Cytokinetics, Incorporated for the year ended December 31, 2020.

/s/ Ernst & Young LLP

Redwood City, California

February 26, 2021

**CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER PURSUANT TO
SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002**

I, Robert I. Blum, certify that:

1. I have reviewed this Annual Report on Form 10-K of Cytokinetics, Incorporated;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
 - a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
 - c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

By: /s/ ROBERT I. BLUM
Robert I. Blum,
President, Chief Executive Officer and Director
(Principal Executive Officer)

Date: February 26, 2021

**CERTIFICATION OF PRINCIPAL FINANCIAL OFFICER PURSUANT TO
SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002**

I, Ching W. Jaw, certify that:

1. I have reviewed this Annual Report on Form 10-K of Cytokinetics, Incorporated;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
 - a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
 - c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

By: /s/ CHING W. JAW
Ching W. Jaw,
Senior Vice President, Chief Financial Officer
(Principal Financial Officer)

Date: February 26, 2021

**CERTIFICATION OF PRINCIPAL ACCOUNTING OFFICER PURSUANT TO
SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002**

I, Robert C. Wong, certify that:

1. I have reviewed this Annual Report on Form 10-K of Cytokinetics, Incorporated;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
 - a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
 - c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

By: /s/ ROBERT C. WONG
Robert C. Wong,
Vice President, Chief Accounting Officer (Principal
Accounting Officer)

Date: February 26, 2021

**CERTIFICATIONS PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002
(18 U.S.C. SECTION 1350)**

In connection with the Annual Report on Form 10-K of Cytokinetics, Incorporated (the "Company") for the year ended December 31, 2020 as filed with the Securities and Exchange Commission on the date hereof (the "Annual Report"), each of the undersigned certifies, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

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

By: /s/ ROBERT I. BLUM
Robert I. Blum,
President, Chief Executive Officer and Director
(Principal Executive Officer)

By: /s/ CHING W. JAW
Ching W. Jaw,
Senior Vice President, Chief Financial Officer
(Principal Financial Officer)

By: /s/ ROBERT C. WONG
Robert C. Wong,
Vice President, Chief Accounting Officer
(Principal Accounting Officer)

Date: February 26, 2021