

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, 2023

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)

350 Oyster Point Boulevard
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.

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements.

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b).

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

The approximate aggregate market value of voting and non-voting common stock held by non-affiliates of the registrant was \$2.0 billion as of June 30, 2023.^(A)

^(A) Excludes 36.1 million shares of common stock held by directors and executive officers, and any stockholders whose ownership exceeds ten percent of the shares outstanding, at June 30, 2023. Exclusion of shares held by any person should not be construed to indicate that such person possesses the power, directly or indirectly, to direct or cause the direction of the management or policies of the registrant, or that such person is controlled by or under common control with the registrant.

As of February 27, 2024, the number of shares outstanding of the Registrant's common stock, par value \$0.001 per share, was 103,004,710 shares.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's Proxy Statement for its 2024 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, 2023
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GLOSSARY OF TERMS

Unless the context requires otherwise, references to “Cytokinetics,” “the Company,” “we,” “us” or “our” in this Form 10-K (defined below) refer to Cytokinetics, Incorporated and its subsidiaries. References to “Notes” in this Form 10-K are to the Notes to the Consolidated Financial Statements in this Form 10-K. We also have used other specific terms in this Form 10-K, most of which are explained or defined below:

Term/Abbreviation	Definition
2004 Plan	Cytokinetics’ Amended and Restated 2004 Equity Incentive Plan
2020 RTW Transactions	The transactions contemplated by the RTW Royalty Purchase Agreement, Ji Xing Aficamten License Agreement and the Common Stock Purchase Agreements, dated July 14, 2020, by and between Cytokinetics and the RTW Investors
2021 RTW Transactions	The transactions contemplated by the Ji Xing OM License Agreement and the Common Stock Purchase Agreements, dated December 20, 2021 by and between Cytokinetics and the RTW Investors
2022 RPI Transactions	The transactions contemplated by the RP Loan Agreement and the RP Aficamten RPA
2026 Notes	Cytokinetics’ 4% convertible senior notes due 2026
2027 Indenture	Indenture Agreement, dated July 6, 2022, between Cytokinetics and U.S. Bank Trust Company, as trustee
2027 Notes	Cytokinetics’ 3.50% convertible senior notes due 2027
ACA	Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act
ACACIA-HCM	Assessment Comparing Aficamten to Placebo on Cardiac Endpoints In Adults with Non-Obstructive HCM
ACC	American College of Cardiology
AHA	American Heart Association
ALS	amyotrophic lateral sclerosis (also known as Lou Gehrig’s Disease)
ALSFRS-R	ALS Functional Rating Scale – Revised
Amended ATM Facility	amended and restated Controlled Equity Offering Sales Agreement
Amgen Agreement	Collaboration and Option Agreement, dated December 29, 2006, as amended, between Cytokinetics and Amgen
ARR	absolute risk reductions
Astellas Agreement	License and Collaboration Agreement, dated June 21, 2013, between Cytokinetics and Astellas
Astellas FSRA Agreement	Fast Skeletal Regulatory Activator Agreement, dated April 23, 2020 between Cytokinetics and Astellas
Astellas OSSA Agreement	License and Collaboration Agreement for Other Skeletal Sarcomere Activators, dated April 23, 2020, as amended, between Cytokinetics and Astellas
ASU 2020-06	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
cGMP	current Good Manufacturing Practice
Cantor	Cantor Fitzgerald & Co.
China	People’s Republic of China (including the Hong Kong and Macau SARs)
CMC	Chemistry, Manufacturing and Controls
CMO	Contract Manufacturing Organizations
Common Stock	our common stock, par value \$0.001 per share
Compensation Committee	Compensation and Talent Committee of Cytokinetics’ Board of Directors
Convertible Notes	2026 Notes and 2027 Notes
COURAGE-ALS	Clinical Outcomes Using Reldesemtiv on ALSFRS-R in a Global Evaluation in ALS

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CPET	cardiopulmonary exercise testing
CRL	Complete Response Letter
CRO	Contract Research Organization
CV	cardiovascular
E.U. or EU	European Union
EEA	European Economic Area
EMA	European Medicines Agency
ESPP	employee stock purchase plan
Exchange Act	Securities Exchange Act of 1934, as amended
FDA	U.S. Food and Drug Administration
Final Payment Amount	As defined in Part II, Item 7 (Management’s Discussion and Analysis of Financial Conditions and Results of Operations) of this Annual Report on Form 10-K – Sources and Uses of Cash, Royalty Pharma Transactions
FOREST-HCM	Five-Year, Open-Label, Research Evaluation of Sustained Treatment with Aficamten in HCM
FSRA	fast skeletal regulatory activator
FSTA	fast skeletal muscle troponin activator
Fundamental Change	As defined in the 2027 Indenture
GAAP	Generally Accepted Accounting Principles in the U.S.
GALACTIC-HF	Global Approach to Lowering Adverse Cardiac Outcomes Through Improving Contractility in Heart Failure
GCP	Good Clinical Practice
GDPR	General Data Protection Regulation ((EU) 2016/679)
HCM	hypertrophic cardiomyopathy
HFpEF	heart failure with preserved ejection fraction
HFrEF	heart failure with reduced ejection fraction
HFSA	Heart Failure Society of America
HHS	U.S. Department of Health and Human Services
HIPAA	The federal Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act
ICER	Institute for Clinical and Economic Review
IND	Investigational New Drug
IRA	Inflation Reduction Act of 2022
IRB	Institutional Review Board
Ji Xing	Ji Xing Pharmaceuticals Limited and/or its affiliates, including Ji Xing Pharmaceuticals Hong Kong Limited
Ji Xing Aficamten License Agreement	License and Collaboration Agreement, dated July 14, 2020, by and between Cytokinetics and Ji Xing Pharmaceuticals Limited
Ji Xing Agreements	Ji Xing Aficamten License Agreement and Ji Xing OM License Agreement
Ji Xing OM License Agreement	License and Collaboration Agreement, dated December 20, 2021, by and between Cytokinetics and Ji Xing Pharmaceuticals Limited
KCCQ	Kansas City Cardiomyopathy Questionnaire
KCCQ-OSS	KCCQ Overall Summary Score
Lenders	Silicon Valley Bank and Oxford Finance LLC
LVEF	left ventricular ejection fraction
LVOT	left ventricular outflow tract
LVOT-G	left ventricular outflow tract gradient

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MAA	Marketing Authorization Application
MAPLE-HCM	Metoprolol vs Aficamten in Patients with LVOT Obstruction on Exercise Endpoints Capacity in HCM
Mavacamten Royalty	certain payments on the net sales of products containing the compound mavacamten pursuant to the Research Collaboration Agreement, dated August 24, 2012, between Cytokinetics and MyoKardia, Inc.
NDA	New Drug Application
nHCM	non-obstructive HCM
NOLs	net operating loss carryforward
NYHA	New York Heart Association
oHCM	obstructive HCM
OLE	Open-Label Extension
Ownership Change	As defined in Part 1, Item 1A (Risk Factors) of this Annual Report on Form 10-K, Financial Risks
Oxford	Oxford Finance LLC
Oyster Point Lease	Lease, dated July 24, 2019, by and between Cytokinetics and KR Oyster Point 1, LLC, as amended
Partial Redemption Limitation	As defined in the 2027 Indenture
PSU	Performance Stock Unit
Radnor Lease	As defined in Part II, Item 8 (Financial Statements and Supplementary Data), Notes to Consolidated Financial Statements of this Annual Report on Form 10-K - Note 9 (Commitments and Contingencies) – Operating Leases
REDWOOD-HCM	Randomized Evaluation of Dosing With CK-274 in Obstructive Outflow Disease in HCM
REDWOOD-HCM OLE	Randomized Evaluation of Dosing With CK-274 in Obstructive Outflow Disease in HCM Open Label Extension
REMS	Risk Evaluation and Mitigation Strategy
RP Aficamten RPA	Revenue Participation Right Purchase Agreement, dated January 7, 2022, by and between Cytokinetics and Royalty Pharma Investments 2019 ICAV
RP Loan Agreement	Development Funding Loan Agreement, dated January 7, 2022, by and among Royalty Pharma Development Funding, LLC and Cytokinetics
RP OM Liability	As defined in Part II, Item 8 (Financial Statements and Supplementary Data), Notes to Consolidated Financial Statements of this Annual Report on Form 10-K - Note 6 (Agreements with Royalty Pharma) – 2017 RP Omecamtiv Mecarbil Royalty Purchase Agreement
RP OM RPA	Royalty Purchase Agreement, dated February 1, 2017, by and between the Cytokinetics and RPI Finance Trust, as amended by Amendment No. 1, dated January 7, 2022
RPDF	Royalty Pharma Development Funding, LLC
RPFT	RPI Finance Trust
RPI ICAV	Royalty Pharma Investments 2019 ICAV
RSU	Restricted Stock Unit
RTW ICAV	RTW Investments ICAV for RTW Fund 1
RTW Investors	RTW Master Fund, Ltd., RTW Innovation Master Fund, Ltd. and RTW Venture Fund Limited
RTW Royalty Holdings	RTW Royalty Holdings Designated Activity Company
RTW Royalty Purchase Agreement	Royalty Purchase Agreement, dated July 14, 2020, between Cytokinetics and RTW Royalty Holdings
Section 382	Section 382 of the Internal Revenue Code

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Securities Act	Securities Act of 1933, as amended
SEQUOIA-HCM	Safety, Efficacy, and Quantitative Understanding of Obstruction Impact of Aficamten in HCM
SGLT2	sodium-glucose cotransporter-2
SMA	spinal muscular atrophy
SPA	Special Protocol Assessment
Tax Act	Tax Cuts and Jobs Act
Term Loan Agreement	Loan and Security Agreement, dated as of October 19, 2015, by and among Cytokinetics, Oxford Finance LLC and Silicon Valley Bank and Loan and Security Agreement, dated as of May 17, 2019, by and among Cytokinetics, Oxford Finance LLC and Silicon Valley Bank
U.S. or US	United States

This Form 10-K includes discussion of certain clinical studies relating to various in-line products and/or product candidates. These studies typically are part of a larger body of clinical data relating to such products or product candidates, and the discussion herein should be considered in the context of the larger body of data. In addition, clinical trial data are subject to differing interpretations, and, even when we view data as sufficient to support the safety and/or effectiveness of a product candidate or a new indication for an in-line product, regulatory authorities may not share our views and may require additional data or may deny approval altogether.

CYTOKINETICS and our C-shaped logo are registered trademarks of Cytokinetics in the U.S. and certain other countries. Other service marks, trademarks and trade names referred to in this report are the property of their respective owners.

The information contained on our website, our Facebook, Instagram, YouTube and LinkedIn pages or our Twitter accounts, or any third-party website, is not incorporated by reference into this Form 10-K.

**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, Section 21E of 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:

- the timing of submissions and potential approvals of marketing authorization applications to FDA, EMA and other foreign regulatory authorities;
- 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 completion and announcement of results of our clinical trials, and anticipated rates of enrollment for clinical trials;
- guidance concerning revenues and net cash use for 2024;
- 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 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 ability to ensure commercial availability of an antibody-based immunoassay for the dose optimization of omecamtiv mecarbil;
- our and our partners' plans or ability to conduct the continued research and development of our drug candidates and other compounds;
- our expected roles in research, development or commercialization under our strategic alliances with our partners and collaborators;
- 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 or commercialized;
- 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 and commercial viability 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 and execute on commercial plans;
- 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 the research and development of drug candidates directed to other areas of muscle biology and 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, and revenue interest agreements and the Convertible Notes;
- potential competitors and competitive products;
- retaining key personnel and recruiting additional key personnel; and
- the potential impact of recent accounting pronouncements on our financial position or results of operations.

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

- decisions by Ji Xing with respect to the timing, design and conduct of development and commercialization activities for aficamten or omecamtiv mecarbil in China and Taiwan;
- our ability to meet any of the conditions for disbursement and our receipt of any loan disbursements under the RP Loan Agreement;
- our ability to enroll patients in our clinical trials by any particular date;
- our ability to complete our clinical trials by any particular date;
- 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 or regulatory approvals of our drug candidates and other compounds;
- the possibility 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 drug candidates;
- 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 products and the potential impacts of health care reform;
- changes in laws and regulations applicable to drug development, commercialization, pricing 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, contract manufacturing organizations, 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 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.

In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this Annual Report on Form 10-K, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements.

SUMMARY OF PRINCIPAL RISK FACTORS

Risks Specific to our Research and Development Activities

- The regulatory approval and marketing authorization 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, including aficamten and omecamtiv mecarbil.
- We received a CRL from FDA in response to our NDA for omecamtiv mecarbil. The CRL stated that results from an additional clinical trial of omecamtiv mecarbil are required to establish substantial evidence of effectiveness for the treatment of HFREF, with benefits that outweigh the risks. No assurance can be given that we will be able to address any of the deficiencies noted in the CRL and/or obtain FDA approval of our NDA for omecamtiv mecarbil.
- Clinical trials may fail to demonstrate the desired safety and efficacy of our drug candidates which could prevent or significantly delay completion of clinical development and regulatory approval.
- Our clinical trials, including FOREST-HCM, MAPLE-HCM and ACACIA-HCM, are expensive, time-consuming and may be subject to delay.
- If we encounter difficulties enrolling patients in our clinical trials, including FOREST-HCM, MAPLE-HCM and ACACIA-HCM, our clinical development activities in relation to aficamten and our other drug candidates could be delayed or otherwise adversely affected.
- The failure to successfully develop, manufacture and obtain regulatory clearance or approval of an antibody-based immunoassay for blood concentrations of omecamtiv mecarbil by Microgenics Corporation, a subsidiary of Thermo Fisher, could harm our development and commercialization strategy for omecamtiv mecarbil in key markets. In addition, if required by regulatory authorities as part of any approved label for omecamtiv mecarbil, we will be dependent on Microgenics to manufacture and commercialize such an immunoassay in sufficient quantities in all key markets in which we may seek to commercialize omecamtiv mecarbil.
- We depend on CROs to conduct our clinical trials as well as other third parties to manufacture drug candidates for use in clinical trial and we 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.

Risks Specific to our Commercial Operations

- 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 such as an ETASU or other form of REMS, all of which may result in significant expense and limit commercialization of our potential drugs.
- Our competitors may develop drugs that are less expensive, safer and/or more effective than ours, which may diminish or eliminate the commercial success of any drugs that we may commercialize.
- Even if our drug candidates are approved, we may experience difficulties or delays in achieving market access, reimbursement and favorable drug pricing for our drug products.
- The commercial success of our products depends on the availability and sufficiency of third party payor coverage and reimbursement.
- We have no manufacturing capabilities and depend on contract manufacturers to produce our clinical trial materials, including our drug candidates, and will have continued reliance on contract manufacturers for the development and commercialization of our potential 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 approved drug products, if any.
- 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.
- If physicians and patients do not accept our drugs, we may be unable to generate significant revenue, if any.

Risks Specific to our Intellectual Property

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

Financial Risks

- 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 will need substantial additional capital in the future to sufficiently fund and maintain our operations.
- We have never generated, and may never generate, revenues from commercial sales of our drugs, and we may not have drugs to commercialize for at least several years, if ever.
- We may not be entitled to obtain additional loan disbursements under the RP Loan Agreement.
- 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, the 2027 Notes and the RP Loan Agreement.

Legal and Compliance Risks

- Recently enacted laws, including the Inflation Reduction Act, or IRA, and potential future legislation may increase the difficulty and cost for us to obtain regulatory approval of, and to commercialize our products and affect the prices we may obtain upon commercialization.
- 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.

PART I

ITEM 1. BUSINESS

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 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 represents a first or next in class molecule 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

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 health span, 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,” designed to enable 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 our research.

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

- *Achieve regulatory approvals for drugs arising from our pipeline.* We are committed to fueling a diverse and expansive pipeline of muscle-directed drug candidates advancing toward regulatory approvals. 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 successes 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.
- *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 franchise 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 potentially in 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. Through prudent investment spending fueled by commercial returns alongside other potential strategic partnerships and structured finance and royalty monetization deals, we seek to provide investor returns while continuing to conduct proprietary research to support future research, development and commercial programs. Additionally, we strive to ensure sustainable growth of product sales and long-term profitability through lifecycle management strategies.
- *Expand our development pipeline.* 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.
- *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, regeneration 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.

Building a Specialty Cardiology Franchise

We believe that we are well positioned to build a specialty cardiology business franchise anchored by our late-stage development program for aficamten, complemented by earlier stage drug candidates that have arisen from our industry leading research and leadership in muscle biology and the mechanics of contractility. We anticipate that aficamten, the first product in our potential franchise opportunity will help serve unmet needs in the growing hypertrophic cardiomyopathy market. If aficamten is approved and indicated for the treatment of patients with oHCM (based upon the positive results of SEQUOIA-HCM, and assuming positive results from MAPLE-HCM), it could be followed by a subsequent approval and indication for the treatment of patients with HCM (assuming positive results from ACACIA-HCM). We further believe that our pioneering leadership and research activities directed to the same biology and emerging pharmacology could result in an expansion of our business franchise with the development and potential approval of CK-586 for the potential treatment of a subset of patients with HFpEF whose hypercontractility resembles that of patients with nHCM.

Our commercial business franchise is focused to the advancement of potential medicines that may address high unmet needs of patients primarily treated by a concentrated segment of cardiologists. Our focus is in contrast to other biopharmaceutical companies focused to cardiology, but whose potential medicines may be targeted to a greater number, and more diffuse geographical base of, primary care physicians. Specifically, HCM is primarily diagnosed with initiation of treatment by approximately 10,000 cardiologists in the U.S., including in centers of excellence and targeted community hospitals. We aim to achieve similar if not higher return on investments relative to comparable biopharmaceutical companies with a relatively limited sales and marketing infrastructure focused to key prescribers and with a specialty distribution model. We aim to achieve commercial returns from our franchise business strategies as would be enabled by experienced sales representatives who bring established rapport with their potential customers and appropriately couple their selling activities with high touch customer support services designed to benefit prescribers and patients alike.

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 \$330.1 million for 2023, \$240.8 million for 2022, and \$159.9 million for 2021.

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 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.

We also have a late stage program based on the hypothesis that activators of cardiac myosin may address certain adverse properties of existing positive inotropic agents. 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.

Aficamten

Aficamten is a novel, oral, small molecule cardiac myosin inhibitor that our company scientists discovered. Aficamten 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. Aficamten was purposely designed to reduce the hypercontractility that is associated with HCM. In preclinical models, aficamten 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. Aficamten 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 aficamten 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 aficamten will include an extensive characterization of its pharmacokinetics/pharmacodynamic (“PK/PD”) relationship as has been a hallmark of Cytokinetics’ development programs in muscle pharmacology. The overall development program will assess the potential of aficamten to improve exercise capacity and relieve symptoms in patients with hyperdynamic ventricular contraction due to HCM.

HCM is a disease in which the heart muscle (myocardium) becomes abnormally thick (hypertrophied). The thickening of cardiac muscle leads to the inside of the left ventricle becoming smaller and stiffer, and thus the ventricle becomes less able to relax and fill with blood. This ultimately limits the heart’s pumping function, resulting in symptoms including chest pain, dizziness, shortness of breath, or fainting during physical activity.

HCM is the most common monogenic inherited cardiovascular disorder, with approximately 280,000 patients diagnosed in the U.S., however, there are an estimated 400,000-800,000 additional patients who remain undiagnosed, a rate that is growing at the same rate as the population. Two-thirds of patients with HCM have obstructive HCM (oHCM), in which the thickening of the cardiac muscle leads to left ventricular outflow tract (LVOT) obstruction, while one-third have non-obstructive HCM (nHCM), in which blood flow isn't impacted, but the heart muscle is still thickened. HCM is fairly evenly split across gender and while patients are typically diagnosed in their early 40s, the average age of an oHCM patient is in the early 60s. People with HCM are at high risk of also developing cardiovascular complications including atrial fibrillation, stroke and mitral valve disease. People with HCM are at risk for potentially fatal ventricular arrhythmias and it is one of the leading causes of sudden cardiac death in younger people or athletes. A subset of patients with HCM are at high risk of progressive disease leading to dilated cardiomyopathy and heart failure necessitating cardiac transplantation.

FDA has granted aficamten orphan drug designation for the treatment of symptomatic HCM and Breakthrough Therapy Designation for aficamten for the treatment of oHCM.

SEQUOIA-HCM

SEQUOIA-HCM was a Phase 3 randomized, placebo-controlled, double-blind, multi-center clinical trial designed to evaluate aficamten in patients with symptomatic oHCM on background medical therapy for 24 weeks. The primary objective was to assess the effect of aficamten on change in peak oxygen uptake (pVO₂) measured by CPET from baseline to week 24. Secondary objectives included change in KCCQ score from baseline to week 12 and week 24, the proportion of patients with ≥1 class improvement in NYHA Functional Class from baseline to week 12 and week 24, change in post-Valsalva LVOT-G to week 12 and week 24, the proportion of patients with post-Valsalva LVOT-G <30 mmHg, and change in total workload during CPET to week 24.

On December 27, 2023, we announced positive topline results of SEQUOIA-HCM. The results of SEQUOIA-HCM show that treatment with aficamten significantly improved exercise capacity compared to placebo, increasing peak oxygen uptake (pVO₂) measured by cardiopulmonary exercise testing (CPET) by a least square mean difference (95% CI) of 1.74 (1.04 - 2.44) mL/kg/min (p=0.00002). The treatment effect with aficamten was consistent across all prespecified subgroups reflective of patient baseline characteristics and treatment strategies, including patients receiving or not receiving background beta-blocker therapy.

Statistically significant (p<0.0001) and clinically meaningful improvements were also observed in all 10 prespecified secondary endpoints, including Kansas City Cardiomyopathy Questionnaire Clinical Summary Score (KCCQ-CSS) at weeks 12 and 24, the proportion of patients with ≥1 class improvement in New York Heart Association (NYHA) functional class at weeks 12 and 24, change in provoked left ventricular outflow tract gradient (LVOT-G) and proportion <30 mmHg at weeks 12 and 24, as well as exercise workload and guideline-eligibility for septal reduction therapy.

Aficamten was well-tolerated in SEQUOIA-HCM with an adverse event profile comparable to placebo. Treatment emergent serious adverse events occurred in 8 (5.6%) and 13 (9.3%) patients on aficamten and placebo, respectively. Core echocardiographic left ventricular ejection fraction (LVEF) was observed to be <50% in 5 patients (3.5%) on aficamten compared to 1 patient (0.7%) on placebo. There were no instances of worsening heart failure or treatment interruptions due to low LVEF.

The full results of SEQUOIA-HCM will be presented at an upcoming medical conference and published in a peer-reviewed medical journal.

MAPLE-HCM

MAPLE-HCM (Metoprolol vs Aficamten in Patients with LVOT Obstruction on Exercise Endpoints in HCM) is our second Phase 3 clinical trial of aficamten as monotherapy in patients with oHCM. It is a Phase 3, multi-center, randomized, double-blind, active-comparator trial in patients with symptomatic oHCM and elevated LVOT gradient, which is expected to enroll approximately 170 patients. The primary endpoint is change in peak oxygen uptake (pVO₂), assessed by CPET from baseline to Week 24. Secondary endpoints include change in NYHA class, KCCQ, N-terminal prohormone brain natriuretic peptide (NT-proBNP), and measures of structural remodeling.

On August 3, 2023, we announced that we had initiated patient enrollment in MAPLE-HCM.

ACACIA-HCM

ACACIA-HCM (Assessment Comparing Aficamten to Placebo on Cardiac Endpoints in Adults with Non-Obstructive HCM) is a Phase 3, multi-center, randomized, double-blind, placebo-controlled clinical trial. The trial is expected to enroll approximately 420 patients with symptomatic nHCM. The primary endpoint is the change in KCCQ Clinical Summary Score from baseline to Week 36. Secondary endpoints include change from baseline to Week 36 in the following: exercise capacity as measured by CPET, proportion of patients with an improvement of at least 1 NYHA Functional Class, NT-proBNP, and left atrial volume index. Additionally, while the primary analysis will take place at 36 weeks, patients will continue treatment with aficamten or placebo for up to 72 weeks in order to evaluate additional secondary and exploratory analyses including the time to first cardiovascular event.

On September 6, 2023, we announced that ACACIA-HCM is open to enrollment of patients.

FOREST-HCM (formerly REDWOOD-HCM OLE)

In May 2021, we announced that the first site had been activated to enroll patients in REDWOOD-HCM OLE, an open-label extension clinical study designed to assess the long-term safety and tolerability of aficamten in patients with symptomatic oHCM. Eligible patients were initially to have completed participation in REDWOOD-HCM. However, since initiation of the open-label extension clinical study, we expanded eligibility to include patients having participated in SEQUOIA-HCM, our first Phase 3 clinical trial of aficamten for the treatment of oHCM, and as a result, the trial has been renamed FOREST-HCM.

On March 4, 2023, we announced 48-week data from FOREST-HCM at the American College of Cardiology 72nd Annual Scientific Session. Specifically, we announced that new data through 48 weeks of treatment showed that aficamten was associated with significant reductions in the average resting LVOT-G (mean change from baseline (SD) = -32 (28) mmHg, $p < 0.0002$) and Valsalva LVOT-G (mean change from baseline (SD) = -47 (28) mmHg, $p < 0.0001$). Treatment with aficamten also resulted in significant improvements in NYHA class, with 88% of patients experiencing a ≥ 1 NYHA Functional Class improvement, and significant improvements in NT-proBNP, with an average decrease of 70% from baseline to Week 48 ($p < 0.0001$). At baseline, 19 patients met eligibility criteria for septal reduction therapy (SRT), defined as NYHA Class III and peak LVOT-G ≥ 50 mmHg, but treatment with aficamten eliminated SRT eligibility in all 19 patients at 48 weeks. Aficamten was safe and well-tolerated, with no treatment-related serious adverse events (SAEs). There were no instances of LVEF $< 50\%$ attributed to aficamten. One dose reduction and one temporary dose interruption occurred, neither of which were attributed to treatment with aficamten.

On October 19, 2023, we announced new long-term efficacy and safety data from FOREST-HCM. Specifically, we announced that more than 200 patients had been enrolled in FOREST-HCM as of such date and 143 patients were available for this analysis. Of the 94 patients who had completed the titration period (by Week 12), approximately two-thirds were receiving the 15 mg or 20 mg doses of aficamten. During the titration period, there had been no treatment-related instances of left ventricular ejection fraction (LVEF) $< 50\%$. During the maintenance phase, there had been no instances of LVEF $< 40\%$, which would have required dose interruption, and only three instances of LVEF $< 50\%$ that required a dose down-titration. Therefore, of the 579 monitoring echocardiograms completed during the maintenance phase of treatment, 99.5% of them did not result in a dose reduction. Additionally, after prolonged treatment for more than two years in some patients, the mean resting left ventricular outflow tract gradients (LVOT-G) and mean Valsalva LVOT-Gs remained reduced and below the diagnostic threshold for oHCM. As of such date, patients had also experienced sustained reductions in cardiac biomarkers and improved symptoms. As of such date, the KCCQ increased by ≥ 5 points in 71% of patients, 30% of whom had an improvement of ≥ 10 points. Approximately half of patients were, as of such date, asymptomatic at one year by NYHA Functional Class assessment, and 80% of patients improved by one or more Functional Class at every visit after starting treatment with aficamten. Of patients eligible for septal reduction therapy (SRT) at baseline, 90% were no longer SRT-eligible at the time of the analysis. In addition, as of the date of the analysis, aficamten had been generally well-tolerated, with 60% of patients experiencing at least one treatment emergent adverse event (TEAE) but no treatment-related serious adverse events (SAEs) as assessed by investigators, and no patient deaths.

FOREST-HCM continues to enroll patients.

Ji Xing Collaboration for Greater China

On July 14, 2020, we entered into the Ji Xing Aficamten License Agreement, pursuant to which we granted to Ji Xing an exclusive license to develop and commercialize aficamten in China and Taiwan. Under the terms of the Ji Xing Aficamten License Agreement, 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 aficamten in the field of oHCM, and/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 pharmaceutical products containing aficamten in China and Taiwan, subject to certain reductions for generic competition, patent expiration and payments for licenses to third party patents. The Ji Xing Aficamten License Agreement, unless terminated earlier, will continue on a market-by-market basis until expiration of the relevant royalty term.

Royalty Pharma Revenue Interest

On January 7, 2022, we entered into a Revenue Participation Right Purchase Agreement, which we refer to as the RP Aficamten RPA, with Royalty Pharma Investments 2019 ICAV, which we refer to as RPI ICAV, pursuant to which RPI ICAV purchased rights to certain revenue streams from net sales of pharmaceutical products containing aficamten by us, our affiliates and our licensees in exchange for up to \$150.0 million in consideration, \$50.0 million of which was paid on the closing date, \$50.0 million of which was paid to us on March 10, 2022 following the initiation of the first pivotal trial in oHCM for aficamten and \$50.0 million of which was paid to us in September 2023 following the initiation of the first pivotal clinical trial in nHCM for aficamten. The RP Aficamten RPA also provides that the parties will negotiate terms for additional funding if we achieve proof of concept results in certain other indications for aficamten, with a reduction in the applicable royalty if we and RPI ICAV fail to agree on such terms in certain circumstances.

Pursuant to the RP Aficamten RPA, RPI ICAV purchased the right to receive a percentage of net sales equal to 4.5% for annual worldwide net sales of pharmaceutical products containing aficamten up to \$1 billion and 3.5% for annual worldwide net sales of pharmaceutical products containing aficamten in excess of \$1 billion, subject to reduction in certain circumstances.

Omecamtiv mecarbil

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 a selective, small molecule cardiac myosin activator, the first of a novel class of myotropes designed to directly target the contractile mechanisms of the heart, binding to and recruiting more cardiac myosin heads to interact with actin during systole. Omecamtiv mecarbil is designed to increase the number of active actin-myosin cross bridges during each cardiac cycle and consequently augment the impaired contractility that is associated with heart failure with reduced ejection fraction, or HFrEF.

Heart failure is a grievous condition that is estimated to affect more than 64 million people worldwide an estimated half of whom have reduced left ventricular function. It is the leading cause of hospitalization and readmission in people age 65 and older. Despite broad use of standard treatments and advances in care, the prognosis for patients with heart failure is generally poor. An estimated one in five people over the age of 40 are at risk of developing heart failure, and approximately 50% of people diagnosed with heart failure will die within five years of initial hospitalization. Approximately 2 million people in the U.S. are estimated to have an ejection fraction <30%, indicating they may have worsening heart failure.

GALACTIC-HF

GALACTIC-HF was 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 was 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 an 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 was 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 included time to cardiovascular death; patient reported outcomes as measured by the KCCQ Total Symptom Score; time to first heart failure hospitalization; and time to all-cause death.

GALACTIC-HF: Primary Results

The results of GALACTIC-HF showed 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. 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 LVEF (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.

GALACTIC-HF: Further Analyses

Since our release of the primary results, we have conducted and announced supplemental and subgroup analyses suggesting that certain subgroups of patients treated with omecamtiv mecarbil in GALACTIC-HF may have benefited more than the general patient population in such trial.

For example, additional results 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 LVEF (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 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.

Another analysis assessed the effect of omecamtiv mecarbil on clinical outcomes in relationship to patient baseline ejection fraction by evaluating the effect of patient treatment with omecamtiv mecarbil based on quartiles of baseline EF defined as EF \leq 22%, EF 23-28%, EF 29-32% and EF \geq 33% as well as considering baseline EF as a continuous variable. The incidence of the primary outcome of first heart failure event or cardiovascular death increased with decreasing ejection fraction; in the lowest LVEF quartile (EF \leq 22%) the incidence (35.6 per 100 patient-years) was almost 80% greater than in the highest EF quartile (EF \geq 33%; 20 per 100 patient-years). Treatment with omecamtiv mecarbil demonstrated a 15% (HR 0.85; 95% CI 0.74-0.97; p = 0.016) and 17% (HR 0.83; 95% CI 0.73-0.95; p = 0.005) relative risk reduction in the lower two quartiles, respectively, compared to no difference in the upper two quartiles.

Analysis of ejection fraction as a continuous variable demonstrated a progressively larger treatment effect of omecamtiv mecarbil with decreasing ejection fraction. Accordingly, the absolute treatment effect on the primary composite endpoint also increased between the patients treated with placebo and omecamtiv mecarbil as baseline ejection fraction decreased such that in the lowest ejection fraction quartile, there was an absolute reduction of 7.4 events per 100 patient-years, with a number-needed-to-treat of 11.8 patients necessary to prevent an event over three years.

An analysis of patients with low blood pressure showed that there was a greater treatment effect from omecamtiv mecarbil on the primary composite endpoint of cardiovascular death or first heart failure event than in patients without low blood pressure such that there was an absolute risk reduction of 9.8 events per 100 patient-years (hazard ratio, 0.81; 95% confidence interval [CI] 0.70, 0.94; interaction p=0.051). Patients with low blood pressure treated with omecamtiv mecarbil also experienced improvements in blood pressure over time as did those treated with placebo. Additionally, the incidence of treatment-emergent serious adverse events in patients with low blood pressure who received omecamtiv mecarbil (RR 0.88; 95% CI 0.82, 0.95; p<0.001) and adjudicated first stroke (RR 0.31; 95% CI 0.12, 0.79; p=0.009) was lower compared to placebo.

An analysis of Black patients participating in GALACTIC-HF showed that treatment with omecamtiv mecarbil resulted in a trend towards reduction in the primary endpoint by 18% (HR=0.82, 95% CI 0.64-1.04), corresponding to a reduction in the primary event rate of 7.7/100 patient-years with a number-needed-to-treat of 13 patients. This result, like the overall study results, was driven primarily by a reduction in HF hospitalizations (HR=0.80) and HF events (HR=0.82), with no effect on cardiovascular mortality (HR=1.03). There were no significant differences in adverse events in Black patients between the groups treated with omecamtiv mecarbil and placebo.

A further analysis indicated that the rate of the primary outcome in GALACTIC-HF was higher in hospitalized patients in the placebo group (38.3/100 person-years [PY]) than in outpatients (23.1/100 PY) with an adjusted hazard ratio (HR) of 1.21 (95% CI 1.12, 1.31). There was a stepwise gradient in risk, with those randomized as outpatients in the placebo group within 3 months of a heart failure event at the highest risk (26.6/100 patient years (PY)) as compared with those 9-12 months post-event (19.0/100 PY) with an adjusted hazard ratio (HR) of 1.20 (95% CI 1.01, 1.42), p for trend = 0.008). The effect of omecamtiv mecarbil versus placebo on the primary outcome was similar in hospitalized patients (HR 0.89, 95% CI 0.78, 1.01) and outpatients (HR 0.94, 95% CI 0.86, 1.02), indicating that omecamtiv mecarbil similarly reduced the risk of the primary outcome both when initiated in hospitalized patients and in outpatients. In both hospitalized patients and outpatients, the initiation of omecamtiv mecarbil was safe and well tolerated. Treatment-emergent serious adverse events occurred more frequently in patients randomized during hospitalization but did not differ significantly between the treatment groups.

New Drug Application/Regulatory

On February 28, 2023, we announced that we received a CRL from the FDA's Division of Cardiology and Nephrology regarding our NDA for omecamtiv mecarbil for the treatment of HF_rEF. According to the CRL, GALACTIC-HF is not sufficiently persuasive to establish substantial evidence of effectiveness for reducing the risk of heart failure events and cardiovascular death in adults with chronic heart failure with HF_rEF, in lieu of evidence from at least two adequate and well-controlled clinical investigations. In addition, FDA stated that results from an additional clinical trial of omecamtiv mecarbil are required to establish substantial evidence of effectiveness for the treatment of HF_rEF, with benefits that outweigh the risks. FDA's decision to issue a CRL followed an FDA Cardiovascular and Renal Drugs Advisory Committee's vote of 8 to 3 in December 2022 that the benefits of omecamtiv mecarbil do not outweigh its risks for the treatment of HF_rEF.

In 2023, we participated in a Type A meeting with FDA in order to understand FDA's views regarding the CRL and what may be required to support potential approval of omecamtiv mecarbil in the United States, and subsequently submitted a formal dispute resolution request to FDA, with the objective to appeal the FDA's conclusion, as stated in the CRL, that substantial evidence of effectiveness had not been established to support approval of omecamtiv mecarbil. FDA subsequently denied our appeal in November 2023 and reaffirmed its decision in the CRL that GALACTIC-HF is not sufficiently persuasive to establish substantial evidence of effectiveness for reducing the risk of heart failure events and cardiovascular death in adults with chronic heart failure with HF_rEF, in lieu of evidence from at least two adequate and well-controlled clinical investigations.

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In December 2022, the EMA accepted for review our MAA seeking approval of omecamtiv mecarbil for the treatment of HFREF in the E.U. and the other states of the EEA. We continue to support reviews and address questions related to the marketing application for omecamtiv mecarbil for the treatment of HFREF with the EMA.

In November 2022, our partner, Ji Xing announced that the Center for Drug Evaluation of the National Medical Products Administration of the People's Republic of China had accepted the submission of the NDA for omecamtiv mecarbil for the treatment of HFREF. Subsequently, Ji Xing submitted a request for voluntary withdrawal of the NDA for omecamtiv mecarbil to the Center for Drug Evaluation of the National Medical Products Administration of the People's Republic of China, subject to potential re-submission upon receipt of favorable feedback from EMA or FDA with regard to potential drug approval for omecamtiv mecarbil in the EU or US, respectively.

Ji Xing Collaboration for Greater China

On December 20, 2021, we entered into the Ji Xing OM License Agreement, pursuant to which we granted to Ji Xing an exclusive license to develop and commercialize omecamtiv mecarbil in China and Taiwan. Under the terms of the Ji Xing OM License Agreement, we may be eligible to receive from Ji Xing additional payments totaling up to \$330.0 million for the achievement of certain commercial milestone events in China in connection to omecamtiv mecarbil. In addition, Ji Xing will pay us tiered royalties in the mid-teens to the low twenties range on the net sales of pharmaceutical products containing omecamtiv mecarbil in China and Taiwan, subject to certain reductions for generic competition, patent expiration and payments for licenses to third party patents. The Ji Xing OM License Agreement, unless terminated earlier, will continue on a market-by-market basis until expiration of the relevant royalty term.

Royalty Pharma Revenue Interest

In 2017, we entered into a Royalty Purchase Agreement, which we refer to as the RP OM RPA, with Royalty Pharma Development Funding, LLC, or RPFT, and amended the RP OM RPA on January 7, 2022. Pursuant to the RP OM RPA, as amended, RPFT has a revenue interest entitling it to up to 5.5% of our and our affiliates' and licensees' worldwide net sales of omecamtiv mecarbil. If FDA or EMA approves omecamtiv mecarbil in the future, the royalty rate at which payments are owed to RPFT will be 5.5%.

CK-586

CK-586 is a novel, selective, oral, small molecule cardiac myosin inhibitor designed to reduce the hypercontractility associated with heart failure with preserved ejection fraction, or HFpEF. In preclinical models, CK-586 reduced cardiac hypercontractility by decreasing the number of active myosin cross-bridges during cardiac contraction thereby reducing the contractile force, without effect on calcium transients.

Dosing of patients in a Phase 1 clinical trial of CK-586 commenced in May 2023. The primary objective of this Phase 1 randomized, double-blind, placebo-controlled, double-blind, multi-part single and multiple ascending dose clinical study is to evaluate the safety, tolerability and pharmacokinetics of CK-586 when administered orally as single or multiple doses to healthy participants. The study design includes single ascending dose and multiple ascending dose cohorts. We proceeded to begin the multiple ascending dose cohorts. The study is ongoing.

CK-136

CK-136 is a novel, selective, oral, small molecule cardiac troponin activator. 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.

Dosing of patients in a Phase 1 clinical trial of CK-136 commenced in December 2022. The primary objective of this Phase 1 randomized, double-blind, placebo-controlled, single and multiple ascending dose trial is to assess the safety, tolerability and pharmacokinetics of CK-136 when administered orally as single or multiple doses to healthy participants. The study design, as amended, includes five groups of at least eight participants in single ascending dose cohorts and four groups of at least eight participants in multiple-dose ascending cohorts. A final optional cohort will include eight participants in an open-label, 2-period crossover arm to investigate the effect of food on CK-136. We have completed the single ascending dose cohorts in the Phase 1 study of CK-136 in healthy participants and have begun analyses of the data.

Skeletal Muscle 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.

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, chronic obstructive pulmonary disease (COPD) or sarcopenia (general frailty associated with aging).

We currently have no clinical stage drug candidates arising from our skeletal muscle contractility program.

Ongoing Research in Skeletal Muscle Activators

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.

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 cardiac or skeletal 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.

Commercial Readiness

We began building our commercial capabilities in the U.S. prior to the potential FDA approval and launch of omecamtiv mecarbil, our cardiac myosin activator. Upon receipt of the CRL from FDA in response to our NDA for omecamtiv mecarbil, we maintained the infrastructure that had been built and further refined the team and activities in anticipation of what may now be our first commercial launch with aficamten, our cardiac myosin inhibitor, as early as 2025. We had hired a number of headquarter and other positions, including our field sales leadership team with substantial cardiovascular experience, as well as market access team that includes filed payer professionals and other professionals with experience in HEOR, pricing, market analyses and commercial strategies, systems, and operational execution. We plan to expand the team with customer-facing positions as we near potential FDA approval in 2025. Additionally, we have established our field-based medical affairs team, inclusive of medical directors, medical education and medical communications functions, as well as medical science liaisons in key geographies across the U.S.. In Europe, we have filled key leadership positions in medical affairs and market access and hired an experienced executive as Head of Europe.

Our go-to-market approach will include three phases; learn, design, and build. Our focus in 2023 was on learning. We have commissioned market research with nearly 850 healthcare professionals and more than 160 individuals suffering from HCM. Market research and clinical data has informed our target product profile, positioning, potential customer profiles and anticipated differentiators for a proposed REMS program. Based on our market research, we have learned the overall journey to diagnosis is complex and challenging due to the unique symptoms present in each patient along with limited disease awareness across the broader health care system, leading to confusion and complexity for patients and the healthcare professionals who treat them. HCM patients experience many complications, and, in addition to the physical impact, patients experience profound psychological effects that impact social involvement and other aspects of everyday life.

With a refined understanding of the patient experience, we have also begun to design a comprehensive patient and HCP support program to help address patient needs to facilitate ease of transitioning to therapy with a cardiac myosin inhibitor. The program design will include reimbursement support, affordability programs and patient education resources to support the patient journey.

Market research has revealed challenges that have impacted the adoption and uptake of another cardiac myosin inhibitor related to the ETASU REMs program, including echo monitoring, pharmacy certification, drug-drug interactions, down titration challenges and overall REMS process complexity. We believe aficamten may have attributes that could impact differentiation, including time to onset and reversibility, predictable dose response, no clinically meaningful P450 liabilities resulting in REMS related drug-drug interaction monitoring and frequency of echo monitoring. We have also begun development of a market development and education campaign, building out the field commercial training modules, starting to engage with payers with compliant, pre-approval information planning and planning to build out the necessary technologies to optimize customer engagement.

We recognize the critical importance of market access; critical to contracting with payers is our experienced account team with established relationships with key payer customers. We have hired a seasoned account management team that covers over 100 plans that represent greater than 90% of covered lives for our priority segment. The team has interacted with every major payer in introducing our company and will engage further in 2024 to share results from SEQUOIA-HCM with the goal to educate payers on the potential clinical meaningfulness of the results thereof, as well as health economic data and the anticipated launch timeline for aficamten. We maintain a strong commitment to health economics research, which is intended to facilitate us in effectively conveying the potential value proposition of aficamten to a broad range of stakeholders. The two platforms that we expect to generate this value include the results of SEQUOIA-HCM and the clinical attributes of aficamten. Our customer-facing strategy and deployment has been informed by insights gathered from potential health care professional customers through market research, focus groups and advisory boards. This strategy and deployment, coupled with secondary data, patient diagnosis data, prescriptions and treatment data, have identified a universe of approximately 10,000 treaters across 500 to 700 healthcare organizations, which represent approximately 75% of HCM patient volume, a focused group covering the vast majority of patients, enabling the design of an efficient and impactful customer-facing structure.

Manufacturing Resources and Product Supply

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 in North America and Western Europe 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. For our portfolio of small molecules, we continue to expand our network through well-established and reputable third-party contract manufacturers for our CMC development and manufacturing that have good regulatory standing, suitable manufacturing capabilities and capacities. These third parties must comply with applicable regulatory requirements, including FDA's cGMP, the E.U.'s Guidelines on Good Distribution Practice (cGDP), as well as other stringent regulatory requirements enforced by the FDA or foreign regulatory agencies, as applicable, and are subject to routine inspections by such regulatory agencies. In addition, through our third-party contract manufacturers and data service providers, we continue to provide serialized commercial products as required to comply with the Drug Supply Chain Security Act.

We monitor and evaluate the performance of our third-party contract manufacturers on an ongoing basis for compliance with these requirements and to affirm their continuing capabilities to meet both our commercial and clinical needs. We employ highly skilled personnel with both technical and manufacturing experience to diligently manage the activities at our third-party contract manufacturers and other supply chain partners, and our quality department audits them on a periodic basis.

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.

We have contract manufacturing arrangements in place with leading contract manufacturers for the development and supply of the active pharmaceutical ingredient and finished drug product for aficamten for use in our clinical trials.

Competition

There are many companies focused on the development of small molecules for the treatment HCM, HFrEF and other diseases that our drug candidates are intended to treat. Our competitors and potential competitors include major pharmaceutical and biotechnology companies, as well as academic research institutions, clinical reference laboratories and government agencies that are pursuing research activities similar to ours. Many of the organizations competing with us have greater capital resources, larger research and development staff and facilities, deeper regulatory expertise and more extensive product manufacturing and commercial capabilities than we do, which may afford them a competitive advantage.

Competition for Aficamten

If aficamten is approved for sales and marketing by the FDA or other regulatory authorities for the treatment of HCM, we believe it will likely compete with Camzyostm (mavacamten), a first in class cardiac myosin inhibitor marketed by Bristol Myers Squibb. In addition to Camzyostm, other companies, including but not limited to Edgewise Therapeutics, Tenaya Therapeutics, Novartis AG, Eli Lilly, Boehringer Ingelheim, Gilead and Imbria are conducting clinical trials and pre-clinical activities in HCM and could compete with aficamten.

As a condition to its FDA approval, Camzyostm is subject to a REMS program that may be slowing its market uptake. We cannot predict whether FDA will impose a similar REMS program as a condition to a potential, future approval of aficamten or whether the FDA will alter or lessen the REMS program for CAMZYOS™ altering the competitive landscape. Despite the challenges associated with a REMS program, Bristol Myers Squibb has been able to enroll many physicians in its training program and has been able to start new patients on therapy. We expect that this will increase over time with more experience with this class of drugs.

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

- efficacy, safety and reliability of aficamten, both alone and in combination with other therapies;
- the timing and scope of regulatory approval;
- our ability to obtain regulatory approvals and marketing authorizations for aficamten;
- the imposition by FDA or other regulatory authorities of a REMS program that is differentiated and less burdensome to healthcare providers, pharmacists and patients than the REMS program to which CAMZYOS™ is subject;
- our ability to manufacture and sell commercial quantities of aficamten product to the market;
- our ability to gain market access, successfully commercialize aficamten and secure coverage and adequate reimbursement in approved indications;
- product acceptance by physicians and other health care providers;
- protection of our intellectual property, including our ability to enforce our intellectual property rights against potential generic competition; and
- the availability of substantial capital resources to fund development and commercialization activities.

Competition for Omecamtiv Mecarbil

We believe the principal competition for omecamtiv mecarbil, if ultimately approved for sales and marketing by FDA and/or other regulatory agencies for the treatment of HFrEF includes generic drugs, such as milrinone, dobutamine or digoxin, categories of generic therapies, including beta-blockers, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), Mineralocorticoid receptor antagonists (MRAs), 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 inhibitor class, that have either expanded or are planning to expand their labels to include treatment of patients with heart failure, including FORXIGA® (dapagliflozin), INVOKANA® (canagliflozin), and JARDIANCE® (empagliflozin). The competitive landscape for HFrEF is already crowded and evolving rapidly, especially given the addition of SGLT2 inhibitors as AHA/ACC/HFSA guideline directed medical therapy for HFrEF. SGLT2 inhibitors have steadily gained market share over the previous two years. In addition, there are a number of medical devices both marketed and in development for the potential treatment of patients living with heart failure.

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

- efficacy, safety and reliability of omecamtiv mecarbil, both alone and in combination with other therapies;
- in the U.S., the ability to fund and successfully complete an additional confirmatory phase 3 clinical trial of omecamtiv mecarbil in HFREF and resolve to the satisfaction of FDA the other deficiencies stipulated in the CRL we received in response to our initial NDA submission for omecamtiv mecarbil;
- in the E.U. and other jurisdictions outside of the U.S., the timing and scope of regulatory approval by EMA and other regulatory bodies;
- our ability to manufacture and sell commercial quantities of omecamtiv mecarbil product to the market;
- our ability to successfully commercialize omecamtiv mecarbil and secure coverage and adequate reimbursement with affordable patient copay in approved indications;
- product acceptance by physicians and other health care providers;
- if required in connection to regulatory approval by FDA, EMA and/or other regulatory authorities, the availability of an antibody-based immunoassay to timely and properly perform blood tests for omecamtiv mecarbil concentration levels on patients to whom omecamtiv mecarbil is prescribed;
- price competition, particularly of generic products;
- protection of our intellectual property, including our ability to enforce our intellectual property rights against potential generic competition; and
- the availability of substantial capital resources to fund development and commercialization activities.

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, 2023, we owned, co-owned or licensed 76 issued U.S. patents, over 700 issued patents in various foreign jurisdictions, and over 480 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.

We have a U.S. patent covering aficamten, which expires in 2039 unless extended or otherwise adjusted. We also have a U.S. patent covering omecamtiv mecarbil, which expires in 2027, inclusive of 605 days of Patent Term Adjustment, unless extended or otherwise adjusted. A recent U.S. Federal Circuit decision could have implications for patents whose expiration dates include Patent Term Adjustment, including the U.S. patent covering omecamtiv mecarbil. The implications of this decision may lead to loss of the portion of the patent term that is due to Patent Term Adjustment. 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.

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.

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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, 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.

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 omecantiv 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.

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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 GCP;
- 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 cGMP regulations and FDA audits of select clinical investigator sites to assess compliance with 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 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.

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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 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 EEA. 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 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 also require preapproval inspections of manufacturing operations and clinical trial sites during the course of NDA review, and findings arising from any of these inspections may delay or prevent the approval of the NDA. The FDA may deny approval of an NDA by issuing a CRL 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.

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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 an 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.

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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. Such federal and state healthcare laws and regulations, including, 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.
- HIPAA 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.
- In addition, HIPAA, as amended by Health Information Technology for Economic and Clinical Health Act of 2009 (“HITECH”), imposes certain requirements on covered entities, which include certain healthcare providers, health plans and healthcare clearinghouses, and their business associates and covered subcontractors that receive or obtain protected health information in connection with providing a service on behalf of a covered entity relating to the privacy, security and transmission of individually identifiable health information.
- 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), other health care professionals (such as physician assistants and nurse practitioners), and teaching hospitals, as well as information regarding ownership and investment interests held by physicians and their immediate family members. Payments made to physicians and research institutions for clinical trials are included within the ambit of this law.

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 payor. 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.

Health Care Reform. 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. In particular, in March 2010, the ACA, was enacted, which substantially changed the way health care is financed by both governmental and private insurers, and continues to significantly impact the U.S. pharmaceutical 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. Moreover, in the United States, there have been several recent Congressional inquiries, presidential executive orders 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. For example, in August 2022, the IRA was signed into law, which, among other things, includes prescription drug provisions that may impact product pricing including the potential for net price reductions and/or the ability to increase price beyond the level of inflation over the lifecycle of our products, and/or may increase our rebate obligation to Medicare. Provisions include a requirement that the HHS negotiate drug prices for single-source brand-name drugs and biologics that are among the 50 drugs with the highest total Medicare Part D spending. The law establishes a maximum fair price, outlines the process by which the Secretary of HHS will identify drugs for negotiations, and establishes non-compliance penalties for manufacturers. The Act implements inflation rebates in Medicare when a drug's Average Manufacturer Price (AMP, in Part D) or Average Sale Price (ASP, in Part B) rises faster than the inflation index (CPI-U). In addition, the Part D drug benefit caps beneficiary spending at \$2,000, eliminates the coverage gap for patients, and modifies, beginning in 2025, liabilities for drug manufacturers by replacing the 70% discount in the Coverage gap with a 10% discount in the Initial Coverage phase and a 20% discount in the Catastrophic phase. The IRA permits HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. These provisions take effect progressively starting in fiscal year 2023. On August 29, 2023, HHS announced the list of the first ten drugs that will be subject to price negotiations, although the Medicare drug price negotiation program is currently subject to legal challenges. In response to the Biden administration's October 2022 executive order, on February 14, 2023, HHS released a report outlining three new models for testing by the Centers for Medicare & Medicaid Services Innovation Center which will be evaluated on their ability to lower the cost of drugs, promote accessibility, and improve quality of care. It is unclear whether the models will be utilized in any health reform measures in the future. Further, on December 7, 2023, the Biden administration announced an initiative to control the price of prescription drugs through the use of march-in rights under the Bayh-Dole Act. On December 8, 2023, the National Institute of Standards and Technology published for comment a Draft Interagency Guidance Framework for Considering the Exercise of March-In Rights which for the first time includes the price of a product as one factor an agency can use when deciding to exercise march-in rights. While march-in rights have not previously been exercised, it is uncertain if that will continue under the new framework. 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. For example, on January 5, 2024, the FDA approved Florida's Section 804 Importation Program (SIP) proposal to import certain drugs from Canada for specific state healthcare programs. It is unclear how this program will be implemented, including which drugs will be chosen, and whether it will be subject to legal challenges in the United States or Canada. Other states have also submitted SIP proposals that are pending review by the FDA. Any such approved importation plans, when implemented, may result in lower drug prices for products covered by those programs.

Coverage and Reimbursement. 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 U.S. Reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that a product is safe, effective and medically necessary; and neither cosmetic, experimental nor investigational. To support securing coverage and reimbursement for any product that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our approved products. There may be significant delays in obtaining coverage and reimbursement as the process of determining coverage and reimbursement is often time-consuming and costly. Further, coverage policies and third party reimbursement rates may change at any time. Additionally, we or our partners may develop companion diagnostic tests for use with our product candidates. Companion diagnostic tests require coverage and reimbursement separate and apart from the coverage and reimbursement for their companion pharmaceutical or biological products. Similar challenges to obtaining coverage and reimbursement, applicable to pharmaceutical products, will apply to companion diagnostics.

Cytokinetics Human Capital

As of December 31, 2023, we had 423 employees and 141 consultants. 28 of those employees have more than 10 years tenure with us and 75 have over 5 years of service. In 2023, employee turnover was 10.6%, which we believe is a lower attrition rate compared to the industry.

We are committed to fostering and maintaining a culture that engenders collaboration and teamwork, inclusion, respect, transparency and candor. We provide our employees with an array of professional development resources and tools to support their learning, growth and development opportunities. We were honored to be recognized as a San Francisco Times Best Place to Work and Great Places to Work in 2023.

Our compensation and benefit programs are designed to enable us to attract and retain the best employees in a very competitive life science sector and regularly benchmark and survey the market to ensure we maintain competitive programs. In addition, we routinely survey our employees to measure engagement, identify and take action on opportunities for improvement, and share these results with 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.

We are going into our third year of implementing a Diversity, Equity, Inclusion and Respect program and are fully committed across all aspects of our organization including recruiting and hiring, development and promotion practices. Employees identifying as ethnic or racial minorities held 43% of director-level and above positions. Employees identifying as women held 43% of director-level and above positions.

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.

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 Specific to our Company in connection with our Research and Development Activities

The regulatory approval and marketing authorization 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, including aficamten and omecamtiv mecarbil.

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 an NDA from the FDA. Neither we nor our partners have ever 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.

Although we have announced positive results from SEQUOIA-HCM for aficamten and GALACTIC-HF for omecamtiv mecarbil, regulatory approval of an NDA or NDA supplement is never guaranteed, and the approval process typically takes several years and is extremely expensive. For example, our NDA for omecamtiv mecarbil for the treatment of HFrEF resulted in a CRL notwithstanding the fact that GALACTIC-HF met its primary efficacy endpoint. 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. For example, the CRL we received from FDA in connection with our NDA for omecamtiv mecarbil stated that results from an additional clinical trial of omecamtiv mecarbil are required to establish substantial evidence of effectiveness for the treatment of HFrEF, with benefits that outweigh the risks. 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 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. Moreover, the refusal of one regulatory authority to approve one of our drug candidates may influence the decision-making of another regulatory authority in a different jurisdiction in a manner that is adverse to us. For example, FDA's recent CRL in response to our NDA for omecamtiv mecarbil may influence EMA to decline to approve our MAA for omecamtiv mecarbil in the E.U. or other regulatory authorities in other jurisdictions to decline to approve our potential marketing applications for omecamtiv mecarbil in such other jurisdictions.

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.

We received a CRL from FDA in response to our NDA for omecamtiv mecarbil. The CRL stated that results from an additional clinical trial of omecamtiv mecarbil are required to establish substantial evidence of effectiveness for the treatment of HFrEF, with benefits that outweigh the risks. No assurance can be given that we will be able to address any of the deficiencies noted in the CRL and/or obtain FDA approval of our NDA for omecamtiv mecarbil.

On February 28, 2023, we announced that we received a CRL from the FDA's Division of Cardiology and Nephrology regarding our NDA for omecamtiv mecarbil for the treatment of HFrEF. According to the CRL, GALACTIC-HF is not sufficiently persuasive to establish substantial evidence of effectiveness for reducing the risk of heart failure events and cardiovascular death in adults with chronic heart failure with HFrEF, in lieu of evidence from at least two adequate and well-controlled clinical investigations. In addition, FDA stated that results from an additional clinical trial of omecamtiv mecarbil are required to establish substantial evidence of effectiveness for the treatment of HFrEF, with benefits that outweigh the risks. FDA's decision to issue a CRL followed an FDA Cardiovascular and Renal Drugs Advisory Committee's vote of 8 to 3 in December 2022 that the benefits of omecamtiv mecarbil do not outweigh its risks for the treatment of HFrEF. No assurance can be given that we will be able to address any of the deficiencies noted in the CRL and/or obtain FDA approval of our NDA for omecamtiv mecarbil.

In 2023, we participated in a Type A meeting with FDA in order to understand FDA's views regarding the CRL and what may be required to support potential approval of omecamtiv mecarbil in the United States, and subsequently submitted a formal dispute resolution request to FDA, with the objective to appeal the FDA's conclusion, as stated in the CRL, that substantial evidence of effectiveness had not been established to support approval of omecamtiv mecarbil. FDA subsequently denied our appeal in November 2023 and reaffirmed its decision in the CRL that GALACTIC-HF is not sufficiently persuasive to establish substantial evidence of effectiveness for reducing the risk of heart failure events and cardiovascular death in adults with chronic heart failure with HFrEF, in lieu of evidence from at least two adequate and well-controlled clinical investigations.

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

Prior to receiving approval to commercialize any of our drug candidates, we or our partners must adequately demonstrate to the satisfaction of FDA and foreign regulatory authorities that the drug candidate is sufficiently safe and effective with substantial evidence from well-controlled clinical trials. We or our partners will need to demonstrate efficacy in clinical trials for the treatment of specific indications and monitor safety throughout the clinical development process and following approval. None of our drug candidates have yet met the safety and efficacy standards required for regulatory approval for commercialization and they may never do so. For example, the CRL we received on February 28, 2023 in connection to our NDA for omecamtiv mecarbil stated the results of GALACTIC-HF are not sufficiently persuasive to establish substantial evidence of effectiveness for reducing the risk of heart failure events and cardiovascular death in adults with chronic heart failure with HFrEF, and on March 31, 2023, we announced the discontinuation of COURAGE-ALS, our Phase 3 clinical trial of reldesemtiv in patients with ALS, due to futility.

In addition, for each of our preclinical compounds, we or our partners must adequately demonstrate satisfactory chemistry, formulation, quality, stability and toxicity in order to submit an IND to the FDA, or an equivalent application in foreign jurisdictions, that would allow us to advance that compound into clinical trials. Furthermore, we or our partners may need to submit separate INDs (or foreign equivalent) to different divisions within the FDA (or foreign regulatory authorities) in order to pursue clinical trials in different therapeutic areas. Each new IND (or foreign equivalent) must be reviewed by the new regulatory division before the clinical trial under its jurisdiction can proceed, entailing all the risks of delay inherent to regulatory review. If our or our partners' current or future preclinical studies or clinical trials are unsuccessful, our business will be significantly harmed and our stock price could be negatively affected.

All of our drug candidates are prone to the risks of failure inherent in drug development. Preclinical studies may not yield results that would adequately support the filing of an IND (or a foreign equivalent) with respect to our potential drug candidates. Even if the results of preclinical studies for a drug candidate are sufficient to support such a filing, the results of preclinical studies do not necessarily predict the results of clinical trials. As an example, because the physiology of animal species used in preclinical studies may vary substantially from other animal species and from humans, it may be difficult to assess with certainty whether a finding from a study in a particular animal species will result in similar findings in other animal species or in humans. For any of our drug candidates, the results from Phase 1 clinical trials in healthy volunteers and clinical results from Phase 1 and 2 trials in patients are not necessarily indicative of the results of later and larger clinical trials that are necessary to establish whether the drug candidate is safe and effective for the applicable indication. Likewise, interim results from a clinical trial may not be indicative of the final results from that trial, and results from early Phase 2 clinical trials may not be indicative of the results from later clinical trials.

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. 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.

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. Moreover, clinical trials of our drug candidates 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.

Our clinical trials, including FOREST-HCM, MAPLE-HCM and ACACIA-HCM, are expensive, time-consuming and may be 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. In addition, as is the case for omecamtiv mecarbil given the CRL requirement to perform an additional Phase 3 clinical trial, the time and expense associated with an additional clinical trial may limit the commercial returns given the eventual loss of market exclusivity. 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;

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- 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;
- a regulatory authority in one jurisdiction may not accept a clinical trial design that is acceptable in another jurisdiction;
- an 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, including FOREST-HCM, MAPLE-HCM and ACACIA-HCM, 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;

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- 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;
- 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 failure to successfully develop, manufacture and obtain regulatory clearance or approval of an antibody-based immunoassay for blood concentrations of omecamtiv mecarbil by Microgenics Corporation, a subsidiary of Thermo Fisher, could harm our development and commercialization strategy for omecamtiv mecarbil in key markets. In addition, if required by FDA and/or EMA as part of any approved label for omecamtiv mecarbil, we will be dependent on Microgenics to manufacture and commercialize such an immunoassay in sufficient quantities in all key markets in which we may seek to commercialize omecamtiv mecarbil.

In connection with our NDA and our MAA for omecamtiv mecarbil, FDA and/or EMA may require that patients treated with omecamtiv mecarbil have their blood monitored during titration for concentrations of the drug in order to ensure optimized dosing that maximizes benefits without undue increased risk. We have recently contracted with Microgenics Corporation, a subsidiary of Thermo Fisher, to develop and eventually commercialize an antibody-based immunoassay for blood concentrations of omecamtiv mecarbil. The development, manufacture and regulatory approval of an antibody-based immunoassay, however, may be complex and/or time consuming. Such an immunoassay could require regulatory clearance by FDA as a companion diagnostic device or similar regulatory clearance by EMA, and there is no assurance that such regulatory clearance will be obtained. In addition, if required by FDA and/or EMA as part of any approved label for omecamtiv mecarbil, we will be dependent on Microgenics Corporation to successfully manufacture and commercialize its immunoassay in sufficient quantities in all key markets in which we may seek to commercialize omecamtiv mecarbil, failing which, our potential sales of omecamtiv mecarbil could be materially adversely affected.

We depend on CROs to conduct our clinical trials as well as other third parties to manufacture drug candidates for use in clinical trials and we 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. 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.

The mechanisms of action of certain 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. 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 competitor's 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.

We have been granted orphan designation by the FDA for aficamten for the potential treatment of symptomatic HCM; however, there can be no guarantee that we will receive approval for aficamten for this indication, nor that we will be able to prevent third parties from developing and commercializing products that are competitive to aficamten.

We have been granted orphan drug designation in the U.S. by the FDA for aficamten for the 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.

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.

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We are not guaranteed to maintain orphan status from the FDA for aficamten or to receive orphan status for aficamten 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 aficamten 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.

We have been granted Breakthrough Therapy Designation for aficamten by the FDA and we may seek additional special designations from regulatory authorities to expedite the review and approval process for our product candidates. However, these designations may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that our product candidates will receive marketing approval.

We have been granted Breakthrough Therapy Designation for aficamten for oHCM by the FDA and may seek these and/or additional special designations from regulatory authorities to expedite the review and approval process for our product candidates. A breakthrough therapy is defined as a drug candidate that is intended, alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically important endpoints, such as substantial treatment effects observed early in clinical development. For products that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Drug candidates designated as breakthrough therapies by the FDA can also be eligible for accelerated approval. If a drug candidate is intended for the treatment of a serious or life-threatening condition and the product demonstrates the potential to address unmet medical needs for this condition, the drug candidate sponsor may apply for Fast Track Designation.

Fast Track Designation is an FDA process designed to facilitate the development and expedite the review of drugs to treat serious conditions and fill an unmet medical need. The purpose of the program is to make important new drugs available to the patient earlier. Filling an unmet medical need is defined as providing a therapy where none exists or providing a potential improvement upon the current standard of care. Once a drug candidate receives Fast Track Designation, early and frequent communication between the FDA and the sponsor is encouraged throughout the entire drug development and review process. The frequency of communication assures that questions and issues are resolved quickly, often leading to earlier drug approval and access by patients.

The FDA has broad discretion whether or not to grant these designations, so even if we believe a particular drug candidate is eligible for a particular designation, we cannot assure you that the FDA would decide to grant it. Accordingly, even if we believe one of our drug candidates meets the criteria for a designation, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a particular designation for a product candidate may not result in a faster development process, review or approval compared to drug candidates considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our drug candidates qualify as breakthrough therapies, the FDA may later decide that the products no longer meet the conditions for qualification and rescind the breakthrough designation. Further, the FDA may withdraw Fast Track Designation if it believes that the designation is no longer supported by data from a clinical development program.

If we are unable to maintain any existing Breakthrough Therapy Designation or Fast Track Designation or fail to secure such designation for any additional product candidates, this would have an adverse impact on our development timelines and our ability to obtain approval for and commercialize our product candidates.

Disruptions at the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire and retain key leadership and other personnel, or otherwise prevent new products and services from being developed or commercialized in a timely manner, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including for 35 days beginning on December 22, 2018, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Separately, in response to the global COVID-19 pandemic, the FDA had a period during which manufacturing inspections were not conducted, leading to delay, and has resumed on-site inspections of domestic manufacturing facilities subject to a risk-based prioritization system. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Risks Specific to our Company in connection with our Commercial Operations

Our competitors may develop drugs that are less expensive, safer and/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.

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;

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- 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 and/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.

Even if our drug candidates are approved, we may experience difficulties or delays in achieving market access, reimbursement and favorable drug pricing for our drug products.

We currently have limited interactions and relationships with payors. Over time, we anticipate that our drugs will be adopted by our patients as indicated by the labels once they are approved by regulatory authorities. To achieve this adoption, our drugs will need to be covered and listed in formularies of major pharmacy benefit managers and payors in the U.S. These major pharmacy benefit managers and payors include Medicare, Medicaid, VA, DoD, TriCare, and other commercial payors with whom we have had limited interactions. The process to achieve coverage with pharmacy benefit managers and payors can be time consuming, is not guaranteed and if achieved can impact profitability given the level of rebates often required.

Specifically in relation to aficamten and omecamtiv mecarbil, even if such drug candidates are ultimately approved by the FDA or other regulatory authorities for commercialization, they may not become a guideline-directed medical therapy for oHCM or HFrEF respectively or they may not reach such status in a timely manner upon commercialization, which may adversely impact its sales prospects. Furthermore, we assume omecamtiv mecarbil will have a disproportionately larger share of Medicare patients relative to commercial and other payors. Overall coverage could be delayed given Medicare's defined bid timelines for inclusion in the Medicare Part D formulary. In addition, the rebate levels we may have to offer to pharmacy benefit managers and payors to be included in their formularies may also impact the profitability of omecamtiv mecarbil.

Moreover, pricing of our drug candidates, if approved by the FDA or other regulatory authorities for commercialization, may be impacted by cost-effectiveness and economic analyses by a Health Technology Assessment organization such as the Institute for Clinical and Economic Review, or ICER, an independent non-profit research institute that produces reports analyzing the evidence underlying the effectiveness and value of drugs and other medicinal services. ICER assessments and recommended pricing based on cost-effectiveness may affect our ability to obtain favorable pricing terms with Medicare, Medicaid, VA, DoD, TriCare, and other commercial payors. For example, in November 2021, ICER published its final evidence report and policy recommendations related to CAMZYOS™ (mavacamten), a small molecule myosin inhibitor developed formerly by MyoKardia, Inc. and commercialized by Bristol-Myers Squibb Company that has a similar mechanism of action to aficamten. The report concluded that a majority of contributing panelists found that current evidence was not adequate to demonstrate a net health benefit for CAMZYOS™ (mavacamten) added to background therapy when compared to background therapy alone or a net health benefit of CAMZYOS™ (mavacamten) when compared to disopyramide. Moreover, ICER's final report concluded that modeling short-term clinical benefits of CAMZYOS™ (mavacamten) over a longer time period produces a health-benefit price benchmark index for CAMZYOS™ (mavacamten) between \$12,000-\$15,000 per year, significantly lower than Bristol-Myers Squibb Company's current annual list price in the U.S. Whilst not binding on Medicare, Medicaid, VA, DoD, TriCare, and other commercial payors, or indicative of the net health benefits, ICER could conclude for aficamten a similar conclusion that could adversely impact our ability to obtain favorable pricing and/or reimbursement.

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 timeframe from approval to coverage could be lengthy, inadequate, and/or 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.

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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. Coverage policies and third party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

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.

Additionally, we or our partners may develop companion diagnostic tests for use with our product candidates. Companion diagnostic tests require coverage and reimbursement separate and apart from the coverage and reimbursement for their companion pharmaceutical or biological products. Similar challenges to obtaining coverage and reimbursement, applicable to pharmaceutical products, will apply to companion diagnostics.

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.

We have no manufacturing capabilities and depend on contract manufacturers to produce our clinical trial materials, including our drug candidates, and will have 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 and rely on CMOs for the manufacture of finished drug product and active pharmaceutical ingredient. 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.

In addition, under the Ji Xing Agreements, we have committed to providing Ji Xing with supply of aficamten and omecamtiv mecarbil for development and commercialization of aficamten and omecamtiv mecarbil 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 Agreements.

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 one or both of the Ji Xing Agreements, giving rise to the ability to terminate such agreements and other adverse consequences as stipulated in the Ji Xing Agreements. 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 approved drug products, 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.

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 such as an ETASU or other form of REMS, 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. For example, CAMZYOS™ (mavacamten), a small molecule myosin inhibitor developed formerly by MyoKardia, Inc. and commercialized by Bristol-Myers Squibb Company that has a similar mechanism of action to aficamten, is subject to an ETASU REMS, an FDA imposed program designed to reinforce medication use behaviors and actions that support the safe use of certain medication with serious safety concerns to help ensure the benefits of the medication outweigh its risks. The CAMZYOS™ (mavacamten) ETASU REMS program requires, among other things, restrictions and qualifications on pharmacies that dispense the drug and certification, record-keeping and patient counselling obligations on physicians who prescribe the drug. The requirements of an ETASU REMS program may limit the commercial success of a drug due by making it more difficult for physicians to prescribe a drug and patients to obtain and subsequently use a drug. Since aficamten is a small molecule myosin inhibitor with a similar mechanism of action to CAMZYOS™ (mavacamten), it is possible that FDA or other regulatory bodies may condition aficamten's marketing approval on the implementation of a similar ETASU REMS program to that of CAMZYOS™ (mavacamten).

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 patient support;
- 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.

Risks Specific to our Company in connection with our Intellectual Property

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.

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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 of 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.

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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.

Financial Risks

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 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 and maintain our operations.

We have consumed substantial amounts of capital to date, and our operating expenditures will increase over the next several years as we expand our research and development activities and expand our organization to prepare for commercialization of any approved drug. We have funded our operations and capital expenditures with proceeds primarily from private and public sales of our equity securities, royalty monetization agreements, revenue interest agreements, 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, the organizational scale up and associated expenditures with commercial readiness activities to launch approved drugs combined with the absence of any revenues from product sales. 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 loans under the RP Loan Agreement with RPDF and reimbursements, milestone and royalty payments that we may receive under our agreements with Ji Xing. We may not receive any further funds under any of these agreements. Our ability to raise funds may be adversely impacted by worsening economic conditions and the recent disruptions to, and volatility in, the credit and financial markets in the U.S. and worldwide resulting from the effects of inflationary pressures, potential future bank failures, global geopolitical factors including war or other hostilities, or otherwise. 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, and if we cannot raise the funds we need to operate our business, we will need to delay or discontinue certain research and development activities, and our stock price may be negatively affected.

We have never generated, and may never generate, revenues from commercial sales of our drugs and we may not have drugs to commercialize 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 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 late clinical-stage drug candidates include omecamtiv mecarbil for the potential treatment of heart failure, and aficamten 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. For example, our NDA for omecamtiv mecarbil for the treatment of HFrEF resulted in a CRL notwithstanding the fact that GALACTIC-HF met its primary efficacy endpoint, and that the results from an additional clinical trial of omecamtiv mecarbil are required to establish substantial evidence of effectiveness for the treatment of HFrEF, with benefits that outweigh the risks. Our commercial revenues, if any, will be derived from sales of drugs that may not be commercially marketed for 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.

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, the 2027 Notes and the RP Loan Agreement.

As of December 31, 2023, we had \$617.5 million of debt recorded on the balance sheet comprised of the RP Loan Agreement and the 2026 and 2027 Convertible Notes.

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 Convertible 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 and our cash needs may increase in the future. In addition, any required repurchase of the Convertible 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 the RP Loan Agreement, the RP Aficamten RPA, the RP OM RPA, and the indentures related to our Convertible Notes 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 our debt repayment obligations.

The RP Loan Agreement, the RP Aficamten RPA, the RP OM RPA, and the indentures related to the Convertible Notes require 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, the RP Aficamten RPA and the RP OM RPA contain certain covenants applicable to us, including among other things, development and commercialization diligence obligations in connection to aficamten and omecamtiv mecarbil and reporting obligations, which could also restrict our business and operations, particularly in connection to our development and commercialization of aficamten and omecamtiv mecarbil.

Our failure to comply with any of the covenants could result in a default under the RP Loan Agreement, the RP Aficamten RPA, the RP OM RPA, or the indentures related to the Convertible Notes, which could permit the counterparties 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.

We have no rights to repurchase the revenue interests in omecamtiv mecarbil or aficamten sold to RPFT or RPI ICAV respectively, thereby limiting our ability to eliminate future applicability of the covenants contained in the RP OM RPA and the RP Aficamten RPA, and although we do have voluntary prepayment rights under the RP Loan Agreement, any voluntary prepayment rights will require that we pay RPDF 190% of the principal amount of amounts disbursed to us as tranche 1, tranche 4 and tranche 5 loans and 200% for tranche 2 and tranche 3 loans, thereby making it potentially disadvantageous to voluntarily repay RPDF prior to the final maturity date applicable to loans outstanding under the RP Loan Agreement.

In addition, certain provisions in the 2026 Notes, the 2027 Notes and the related indentures 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 Convertible Notes and the related Indentures 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.

Finally, should we be unable to comply with our covenants or if we default on any portion of our outstanding borrowings under the RP Loan Agreement, in addition to its rights to accelerate and demand for immediate repayment of amounts outstanding under the RP Loan Agreement, we would be liable for default interest at a rate of 4% over the prime rate.

We may not be entitled to obtain additional loan disbursements under the RP Loan Agreement.

On January 7, 2022, we announced that we had entered into the RP Loan Agreement with RPDF, such entity being affiliated with Royalty Pharma International plc. The RP Loan Agreement makes available to us up to \$300.0 million in loans, of which a \$50.0 million loan was paid to us at the closing of such transaction. With the positive results of SEQUOIA-HCM, we have satisfied the conditions related to tranche 4 of the RP Loan Agreement and thus an additional \$75 million in loans are currently available to us for disbursement. Tranche 5 of the RP Loan Agreement would be available to us upon acceptance for filing by FDA of an NDA for aficamten. Should we not satisfy such condition for tranche 5 by March 31, 2025, or in the event we fail to meet our obligations or default under the agreement, the actual amount of additional loan disbursements could be substantially less than the maximum amounts available thereunder. For example, as a result of FDA's CRL in response to our NDA for omecamtiv mecarbil, we have not satisfied the conditions for the availability of disbursement of the \$50 million tranche 2 and \$25 million tranche 3 term loans under the RP Loan Agreement.

We are subject to counterparty risk under the RP Loan Agreement

We are subject to counterparty risk in the event that RPDF defaults on its obligations under the RP Loan Agreement. In such event, we have no recourse against Royalty Pharma International plc or any of its other affiliated or controlled entities, and in the event of an RPDF insolvency, we would have no rights to additional loan disbursements from RPDF.

Conversion of our outstanding Convertible 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 Convertible 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 Convertible 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 Convertible Notes could also encourage short sales by third parties, creating additional selling pressure on our stock. The existence of the Convertible 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.

We will depend on Ji Xing for the development and commercialization of aficamten and omecamtiv mecarbil in China and Taiwan.

Under the terms of the Ji Xing Agreements, Ji Xing will be responsible for the development and commercialization of aficamten and omecamtiv mecarbil in China and Taiwan. The timing and amount of any milestone and royalty payments we may receive under the Ji Xing Agreements will depend in part on the efforts and successful commercialization of aficamten and omecamtiv mecarbil 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 aficamten or omecamtiv mecarbil 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 aficamten and omecamtiv mecarbil 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 Agreements 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 aficamten and omecamtiv mecarbil 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.

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 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 our 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. 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. The impact of the 2017 tax legislation on holders of our common stock is also uncertain and could be adverse.

We are obligated to 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 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 our annual or interim financial statements will not be prevented or detected on a timely basis.

If 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.

Legal and Compliance Risks

Recently enacted laws, including the Inflation Reduction Act, or IRA, and potential future legislation may increase the difficulty and cost for us to obtain regulatory approval of, and to commercialize our products and affect the prices we may obtain upon commercialization.

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 ACA was enacted, which substantially changed the way health care is financed by both governmental and private insurers, and continues to 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 until 2032 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 executive, judicial and Congressional challenges to numerous elements of the ACA, as well as efforts to repeal or replace certain aspects of the ACA. For example, on June 17, 2021, the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. It is possible that the ACA will be subject to executive, judicial, and Congressional challenges in the future. It is unclear how any such challenges will impact the ACA and our business. 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.

In August 2022, the Inflation Reduction Act, or IRA, was signed into law, which, among other things, includes prescription drug provisions that may impact product pricing including the potential for net price reductions and/or the ability to increase price beyond the level of inflation over the lifecycle of our products, and/or may increase our rebate obligation to Medicare. Provisions include a requirement that the HHS negotiate drug prices for single-source brand-name drugs and biologics that are among the 50 drugs with the highest total Medicare Part D spending. The law establishes a maximum fair price, outlines the process by which the Secretary of HHS will identify drugs for negotiations, and establishes non-compliance penalties for manufacturers. The IRA implements inflation rebates in Medicare when a drug's Average Manufacturer Price (AMP, in Part D) or Average Sale Price (ASP, in Part B) rises faster than the inflation index (CPI-U). In addition, the Part D drug benefit caps beneficiary spending at \$2,000, eliminates the coverage gap for patients, and modifies, beginning in 2025, liabilities for drug manufacturers by replacing the 70% discount in the Coverage gap with a 10% discount in the Initial Coverage phase and a 20% discount in the Catastrophic phase. The IRA permits HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. These provisions take effect progressively starting in fiscal year 2023. On August 29, 2023, HHS announced the list of the first ten drugs that will be subject to price negotiations, although the Medicare drug price negotiation program is currently subject to legal challenges.

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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. However, we cannot predict the timing or substance of proposals that may be adopted in the future, particularly in light of the difficulty of advancing legislation through Congress. 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 and/or potential sales 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 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. For example, on January 5, 2024, the FDA approved Florida's Section 804 Importation Program (SIP) proposal to import certain drugs from Canada for specific state healthcare programs. It is unclear how this program will be implemented, including which drugs will be chosen, and whether it will be subject to legal challenges in the United States or Canada. Other states have also submitted SIP proposals that are pending review by the FDA. Any such approved importation plans, when implemented, may result in lower drug prices for products covered by those programs. In addition to the enactment of the IRA, in response to the Biden administration's October 2022 executive order, on February 14, 2023, HHS released a report outlining three new models for testing by the Centers for Medicare & Medicaid Services Innovation Center which will be evaluated on their ability to lower the cost of drugs, promote accessibility, and improve quality of care. It is unclear whether the models will be utilized in any health reform measures in the future. Further, on December 7, 2023, the Biden administration announced an initiative to control the price of prescription drugs through the use of march-in rights under the Bayh-Dole Act. On December 8, 2023, the National Institute of Standards and Technology published for comment a Draft Interagency Guidance Framework for Considering the Exercise of March-In Rights which for the first time includes the price of a product as one factor an agency can use when deciding to exercise march-in rights. While march-in rights have not previously been exercised, it is uncertain if that will continue under the new framework. 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.

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.
- HIPAA 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.
- In addition, HIPAA, as amended by Health Information Technology for Economic and Clinical Health Act of 2009 (“HITECH”), imposes certain requirements on covered entities, which include certain healthcare providers, health plans and healthcare clearinghouses, and their business associates and covered subcontractors that receive or obtain protected health information in connection with providing a service on behalf of a covered entity relating to the privacy, security and transmission of individually identifiable health information.
- 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), other health care professionals (such as physician assistants and nurse practitioners), and teaching hospitals, as well as information regarding ownership and investment interests held by physicians and their immediate family members. Payments made to physicians and research institutions for clinical trials are included within the ambit of this law.
- Analogous state laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, and some state laws require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures 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.

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.

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 E.U. in connection with our business, including in connection with conducting clinical trials in the E.U. Additionally, if any of our product candidates are approved, we may seek to commercialize those products in the E.U. The collection and use of personal health data in the E.U. are governed by the provisions of the 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 EEA, including to the U.S., 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 E.U. 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.

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European data protection laws, including the GDPR, generally restrict the transfer of personal information from Europe, including the EEA, 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 EEA, 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.

General Risk Factors

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, commercial and technical personnel. The loss of the services of any member of our senior management or key scientific, technical, commercial 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. 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, commercial and managerial personnel could limit or delay our product development or commercialization activities, which would adversely affect the development of our drug candidates and commercialization of our potential drugs and growth of our business.

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. 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 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. For example, in 2023, the closing price of our common stock on the Nasdaq Global Select Market ranged from \$25.98 to \$87.58. Factors that have caused and could cause in the future 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;

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- 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 have caused and 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.

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.

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.

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:

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- 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 1C. CYBERSECURITY

Risk management and strategy

Cytokinetics recognizes the critical importance of developing, implementing, and maintaining cybersecurity measures designed to safeguard our information systems and protect the confidentiality, integrity, and availability of our critical data.

Managing Material Risks & Integrated Overall Risk Management

Our cybersecurity team, led by our CISO, identifies and assesses risks from cybersecurity threats by monitoring and evaluating our threat environment and the Company's risk profile using various methods including, for example, through manual and automated tools, internal and external audits, third-party threat assessments and third-party conducted red/blue team testing and tabletop incident response exercises and by subscribing to reports and services that identify cybersecurity threats, analyzing reports of threats and actors, conducting scans of the threat environment, evaluating our and our industry's risk profile, evaluating threats reported to us, conducting threat assessments for internal and external threats and conducting vulnerability assessments.

Depending on the environment, we implement and maintain various technical, physical, and organizational measures, processes, standards and policies designed to manage and mitigate material risks from cybersecurity threats to our Information Systems and Data, including, for example: maintaining an incident response plan, a vulnerability management policy, disaster recovery and business continuity plans and a vendor risk management program; conducting employee training, systems monitoring and penetration testing; implementing security standards, network security controls, access controls and physical security; encrypting and segregating data; though asset management, tracking and disposal; and maintaining cybersecurity insurance.

We have strategically integrated cybersecurity risk management into our broader risk management framework to promote a culture of cybersecurity risk management. This integration is designed to make cybersecurity considerations an integral part of our decision-making processes. Our risk management team works closely with our IT department and cybersecurity team to evaluate and address cybersecurity risks connected with our business objectives and operational needs.

Engage Third-parties on Risk Management

Recognizing the complexity and evolving nature of cybersecurity threats, Cytokinetics engages with a range of external experts, including cybersecurity assessors, consultants, and auditors in evaluating and testing our risk management systems. These partnerships enable us to leverage specialized knowledge and insights. Our collaboration with these third parties includes periodic audits, threat assessments, and consultation on security enhancements.

Oversee Third Party Risk

Because we are aware of the potentially material risks from cybersecurity threats associated with third-party service providers, Cytokinetics implements processes to oversee and manage these risks. Depending on the nature of the services provided and the identity of the service provider, we may conduct security assessments of the provider before engagement and may monitor their compliance with our cybersecurity policies after engagement. The monitoring includes periodic assessments by our Chief Information Security Officer (“CISO”) and on an ongoing basis by our security specialists. This approach is designed to mitigate risks related to data breaches or other security incidents originating from third parties.

Risks from Cybersecurity Threats

For a description of the risks from cybersecurity threats that may materially affect the Company and how they may do so, see our risk factors under Part I. Item 1A. Risk Factors in this Annual Report on Form 10-K, including the discussion under the headings “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” and “Significant disruptions of information technology systems or breaches of data security could adversely affect our business”.

Governance

Cytokinetics’ Board of Directors is aware of the critical nature of managing risks associated with cybersecurity threats. Our Board has established oversight mechanisms designed to ensure effective governance in managing material risks associated with cybersecurity threats because we recognize the significance of these threats to our operational integrity and stakeholder confidence.

Board of Directors Oversight

The Audit Committee is central to the Board’s oversight of cybersecurity risks and bears the primary responsibility for this domain. The Audit Committee is composed of board members with diverse expertise, including, risk management, technology, and finance. The Audit Committee reports to the Board of Directors periodically regarding cybersecurity topics presented to the Audit Committee, and all materials made available to the Audit Committee are available to rest of the Board of Directors.

Management’s Role Managing Risk

The CISO, the Vice President, Information Technology (“VP of IT”), the Chief Executive Officer (“CEO”) and the Chief Financial Officer (“CFO”) play a pivotal role in informing the Audit Committee on cybersecurity risks. They provide cybersecurity briefings to the Audit Committee on a regular basis, with a minimum frequency of once per year. These briefings encompass a broad range of topics, including as applicable: the current cybersecurity landscape and emerging threats, the status of ongoing cybersecurity initiatives and strategies, incident reports and learnings from any cybersecurity events, and compliance with regulatory requirements and industry practices.

In addition to our scheduled meetings, the Audit Committee, CISO, VP of IT, CEO and CFO maintain an ongoing dialogue regarding emerging or potential cybersecurity risks. Together, they receive updates from one another, as appropriate, on any significant developments in the cybersecurity domain, ensuring the Board’s oversight is proactive and responsive. The Audit Committee actively participates in strategic decisions related to cybersecurity, offering guidance and approval for major initiatives. This involvement ensures that cybersecurity considerations are integrated into the broader strategic objectives of Cytokinetics. The Audit Committee conducts an annual review of the company’s cybersecurity posture and the effectiveness of its risk management strategies. This review helps in identifying areas for improvement and ensuring the alignment of cybersecurity efforts with the overall risk management framework.

Management Personnel in Cybersecurity

Primary responsibility for assessing, monitoring and managing our risks from cybersecurity threats rests with the CISO, Mr. Eric Brown. With over 10 years of experience in the field of cybersecurity and over 20 years of experience in IT more broadly, Mr. Brown brings a wealth of expertise to his role. His background includes extensive experience as an enterprise CISO. His in-depth knowledge and experience are instrumental in developing and executing our cybersecurity strategies. Our CISO oversees our governance programs, tests our compliance with standards, remediates known risks, and leads our employee training program.

Mr. Brown reports to the VP of IT, Mr. Daniel Casper. With over 20 years of experience in IT leadership roles in biopharma and industry services, Mr. Casper brings expertise in leading the effective business use of technology solutions and services to our industry. Our VP of IT has overall responsibility for the Company’s IT department and operations, including oversight over the CISO and cybersecurity team to ensure efforts to contain and remediate security incidents are sufficient and effective.

Monitor Cybersecurity Incidents

The CISO is responsible for informing himself from appropriate sources about the latest developments in cybersecurity, including potential threats and innovative risk management techniques. The CISO implements and oversees processes for the monitoring of our information systems. This includes the deployment of security measures and system audits to identify potential vulnerabilities. In the event of a cybersecurity incident, the CISO is equipped with a well-defined incident response plan. This plan includes immediate actions designed to mitigate the impact and long-term strategies for remediation and prevention of future incidents.

Reporting to Board of Directors

The CISO, in his capacity, regularly informs the VP of IT, the CFO, the CEO, and the General Counsel or Head of Legal of material cybersecurity risks and incidents. This is how executive management is kept abreast of our cybersecurity posture and potentially material cybersecurity risks facing Cytokinetics. Furthermore, significant cybersecurity matters, and strategic risk management decisions are escalated by any of the CEO, the CFO and the General Counsel or Head of Legal to the Audit Committee, so that the Audit Committee can oversee and provide guidance on critical cybersecurity issues.

ITEM 2. PROPERTIES

Our material facilities consist of 234,892 square feet of leased office and laboratory space at 350 Oyster Point, South San Francisco, California. Our lease over this property expires in 2033.

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

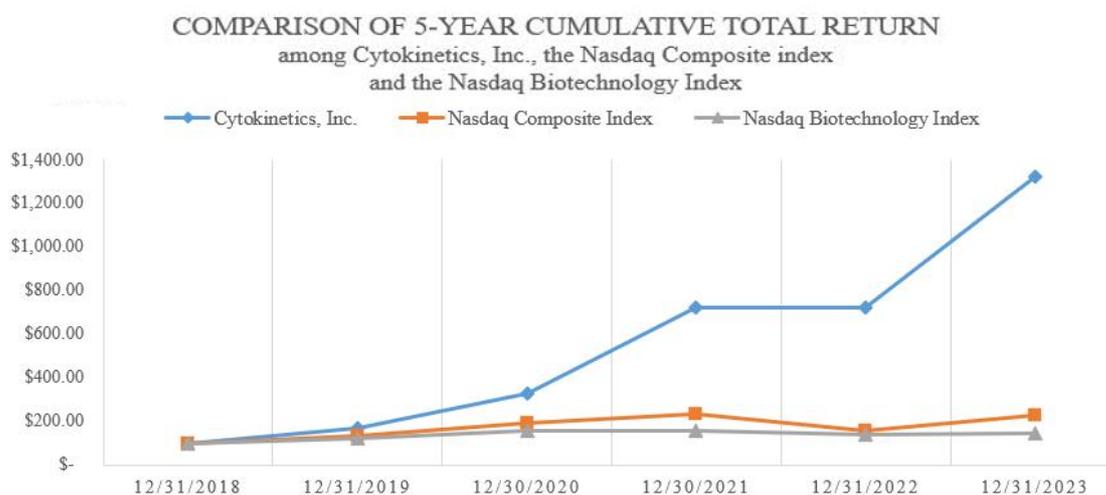
Market information for common stock

Our common stock is listed on the Nasdaq Global Select Market under the symbol “CYTK.” On February 27, 2024, the last reported sale price for our common stock was \$80.99 per share.

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 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, 2018 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	12/31/2018	12/31/2019	12/30/2020	12/30/2021	12/31/2022	12/31/2023
Cytokinetics, Inc.	\$ 100.00	\$ 167.88	\$ 328.80	\$ 721.20	\$ 725.00	\$ 1,321.04
Nasdaq Composite Index	100.00	135.23	194.24	235.78	157.74	226.24
Nasdaq Biotechnology Index	100.00	124.41	156.36	155.37	138.42	143.60

Holders of Record

As of February 27, 2024, we had 45 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.

Unregistered Sales of Equity Securities

None.

Issuer Purchases of Equity Securities

None.

ITEM 6. [RESERVED]

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: aficamten, a next-in-class cardiac myosin inhibitor, omecamtiv mecarbil, a novel cardiac myosin activator, CK-586, an additional cardiac myosin inhibitor, and CK-136, a novel cardiac troponin activator.

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.

Accrued Research and Development Expenditures

Clinical trial costs are a component of research and development expense. We accrue and expense clinical trial activities performed by third parties based upon actual work completed in accordance with agreements established with clinical research and manufacturing organizations and clinical sites. We determine the actual costs through monitoring patient enrollment, communications with internal personnel and external service providers regarding the progress or stage of completion of trials or services and the agreed-upon fee to be paid for such services.

Revenue Participation Right Purchase Agreements

We have entered into certain revenue participation right purchase agreements for omecamtiv mecarbil and aficamten with affiliates of Royalty Pharma, pursuant to which such affiliates purchased rights to royalties from certain revenue streams in exchange for consideration. We typically account for such agreements as liabilities to be amortized under the effective interest rate method over the life of the related royalty stream, when we have continuing involvement with the underlying R&D. We typically account for such agreements as deferred income to be amortized under the units-of-revenue method, when there is no continuing involvement with the underlying R&D. We are required to update our estimates, each reporting period, related to the amount and timing of future royalty payments to be paid to the counterparties of the revenue participation right purchase agreements. The estimates of the future royalty payment determine the measurement of the non-cash interest expense and the carrying value of the liability.

Revenue participation right purchase agreements are measured using significant unobservable inputs. The estimates of future royalties requires the use of several assumptions such as: the probability of clinical success, the probability of regulatory approval, the estimated date of a product launch, estimates of eligible patient populations, estimates of prescribing behavior and patient behavior, estimates of pricing, payor reimbursement and coverage, and sales ramp. As products containing aficamten and omecamtiv mecarbil have not yet been commercialized, the estimates are highly subjective.

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The carrying amount of the liabilities are based on our estimate of the future royalties to be paid over the life of the arrangements as discounted using an imputed rate of interest. The imputed rate of interest on the RP Aficamten Liability was approximately 24.8% as of December 31, 2023 and 22.4% as of December 31, 2022. In 2023, the change in estimate increased our non-cash interest expense and net loss by \$2.0 million. The imputed rate of interest on the RP OM Liability was approximately 0.2% as of December 31, 2023 and 8.5% as of December 31, 2022. In 2023, the change in estimate decreased our non-cash interest expense and net loss by \$12.8 million. We periodically assess the amount and timing of expected royalty payments and account for any changes in such estimates on a prospective basis.

As of December 31, 2023, we have a total carrying value of approximately \$380.0 million of liabilities related to revenue participation right purchase agreements.

Results of Operations

A discussion of our results of operations for the year ended December 31, 2021 and year-to-year comparisons between 2022 and 2021 can be found in Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations in our 2022 Annual Report on Form 10-K under the heading "Results of Operations."

Revenues

Our revenues since inception were primarily from our strategic alliances. We have not generated any revenue from commercial product sales to date.

Revenues in 2023, 2022, and 2021 were as follows (in thousands):

	Years Ended December 31,			Change	
	2023	2022	2021	2023-2022	2022-2021
		(In millions)			
Research and development revenues	\$ 4.0	\$ 6.6	\$ 10.6	\$ (2.6)	\$ (4.0)
License revenues	—	—	54.9	0.0	(54.9)
Milestone revenues	3.5	1.0	5.0	2.5	(4.0)
Realization of revenue participation right purchase agreement	—	87.0	—	(87.0)	87.0
Total revenues	\$ 7.5	\$ 94.6	\$ 70.4	\$ (87.1)	\$ 24.2

Research and development revenues in 2023 were primarily from Astellas for reimbursements under the Astellas FSRA Agreement and from Ji Xing under the Ji Xing Agreements. In 2022, research and development revenues were primarily from Astellas for reimbursements under the Astellas FSRA Agreement.

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 the Company's Phase 3 clinical trial of reldesemtiv in ALS, up to a maximum contribution by Astellas of \$12 million. On March 31, 2023, we announced that we would be discontinuing COURAGE-ALS, our Phase 3 clinical trial of reldesemtiv in patients with ALS, and COURAGE-ALS OLE. As of December 31, 2023 we have billed and collected from Astellas up to the maximum contribution of \$12.0 million, and no further revenue is expected under this arrangement.

Milestone revenues for 2023 consist primarily of a \$2.5 million milestone payment from Ji Xing for the initiation of our Phase 3 clinical trial of aficamten in patients with nHCM (ACACIA-HCM).

In 2022, we recognized revenues of \$87.0 million related to the RTW Royalty Purchase Agreement. On July 14, 2020, we entered the RTW Royalty Purchase Agreement with RTW Royalty Holdings, pursuant to which we sold our 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. On March 31, 2021, RTW Royalty Holdings assigned its rights and obligations under the RTW Royalty Purchase Agreement to its affiliate, RTW ICAV. We understand that on April 18, 2022, RTW ICAV and MyoKardia, Inc. entered into agreements, which purported to assign all of RTW ICAV's rights, title and interest to the Mavacamten Royalty to MyoKardia, Inc., and on April 25, 2022, we entered into a tripartite agreement with RTW ICAV and MyoKardia, Inc. acknowledging the release and discharge of any further obligations by us or MyoKardia, Inc. in connection to the Mavacamten Royalty. As a result of the full extinguishment of the Mavacamten Royalty, we recognized revenue of \$87.0 million in 2022.

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 by program for 2023, 2022, and 2021 were as follows (in thousands):

	Years Ended December 31,			Change	
	2023	2022	2021	2023-2022	2022-2021
	(In millions)				
Cardiac muscle contractility	\$ 231.9	\$ 125.6	\$ 102.5	\$ 106.3	\$ 23.1
Skeletal muscle contractility	52.4	67.1	27.9	(14.7)	39.2
All other research programs	45.8	48.1	29.5	(2.3)	18.6
Total research and development expenses	\$ 330.1	\$ 240.8	\$ 159.9	\$ 89.3	\$ 80.9

Research and development expenses increased to \$330.1 million in 2023 from \$240.8 million in 2022, primarily due to higher expenses for our clinical development activities for our cardiac muscle contractility (i.e. SEQUOIA-HCM) and skeletal muscle contractility (i.e. COURAGE-ALS) and for early research activities.

On March 31, 2023, we announced that we would be discontinuing COURAGE-ALS and COURAGE-ALS OLE. Research and development expenses for COURAGE-ALS and COURAGE-ALS OLE was \$42.9 million in 2023. We expect the related expenses will decrease in 2024.

We continue to develop aficamten to treat both oHCM and nHCM in two phase 3 clinical trials. MAPLE-HCM is our Phase 3 clinical trial of aficamten as a monotherapy for patients with oHCM and ACACIA-HCM is a Phase 3 clinical trial for patients with symptomatic nHCM. Additionally we have FOREST-HCM which is an open label extension study designed to assess the long term safety and tolerability of aficamten in patients with symptomatic oHCM.

On February 28, 2023, we received a CRL from FDA in connection with our NDA for omecamtiv mecarbil for the treatment of HFREF. With the CRL, FDA communicated that GALACTIC-HF is not sufficiently persuasive to establish substantial evidence of effectiveness for reducing the risk of heart failure events and cardiovascular death in adults with chronic heart failure with HFREF, in lieu of evidence from at least two adequate and well-controlled clinical investigations. FDA stated that results from an additional clinical trial of omecamtiv mecarbil are required to establish substantial evidence of effectiveness for the treatment of HFREF, with benefits that outweigh the risks. In 2023, we participated in a Type A meeting with FDA in order to understand FDA's views regarding the CRL and what may be required to support potential approval of omecamtiv mecarbil in the United States, and subsequently submitted a formal dispute resolution request to FDA, with the objective to appeal the FDA's conclusion, as stated in the CRL, that substantial evidence of effectiveness had not been established to support approval of omecamtiv mecarbil. FDA subsequently denied our appeal in November 2023 and reaffirmed its decision in the CRL that GALACTIC-HF is not sufficiently persuasive to establish substantial evidence of effectiveness for reducing the risk of heart failure events and cardiovascular death in adults with chronic heart failure with HFREF, in lieu of evidence from at least two adequate and well-controlled clinical investigations.

Under our strategic alliances with Ji Xing, Ji Xing is responsible for the development of aficamten and omecamtiv mecarbil in China and Taiwan.

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 by program for 2023, 2022, and 2021 were as follows (in thousands):

	Years Ended December 31,			Change	
	2023	2022	2021	2023-2022	2022-2021
	(In millions)				
Total general and administrative expenses	\$ 173.6	\$ 178.0	\$ 96.8	\$ (4.4)	\$ 81.2

General and administrative expenses decreased to \$173.6 million in 2023 from \$178.0 million in 2022, primarily due to lower outside service spend related to commercial activities, offset by an increase in personnel related costs including stock-based compensation recorded in 2023.

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

Interest Expense

Interest expense for 2023, 2022, and 2021 were as follows (in thousands):

	Years Ended December 31,			Change	
	2023	2022	2021	2023-2022	2022-2021
	(In millions)				
Term loan	\$ 5.1	\$ 4.8	\$ 4.8	\$ 0.3	\$ —
2026 Notes	1.0	3.6	11.5	(2.6)	(7.9)
2027 Notes	22.0	10.7	—	11.3	10.7
Other	0.2	0.3	0.1	(0.1)	0.2
Total interest expense	\$ 28.3	\$ 19.4	\$ 16.4	\$ 8.9	\$ 3.0

Interest expense in 2023 consists primarily of interest expense related to the RP Loan Agreement between us and RPDF and interest expense related to the 2026 Notes and 2027 Notes. Commensurate with our entry into the RP Loan Agreement, we terminated the Term Loan Agreement with Silicon Valley Bank and Oxford Finance LLC and repaid all amounts outstanding thereunder in January 2022. The RP Loan Agreement effectively replaced the Term Loan Agreement. In July 2022, we issued the 2027 Notes and used the net proceeds and common stock to partially repurchase the 2026 Notes.

Non-cash interest expense on liabilities related to revenue participation right purchase agreements

Non-cash interest expense results from the accretion of our liabilities to RPFT and RP ICAV related to the sale of future royalties under the RP OM RPA and the RP Aficamten RPA, respectively.

On January 7, 2022, we entered into the RP Aficamten RPA with RPI ICAV. Pursuant to the RP Aficamten RPA, RPI ICAV purchased the right to receive a percentage of net sales equal to 4.5% for annual worldwide net sales of pharmaceutical products containing aficamten up to \$1 billion and 3.5% for annual worldwide net sales of pharmaceutical products containing aficamten in excess of \$1 billion, subject to reduction in certain circumstances (the “RP Aficamten Liability”). The carrying amount of the RP Aficamten Liability is based on our estimate of the future royalties to be paid to RPI ICAV over the life of the arrangement as discounted using an imputed rate of interest. The imputed rate of interest on the unamortized portion of the RP Aficamten Liability was approximately 24.8% as of December 31, 2023.

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In 2023, we updated our analyses of the RP Aficamten RPA to reflect our assumptions resulting from ongoing global market research and to reflect other adjustments in connection with our anticipated commercialization, including the additional consideration of \$50.0 million which was paid to us in September 2023 following the initiation of the first pivotal clinical trial in nHCM for aficamten. Our estimates regarding the amount of future royalty payments under the RP Aficamten RPA changed from the fourth quarter of 2022 due to changes in management's estimates of unobservable inputs related to market conditions and timing to include projections of future royalty payments. The resulting sales forecast for aficamten has increased year over year mainly due to the receipt of positive topline results from SEQUOIA-HCM, the Phase 3 trial for aficamten, in December 2023. The adjustment is accounted for on a prospective basis in our liability calculation and resulted in changes in our imputed interest rate and non-cash interest expense from 22.4% and \$5.2 million in the fourth quarter of 2022, 22.4% and \$5.4 million in the first quarter of 2023, 19.0% and \$4.9 million in the second quarter of 2023, 18.0% and \$5.4 million in the third quarter of 2023, to 24.8% and \$9.8 million in the fourth quarter of 2023. The non-cash interest expense was \$25.5 million and \$15.5 million in 2023 and 2022, respectively. In 2023, the change in estimate increased our non-cash interest expense and net loss by \$2.0 million. The change in accounting estimate increased the net loss per share by \$0.02 in 2023.

In 2023, we updated our analyses of the RP OM RPA to reflect our current assumptions resulting from ongoing global market research and to reflect other adjustments in connection with our anticipated commercialization, including the result of our receipt of a CRL in connection to our NDA for omecamtiv mecarbil. As a consequence of our receipt of the CRL from FDA, the royalty rate under the RP OM RPA will increase to no more than 5.5%. The resulting sales forecast for omecamtiv mecarbil has decreased year over year because commercialization and sales of omecamtiv mecarbil will be delayed. The adjustment is accounted for on a prospective basis in our liability calculation and resulted in changes in our imputed interest rate and non-cash interest expense from 8.5% and \$4.0 million in the fourth quarter of 2022, 1.9% and \$0.9 million in the first quarter of 2023, 2.9% and \$1.4 million in the second and third quarter of 2023, and to 0.1% and \$0.1 million in the fourth quarter of 2023, respectively. The non-cash interest expense was \$3.9 million, \$16.2 million, and \$12.9 million in 2023, 2022, and 2021, respectively. In 2023, the change in estimate decreased our non-cash interest expense and net loss by \$12.8 million. The change in accounting estimate reduced the net loss per share by \$0.13 in 2023.

We review our assumptions on a regular basis and our estimates may change in the future as we refine and reassess our assumptions.

Non-cash interest expense on liability related to the RP OM RPA and the RP Aficamten RPA for 2023, 2022, and 2021 were as follows (in thousands):

	Years Ended December 31,			Change	
	2023	2022	2021	2023-2022	2022-2021
	(In millions)				
RP OM Liability	\$ 3.9	\$ 16.2	\$ 12.9	\$ (12.3)	\$ 3.3
RP Aficamten Liability	25.5	15.5	—	10.0	15.5
Total non-cash interest expense recognized	<u>\$ 29.4</u>	<u>\$ 31.7</u>	<u>\$ 12.9</u>	<u>\$ (2.3)</u>	<u>\$ 18.8</u>

Interest and Other Income, net

Interest and other income, net for 2023, 2022, and 2021 consisted primarily of interest income generated from our cash, cash equivalents and investments.

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, 2023	December 31, 2022
	(In millions)	
Financial assets:		
Cash and cash equivalents	\$ 113.0	\$ 65.6
Short-term investments	501.8	717.0
Long-term investments	40.5	46.7
Total cash, cash equivalents, and marketable securities	<u>\$ 655.3</u>	<u>\$ 829.3</u>
Borrowings:		
Term loan, net	\$ 58.4	\$ 63.8
2026 Notes, net	20.8	20.7
2027 Notes, net	528.2	525.1
Total borrowings	<u>\$ 607.4</u>	<u>\$ 609.6</u>
Working capital:		
Current assets	\$ 628.1	\$ 795.2
Current liabilities	102.7	84.6
Working capital	<u>\$ 525.4</u>	<u>\$ 710.6</u>

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

	Years Ended December 31,		
	2023	2022	2021
	(In millions)		
Net cash used in operating activities	\$ (414.3)	\$ (299.5)	\$ (142.5)
Net cash provided by (used in) investing activities	239.3	(262.1)	(147.8)
Net cash provided by financing activities	221.3	516.2	320.0
Net increase (decrease) in cash, cash equivalents, and restricted cash	<u>\$ 46.3</u>	<u>\$ (45.4)</u>	<u>\$ 29.7</u>

Sources and Uses of Cash

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

Cash Flows Used in Operating Activities

Net cash used in operating activities of \$414.3 million and \$299.5 million for 2023 and 2022, respectively, was largely due to ongoing research and development activities and general and administrative expenses to support those activities. In 2022, the net cash used in operating activities was offset by collection of receivables primarily from our 2021 RTW Transactions. Net loss for 2023 and 2022 included, among other items: non-cash stock-based compensation, non-cash interest expense on liabilities related to revenue participation right purchase agreements, and non-cash interest expense related to debt.

Cash Flows Used in Investing Activities

Net cash provided by investing activities of \$239.3 million for 2023 was primarily due to sales and maturities of investments offset by purchases of investments.

Net cash used in investing activities of \$262.1 million for 2022 was primarily due to purchases of investments and property and equipment offset by proceeds from maturity of investments.

Cash Flows Provided by Financing Activities

Net cash provided by financing activities of \$221.3 million in 2023 was due to proceeds from public offerings of common stock of \$164.2 million under the Controlled Equity Offering Sales Agreement with Cantor Fitzgerald & Co discussed below and \$50.0 million of additional consideration associated with the 2022 RP Aficamten Royalty Purchase Agreement which was paid to us in September 2023 and stock-based award activities.

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Net cash provided by financing activities of \$516.2 million in 2022 was primarily due to proceeds related to RP Aficamten RPA and the RP Loan Agreement and offset by the repayment of amounts owed under our Term Loan Agreement and stock-based award activities.

Royalty Pharma Transactions

On January 7, 2022, we announced that we had entered into that certain RP Loan Agreement and the RP Aficamten RPA with RPDF and RPI ICAV respectively, each of which were at the time of our entry into such agreements affiliated with Royalty Pharma International plc.

Under the RP Loan Agreement, we were initially entitled to receive up to \$300.0 million in term loans, \$50.0 million of which was disbursed to us on closing and the remaining \$250.0 million scheduled to have been available to us upon our satisfaction of customary disbursement conditions and certain development conditions by specific deadlines, as follows:

- \$50.0 million of tranche 2 term loans during the one year period following the receipt on or prior to March 31, 2023 of marketing approval from FDA of omeamtiv mecarbil;
- \$25.0 million of tranche 3 term loans during the one year period following the commercial availability of a diagnostic test measuring levels of omeamtiv mecarbil to support the final FDA label language applicable to such drug, subject to such commercial availability and the conditions to the tranche 2 term loans having occurred on or prior to March 31, 2023;
- \$75.0 million of tranche 4 term loans during the one year period following the receipt on or prior to September 30, 2024 of positive results from SEQUOIA-HCM, the Phase 3 trial for aficamten; and
- \$100.0 million of tranche 5 term loans during the one year period following the acceptance by the FDA on or prior to March 31, 2025 of an NDA for aficamten, subject to the conditions to the tranche 4 term loans having occurred on or prior to September 30, 2024.

As a result of our receipt of a CRL in connection to our NDA for omeamtiv mecarbil, we have not satisfied the conditions to the availability of the tranche 2 and tranche 3 loans under the RP Loan Agreement.

In December 2023, we announced positive topline results from SEQUOIA-HCM, the Phase 3 trial for aficamten. This entitled us to receive \$75.0 million under tranche 4 during the one year period following the receipt of the positive results and requires us to draw a minimum of at least \$50.0 million of the \$75.0 million available under tranche 4.

The remaining \$100.0 million under tranche 5 remains available for disbursement to us, subject to satisfaction of the conditions described above.

Each term loan under the RP Loan Agreement matures on the 10 year anniversary of the funding date for such term loan and is repayable in quarterly installments of principal, interest and fees commencing on the last business day of the seventh full calendar quarter following the calendar quarter of the applicable funding date for such term loan, with the aggregate amount payable in respect of each term loan (including interest and other applicable fees) equal to 190% of the principal amount of the tranche 1, tranche 4 and tranche 5 term loans and 200% of the principal amount of the tranche 2 and tranche 3 loans (such amount with respect to each term loan, "Final Payment Amount"). We have made our first payment in the fourth quarter of 2023.

We may prepay the term loans in full (but not in part) at any time at our option by paying an amount equal to the unpaid portion of Final Payment Amount for the outstanding term loans under the RP Loan Agreement; provided that if the conditions for either the tranche 4 term loans or the tranche 5 term loans have been met, we must have borrowed at least \$50 million principal amount of the tranche 4 or 5 term loans. In addition, the term loans under the RP Loan Agreement are repayable in full at the option of either us or the lender in an amount equal to the unpaid portion of Final Payment Amount for the outstanding term loans upon a change of control of Cytokinetics.

In addition, on January 7, 2022, we entered into the RP Aficamten RPA with RPI ICAV, pursuant to which RPI ICAV purchased rights to certain revenue streams from net sales of pharmaceutical products containing aficamten by us, our affiliates and our licensees in exchange for up to \$150.0 million in consideration, \$50.0 million of which was paid on the closing date, \$50.0 million of which was paid to us in March 2022 following the initiation of the first pivotal trial in oHCM for aficamten, and \$50.0 million of which was paid to us in September 2023 following the initiation of the first pivotal clinical trial in nHCM for aficamten.

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The RP Aficamten RPA also provides that the parties will negotiate terms for additional funding if we achieve proof of concept results in certain other indications for aficamten, with a reduction in the applicable royalty if we and RPI ICAV fail to agree on such terms in certain circumstances.

Pursuant to the RP Aficamten RPA, RPI ICAV purchased the right to receive a percentage of net sales equal to 4.5% for annual worldwide net sales of pharmaceutical products containing aficamten up to \$1 billion and 3.5% for annual worldwide net sales of pharmaceutical products containing aficamten in excess of \$1 billion, subject to reduction in certain circumstances.

Convertible Notes

On November 13, 2019, we issued \$138.0 million aggregate principal amount of 2026 Notes. On July 6, 2022, we issued \$540.0 million aggregate principal amount of 2027 Notes and used approximately \$140.3 million of the net proceeds from the offering of 2027 Notes and issued 8,071,343 shares of common stock to repurchase approximately \$116.9 million aggregate principal amount of the 2026 Notes pursuant to privately negotiated exchange agreements entered into with certain holders of the 2026 Notes concurrently with the pricing of the offering of the 2027 Notes. As a result of the partial repurchase of the 2026 Notes, we recorded an inducement loss of \$22.2 million, consisting of the difference between the consideration to the holders pursuant to the exchange agreements and the if-converted value of the 2026 Notes under the original terms. As of December 31, 2023, there remains \$21.1 million aggregate principal amount of 2026 Notes outstanding and \$540.0 million of aggregate principal amount of 2027 Notes outstanding. The 2026 Notes are redeemable, in whole or in part, at our option at any time, and from time to time, 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 our 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 we may send the related redemption notice; and (2) the trading day immediately before the date we may send such notice.

2021 Ji Xing and RTW Transactions

On December 20, 2021, we entered into the Ji Xing OM License Agreement, pursuant to which we granted to Ji Xing an exclusive license to develop and commercialize omecamtiv mecarbil in China and Taiwan. Under the terms of the Ji Xing OM License Agreement, we received a \$50.0 million nonrefundable payment from Ji Xing comprised of a \$40.0 million payment as consideration for the rights granted by us to Ji Xing and \$10.0 million attributable to our having submitted to FDA an NDA for omecamtiv mecarbil. We may be eligible to receive from Ji Xing additional payments totaling up to \$330.0 million for the achievement of certain commercial milestone events in China in connection to omecamtiv mecarbil. In addition, Ji Xing will pay us tiered royalties in the mid-teens to the low twenties range on the net sales of pharmaceutical products containing omecamtiv mecarbil in China and Taiwan, subject to certain reductions for generic competition, patent expiration and payments for licenses to third party patents. The Ji Xing OM License Agreement, unless terminated earlier, will continue on a market-by-market basis until expiration of the relevant royalty term. We recognized a \$2.5 million milestone from Ji Xing in 2023 for the initiation of a phase 3 clinical trial for aficamten in nHCM, which was collected in the fourth quarter of 2023.

In addition to the Ji Xing OM License Agreement, we entered into common stock purchase agreements with each of the RTW Investors, pursuant to which we sold and issued an aggregate of 0.5 million shares of our common stock at a price per share of \$39.125 and an aggregate purchase price of \$20.0 million.

Controlled Equity Offering Sales Agreement with Cantor Fitzgerald & Co.

On March 1, 2023, we entered into the Amended ATM Facility, with Cantor, under which we may offer and sell, from time to time at our sole discretion, shares of the Common Stock having an aggregate offering price of up to \$300.0 million through Cantor, as sales agent. The Amended ATM Facility amends, restates and supersedes the Controlled Equity Offering Sales Agreement dated as of March 6, 2019 between the Company and Cantor.

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

In 2023, we issued 5,016,170 shares of our common stock for net proceeds of \$164.2 million pursuant to the Amended ATM Facility.

Future Uses of Cash

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, and we plan to file one to two investigational new drug applications in 2023. We may also incur significant sales and marketing expenses in anticipation of regulatory approval of one of our drug candidates.

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, 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;
- our revenues, if any, from successful development of our drug candidates and commercialization of potential drugs;
- the cost of additional construction to expand our headquarters in South San Francisco and in relation to our leased office facilities in Radnor, Pennsylvania; and
- the payments due for interest on the term loan and convertible debt;

We have incurred an accumulated deficit of approximately \$2.1 billion 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. Therefore, 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.

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Based on the current status of our development plans, we believe that our existing cash and cash equivalents, investments and interest earned on investments will be sufficient to meet our projected operating requirements for at least the next 12 months. If, at any time, our prospects for internally financing our research and development programs decline, we may decide to reduce research and development expenses by delaying, discontinuing or reducing our funding of development of one or more of our drug candidates or of other research and development programs. Alternatively, we might raise funds through strategic relationships, public or private financings or other arrangements. There can be no assurance that funding, if needed, will be available on attractive terms, or at all, or in accordance with our planned timelines. Furthermore, financing obtained through future strategic relationships may require us to forego certain commercialization and other rights to our drug candidates. Similarly, any additional equity financing may be dilutive to stockholders and debt financing, if available, may involve restrictive covenants. Our failure to raise capital as and when needed could have a negative impact on our financial condition and our ability to pursue our business strategy.

Segment Information

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

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.

Market Risk and Interest Rate Risk

We are exposed to market risk related to changes in interest rates. As of December 31, 2023, we had cash and investments of \$655.4 million, which consist of U.S. Treasury securities, U.S. and non-U.S. government agency bonds, commercial paper, global portfolio of corporate debt, money market fund, and repurchase agreements backed by U.S. Treasury securities. 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. We have not been exposed to, nor do we anticipate being exposed to, material risks due to changes in interest rates. A 1% increase or decrease in current interest rates would not have a material effect on our financial results.

We had \$21.1 million under 2026 Notes with a fixed rate of 4.0% and \$540.0 million under 2027 Notes with a fixed rate of 3.5% outstanding as of December 31, 2023. The convertible notes issued at fixed interest rates are exposed to fluctuations in fair value resulting from changes in market price and interest rates. We do not record our convertible debt at fair value but present the fair value for disclosure purposes (see Note 7 to our Consolidated Financial Statements). As of December 31, 2022, the fair value of the 2026 Notes and 2027 Notes was estimated at \$168.4 million and \$990.4 million using quoted market prices.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

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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, 2023 and 2022, the related consolidated statements of operations and comprehensive loss, stockholders’ (deficit) equity, and cash flows for each of the three years in the period ended December 31, 2023, and the related notes (collectively referred to as the “consolidated financial statements”). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2023 and 2022, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2023, 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, 2023, 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 28, 2024 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 Matter

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of the critical audit matter 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 matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Measurement of Revenue Participation Right Purchase Agreements

Description of the Matter

As of December 31, 2023, the liabilities related to revenue participation right purchase agreements, net were \$380.0 million. The Company recognized non-cash interest expense on the liabilities related to revenue participation right purchase agreements of \$29.4 million for the year ended December 31, 2023. As described in Note 6 to the consolidated financial statements, the Company has entered into agreements, pursuant to which counterparties purchased rights to receive royalty streams from the net sales of pharmaceutical products containing Aficamten and Omecamtiv Mecarbil. The cash received by the Company from these royalty purchase agreements was initially recognized as a liability related to revenue participation right purchase agreements. The Company is required to update its estimate, each reporting period, related to the amount and timing of future royalty payments to be paid to the counterparties of the revenue participation right purchase agreements. The estimates of the future royalty payment determine the measurement of the non-cash interest expense and the carrying value of the liability.

Auditing the Company's measurement of the revenue participation right purchase agreements was complex due to the significant estimation uncertainty in projecting future royalty payments to be paid to the counterparties of the revenue participation right purchase agreements. The estimates of future royalties requires the use of several assumptions such as: the probability of clinical success, the probability of regulatory approval, the estimated date of a product launch, estimates of eligible patient populations, estimates of prescribing behavior and patient behavior, estimates of pricing and payor reimbursement and coverage, and sales ramp. As products containing Aficamten and Omecamtiv Mecarbil have not yet been commercialized, the estimates are highly subjective.

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.

To test the amount and timing of future royalty payments to be paid to the counterparties of the revenue participation right purchase agreements, our audit procedures included, among others, evaluating the reasonableness of significant assumptions used by management. Evaluating the reasonableness of management's assumptions included consideration of (i) relevant industry forecasts and data, (ii) consistency with observable data for competitor products, and (iii) whether the assumptions were consistent with evidence obtained in other areas of the audit.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2018.
San Jose, California
February 28, 2024

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

	December 31,	
	2023	2022
ASSETS		
Current assets:		
Cash and cash equivalents	\$ 113,024	\$ 65,582
Short-term investments	501,800	716,995
Accounts receivable	1,283	147
Prepaid expenses and other current assets	11,944	12,462
Total current assets	628,051	795,186
Long-term investments	40,534	46,708
Property and equipment, net	68,748	80,453
Operating lease right-of-use assets	78,987	82,737
Other assets	7,996	9,691
Total assets	\$ 824,316	\$ 1,014,775
LIABILITIES AND STOCKHOLDERS' DEFICIT		
Current liabilities:		
Accounts payable	\$ 21,507	\$ 25,611
Accrued liabilities	42,641	44,096
Short-term operating lease liabilities	17,891	12,829
Current portion of long-term debt	10,080	958
Other current liabilities	10,559	1,123
Total current liabilities	102,678	84,617
Term loan, net	58,384	63,810
Convertible notes, net	548,989	545,808
Liabilities related to revenue participation right purchase agreements, net	379,975	300,501
Long-term operating lease liabilities	120,427	126,895
Other non-current liabilities	186	1,044
Total liabilities	1,210,639	1,122,675
Commitments and contingencies		
Stockholders' 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: 101,637,922 shares at December 31, 2023 and 94,833,975 shares at December 31, 2022	102	94
Additional paid-in capital	1,725,823	1,481,590
Accumulated other comprehensive loss	(10)	(3,590)
Accumulated deficit	(2,112,238)	(1,585,994)
Total stockholders' deficit	(386,323)	(107,900)
Total liabilities and stockholders' deficit	\$ 824,316	\$ 1,014,775

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,		
	2023	2022	2021
Revenues:			
Research and development revenues	\$ 4,030	\$ 6,588	\$ 10,572
License revenues	—	—	54,856
Milestone revenues	3,500	1,000	5,000
Realization of revenue participation right purchase agreement	—	87,000	—
Total revenues	<u>7,530</u>	<u>94,588</u>	<u>70,428</u>
Operating expenses:			
Research and development	330,123	240,813	159,938
General and administrative	173,612	177,977	96,803
Total operating expenses	<u>503,735</u>	<u>418,790</u>	<u>256,741</u>
Operating loss	(496,205)	(324,202)	(186,313)
Interest expense	(28,306)	(19,414)	(16,440)
Loss on extinguishment of debt	—	(24,939)	—
Non-cash interest expense on liabilities related to revenue participation right purchase agreements	(29,362)	(31,742)	(12,892)
Interest and other income, net	27,629	11,342	331
Net loss	<u>\$ (526,244)</u>	<u>\$ (388,955)</u>	<u>\$ (215,314)</u>
Net loss per share — basic and diluted	<u>\$ (5.45)</u>	<u>\$ (4.33)</u>	<u>\$ (2.80)</u>
Weighted-average number of shares used in computing net loss per share — basic and diluted	<u>96,524</u>	<u>89,825</u>	<u>76,886</u>
Other comprehensive gain (loss):			
Unrealized gain (loss) on available-for-sale securities, net	3,600	(2,721)	(1,018)
Foreign currency translation adjustments	(20)	—	—
Comprehensive loss	<u>\$ (522,664)</u>	<u>\$ (391,676)</u>	<u>\$ (216,332)</u>

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

CYTOKINETICS, INCORPORATED
CONSOLIDATED STATEMENTS OF STOCKHOLDERS' (DEFICIT) EQUITY
(In thousands, except shares)

	Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' (Deficit) Equity
	Shares	Amount				
Balance, December 31, 2020	71,015,183	\$ 70	\$ 1,105,470	\$ 149	\$ (992,306)	\$ 113,383
Exercise of stock options	1,304,347	3	11,017	—	—	11,020
Vesting of restricted stock units, net of taxes withheld	360,050	—	(4,449)	—	—	(4,449)
Net share settlement	—	—	(418)	—	—	(418)
Underwritten public offering of common stock, net of discounts, commissions and offering cost	11,500,000	11	296,894	—	—	296,905
Issuance of common stock upon private placement	511,182	—	15,144	—	—	15,144
Issuance of common stock under Employee Stock Purchase Plan	108,780	—	1,778	—	—	1,778
Stock-based compensation	—	—	26,832	—	—	26,832
Other comprehensive loss	—	—	—	(1,018)	—	(1,018)
Net loss	—	—	—	—	(215,314)	(215,314)
Balance, December 31, 2021	84,799,542	84	1,452,268	(869)	(1,207,620)	243,863
ASU 2020-06 adoption	—	—	(49,476)	—	10,581	(38,895)
Exercise of stock options	1,389,031	2	14,314	—	—	14,316
Issuance of common stock under restricted stock units	707,772	—	—	—	—	—
Shares withheld related to net share settlement of equity awards	(260,172)	—	(9,602)	—	—	(9,602)
Issuance of common stock under Employee Stock Purchase Plan	98,153	—	3,227	—	—	3,227
Induced conversion of convertible notes	8,071,343	8	(3,386)	—	—	(3,378)
Exercise of warrants	28,306	—	—	—	—	—
Settlement of capped call on 2026 Notes	—	—	26,392	—	—	26,392
Stock-based compensation	—	—	47,853	—	—	47,853
Other comprehensive loss	—	—	—	(2,721)	—	(2,721)
Net loss	—	—	—	—	(388,955)	(388,955)
Balance, December 31, 2022	94,833,975	94	1,481,590	(3,590)	(1,585,994)	(107,900)
Exercise of stock options	1,193,325	2	14,317	—	—	14,319
Vesting of restricted stock units	721,216	1	—	—	—	1
Shares withheld related to net share settlement of equity awards	(262,829)	—	(10,517)	—	—	(10,517)
Issuance of common stock under Employee Stock Purchase Plan	136,065	—	4,140	—	—	4,140
Issuance of common stock under at-the-market offering, net of issuance costs	5,016,170	5	164,228	—	—	164,233
Stock-based compensation	—	—	72,065	—	—	72,065
Other comprehensive income	—	—	—	3,580	—	3,580
Net loss	—	—	—	—	(526,244)	(526,244)
Balance, December 31, 2023	101,637,922	\$ 102	\$ 1,725,823	\$ (10)	\$ (2,112,238)	\$ (386,323)

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,		
	2023	2022	2021
Cash flows from operating activities:			
Net loss	\$ (526,244)	\$ (388,955)	\$ (215,314)
Adjustments to reconcile net loss to net cash used in operating activities:			
Non-cash interest expense on liabilities related to revenue participation right purchase agreement	29,474	31,858	13,004
Stock-based compensation expense	72,065	47,853	26,832
Non-cash lease expense	3,750	2,585	7,361
Impairment of right-of-use assets	—	—	2,844
Depreciation of property and equipment	11,892	5,814	2,276
Realized gain on investment, net	35	107	—
Interest receivable and amortization on investments	(15,735)	(4,710)	4,894
Non-cash interest expense related to debt	7,341	5,697	7,125
Loss on extinguishment of debt	—	2,693	—
Loss on inducement of convertible debt	—	22,246	—
Changes in operating assets and liabilities:			
Accounts receivable	(1,136)	56,672	(47,399)
Prepaid and other assets	1,596	(7,414)	(7,381)
Accounts payable	(3,483)	4,524	1,055
Accrued and other liabilities	17,103	10,844	15,060
Deferred revenue	—	(87,000)	—
Operating lease liabilities	(1,406)	1,728	43,472
Other non-current liabilities	(9,585)	(4,058)	3,649
Net cash used in operating activities	(414,333)	(299,516)	(142,522)
Cash flows from investing activities:			
Purchases of investments	(635,211)	(855,393)	(525,042)
Maturities of investments	870,905	604,594	422,837
Sales of investments	4,975	—	3,300
Purchases of property and equipment	(1,416)	(11,335)	(48,872)
Net cash provided by (used in) investing activities	239,253	(262,134)	(147,777)
Cash flows from financing activities:			
Repayment of finance lease liabilities	(858)	(944)	—
Repayment of term loan	—	(47,651)	—
Debt extinguishment costs	—	(2,409)	—
Repayment of convertible debt	—	(140,330)	—
Proceeds from issuance of convertible debt, net	—	523,586	—
Proceeds from public offerings of common stock, net of discounts, commissions and offering cost	—	—	296,905
Proceeds from private placement, net	—	—	15,144
Proceeds from 2022 RPI Transactions, net	50,000	149,581	—
Proceeds from issuance of common stock related to at-the-market offering, net of issuance costs	164,233	—	—
Proceeds from issuance of common stock under equity incentive and stock purchase plans	18,459	17,543	12,380
Taxes paid related to net share settlement of equity awards	(10,517)	(9,602)	(4,449)
Cash settlement of capped call options associated with 2026 Notes	—	26,392	—
Net cash provided by financing activities	221,317	516,166	319,980
Effect of exchange rate changes	(20)	—	—
Net increase (decrease) in cash, cash equivalents, and restricted cash	46,217	(45,484)	29,681
Cash, cash equivalents, and restricted cash, beginning of period	67,182	112,666	82,985
Cash, cash equivalents, and restricted cash, end of period	\$ 113,399	\$ 67,182	\$ 112,666
Supplemental cash flow disclosures:			
Cash paid for interest	\$ 10,295	\$ 15,165	\$ 9,175
Non-cash investing and financing activities:			
Right-of-use assets recognized in exchange for operating lease obligations	\$ —	\$ 10,904	\$ 80,395
Right-of-use assets recognized in exchange for finance lease obligations	\$ —	\$ 1,055	\$ 1,294
Amounts unpaid for purchases of property and equipment	\$ —	\$ 621	\$ 11,982
Issuance of common stock in connection with repurchase of convertible note	\$ —	\$ 317,123	\$ —

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

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

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 approximately \$2.1 billion since inception and there can be no assurance that we will attain profitability. We had a net loss of \$526.2 million and net cash used in operations of \$414.3 million for the year ended December 31, 2023. Cash, cash equivalents, and investments decreased to \$655.4 million as of December 31, 2023 from \$829.3 million as of December 31, 2022. 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, sales of future revenues and 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 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. 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 activities, we believe that our existing cash, cash equivalents, and investments will be sufficient to fund cash requirements for at least the next 12 months after the issuance of these 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 GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosures of contingent liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting periods. We evaluate our estimates on an ongoing basis. We base our estimates on our historical experience and also on assumptions that we believe are reasonable; however, actual results could significantly differ from those estimates.

Basis of Presentation

The consolidated financial statements include the accounts of Cytokinetics, Incorporated and its wholly-owned subsidiaries and have been prepared in accordance with 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, cash equivalents, restricted cash, investments, and accounts receivable.

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

Our cash, cash equivalents, restricted cash, and investments held with large financial institutions in the United States and deposits may exceed the Federal Deposit Insurance Corporation’s insurance limit.

Drug candidates we develop may require approvals or clearances from the 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, Cash Equivalents, and Restricted Cash

We consider all highly liquid investments with a maturity of three months or less at the time of purchase to be cash equivalents, which consist of money market funds and repurchase agreements backed by U.S. Treasury securities. Repurchase agreements are collateralized by US Treasury securities for an amount not less than 102% of their value and are reported at a carrying value which approximates fair value due to their short duration.

A reconciliation of cash, cash equivalents, and restricted cash reported in our consolidated balance sheets to the amount reported within our consolidated statements of cash flows was as follows (in thousands):

	December 31,	
	2023	2022
Cash and cash equivalents	\$ 113,024	\$ 65,582
Restricted cash	375	1,600
Total cash, cash equivalents, and restricted cash as reported within our consolidated statement of cash flows	\$ 113,399	\$ 67,182

As of December 31, 2023, our restricted cash balance of \$0.4 million is used to collateralize letters of credit.

Investments

Our investments consist of U.S. Treasury securities, U.S. government agency securities, commercial paper, corporate obligations, 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 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.

All of our available-for-sale investments are subject to a periodic impairment review. For each available-for-sale investment whose fair value is below its amortized cost, we determine if the impairment is a result of a credit-related loss or other factors using both quantitative and qualitative factors. If the impairment is a result of a credit-related loss, we recognize an allowance for credit losses. If the impairment is not a result of a credit loss, we recognize the loss in other comprehensive loss.

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 and finance lease right-of-use assets are 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 twelve years. Upon sale or retirement of assets, the costs and related accumulated depreciation and amortization are removed from the balance sheet and the resulting gain or loss is reflected in operations.

Impairment of Long-lived Assets

We review long-lived assets, including property, equipment and right-of-use assets, 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 less than its carrying amount.

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

Leases

We determine if the arrangement contains a lease at inception based on whether the contract conveys the right to control the use of an identified asset. The lease classification is determined at lease commencement, which is the date the underlying asset is available for use by the Company, and preliminary based on whether the arrangement is effectively a financed purchase of the underlying asset (finance lease) or not (operating lease). We determined the lease term at the commencement date by considering whether renewal options and termination options are reasonably assured of exercise. In addition to the fixed minimum lease payments required under the lease arrangements, certain leases include payments of operating expenses that may be revised based on the landlord's estimate. These variable payments are excluded from the lease payments used to determine the right-of-use asset and lease liability and are recognized when the associated activity occurs.

We recognize right-of-use assets and short-term and long-term lease liabilities on our consolidated balance sheets for operating leases. The right-of-use asset and short-term and long-term lease liabilities for finance leases are recognized in property and equipment, other current liabilities, and other non-current liabilities, respectively, on the consolidated balance sheets.

In determining the present value of lease payments, we estimated our incremental borrowing rate based on information available upon commencement. We base the lease liabilities on the present value of remaining lease payments over the remaining terms of the leases using an estimated rate of interest that we would pay to borrow equivalent funds on a collateralized basis at the lease commencement date. The initial right-of-use asset, for both operating and finance leases, is measured based on the lease liability adjusted for any initial direct costs, lease prepayments, and lease incentives.

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. Finance lease right-of-use assets are amortized on a straight-line basis over the shorter of the expected useful life or the lease term, and the carrying amount of the lease liability is adjusted to reflect interest, which is recorded in interest expense.

We exclude from our consolidated balance sheets recognition of leases having a term of 12 months or less (short-term leases). We account for lease and non-lease components as a single component for our operating leases.

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.

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. For example, a license to our intellectual property is determined to be distinct from other performance obligations if licensee is able to use and benefit from the license on its own. Otherwise, licenses are bundled with other promises, such as ongoing research and development services, as combined performance obligation.

We enter into collaborative arrangements with partners that typically include payment to us for one of more of the following: (i) up-front 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. Up-front license fees are included in the transaction price. Development and regulatory milestone payments are included in the transaction price using the most likely amount method, if we conclude it is probable that a significant revenue reversal would not occur. For contracts that include sales-based royalties or sales-based milestones, 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 or sales-based milestone has been allocated has been satisfied.

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

Our joint programs with Astellas under the Astellas OSSA Agreement, and with Amgen under the Amgen Agreement (both of the Astellas OSSA Agreement and the Amgen Agreement having now been terminated), included promises of research and development services. We also entered into the Astellas FSRA Agreement on April 23, 2020. 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 the Company's Phase 3 clinical trial of reldesemtiv in ALS, up to a maximum contribution by Astellas of \$12.0 million. We determined that these services collectively were distinct from any licenses provided to Astellas and Amgen under such agreements, and as such, these services were accounted for as a separate performance obligation recorded over time. We recognized revenue for these services as the performance obligations were satisfied, which we estimated using internal research and development costs incurred.

When a collaborative agreement has more than one performance obligation, 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 performance obligations that consist of the delivery of an intellectual property license, the revenue is recognized at the point in time that the license is delivered. For combined performance obligations consisting of an intellectual property license and research and development services, we recognize the combined performance obligation over time, using an input method, as the research and development services are performed.

We are required to make estimates related to the determination of the transaction price and our measurement of how revenue is recognized over time, using the input method. Any changes in these estimates are recorded on a cumulative catch-up basis, which would affect license, collaboration and other revenues and earnings in the period of adjustment.

Accrued Research and Development Expenditures

Clinical trial costs are a component of research and development expense. We accrue and expense clinical trial activities performed by third parties based upon actual work completed in accordance with agreements established with clinical research and manufacturing organizations and clinical sites. We determine the actual costs through monitoring patient enrollment, discussions with internal personnel and external service providers regarding the progress or stage of completion of trials or services and the agreed-upon fee to be paid for such services.

Revenue Participation Right Purchase Agreements

We have entered into certain revenue participation right purchase agreements with certain investors, pursuant to which such investors purchased rights to royalties from certain revenue streams in exchange for consideration. We typically account for such agreements as liabilities to be amortized under the effective interest rate method over the life of the related royalty stream, when we have continuing involvement with the underlying R&D. We typically account for such agreements as deferred income to be amortized under the units-of-revenue method, when there is no continuing involvement with the underlying R&D. We are required to update our estimates, at each reporting period, related to the amount and timing of future royalty payments to be paid to the counterparties of the revenue participation right purchase agreements. The estimates of the future royalty payment determine the measurement of the non-cash interest expense and the carrying value of the liability.

Revenue participation right purchase agreements are measured using significant unobservable inputs. The estimates of future royalties requires the use of several assumptions such as: the probability of clinical success, the probability of regulatory approval, the estimated date of a product launch, estimates of eligible patient populations, estimates of prescribing behavior and patient compliance behavior, estimates of pricing, payor reimbursement and coverage, and sales ramp. As products containing aficamten and omecamtiv mecarbil have not yet been commercialized, the estimates are highly subjective.

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

In 2020, we entered into a royalty purchase agreement, pursuant to which we sold our right to receive certain payments on the net sales of products containing the compound mavacamten. The consideration received was deferred income to be amortized under the units-of-revenue method, as there was no continuing involvement with the underlying R&D. In 2022, we entered into a tripartite agreement with RTW ICAV and MyoKardia, Inc. acknowledging the release and discharge of any further obligations by us or MyoKardia, Inc. in connection to the Mavacamten Royalty and consequently we recognized the deferred revenue as Realization of revenue participation right purchase agreement on the income statement.

As of December 31, 2023, we have a total carrying value of approximately \$380.0 million of liabilities related to revenue participation right purchase agreements.

Research and Development Expenditures

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

Income Taxes

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

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

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

Stock-Based Compensation

We maintain equity incentive plans under which incentive stock options may be granted to employees and nonqualified stock options, restricted stock awards, performance-based stock units and stock appreciation rights may be granted to employees, directors, consultants and advisors. In addition, we maintain an 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 performance-based 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 when the underlying performance conditions are deemed probable.

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.

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

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,		
	2023	2022	2021
Options to purchase common stock	11,780	10,992	9,373
Warrants to purchase common stock	13	13	48
Restricted stock and performance units	1,375	1,260	1,415
Shares issuable related to the ESPP	16	13	8
Shares issuable upon conversion of 2026 Notes	2,003	2,003	16,675
Shares issuable upon conversion of 2027 Notes	10,572	10,572	—
Total shares	25,759	24,853	27,519

Note 3 — Research and Development Arrangements

2021 Ji Xing and RTW Transactions

In December 2021, we entered into the 2021 RTW Transactions as described below, related to omecamtiv mecarbil.

Ji Xing Omecamtiv Mecarbil License and Collaboration Agreement

On December 20, 2021, we entered into the Ji Xing OM License Agreement, pursuant to which we granted to Ji Xing an exclusive license to develop and commercialize omecamtiv mecarbil in China and Taiwan. Under the terms of the Ji Xing OM License Agreement, we are the beneficiary of a nonrefundable \$50.0 million payment obligation from Ji Xing comprised of a \$40.0 million payment as consideration for the rights granted by us to Ji Xing and \$10.0 million attributable to our having submitted to the FDA an NDA for omecamtiv mecarbil. The \$50.0 million payment was received by the Company in January 2022. We may be eligible to receive from Ji Xing additional payments totaling up to \$330.0 million for the achievement of certain commercial milestone events in connection to omecamtiv mecarbil. In addition, Ji Xing will pay us tiered royalties in the mid-teens to the low twenties range on the net sales of pharmaceutical products containing omecamtiv mecarbil 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 omecamtiv mecarbil at its own cost and is required to use diligent efforts to develop and commercialize omecamtiv mecarbil in China and Taiwan. The development of omecamtiv mecarbil will be initially focused on HFrEF, and Ji Xing will have the opportunity to participate in Cytokinetics' global clinical trials of omecamtiv mecarbil. Cytokinetics will supply omecamtiv mecarbil to Ji Xing either as a finished product or as an active pharmaceutical ingredient. Ji Xing may reimburse Cytokinetics for certain costs related to development and supply activities that we perform on their behalf.

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

The Ji Xing OM 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 OM License Agreement for convenience. Each party may terminate the Ji Xing OM 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 OM License Agreement if Ji Xing challenges Cytokinetics' patents or undergoes certain change of control transactions. Rights granted to Ji Xing in relation to omecamtiv mecarbil 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 omecamtiv mecarbil in China and Taiwan. 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 \$54.9 million in 2021. 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 excluded any potential 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.

Common Stock Purchase Agreements

On December 20, 2021, as part of the 2021 RTW Transactions, we entered into common stock purchase agreements with each of the RTW Investors. These common stock purchase agreements provided for the sale and issuance of an aggregate of 511,182 shares of our common stock at a price per share of \$39.125 and an aggregate purchase price of \$20.0 million. The closing occurred on December 20, 2021. The RTW Investors have agreed to certain trading and other restrictions with respect to the shares of common stock they purchased pursuant to these agreements, including a restriction on sales or other transfers of the shares, subject to certain exceptions, for a period of one year from the closing date. The restrictions resulted in a premium paid by the RTW Investors of \$4.9 million, which represents the excess amount paid over the fair value of the shares of common stock purchased. The premium was determined by analyzing the restrictions discount applied to the closing stock price as of December 20, 2021, which is a Level 2 fair value input. The cash received less the calculated premium is the \$15.1 million fair value of the common stock recorded.

2020 Ji Xing and RTW Transactions

On July 14, 2020, we entered in the 2020 RTW Transactions, as described below, with RTW Royalty Holdings and Ji Xing, related to aficamten, our proprietary small molecule cardiac myosin inhibitor product, a novel cardiac myosin inhibitor, and other assets.

Ji Xing Aficamten License and Collaboration Agreement

On July 14, 2020, we entered into the Ji Xing Aficamten License Agreement with Ji Xing, pursuant to which we granted to Ji Xing an exclusive license to develop and commercialize aficamten in China and Taiwan. Under the terms of the Ji Xing Aficamten 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 aficamten in the field of oHCM and/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 the products containing aficamten 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 aficamten at its own cost and is required to use diligent efforts to develop and commercialize aficamten in China and Taiwan. The development of aficamten will be initially focused on HCM, and Ji Xing will have the opportunity to participate in Cytokinetics' global pivotal clinical trials of aficamten. Cytokinetics or a designated supplier will supply aficamten to Ji Xing either as a finished product or as an active pharmaceutical ingredient.

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

The Ji Xing Aficamten 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 Aficamten License Agreement for convenience. Each party may terminate the Ji Xing Aficamten 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 Aficamten License Agreement if Ji Xing challenges Cytokinetics' patents or undergoes certain change of control transactions. Rights granted to Ji Xing in relation to aficamten 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 aficamten in China and Taiwan.

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 of ASC 606 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 recognized a \$2.5 million milestone from Ji Xing in 2023 for the initiation of a phase 3 clinical trial for aficamten in nHCM which was collected in the fourth quarter of 2023.

We recognized a \$5.0 million milestone from Ji Xing during the third quarter of 2021 for initiation of a phase 3 clinical trial for aficamten in oHCM. Although our contractual right to payment had not arisen under the Ji Xing Aficamten License Agreement, we determined recognition of the milestone in 2021 was appropriate based on our expected initiation of a phase 3 clinical trial of aficamten in oHCM and was recorded as a corresponding contract asset in other current assets in our consolidated balance sheet as of December 31, 2021.

Research and development revenue from Ji Xing for 2023 and 2022 was \$1.3 million and \$0.9 million, respectively, related to certain development cost reimbursements. We had no research and development revenue from Ji Xing in 2021.

We had accounts receivable from Ji Xing of \$0.3 million as of December 31, 2023 and \$0.1 million as of December 31, 2022.

Royalty Purchase Agreement

On July 14, 2020, we entered the RTW Royalty Purchase Agreement with RTW Royalty Holdings, pursuant to which we sold our 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. On March 31, 2021, RTW Royalty Holdings assigned its rights and obligations under the RTW Royalty Purchase Agreement to its affiliate, RTW ICAV. We understand that on April 18, 2022, RTW ICAV and MyoKardia, Inc. entered into agreements, which purported to assign all of RTW ICAV's rights, title and interest to the Mavacamten Royalty to MyoKardia, Inc., and on April 25, 2022, we entered into a tripartite agreement with RTW ICAV and MyoKardia, Inc. acknowledging the release and discharge of any further obligations by us or MyoKardia, Inc. in connection to the Mavacamten Royalty.

The allocation of the consideration for the 2020 RTW Transactions resulted in \$87.0 million being allocated to the RTW Royalty Purchase Agreement representing its fair value. The \$87.0 million was initially recorded as deferred revenue. On April 25, 2022, as discussed above, we entered into a tripartite agreement with RTW ICAV and MyoKardia, Inc. acknowledging the release and discharge of any further obligations by us or MyoKardia, Inc. in connection to the Mavacamten Royalty. As a result of the full extinguishment of the Mavacamten Royalty, we recognized revenue of \$87.0 million in 2022.

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

Astellas

Our strategic alliance with Astellas to advance novel therapies for diseases and medical conditions associated with skeletal muscle impairment and weakness commenced in 2013 under the Astellas Agreement.

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 the Astellas FSRA Agreement on April 23, 2020. 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 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 agreed to pay one-third of the out-of-pocket clinical development costs which may be incurred in connection with the Company's Phase 3 clinical trial of reldesemtiv in ALS, up to a maximum contribution by Astellas of \$12 million. Astellas also agreed to non-cash contributions to the Company, which included the transfer of its existing inventories of active pharmaceutical ingredient of reldesemtiv and CK-601. As of December 31, 2023, we have billed and collected from Astellas up to the maximum contribution of \$12.0 million. On March 31, 2023, we announced that we discontinued COURAGE-ALS, our Phase 3 clinical trial of reldesemtiv in patients with ALS, and COURAGE-ALS OLE.

Research and development revenue from Astellas for 2023, 2022, and 2021 was \$2.7 million, \$5.7 million, and \$3.2 million, respectively.

We had no accounts receivable from Astellas as of December 31, 2023 and 2022.

Amgen

On November 23, 2020, we received written notice of termination from Amgen of the Amgen Agreement pertaining to the discovery, development and commercialization of novel small molecule therapeutics, including omecamtiv mecarbil, a novel cardiac myosin activator, and CK-136 (formerly AMG 594), a novel cardiac troponin activator. The termination of the Amgen Agreement was effective May 20, 2021.

We recognized 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 terminated effective May 20, 2021. Research and development revenue from Amgen was \$7.4 million in 2021 and consisted of reimbursement of costs we incurred related to METEORIC-HF. There was no research and development revenue from Amgen in 2023 and 2022.

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.

We primarily apply the market approach for recurring fair value measurements and endeavor 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.

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

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, 2023				
	Fair Value Hierarchy Level	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Money market funds	Level 1	\$ 77,429	\$ —	\$ —	\$ 77,429
U.S. Treasury securities	Level 1	34,625	13	(15)	34,623
U.S. Government agency securities	Level 2	175,301	87	(133)	175,255
Commercial paper	Level 2	252,956	156	(59)	253,053
Corporate obligations	Level 2	92,384	103	(142)	92,345
		<u>\$ 632,695</u>	<u>\$ 359</u>	<u>\$ (349)</u>	<u>\$ 632,705</u>

	December 31, 2022				
	Fair Value Hierarchy Level	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Money market funds	Level 1	\$ 45,887	\$ —	\$ —	\$ 45,887
U.S. Treasury securities	Level 1	172,568	—	(1,102)	171,466
U.S. Treasury securities backed repurchase agreements	Level 2	16,003	—	—	16,003
U.S. Government agency securities	Level 2	129,174	12	(820)	128,366
Foreign government agency securities	Level 2	7,599	—	(69)	7,530
Commercial paper	Level 2	329,359	28	(431)	328,956
Corporate obligations	Level 2	128,594	—	(1,209)	127,385
		<u>\$ 829,184</u>	<u>\$ 40</u>	<u>\$ (3,631)</u>	<u>\$ 825,593</u>

No credit losses on debt securities were recognized in 2023 or 2022. 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.

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

Note 5 — Balance Sheet Components

Our property and equipment consisted of (in thousands):

	December 31,	
	2023	2022
Property and equipment, net:		
Laboratory equipment	\$ 18,839	\$ 18,490
Computer equipment and software	3,263	3,900
Office equipment, furniture and fixtures	6,061	6,056
Leasehold improvements	66,874	65,912
Construction in progress	220	741
Right-of-use assets, finance lease	1,839	2,448
Total property and equipment	97,096	97,547
Less: Accumulated depreciation	(28,348)	(17,094)
	<u>\$ 68,748</u>	<u>\$ 80,453</u>

Depreciation expense was \$11.9 million, \$5.8 million, and \$2.3 million for 2023, 2022, and 2021, respectively.

Our accrued liabilities were as follows (in thousands):

	December 31,	
	2023	2022
Accrued liabilities:		
Clinical and preclinical costs	\$ 5,880	\$ 16,105
Compensation related	29,255	21,767
Other accrued expenses	7,506	6,224
Total accrued liabilities	<u>\$ 42,641</u>	<u>\$ 44,096</u>

We sponsor a 401(k) defined contribution plan covering all employees and contributed \$2.5 million, \$1.8 million, and \$1.1 million to this plan in 2023, 2022, and 2021, respectively.

Note 6 — Agreements with Royalty Pharma

On January 7, 2022, we announced that we had entered into the 2022 RPI Transactions with affiliates of Royalty Pharma International plc.

The RP Loan Agreement and the RP Aficamten RPA described below, are determined to be debt instruments subsequently measured at amortized cost and were entered into with parties that were at the time of our entry into the 2022 RPI Transactions affiliated and in contemplation of one another. We used the relative fair value method and made separate estimates of the fair value of each freestanding financial instrument and then allocated the proceeds in proportion to those fair value amounts. Arrangement consideration for the RP Loan Agreement and the RP Aficamten RPA totaled \$150 million, consisting of the two \$50 million upfront payments for the signing of the RP Loan Agreement and the RP Aficamten RPA and milestone of \$50 million for initiation of the first pivotal trial in oHCM for aficamten that was deemed probable at the signing of the agreements.

The initial consideration was allocated as follows (in thousands):

	Fair Value	Proceeds	Allocation
Units of Accounting:			
Revenue Participation Right Purchase Agreement	\$ 69,498	\$ 100,000	\$ 89,571
Development Funding Loan Agreement	46,887	50,000	60,429
Total consideration	<u>\$ 116,385</u>	<u>\$ 150,000</u>	<u>\$ 150,000</u>

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

2022 RP Loan Agreement

Under the RP Loan Agreement, we were initially entitled to receive up to \$300.0 million in term loans, \$50.0 million of which was disbursed to us on closing and the remaining \$250.0 million scheduled to have been available to us upon our satisfaction of customary disbursement conditions and certain development conditions by specific deadlines, as follows:

- \$50.0 million of tranche 2 term loans during the one year period following the receipt on or prior to March 31, 2023 of marketing approval from FDA of omecamtiv mecarbil;
- \$25.0 million of tranche 3 term loans during the one year period following the commercial availability of a diagnostic test measuring levels of omecamtiv mecarbil to support the final FDA label language applicable to such drug, subject to such commercial availability and the conditions to the tranche 2 term loans having occurred on or prior to March 31, 2023;
- \$75.0 million of tranche 4 term loans during the one year period following the receipt on or prior to September 30, 2024 of positive results from SEQUOIA-HCM, the Phase 3 trial for aficamten; and
- \$100.0 million of tranche 5 term loans during the one year period following the acceptance by the FDA on or prior to March 31, 2025 of an NDA for aficamten, subject to the conditions to the tranche 4 term loans having occurred on or prior to September 30, 2024.

As a result of our receipt of a CRL on February 28, 2023, in connection to our NDA for omecamtiv mecarbil, we have not satisfied the conditions to the availability of the tranche 2 and tranche 3 loans under the RP Loan Agreement.

In December 2023, we announced positive topline results from SEQUOIA-HCM, the Phase 3 trial for aficamten. This entitled us to receive \$75.0 million under tranche 4 during the one year period following the receipt of the positive results and requires us to complete a minimum mandatory draw of at least \$50.0 million of the \$75.0 million available.

The remaining \$100.0 million under tranche 5 remains available for disbursement to us, subject to satisfaction of the conditions described above.

Each term loan under the RP Loan Agreement matures on the 10 year anniversary of the funding date for such term loan and is repayable in quarterly installments of principal, interest and fees commencing on the last business day of the seventh full calendar quarter following the calendar quarter of the applicable funding date for such term loan, with the aggregate amount payable in respect of each term loan (including interest and other applicable fees) equal to 190% of the principal amount of the term loan for the tranche 1, tranche 4 and tranche 5 term loans and 200% of the principal amount of the term loan for tranche 2 and tranche 3 term loans (such amount with respect to each term loan, "Final Payment Amount"). We accounted for amounts initially drawn under the RP Loan Agreement using the effective interest method which resulted in an effective interest rate of 7.65% over the ten-year term. As of the date of the prepayment or maturity of the term loan (or the date such prepayment or repayment is required to be paid), we will be required to pay an additional amount equal to \$34.6 million accreted over the term of the loan. We have made our first payment in the fourth quarter of 2023.

We may prepay the term loans in full (but not in part) at any time at our option by paying an amount equal to the unpaid portion of Final Payment Amount for the outstanding term loans under the RP Loan Agreement; provided that if the conditions for either the tranche 4 term loans or the tranche 5 term loans have been met, we must have borrowed at least \$50 million principal amount of the tranche 4 or 5 term loans. In addition, the term loans under the RP Loan Agreement are repayable in full at the option of either us or the lender in an amount equal to the unpaid portion of Final Payment Amount for the outstanding term loans upon a change of control of Cytokinetics.

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

Future minimum payments under the existing borrowing under RP Loan Agreement are (in thousands):

Years ending December 31:

2024	\$	10,080
2025		11,520
2026		11,520
2027		11,520
2028		11,520
Thereafter		37,440
Future minimum payments		93,600
Less: Unamortized interest and loan costs		(25,136)
Term Loan, net	\$	68,464

As of December 31, 2023, the estimated fair value of our RP Loan Agreement was \$59.9 million. The fair value was estimated based on Level 3 inputs.

Concurrent with our entry into the RP Loan Agreement discussed above, we terminated the Term Loan Agreement with Silicon Valley Bank and Oxford Finance LLC and repaid all amounts outstanding thereunder as further described in Note 7.

2022 RP Aficamten Royalty Purchase Agreement

In addition, on January 7, 2022, we entered into the RP Aficamten RPA with RPI ICAV, pursuant to which RPI ICAV purchased rights to certain revenue streams from net sales of pharmaceutical products containing aficamten by us, our affiliates and our licensees in exchange for up to \$150.0 million in consideration, \$50.0 million of which was paid on the closing date, \$50.0 million of which was paid to us in March 2022 following the initiation of the first pivotal trial in oHCM for aficamten, and \$50.0 million of which was paid to us in September 2023 following the initiation of the first pivotal clinical trial in nHCM for aficamten. The RP Aficamten RPA also provides that the parties will negotiate terms for additional funding if we achieve proof of concept results in certain other indications for aficamten, with a reduction in the applicable royalty if we and RPI ICAV fail to agree on such terms in certain circumstances.

Pursuant to the RP Aficamten RPA, RPI ICAV purchased the right to receive a percentage of net sales equal to 4.5% for annual worldwide net sales of pharmaceutical products containing aficamten up to \$1 billion and 3.5% for annual worldwide net sales of pharmaceutical products containing aficamten in excess of \$1 billion, subject to reduction in certain circumstances. Our liability to RPI ICAV is referred to as the “RP Aficamten Liability”.

We account for the RP Aficamten Liability as a liability primarily because we have significant continuing involvement in generating the related revenue stream from which the liability will be repaid. If and when aficamten is commercialized and royalties become due, we will recognize the portion of royalties paid to RPI ICAV as a decrease to the RP Aficamten Liability and a corresponding reduction in cash.

The carrying amount of the RP Aficamten Liability is based on our estimate of the future royalties to be paid to RPI ICAV over the life of the arrangement as discounted using an imputed rate of interest. The imputed rate of interest on the carrying value of the RP Aficamten Liability was approximately 24.8% as of December 31, 2023 and 22.4% as of December 31, 2022.

In 2023, we updated our analyses of the RP Aficamten RPA to reflect our assumptions resulting from ongoing global market research and to reflect other adjustments in connection with our anticipated commercialization, including the additional consideration of \$50.0 million which was paid to us in September 2023 following the initiation of the first pivotal clinical trial in nHCM for aficamten. Our estimates regarding the amount of future royalty payments under the RP Aficamten RPA changed from the fourth quarter of 2022 due to changes in management’s estimates of unobservable inputs related to market conditions and timing to include projections of future royalty payments. The resulting probability-adjusted sales forecast for aficamten has increased year over year mainly due to the receipt of positive topline results from SEQUOIA-HCM, the Phase 3 trial for aficamten, in December 2023.

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

The change in estimates are accounted for on a prospective basis in our liability calculation and resulted in changes in our imputed interest rate and non-cash interest expense from 22.4% and \$5.2 million in the fourth quarter of 2022, 22.4% and \$5.4 million in the first quarter of 2023, 19.0% and \$4.9 million in the second quarter of 2023, 18.0% and \$5.4 million in the third quarter of 2023, to 24.8% and \$9.8 million in the fourth quarter of 2023. The non-cash interest expense was \$25.5 million and \$15.5 million in 2023 and 2022, respectively. In 2023, the change in estimate increased our non-cash interest expense and net loss by \$2.0 million. The change in accounting estimate increased the net loss per share by \$0.02 in 2023.

2017 RP Omecamtiv Mecarbil Royalty Purchase Agreement

In February 2017, we entered into the RP OM RPA pursuant to which we sold a portion of our right to receive royalties from Amgen on future net sales of omecamtiv mecarbil to RPFT for a one-time payment of \$90 million, which is non-refundable even if omecamtiv mecarbil is never commercialized. Concurrently, we entered into a common stock purchase agreement with RPFT through which RPFT purchased 875,656 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 our liability to RPFT related to sale of future royalties under the RP OM RPA (the "RP OM Liability") and the common stock sold to RPFT, which resulted in the RP OM Liability being initially recognized at \$92.3 million. The RP OM RPA provides for the sale of a royalty to RPFT of 4.5% on worldwide net sales of omecamtiv mecarbil, subject to a potential increase of up to an additional 1% under certain circumstances. As a result of our receipt of a CRL on February 28, 2023 in connection to our NDA for omecamtiv mecarbil, pursuant to the terms of the RP OM RPA, the applicable royalty rate will increase to a maximum of 5.5% if omecamtiv approval obtains FDA approval at any time after June 30, 2023.

As a result of the termination of the Amgen Agreement and pursuant to our obligations under the RP OM RPA, we and RPFT amended the RP OM RPA on January 7, 2022 to preserve RPFT's rights under the RP OM RPA by providing for direct payments by us to RPFT of up to 5.5% of our and our affiliates and licensees worldwide net sales of omecamtiv mecarbil. The RP OM RPA, as amended, had no impact on the original accounting for the \$92.3 million associated with the RP OM Liability established in February 2017.

We account for the RP OM Liability as a liability primarily because we have significant continuing involvement in generating the related revenue stream from which the liability will be repaid. If and when omecamtiv mecarbil is commercialized and royalties become due, we will recognize the portion of royalties paid to RPFT as a decrease to the RP OM Liability and a corresponding reduction in cash.

The carrying amount of the RP OM Liability is based on our estimate of the future royalties to be paid to RPFT 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 carrying value of the RP OM Liability was approximately 0.1% as of December 31, 2023 and 8.5% as of December 31, 2022.

In 2023, we updated our analyses of the RP OM RPA to reflect our current assumptions resulting from ongoing global market research and to reflect other adjustments in connection with our anticipated commercialization, including the result of our receipt of a CRL in connection to our NDA for omecamtiv mecarbil. As a consequence of our receipt of the CRL from FDA, the royalty rate under the RP OM RPA will increase to no more than 5.5%. The resulting probability-adjusted sales forecast for omecamtiv mecarbil has decreased year over year because commercialization and sales of omecamtiv mecarbil will be delayed.

Changes in estimates are accounted for on a prospective basis in our liability calculation and resulted in changes in our imputed interest rate and non-cash interest expense from 8.5% and \$4.0 million in the fourth quarter of 2022, 1.9% and \$0.9 million in the first quarter of 2023, 2.9% and \$1.4 million in the second and third quarter of 2023, and to 0.1% and \$0.1 million in the fourth quarter of 2023, respectively. The non-cash interest expense was \$3.9 million, \$16.2 million, and \$12.9 million in 2023, 2022, and 2021, respectively. In 2023, the change in estimate decreased our non-cash interest expense and net loss by \$12.8 million. The change in accounting estimate reduced the net loss per share by \$0.13 in 2023.

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

Accounting for the Royalty Pharma Royalty Purchase Agreements

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 RP OM Liability and the RP Aficamten Liability and the effective interest rate.

There are a number of factors that could materially affect the amount and timing of royalty payments, a number of which are not within our control. The RP OM Liability and the RP Aficamten Liability are recognized using significant unobservable inputs. The estimates of future royalties requires the use of several assumptions such as: the probability of clinical success, the probability of regulatory approval, the estimated date of a product launch, estimates of eligible patient populations, estimates of prescribing behavior and patient compliance behavior, estimates of pricing, payor reimbursement and coverage, and sales ramp. A significant change in unobservable inputs could result in a material increase or decrease to the effective interest rate of the RP OM Liability and the RP Aficamten Liability.

We recorded \$50.0 million of additional consideration associated with the 2022 RP Aficamten Royalty Purchase Agreement upon receipt of the cash in the third quarter of 2023.

We review our assumptions on a regular basis and our estimates may change in the future as we refine and reassess our assumptions.

Changes to the RP Aficamten Liability and the RP OM Liability are as follows (in thousands):

	RP Aficamten Liability		RP OM Liability		
	2023	2022	2023	2022	2021
Beginning balance, January 1	\$ 105,117	\$ —	\$ 195,384	\$ 179,072	\$ 166,068
Initial carrying value	—	89,571	—	—	—
Additional consideration	50,000	—	—	—	—
Interest accretion	25,474	15,546	3,888	16,196	12,892
Amortization of issuance costs	—	—	112	116	112
Ending balance, December 31	<u>\$ 180,591</u>	<u>\$ 105,117</u>	<u>\$ 199,384</u>	<u>\$ 195,384</u>	<u>\$ 179,072</u>

Note 7 — Debt

Silicon Valley Bank and Oxford Finance Term Loans

Prior to January 7, 2022, we maintained \$45.0 million aggregate principal amount of the Term Loan Agreement with Silicon Valley Bank and Oxford Finance LLC.

The Term Loan Agreement was terminated, and all amounts thereunder repaid in connection to our entry into that certain RP Loan Agreement, between us and RPDF, as further described above.

As a result of the termination of the Term Loan Agreement and the repayment to the Lenders, in 2022, we recorded \$2.7 million in loss on debt extinguishment in the consolidated statements of operations and comprehensive loss, consisting of the premium on debt repayments and the write-off of the remaining term loan fees and debt issuance costs.

Interest expense for the Term Loan Agreement was immaterial for 2022 because it represented approximately one week of interest before extinguishment. Interest expense for the Term Loan Agreement was \$4.8 million for 2021.

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Convertible Notes

On November 13, 2019, we issued \$138.0 million aggregate principal amount of 2026 Notes. On July 6, 2022, we issued \$540.0 million aggregate principal amount of 2027 Notes and used approximately \$140.3 million of the net proceeds from the offering of 2027 Notes and issued 8,071,343 shares of common stock to repurchase approximately \$116.9 million aggregate principal amount of the 2026 Notes pursuant to privately negotiated exchange agreements entered into with certain holders of the 2026 Notes concurrently with the pricing of the offering of the 2027 Notes. As a result of the partial repurchase of the 2026 Notes, the Company recorded an inducement loss of \$22.2 million, consisting of the difference between the consideration to the holders pursuant to the exchange agreements and the if-converted value of the 2026 Notes under the original terms. As of December 31, 2023, there remain \$21.1 million aggregate principal amount of 2026 Notes outstanding.

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 we entered into with U.S. Bank National Association, as trustee. The 2026 Notes will mature on November 15, 2026, unless earlier repurchased or redeemed by us or converted at the option of the holders. We may redeem the 2026 Notes prior to the maturity date but we are 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), we 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 2026 Notes are convertible at December 31, 2023 at the option of the holder.

The 2026 Notes will be redeemable, in whole or in part, at our 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 our 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 we may send the related redemption notice; and (2) the trading day immediately before the date we may send such notice. If a “fundamental change” (as defined in the indenture agreement, dated November 13, 2019 between us and U.S. Bank National Association, as trustee, as supplemented by the first supplemental indenture dated as of November 13, 2019 between us and such trustee) occurs, then, subject to certain exceptions, holders may require us 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.

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

	Years Ended December 31,		
	2023	2022	2021
Contractual interest expense	\$ 844	\$ 3,265	\$ 5,520
Accretion of debt discount	—	—	5,907
Amortization of debt issuance costs	108	355	59
Total interest expense recognized	\$ 952	\$ 3,620	\$ 11,486

The effective interest rate of the 2026 Notes was 4.6% as of December 31, 2023 and 2022 and 12.5% as of December 31, 2021. As of December 31, 2023, the unamortized debt issuance cost for the 2026 Notes was \$0.3 million and will be amortized over approximately 2.9 years.

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

The 2027 Notes (\$540.0 million of aggregate principal) are our senior, unsecured obligations and are (i) senior in right of payment to our future indebtedness that is expressly subordinated to the 2027 Notes in right of payment; (ii) equal in right of payment with all of our indebtedness that is not so subordinated (including the 2026 Notes); (iii) effectively subordinated to our existing and future secured indebtedness, to the extent of the value of the collateral securing that indebtedness; and (iv) structurally subordinated to all existing and future indebtedness and other liabilities, including trade payables, and (to the extent we are not a holder thereof) preferred equity, if any, of our subsidiaries. The net proceeds of the 2027 Notes were approximately \$523.6 million after deducting issuance costs related to the 2027 Notes. The 2027 Notes bear interest at a rate of 3.5% per year, payable semiannually in arrears on January 1 and July 1 of each year, beginning on January 1, 2023. The 2027 Notes will mature on July 1, 2027, unless earlier converted, redeemed or repurchased.

The 2027 Notes are convertible into cash, shares of our common stock or a combination of cash and shares of our common stock, at our election, based on the applicable conversion rate(s). The initial conversion rate for the 2027 Notes is 19.5783 shares of our common stock per \$1,000 principal amount of such Notes, which is equivalent to an initial conversion price of approximately \$51.08 per share. Holders of the 2027 Notes may convert all or any portion of their convertible notes at their option only in the following circumstances: (i) during any calendar quarter (and only during such calendar quarter) commencing after the calendar quarter ending on September 30, 2022, if the last reported sale price per share of our common stock, \$0.001 par value per share, exceeds 130% of the conversion price for each of at least 20 trading days, whether or not consecutive, during the 30 consecutive trading days ending on, and including, the last trading day of the immediately preceding calendar quarter; (ii) during the five 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 2027 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 our common stock on such trading day and the conversion rate on such trading day; (iii) upon the occurrence of certain corporate events or distributions on our common stock, as described in the 2027 Indenture; (iv) if we call such 2027 Notes for redemption; and (v) at any time from, and including, March 1, 2027 until the close of business on the scheduled trading day immediately before the maturity date.

We may not redeem the 2027 Notes at our option at any time before July 7, 2025. The 2027 Notes will be redeemable, in whole or in part (subject to the “Partial Redemption Limitation” (as defined in the 2027 Indenture)), at our option at any time, and from time to time, on or after July 7, 2025 and, in the case of a partial redemption, on or before the 60th scheduled trading day immediately before the maturity date, at a cash redemption price equal to the principal amount of the 2027 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 our common stock exceeds 130% of the conversion price on (i) 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 we may send the related redemption notice; and (ii) the trading day immediately before the date we may send such notice. In addition, calling any of the 2027 Notes for redemption will constitute a Make-Whole Fundamental Change with respect to that convertible note, in which case the conversion rate applicable to the conversion of that Note will be increased in certain circumstances if it is converted after it is called for redemption. The conversion rate for the 2027 Notes shall not exceed 25.4517 shares per \$1,000 principal amount of such Notes, subject to certain customary anti-dilution adjustments (as defined in the 2027 indenture). Pursuant to the Partial Redemption Limitation, we may not elect to redeem less than all of the outstanding 2027 Notes unless at least \$75.0 million aggregate principal amount of 2027 Notes are outstanding and not subject to redemption as of the time we may send the related redemption notice.

If a “Fundamental Change” (as defined in the 2027 Indenture) occurs, then, subject to a limited exception for certain cash mergers, noteholders may require us to repurchase their 2027 Notes at a cash repurchase price equal to the principal amount of the 2027 Notes to be repurchased, plus accrued and unpaid interest, if any, to, but excluding, the fundamental change repurchase date. The definition of Fundamental Change includes certain business combination transactions involving us and certain de-listing events with respect to our common stock.

The following table presents the total amount of interest cost recognized relating to the 2027 Notes (in thousands):

	2023	2022
Contractual interest expense	\$ 18,900	\$ 9,188
Amortization of debt issuance costs	3,074	1,542
Total interest expense recognized	<u>\$ 21,974</u>	<u>\$ 10,730</u>

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

The effective interest rate of the 2027 Notes was 4.2% as of December 31, 2023 and 2022. As of December 31, 2023, the unamortized debt issuance cost for the 2027 Notes was \$11.8 million and will be amortized over approximately 3.6 years. In 2023, the conditions allowing holders of the Notes to convert were not met. As a result, the 2027 Notes are not convertible at December 31, 2023.

Future minimum payments under the 2027 Notes and 2026 Notes are (in thousands):

Years ending December 31:	2027 Notes	2026 Notes	Total
2024	\$ 18,900	\$ 845	\$ 19,745
2025	18,900	845	19,745
2026	18,900	21,978	40,878
2027	558,900	—	558,900
Future minimum payments	615,600	23,668	639,268
Less: Interest	(75,600)	(2,536)	(78,136)
Convertible notes, principal amount	540,000	21,132	561,132
Less: Debt issuance costs on the convertible notes	(11,799)	(344)	(12,143)
Net carrying amount of the convertible notes	<u>\$ 528,201</u>	<u>\$ 20,788</u>	<u>\$ 548,989</u>

As of December 31, 2023, the estimated fair value of the 2027 Notes and 2026 Notes was \$990.4 million and \$168.4 million, respectively, and was based upon observable, Level 2 inputs, including pricing information from recent trades of the convertible notes.

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. On October 24, 2022, we entered into a termination agreement in connection to the capped call transactions and thereby released the capped call counterparties of any further obligations in relation to the capped call transactions. As a result of the termination agreement and unwinding of the capped call transactions, we received gross proceeds of \$26.4 million in cash.

Note 8 — Stockholders' Equity

Equity Incentive Plan

Our 2004 Plan provides for us to grant incentive stock options, non-statutory 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.

In May 2022, our stockholders approved an amendment to the 2004 Plan to increase the number of authorized shares reserved for issuance under the 2004 Plan by an additional 6.0 million shares. In May 2022 and February 2023, our 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 an additional 1.6 million shares and 1.0 million shares, respectively, for inducement grants to new employees. As of December 31, 2023, the total authorized shares under the 2004 Plan available for grant was 7.6 million.

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

Our annual grant of stock-based compensation takes place during the first quarter of each year. Stock option activity in 2023, 2022, and 2021 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, 2020	8,501,949	\$ 10.02		
Granted	2,513,350	22.43		
Exercised	(1,346,194)	9.01		
Forfeited	(296,146)	14.56		
Balance at December 31, 2021	9,372,959	\$ 13.35		
Granted	3,424,150	39.79		
Exercised	(1,389,031)	10.13		
Forfeited	(415,675)	28.94		
Balance at December 31, 2022	10,992,403	\$ 22.13		
Granted	2,447,225	38.59		
Exercised	(1,200,895)	12.13		
Forfeited	(458,503)	35.01		
Balance at December 31, 2023	11,780,230	\$ 26.07	6.8	\$ 676.4
Exercisable at December 31, 2023	7,279,310	\$ 19.29	5.7	\$ 467.3

We have elected to account for forfeitures as they occur. 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 \$33.8 million for 2023, \$46.3 million for 2022, and \$29.3 million for 2021. The intrinsic value of stock options outstanding at December 31, 2023 was \$676.4 million.

RSU, including PSU, activity in 2023, 2022, and 2021 was as follows:

	Number of Restricted Stock Units	Weighted Average Award Date Fair Value per Share
Balance at December 31, 2020	1,116,642	\$ 11.88
Granted	1,093,450	21.69
Exercised	(606,240)	11.13
Forfeited	(189,025)	21.32
Balance at December 31, 2021	1,414,827	\$ 18.52
Granted	780,519	37.69
Exercised	(707,772)	16.72
Forfeited	(273,310)	26.65
Balance at December 31, 2022	1,214,264	\$ 30.07
Granted	965,863	39.09
Exercised	(721,215)	27.40
Forfeited	(84,290)	35.46
Balance at December 31, 2023	1,374,622	\$ 37.47

RSUs generally vest annually over two to three years. For 2023, 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 \$28.6 million.

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

Performance Stock Units

In May 2021, the Compensation Committee granted a total of 375,000 PSUs to certain employees with a weighted average grant date fair value of \$25.32 per unit. The fair value of the PSUs was determined on the grant date based on the fair value of the Company's common stock at such time. The PSUs consist of two equal tranches with 50% of each tranche vesting upon achieving certain performance criteria and 50% vesting at the one-year anniversary of such achievement provided the recipient has been continuously employed by the Company. The first tranche vests upon certification by the Compensation Committee that the NDA for omecantiv mecarbil has been filed and accepted by the FDA by December 31, 2021 or June 30, 2022 and the second tranche vests upon certification by the Compensation Committee that the FDA approval of the NDA is with an approved label that is consistent with the expectations underlying the Company's commercial launch plans for omecantiv mecarbil in effect immediately prior to such approval by June 30, 2022 or December 31, 2022.

In 2022, the performance target for the first tranche of PSUs was met. As a result, the Company recognized expense of \$0.7 million in 2022 for the first tranche of PSUs. The performance target for the second tranche of PSUs was not met, and therefore, such second tranche of PSUs consisting of 182,500 PSUs were deemed forfeited as of December 31, 2022. No expense was recognized for the second tranche.

Employee Stock Purchase Plan

Under our 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 136,065 shares at an average price of \$30.43 per share during 2023, 98,153 shares at an average price of \$32.89 per share in 2022, and 108,780 shares at an average price of \$16.33 per share in 2021 pursuant to the ESPP. At December 31, 2023, we have 103,822 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, 2023		Year Ended December 31, 2022		Year Ended December 31, 2021	
	Options	ESPP	Options	ESPP	Options	ESPP
Risk-free interest rate	3.57% to 4.6%	5.33% to 5.44%	1.41% to 4.01%	1.63% to 4.65%	0.58% to 1.28%	0.05%
Volatility	67%	49% to 50%	66% to 67%	64% to 65%	66% to 67%	66% to 67%
Expected term in years	6.3	0.5	6.3 to 6.4	0.5	6.4 to 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 our stock trading history and our own historical exercise 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 2023, 2022, and 2021 was as follows (in thousands):

	Years Ended December 31,		
	2023	2022	2021
Research and development	\$ 32,134	\$ 19,100	\$ 10,463
General and administrative	39,931	28,753	16,369
	<u>\$ 72,065</u>	<u>\$ 47,853</u>	<u>\$ 26,832</u>

As of December 31, 2023, we expect to recognize \$102.2 million of unrecognized compensation cost related to unvested stock options over a weighted-average period of 2.5 years, \$29.2 million of unrecognized compensation cost related to unvested restricted stock over a weighted-average period of 1.6 years.

Warrants

In May 2022, Silicon Valley Bank exercised 16,901 warrants issued pursuant to the Term Loan Agreement with a strike price of \$7.10 per share and elected the cashless settlement method. In June 2022, Silicon Valley Bank exercised additional 9,226 warrants and 8,638 warrants with a strike price of \$9.76 per share and \$10.42 per share, respectively. Accordingly, in 2022, we issued to Silicon Valley Bank a total of 28,306 shares of our common stock.

As of December 31, 2023 and 2022, we had the following warrants outstanding to purchase shares of our common stock:

Issuance Date	Expiration Date	Exercise Price	Warrants Outstanding at December 31, 2022	Warrants Outstanding at December 31, 2023
January 2020	January 2030	\$ 10.42	12,957	12,957

The remaining 12,957 warrants outstanding at December 31, 2023 were exercised in January 2024.

Controlled Equity Offering Sales Agreement with Cantor Fitzgerald & Co.

On March 1, 2023, we entered into the Amended ATM Facility, with Cantor, under which we may offer and sell, from time to time at our sole discretion, shares of the Common Stock having an aggregate offering price of up to \$300.0 million through Cantor, as sales agent. The Amended ATM Facility amends, restates and supersedes the Controlled Equity Offering Sales Agreement dated as of March 6, 2019 between the Company and Cantor.

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

In 2023, we issued 5,016,170 shares of our common stock for net proceeds of \$164.2 million under the Amended ATM Facility.

Note 9 — Commitments and Contingencies

Operating Leases

In July 2019, we entered into the Oyster Point Lease of office and laboratory space at a facility located in South San Francisco, California, and we entered into amendments to the Oyster Point Lease in 2020, 2021, 2022, and 2023. The Oyster Point Lease commenced on March 31, 2021 and has an expiration date of October 31, 2033.

In January 2022, we entered into a series of lease agreements with the sub-landlord and landlord and leased an office space at a facility located in Radnor, Pennsylvania (the "Radnor Lease"). The Radnor Lease commenced on September 1, 2022, when the leasehold improvements were substantially completed, and we gained control over the use of the underlying assets. The Radnor Lease has an expiration date of July 31, 2027 with one five-year option to extend the lease.

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

The weighted-average remaining lease term of the operating leases was 9.7 years, 10.7 years, and 11.7 years as of December 31, 2023, 2022, and 2021, respectively. The weighted-average discount rate used to determine the related operating lease liabilities was 8.7% as of December 31, 2023 and 2022, and 10.0% as of December 31, 2021.

Cash paid for operating leases for the years ended December 31, 2023, 2022, and 2021 was \$17.8 million, \$24.1 million, and \$6.1 million, respectively, and was included in net cash used in operating activities in our consolidated statements of cash flows.

Finance Leases

During the third quarter of 2021, we entered into a master lease agreement for laboratory equipment leases that commenced in the fourth quarter of 2021. The leases have an initial term of 3 years, commenced through the second quarter of 2022 and expire in 2025. The master lease agreement provides a purchase option with a bargain purchase price, which we expect to exercise at the end of the term. The Company classified the leases as finance leases.

Finance leases are accounted for on the consolidated balance sheets with right-of-use assets and lease liabilities recognized in property and equipment, other current liabilities, and other non-current liabilities, respectively. The finance lease cost is recognized as a combination of the amortization expense for the right-of-use assets calculated on a straight-line basis over the five-year estimated useful life for laboratory equipment and interest expense for the outstanding lease liabilities using the determined discount rates. As of December 31, 2023, we have recognized finance lease right-of-use assets of \$1.8 million, short-term finance lease liabilities of \$1.0 million, and long-term finance lease liabilities of \$0.2 million.

As of December 31, 2023, 2022, and 2021, the weighted average remaining lease term for the finance leases is 3.0 years, 4.0 years, and 4.9 years, respectively. The weighted average discount rate used to determine the finance lease liabilities is 9.5% as of December 31, 2023, 2022, and 2021.

The cash paid for finance lease for the years ended December 31, 2023 and 2022 was \$0.9 million and was included in financing activities in our consolidated statement of cash flows. No cash was paid for finance lease in 2021.

Future minimum lease payments under non-cancellable leases as of December 31, 2023 is as follows (in thousands):

Years ending December 31:	Operating Leases	Finance Leases
2024	\$ 18,738	\$ 990
2025	19,563	204
2026	20,180	-
2027	20,514	—
2028	20,738	—
Thereafter	109,981	—
Total future minimum lease payments	209,714	1,194
Less: Imputed interest	(71,396)	(51)
Total lease liability	\$ 138,318	\$ 1,143

Rent expense for operating and finance leases was \$22.1 million, \$21.6 million, and \$23.1 million for 2023, 2022, and 2021, respectively.

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

Note 10 — Income Taxes

We did not record an income tax provision in 2023, 2022, and 2021 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,		
	2023	2022	2021
Tax at federal statutory tax rate	21 %	21 %	21 %
State tax, net of federal benefits	1 %	1 %	0 %
Change in state effected rates	0 %	0 %	(1) %
Tax credits, net	4 %	4 %	3 %
Change in valuation allowance	(24) %	(26) %	(24) %
Stock-based compensation	1 %	2 %	2 %
Other	(3) %	(2) %	(1) %
Total	0 %	0 %	0 %

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,	
	2023	2022
Deferred tax assets:		
Net operating loss carryforwards	\$ 231,915	\$ 202,459
Tax credits	119,815	98,292
Liability related to sale of future royalties	85,501	68,366
Reserves and accruals	35,466	23,950
Capitalized R&D	95,437	48,047
Long-term lease liability	28,634	28,901
Total noncurrent deferred tax assets	596,768	470,015
Deferred tax liabilities:		
Depreciation and amortization	(6,842)	(7,909)
Operating lease right-of-use assets	(17,392)	(18,192)
Unrealized Loss	(6)	—
Total noncurrent deferred tax liabilities	(24,240)	(26,101)
Less: Valuation allowance	(572,528)	(443,914)
Net deferred tax assets	\$ —	\$ —

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, 2023 and 2022. The valuation allowance increased by \$128.6 million in 2023 and increased by \$116.5 million in 2022.

At December 31, 2023 federal NOL carryforwards were \$955.7 million, apportioned state NOL carryforwards before federal benefits were \$423.7 million, and foreign NOL carryforwards were \$0.8 million. If not utilized, federal and state net operating loss carryforwards incurred prior to 2018 will begin to expire in various amounts beginning 2024 and 2028, respectively, and the foreign net operating loss carryforwards will begin to expire in 2030.

At December 31, 2023, tax credits of \$126.3 million and \$22.8 million for federal and California 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 2024. California based credit carryforwards do not expire.

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

In general, under 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,		
	2023	2022	2021
Balance at the beginning of the year	\$ 18,355	\$ 11,295	\$ 10,522
Increase related to prior year tax positions	—	4,438	—
Decrease related to prior year tax positions	(97)	(1,804)	(29)
Increase related to current year tax positions	6,974	4,426	802
Balance at the end of the year	<u>\$ 25,232</u>	<u>\$ 18,355</u>	<u>\$ 11,295</u>

We are subject to federal and various state & local and foreign income tax examinations for all fiscal years with unutilized NOLs and tax credit carryforwards. Included in the balance of unrecognized tax benefits as of December 31, 2023, 2022, and 2021 are \$24.5 million, \$17.7 million, and \$10.3 million of tax benefits, respectively, that, if recognized, would result in adjustments to other tax accounts, primarily deferred taxes.

The Inflation Reduction Act of 2022, or IRA, was signed into law on August 16, 2022. The bill was meant to address the high inflation rate in the United States through various climate, energy, healthcare, and other incentives. These incentives are meant to be paid for by the tax provisions included in the IRA, such as a new 15 percent corporate minimum tax, a 1 percent new excise tax on stock buybacks, additional IRS funding to improve taxpayer compliance, and others. The IRA provisions are effective for tax years beginning after December 31, 2022. At this time, none of the IRA tax provisions are expected to have a material impact to our consolidated tax provision for the year ending December 31, 2023. The Company will continue to closely monitor any effects from future legislation.

In October 2021, the Organization for Economic Co-operation and Development (“OECD”)/G20 finalized the significant components of a two-pillar global tax reform plan, which has now been agreed to by the majority of OECD members. Pillar Two requires multinational enterprises with annual global revenue exceeding €750 million to pay a global minimum tax of 15%. The Company does not currently expect to meet the €750 million revenue threshold. The Company will continue to evaluate the potential impact on future periods of the Pillar Two framework and the implementation of the Pillar Two rules in the jurisdictions in which it operates.

Note 11 — Subsequent Events

During the period January 1, 2024 through and inclusive of February 27, 2024, we sold 1,237,460 shares of our common stock for net proceeds of \$93.6 million under the Amended ATM Facility.

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, and interim principal 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 interim 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, 2023. Based on such evaluation, our principal executive officer and interim principal financial officer has concluded that, as of December 31, 2023, 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, and interim principal financial officer and Chief Accounting Officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting as of December 31, 2023 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, 2023.

Our independent registered public accounting firm, Ernst & Young LLP, has audited the financial statements included in this Annual Report and has issued an attestation 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 changes in our internal control 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, 2023 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

During the fourth quarter ended December 31, 2023, none of our directors or officers (as defined in Rule 16a-1(f) under the Exchange Act) adopted or terminated a "Rule 10b5-1 trading arrangement" or "non-Rule 10b5-1 trading arrangement," as those terms are defined in Item 408 of Regulation S-K.

Interim Principal Financial Officer

As previously disclosed, effective February 23, 2024 (the "Resignation Date"), Ching W. Jaw resigned from the office of Senior Vice President & Chief Financial Officer and from his employment with the Company. Effective as of the Resignation Date, Robert I. Blum, the Company's Chief Executive Officer, assumed the duties and responsibilities of the Company's principal financial officer on an interim basis while the Company conducts a search for a Chief Financial Officer. Mr. Blum, age 60, joined the Company in 1998 and has served as the Company's Chief Executive Officer and a member of the Company's Board of Directors since January 2007. Additional biographical information for Mr. Blum may be found in the Company's definitive proxy statement on Schedule 14A filed with the Securities and Exchange Commission on April 7, 2023.

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, 2023, 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, 2023, 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 2023 consolidated financial statements of the Company and our report dated February 28, 2024 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

San Jose, California
February 28, 2024

ITEM 9B. OTHER INFORMATION

None.

ITEM 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS

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 2024 Annual Meeting of Stockholders, where it appears under the headings “Board of Directors,” “Executive Officers,” and, if applicable, “Delinquent Section 16(a) Reports.”

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 investor relations website, ir.cytokinetics.com. We will disclose on our investor relations website any waivers of, or amendments to, our Code of Ethics that applies to the Company's principal executive officer, principal financial officer, principal accounting officer or any person performing similar functions within four business days following the date of such amendment or waiver rather than filing a Current Report on Form 8-K.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this item is incorporated by reference from our definitive Proxy Statement for our 2024 Annual Meeting of Stockholders, where it appears under the heading “Executive Compensation” and “Director 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 2024 Annual Meeting of Stockholders, where it appears under the headings “Security Ownership of Certain Beneficial Owners and Management” and “Executive Compensation – Equity Compensation Plans at December 31, 2023.”

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 2024 Annual Meeting of Stockholders, where it appears under the headings “Certain Business Relationships and Related Party Transactions” and “Board of Directors – Independence of Directors.”

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

The information required by this item is incorporated by reference from our definitive Proxy Statement for our 2024 Annual Meeting of Stockholders, where it appears under the headings “Proposal Three – Ratification of Selection of Ernst & Young LLP as our Independent Registered Public Accounting Firm for the Fiscal Year Ending December 31, 2024.”

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	Certificate of Amendment of Amended and Restated Certificate of Incorporation	10-Q	000-50633	August 3, 2023	3.5	
3.6	Amended and Restated Bylaws.	8-K	000-50633	November 17, 2023	3.1	
4.1	Specimen Common Stock Certificate.	10-Q	000-50633	May 9, 2007	4.1	
4.2	Form of Warrant Issuable to Oxford Finance LLC pursuant to that certain 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	4.2	
4.3	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	
4.4	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	
4.5	Indenture, dated July 6, 2022, between the Company and U.S. Bank Trust Company, National Association, as Trustee (including the form of 3.50% Convertible Senior Notes due 2027).	8-K	000-50633	July 6, 2022	4.1	

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4.6	Description of Securities	10-K	000-50633	March 1, 2023	4.6
4.7	Certificate of Designation	8-K	000-50633	April 18, 2011	4.5
4.8	Certificate of Designation	8-K	000-50633	June 30, 2012	4.1
4.9	Certificate of Change of Registered Agent	10-K	000-50633	March 1, 2023	4.9
10.1	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
10.2	First Amendment to Lease, dated May 12, 2020, by and between the Company and KR Oyster Point 1, LLC	10-K	000-50633	February 26, 2021	10.59
10.3	Second Amendment to Lease, dated January 26, 2021, by and between the Company and KR Oyster Point 1, LLC	10-K	000-50633	February 26, 2021	10.60
10.4	Third Amendment to Lease, dated November 12, 2021, by and between the Company and KR Oyster Point 1, LLC	10-K	000-50633	February 25, 2022	10.4
10.5	Fourth Amendment to Lease, dated October 12, 2022, by and between the Company and KR Oyster Point 1, LLC	10-K	000-50633	March 1, 2023	10.5
10.6	Fifth Amendment to Lease, dated November 27, 2023, by and between the Company and KR Oyster Point 1, LLC				X
10.7	Form of Indemnification Agreement between the Company and each of its directors and executive officers	10-Q	000-50633	August 5, 2008	10.1
10.8+	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
10.9+	Form of Amendment No. 1 to Amended and Restated Executive Employment Agreements	10-K	000-50633	March 12, 2009	10.68
10.10+	Amended and Restated 2004 Equity Incentive Plan	10-K	000-50633	March 1, 2023	10.9
10.11+	Amended and Restated 2015 Employee Stock Purchase Plan	DEF 14A	000-50633	March 26, 2020	Appendix A
10.12+	Form of Option Agreement (Employee Annual Grant)	10-K	000-50633	March 1, 2023	10.11
10.13+	Form of Option Agreement (New Hire Inducement)	10-K	000-50633	March 1, 2023	10.12
10.14+	Form of Option Agreement (Director Annual Grant)	10-K	000-50633	March 1, 2023	10.13
10.15+	Form of Option Agreement (Director Onboarding)	10-K	000-50633	March 1, 2023	10.14
10.16+	Form of Restricted Stock Unit Award Agreement (Employee Annual Grant)	10-K	000-50633	March 1, 2023	10.15

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10.17+	Form of Restricted Stock Unit Award Agreement (Employee Key Performer)	10-K	000-50633	March 1, 2023	10.16
10.18+	Form of Restricted Stock Unit Award Agreement (Director Annual Grant)	10-K	000-50633	March 1, 2023	10.17
10.19+	Form of Executive Employment Agreement between the Company and its executive officers	10-K	000-50633	March 7, 2014	10.39
10.20#†	License and Collaboration Agreement, dated July 14, 2020, by and between the Company and Ji Xing Pharmaceuticals Limited	10-Q/A	000-50633	March 11, 2021	10.1
10.21#†	License and Collaboration Agreement, dated December 20, 2021, by and between the Company and Ji Xing Pharmaceuticals Limited	10-K	000-50633	February 25, 2022	10.14
10.22#	Development Funding Loan Agreement, dated January 7, 2022, by and among Royalty Pharma Development Funding, LLC and the Company	10-K	000-50633	February 25, 2022	10.18
10.23	First Amendment to Development Funding Loan Agreement, dated July 6, 2022, by and among Royalty Pharma Development Funding, LLC and the Company	10-K	000-50633	March 1, 2023	10.22
10.24	Second Amendment to Development Funding Loan Agreement, dated December 8, 2022, by and among Royalty Pharma Development Funding, LLC and the Company	10-K	000-50633	March 1, 2023	10.23
10.25#†	Royalty Purchase Agreement, dated February 1, 2017, by and between the Company and RPI Finance Trust	10-K	000-50633	March 6, 2017	10.44
10.26#	Amendment No. 1 to Royalty Purchase Agreement, dated January 7, 2022, by and between the Company and RPI Finance Trust	10-K	000-50633	February 25, 2022	10.20
10.27#	Revenue Participation Right Purchase Agreement, dated January 7, 2022, by and between the Company and Royalty Pharma Investments 2019 ICAV	10-K	000-50633	February 25, 2022	10.21
10.28+	Description of Director Compensation	10-Q	000-50633	November 4, 2022	10.1
10.29	Amended and Restated Controlled Equity OfferingSM Sales Agreement, dated as of March 1, 2023, by and between the Company and Cantor Fitzgerald & Co.	10-K	000-50633	March 1, 2023	10.28
10.30	Cytokinetics, Incorporated Executive Severance Plan and Summary Plan Description	8-K	000-50633	October 3, 2023	10.1
23.1	Consent of independent registered public accounting firm				X

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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 Accounting Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002	X
32.1	Certifications of the Principal Executive Officer, the Principal Financial Officer, and the Principal Accounting Officer pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 (18 U.S.C. Section 1350)(1)	X
97.1	Incentive Compensation Recoupment Policy	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 have been omitted as being immaterial and would be competitively harmful if publicly disclosed or is of the type of information Cytokinetics treats as confidential.

† 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.

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(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 28, 2024

POWER OF ATTORNEY

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

Pursuant to the requirements of the Securities 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.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ ROBERT I. BLUM</u> Robert I. Blum	President, Chief Executive Officer and Director (Principal Executive Officer, Principal Financial Officer)	February 28, 2024
<u>/s/ ROBERT C. WONG</u> Robert C. Wong	Vice President, Chief Accounting Officer (Principal Accounting Officer)	February 28, 2024
<u>/s/ JOHN T. HENDERSON</u> John T. Henderson, M.B. Ch.B.	Chairman of the Board of Directors	February 28, 2024
<u>/s/ MUNA BHANJI</u> Muna Bhanji	Director	February 28, 2024
<u>/s/ SANTO J. COSTA</u> Santo J. Costa	Director	February 28, 2024
<u>/s/ ROBERT A. HARRINGTON</u> Robert A. Harrington, M.D.	Director	February 28, 2024
<u>/s/ EDWARD M. KAYE</u> Edward M. Kaye, M.D.	Director	February 28, 2024
<u>/s/ B. LYNNE PARSHALL</u> B. Lynne Parshall	Director	February 28, 2024
<u>/s/ SANDFORD D. SMITH</u> Sandford D. Smith	Director	February 28, 2024
<u>/s/ WENDELL WIERENGA</u> Wendell Wierenga, Ph.D.	Director	February 28, 2024
<u>/s/ NANCY J. WYSENSKI</u> Nancy J. Wysenski	Director	February 28, 2024

FIFTH AMENDMENT TO LEASE

This FIFTH AMENDMENT TO LEASE ("**Fifth Amendment**") is made and entered into as of November 27, 2023 (the "**Effective Date**"), 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 "**Original Lease**"), as amended by that certain First Amendment to Lease dated May 12, 2020 (the "**First Amendment**"), that certain Second Amendment to Lease dated January 26, 2021 (the "**Second Amendment**"), that certain Third Amendment to Lease dated November 12, 2021 (the "**Third Amendment**"), and that certain Fourth Amendment to Lease dated October 12, 2022 (the "**Fourth Amendment**"), together with the Original Lease, First Amendment, Second Amendment, and Third Amendment, the "**Lease**") whereby Tenant leases certain space (the "**Premises**") within Building 3 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 Fifth 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 Fifth Amendment.

2. **Fitness Center.** Notwithstanding anything to the contrary contained in Section 1.1.1.2 of the Original Lease, Tenant shall be solely responsible for the operation of the Fitness Center, as further set forth in this Section 2, and Landlord shall no longer have any obligation to operate the Fitness Center. To the extent permitted by Applicable Laws, Tenant may use the Fitness Center for weight and aerobic training, personal training, group training, aerobics, free weights, and treadmills, stationary bicycles, elliptical machines, and stair-climbing machines, but shall in no event include installation or operation of a swimming pool, sauna or whirlpool facilities. The Fitness Center shall be for the exclusive use of Tenant's employees and guests and Tenant shall not make the Fitness Center available to other tenants or occupants of the Project (or their employees) or to members of the general public.

Kilroy Oyster Point
[Fifth Amendment]
[Cytokinetics Incorporated]

2.1. **Fitness Equipment Maintenance.** Retroactively effective as of February 23, 2023, Tenant shall be responsible for directly entering into a contract with ArchAmenities, its subcontractor, or another reputable and experienced vendor subject to Landlord's approval, which approval shall not be unreasonably withheld (the "**Fitness Equipment Contractor**"), for the quarterly maintenance of the fitness equipment in the Fitness Center (the "**Fitness Equipment**"). Tenant shall deliver a copy of its contract with the Fitness Equipment Contractor to Landlord concurrently with execution of this Fifth Amendment, and shall deliver a copy of any contract with any other vendor relating to the repair or maintenance of the Fitness Equipment within ten (10) business days of execution thereof. Notwithstanding the fact that Landlord purchased the Fitness Equipment, Tenant shall (i) be solely responsible for the payment directly to Fitness Equipment Contractor of all costs and expenses in connection with the quarterly maintenance of the Fitness Equipment, as well as any repairs of the Fitness Equipment, as needed from time-to-time in accordance with the terms of Section 7.2.1 of the Original Lease, and (ii) maintain insurance for the Fitness Equipment as if it were Tenant's property in accordance with Section 10.3 of the Original Lease. In the event that any Fitness Equipment requires repairs or maintenance to ensure the safety and proper function of such Fitness Equipment, Tenant agrees to place such Fitness Equipment "out of service" until such repair is complete. Following the expiration or earlier termination of the Lease, the Fitness Equipment shall remain in the Fitness Center and shall be Landlord's property. Tenant shall send Landlord a copy of all maintenance records and reports generated by the Fitness Equipment Contractor in connection with its repair and maintenance activities in the Fitness Center, including, without limitation, an annual report of all repair and maintenance activities for the Fitness Center occurring in the preceding Lease Year.

2.2. **Fitness Center Janitorial Service.** Effective as of January 1, 2024, Tenant shall be responsible for directly entering into a contract with a janitorial vendor (the "**Fitness Center Janitorial Contractor**") for recurring janitorial service of Fitness Center. Notwithstanding anything to the contrary contained in the Lease, as amended, Tenant shall be solely responsible for the direct payment of all costs and expenses related to the daily/weekly/monthly/quarterly/annual janitorial services for the Fitness Center to the Fitness Center Janitorial Contractor. Tenant shall not use (and upon notice from Landlord shall cease using) any Fitness Center Janitorial Contractor who would, in Landlord's reasonable and good faith judgment, disturb labor harmony with the workforce or trades engaged in performing other work, labor or services in or about the Building or the Common Areas. Tenant shall deliver a copy of its contract with the Fitness Center Janitorial Contractor to Landlord concurrently with execution of this Fifth Amendment, and shall deliver a copy of (a) the janitorial scope and safety data sheet for all products that will be utilized in connection with the cleaning of the Fitness Center, and (b) any contract with any other vendor relating to the cleaning of the Fitness Center within ten (10) business days of execution thereof. All cleaning solutions used must comply with Project LEED guidelines and all Fitness Equipment warranty specifications.

2.3. **Fitness Center Towel Service.** Effective as of January 1, 2024, Tenant shall be responsible for directly entering into a contract with a towel service vendor of Tenant's choosing (the "**Fitness Center Towel Contractor**") for recurring service to the Fitness Center. Tenant shall deliver a copy of its contract with the Fitness Center Towel Contractor to Landlord concurrently with execution of this Fifth Amendment. Tenant shall be solely responsible for the payment directly to Fitness Center Towel Contractor of all costs and expenses in connection with the provision of towel service to the Fitness Center.

2.4. **Fitness Center and Premises Rubbish Service.** Effective as of January 1, 2024, Tenant shall be responsible for directly entering into a contract with SSF Scavenger Company, Inc., its subcontractor, or another reputable and experienced vendor subject to Landlord's approval, which approval shall not be unreasonably withheld (the "**Rubbish Disposal Contractor**"), for recurring rubbish removal service for the Fitness Center and the Premises. Tenant shall deliver a copy of its contract with the Rubbish Disposal Contractor to Landlord concurrently with execution of this Fifth Amendment. Tenant shall be solely responsible for the payment directly to Rubbish Disposal Contractor of all costs and expenses in connection with the provision of rubbish removal service for the Fitness Center and the Premises. Tenant shall ensure that all rubbish containment receptacles in the Fitness Center are kept clean and free of pests at all times. Tenant shall cause the Rubbish Disposal Contractor to comply with all Applicable Laws relating to sorting requirements in connection with its provision of services. Within ten (10) business days following request from Landlord, Tenant shall provide all service records necessary to ensure compliance with Landlord's sustainability metrics and environmental reporting requirements.

2.5. **Third Party Contractors.** For the avoidance of doubt, Fitness Equipment Contractor, Fitness Center Janitorial Contractor, Fitness Center Towel Contractor, Rubbish Disposal Contractor, and any other third party contractors accessing the Fitness Center (e.g., any third party Fitness Center staff, trainers, and coaches) shall each be deemed to be a Third Party Contractor for all purposes under the Lease, as amended.

2.6. **Fitness Center Liability Waiver.** Use of the Fitness Center by Tenant shall be at the sole risk of Tenant and Landlord assumes no liability or risk associated with Tenant's use of the Fitness Center. Notwithstanding anything to the contrary contained in Section 1.1.1.2 of the Original Lease, prior to accessing the Fitness Center, each officer or employee of Tenant who desires to access the Fitness Center shall be required to sign and deliver to Landlord a liability waiver in the form attached hereto as **Exhibit A**.

3. **Construction of Phase 2; Construction Deadline Date.** Notwithstanding anything to the contrary contained in Section 2 of the Fourth Amendment, Tenant agrees to use commercially reasonable efforts to commence construction of Phase 2 (as defined in Section 5 of the Second Amendment) by June 30, 2025 and to cause substantial completion of construction of Phase 2 on or before December 31, 2025, as evidenced by a certificate of substantial completion signed by the Architect (as that term is defined in the Work Letter). Notwithstanding anything to the contrary contained in Section 2 of the Fourth Amendment, in the event construction of the Phase 2 is not complete (as evidenced per the prior sentence) by December 31, 2025 (the "**Construction Deadline Date**"), then Landlord may elect, in its sole and absolute discretion, that the entirety of the amount of any Partial Base Rent Abatement (as defined in Section 2 of the Fourth Amendment) that has not then been repaid by Tenant on an amortized basis pursuant to the schedule set forth in Section 2 of the Fourth Amendment as of the Construction Deadline Date (i.e., a total of \$3,856,755.64) shall become immediately due and payable as Additional Rent.

4. **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 Fifth Amendment and that they know of no real estate broker or agent who is entitled to a commission in connection with this Fifth 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 4 shall survive the expiration or earlier termination of the term of the Lease, as hereby amended.

5. **Signatures.** The parties hereto consent and agree that this Fifth 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 Fifth Amendment using electronic signature technology, by clicking "SIGN", such party is signing this Fifth Amendment electronically, and (2) the electronic signatures appearing on this Fifth Amendment shall be treated, for purposes of validity, enforceability and admissibility, the same as handwritten signatures.

6. **No Further Modification.** Except as set forth in this Fifth Amendment, all of the terms and provisions of the Lease shall remain unmodified and in full force and effect.

[Signatures follow on next page]

IN WITNESS WHEREOF, this Fifth Amendment has been executed as of the Effective Date.

"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/ John Osmond
Name: John Osmond
Title: EVP, Asset Management

By: /s/ Eileen Kong
Name: Eileen Kong
Title: SVP, Asset Management

"TENANT"

CYTOKINETICS, INCORPORATED,
a Delaware corporation

By: /s/ Robert Blum
Name: Robert I. Blum
Title: President and CEO

EXHIBIT A

FORM OF FITNESS CENTER LIABILITY WAIVER

RELEASE OF LIABILITY

KR Oyster Point I, LLC., a Delaware limited liability company (“Owner”) is the owner of the properties commonly known as “Kilroy Oyster Point” which contain the building(s) located at 348, 350, 352 and 354 Oyster Point Boulevard, South San Francisco, California 94080 (each, a “Building”). The Building located at “350 Oyster Point Boulevard, Building 3” contains a fitness center containing various types of exercise machines and related equipment (the “Fitness Center”).

Owner cannot prevent you from becoming exposed to, contracting, or spreading COVID-19 while visiting Owner’s Buildings and/or the Fitness Center. It is not possible to prevent against the presence of the disease. Therefore, if you choose to enter onto Owner’s Buildings and/or the Fitness Center you may be exposing yourself to and/or increasing your risk of contracting or spreading COVID-19.

The undersigned represents that he/she is currently employed by a tenant or occupant of one of the Buildings and that such Building is his/her primary place of work (as opposed to other buildings occupied by his/her employer in the surrounding areas). The undersigned acknowledges that he/she has voluntarily chosen to utilize the Fitness Center and participate in exercise and/or sport programs in connection therewith, and hereby confirms and agrees as follows:

1. I have read and understood the above warning concerning COVID-19. I hereby choose to accept the risk of contracting COVID-19 for myself in order to voluntarily enter the Fitness Center. I accept the risk of being exposed to, contracting, and/or spreading COVID-19 in order to enter the Fitness Center.

2. I am aware that exercise and related sport activities are strenuous and may be hazardous, depending upon the nature and extent of my participation or involvement and the equipment or sport activity in which I am involved, and I hereby agree to accept any and all risk of injury or death, occasioned by my participation in such activities.

3. In consideration for being permitted to utilize the Fitness Center, or for my engaging in any contest, game, sports activity, exercise, function, competition or other activity at the Fitness Center or organized, arranged or sponsored by Owner or any other person or entity having the right to manage or utilize the Fitness Center, whether such activity is on or off the Fitness Center premises, I, on behalf of myself and my heirs, personal representatives, successors and assigns (collectively, the “Releasing Parties”) agree that the Releasing Parties:

- a. shall not make any claim against or sue Owner, its affiliates and their respective partners, principals, officers, directors, employees, representatives, agents, contractors, managers and assigns (collectively, the “Released Parties”) for any act or omission or in connection with any injury or damage to persons or property occasioned by or resulting from the Releasing Parties’ use of the Fitness Center;
- b. do hereby release and discharge the Released Parties from any and all actions, claims and demands the Releasing Parties have or may hereafter have for any injury or damage, including death, that any of the Releasing Parties may sustain or incur that is in any way related to a Releasing Parties’ use of the Fitness Center;

EXHIBIT A

-1-

Kilroy Oyster Point
[Fifth Amendment]
[Cytokinetics Incorporated]

- c. do hereby forever release and waive my right to bring suit against the Released Parties in connection with exposure, infection, and/or spread of COVID-19 related to utilizing the Fitness Center. I understand that this waiver means I give up my right to bring any claims including for personal injuries, death, disease or property losses, or any other loss, including but not limited to claims of negligence and give up any claim I may have to seek damages, whether known or unknown, foreseen or unforeseen; and
- d. do hereby hold the Released Parties free and harmless from and indemnified against any and all loss, cost, claim, injury, damage or liability (including, without limitation, reasonable court costs and attorney's fees) sustained or resulting to me or any of the Releasing Parties.

4. Neither Owner nor any Released Parties shall be liable to me or my guests at the Fitness Center for loss or theft of personal property. Any property left by me or my guests on the premises of the Fitness Center, without provision for its storage, may be disposed of or sold without notice.

5. In consideration of my entry upon the Fitness Center, I acknowledge and agree to the following:

- a. I have not experienced symptoms of fever, fatigue, difficulty of breathing, dry cough or exhibited any other symptoms relating to COVID-19 or any communicable disease within the last fourteen (14) days. If I experience any of these symptoms, I will immediately cease use of the Fitness Center.
- b. I have not been diagnosed with the COVID-19 virus within the last thirty (30) days.
- c. I will follow any and all federal, state, and local government and federal and state health agencies' orders, recommendations and guidelines concerning COVID-19, as the same may be updated from time to time.
- d. I agree to comply with all posted signage within Owner's Buildings and the Fitness Center and comply with all verbal logistical instructions provided by Owner to maximize safety.

I, THE UNDERSIGNED, CONFIRM I HAVE CAREFULLY READ THIS AGREEMENT AND FULLY UNDERSTAND ITS CONTENTS AND ALL PROVISIONS OF THIS RELEASE. I FREELY AND KNOWINGLY ASSUME THE RISK AND WAIVE MY RIGHTS CONCERNING LIABILITY AS DESCRIBED ABOVE.

Signed: _____

Date: _____

Name (please print): _____

Tenant Access Card #: _____

Phone: _____

Company: _____

Email: _____

Cyto Facilities Approved: By: _____ Date: _____

EXHIBIT A

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

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

- 1) Registration Statement (Form S-3 No. 333-268483) 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, 333-238786, 333-256054, 333-260840, 333-265316 and 333-270182) pertaining to the Amended and Restated 2004 Equity Incentive Plan of Cytokinetics, Incorporated;

of our reports dated February 28, 2024, 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, 2023.

/s/ Ernst & Young LLP

San Jose, California
February 28, 2024

**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, Principal Financial Officer)

Date: February 28, 2024

**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 28, 2024

**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, 2023 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, Principal Financial Officer)

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

Date: February 28, 2024

CYTOKINETICS, INCORPORATED

INCENTIVE COMPENSATION RECOUPMENT POLICY

1. INTRODUCTION

The Board of Directors (the “**Board**”) of Cytokinetics, Incorporated, a Delaware corporation (the “**Company**”), has determined that it is in the best interests of the Company and its stockholders to adopt this Incentive Compensation Recoupment Policy (this “**Policy**”) providing for the Company’s recoupment of Recoverable Incentive Compensation that is received by Covered Officers of the Company under certain circumstances. Certain capitalized terms used in this Policy have the meanings given to such terms in Section 3 below.

This Policy is designed to comply with, and shall be interpreted to be consistent with, Section 10D of the Exchange Act, Rule 10D-1 promulgated thereunder (“**Rule 10D-1**”) and Nasdaq Listing Rule 5608 (the “**Listing Standards**”).

2. EFFECTIVE DATE

This Policy shall apply to all Incentive Compensation that is received by a Covered Officer on or after October 2, 2023 (the “**Effective Date**”). Incentive Compensation is deemed “**received**” in the Company’s fiscal period in which the Financial Reporting Measure specified in the Incentive Compensation award is attained, even if the payment or grant of such Incentive Compensation occurs after the end of that period.

3. DEFINITIONS

“**Accounting Restatement**” means an accounting restatement that the Company is required to prepare due to the material noncompliance of the Company with any financial reporting requirement under the securities laws, including any required accounting restatement to correct an error in previously issued financial statements that is material to the previously issued financial statements, or that would result in a material misstatement if the error were corrected in the current period or left uncorrected in the current period.

“**Accounting Restatement Date**” means the earlier to occur of (a) the date that the Board, a committee of the Board authorized to take such action, or the officer or officers of the Company authorized to take such action if Board action is not required, concludes, or reasonably should have concluded, that the Company is required to prepare an Accounting Restatement, or (b) the date that a court, regulator or other legally authorized body directs the Company to prepare an Accounting Restatement.

“**Administrator**” means the Compensation Committee or, in the absence of such committee, the Board.

“**Code**” means the U.S. Internal Revenue Code of 1986, as amended, and the regulations promulgated thereunder.

“**Compensation Committee**” means the Compensation and Talent Committee of the Board.

“**Covered Officer**” means each current and former Executive Officer.

“**Exchange**” means the Nasdaq Stock Market.

“**Exchange Act**” means the U.S. Securities Exchange Act of 1934, as amended.

“**Executive Officer**” means the Company’s president, principal financial officer, principal accounting officer (or if there is no such accounting officer, the controller), any vice-president of the Company in charge of a principal business unit, division, or function (such as sales, administration, or finance), any other officer who performs a policy-making function, or any other person who performs similar policy-making functions for the Company. Executive officers of the Company’s parent(s) or subsidiaries are deemed executive officers of the Company if they perform such policy-making functions for the Company. Policy-making function is not intended to include policy-making functions that are not significant. Identification of an executive officer for purposes of this Policy would include at a minimum executive officers identified pursuant to Item 401(b) of Regulation S-K promulgated under the Exchange Act.

“**Financial Reporting Measures**” means measures that are determined and presented in accordance with the accounting principles used in preparing the Company’s financial statements, and any measures derived wholly or in part from such measures, including Company stock price and total stockholder return (“**TSR**”). A measure need not be presented in the Company’s financial statements or included in a filing with the SEC in order to be a Financial Reporting Measure.

“**Incentive Compensation**” means any compensation that is granted, earned or vested based wholly or in part upon the attainment of a Financial Reporting Measure.

“**Lookback Period**” means the three completed fiscal years immediately preceding the Accounting Restatement Date, as well as any transition period (resulting from a change in the Company’s fiscal year) within or immediately following those three completed fiscal years (except that a transition period of at least nine months shall count as a completed fiscal year). Notwithstanding the foregoing, the Lookback Period shall not include fiscal years completed prior to the Effective Date.

“**Recoverable Incentive Compensation**” means Incentive Compensation received by a Covered Officer during the Lookback Period that exceeds the amount of Incentive Compensation that would have been received had such amount been determined based on the Accounting Restatement, computed without regard to any taxes paid (*i.e.*, on a gross basis without regarding to tax withholdings and other deductions). For any compensation plans or programs that take into account Incentive Compensation, the amount of Recoverable Incentive Compensation for purposes of this Policy shall include, without limitation, the amount contributed to any notional account based on Recoverable Incentive Compensation and any earnings to date on that notional amount. For any Incentive Compensation that is based on stock price or TSR, where the Recoverable Incentive Compensation is not subject to mathematical recalculation directly from the information in an Accounting Restatement, the Administrator will determine the amount of Recoverable Incentive Compensation based on a reasonable estimate of the effect of the Accounting Restatement on the stock price or TSR upon which the Incentive Compensation was received. The Company shall maintain documentation of the determination of that reasonable estimate and provide such documentation to the Exchange in accordance with the Listing Standards.

“**SEC**” means the U.S. Securities and Exchange Commission.

4. RECOUPMENT

(a) Applicability of Policy. This Policy applies to Incentive Compensation received by a Covered Officer (i) after beginning services as an Executive Officer, (ii) who served as an Executive Officer at any time during the performance period for such Incentive Compensation, (iii) while the Company had a class of securities listed on a national securities exchange or a national securities association, and (iv) during the Lookback Period.

(b) Recoupment Generally. Pursuant to the provisions of this Policy, if there is an Accounting Restatement, the Company must reasonably promptly recoup the full amount of the Recoverable Incentive Compensation, unless the conditions of one or more subsections of Section 4(c) of this Policy are met and the Compensation Committee, or, if such committee does not consist solely of independent directors, a majority of the independent directors serving on the Board, has made a determination that recoupment would be impracticable. Recoupment is required regardless of whether the Covered Officer engaged in any misconduct and regardless of fault, and the Company's obligation to recoup Recoverable Incentive Compensation is not dependent on whether or when any restated financial statements are filed.

(c) Impracticability of Recovery. Recoupment may be determined to be impracticable if, and only if:

(i) the direct expense paid to a third party to assist in enforcing this Policy would exceed the amount of the applicable Recoverable Incentive Compensation; provided that, before concluding that it would be impracticable to recover any amount of Recoverable Incentive Compensation based on expense of enforcement, the Company shall make a reasonable attempt to recover such Recoverable Incentive Compensation, document such reasonable attempt(s) to recover, and provide that documentation to the Exchange in accordance with the Listing Standards; or

(ii) recoupment of the applicable Recoverable Incentive Compensation would likely cause an otherwise tax-qualified retirement plan, under which benefits are broadly available to employees of the Company, to fail to meet the requirements of Code Section 401(a)(13) or Code Section 411(a) and regulations thereunder.

(d) Sources of Recoupment. To the extent permitted by applicable law, the Administrator shall, in its sole discretion, determine the timing and method for recouping Recoverable Incentive Compensation hereunder, provided that such recoupment is undertaken reasonably promptly. The Administrator may, in its discretion, seek recoupment from a Covered Officer from any of the following sources or a combination thereof, whether the applicable compensation was approved, awarded, granted, payable or paid to the Covered Officer prior to, on or after the Effective Date: (i) direct repayment of Recoverable Incentive Compensation previously paid to the Covered Officer; (ii) cancelling prior cash or equity-based awards (whether vested or unvested and whether paid or unpaid); (iii) cancelling or offsetting against any planned future cash or equity-based awards; (iv) forfeiture of deferred compensation, subject to compliance with Code Section 409A; and (v) any other method authorized by applicable law or contract. Subject to compliance with any applicable law, the Administrator may effectuate recoupment under this Policy from any amount otherwise payable to the Covered Officer, including amounts payable to such individual under any otherwise applicable Company plan or program, *e.g.*, base salary, bonuses or commissions and compensation previously deferred by the Covered Officer. The Administrator need not utilize the same method of recovery for all Covered Officers or with respect to all types of Recoverable Incentive Compensation.

(e) No Indemnification of Covered Officers. Notwithstanding any indemnification agreement, applicable insurance policy or any other agreement or provision of the Company's certificate of incorporation or bylaws to the contrary, no Covered Officer shall be entitled to indemnification or advancement of expenses in connection with any enforcement of this Policy by the Company, including paying or reimbursing such Covered Officer for insurance premiums to cover potential obligations to the Company under this Policy.

(f) Indemnification of Administrator. Any members of the Administrator, and any other members of the Board who assist in the administration of this Policy, shall not be personally liable for any action, determination or interpretation made with respect to this Policy and shall be indemnified by the Company to the fullest extent under applicable law and Company policy with respect to any such action, determination or interpretation. The foregoing sentence shall not limit any other rights to indemnification of the members of the Board under applicable law or Company policy.

5. ADMINISTRATION

Except as specifically set forth herein, this Policy shall be administered by the Administrator. The Administrator shall have full and final authority to make any and all determinations required under this Policy. Any determination by the Administrator with respect to this Policy shall be final, conclusive and binding on all interested parties and need not be uniform with respect to each individual covered by this Policy. In carrying out the administration of this Policy, the Administrator is authorized and directed to consult with the full Board or such other committees of the Board as may be necessary or appropriate as to matters within the scope of such other committee's responsibility and authority. Subject to applicable law, the Administrator may authorize and empower any officer or employee of the Company to take any and all actions that the Administrator, in its sole discretion, deems necessary or appropriate to carry out the purpose and intent of this Policy (other than with respect to any recovery under this Policy involving such officer or employee).

6. SEVERABILITY

If any provision of this Policy or the application of any such provision to a Covered Officer shall be adjudicated to be invalid, illegal or unenforceable in any respect, such invalidity, illegality or unenforceability shall not affect any other provisions of this Policy, and the invalid, illegal or unenforceable provisions shall be deemed amended to the minimum extent necessary to render any such provision or application enforceable.

7. NO IMPAIRMENT OF OTHER REMEDIES

Nothing contained in this Policy, and no recoupment or recovery as contemplated herein, shall limit any claims, damages or other legal remedies the Company or any of its affiliates may have against a Covered Officer arising out of or resulting from any actions or omissions by the Covered Officer. This Policy does not preclude the Company from taking any other action to enforce a Covered Officer's obligations to the Company, including, without limitation, termination of employment and/or institution of civil proceedings. This Policy is in addition to the requirements of Section 304 of the Sarbanes-Oxley Act of 2002 that are applicable to the Company's Chief Executive Officer and Chief Financial Officer and to any other compensation recoupment policy and/or similar provisions in any employment, equity plan, equity award, or other individual agreement, to which the Company is a party or which the Company has adopted or may adopt and maintain from time to time.

8. AMENDMENT; TERMINATION

The Administrator may amend, terminate or replace this Policy or any portion of this Policy at any time and from time to time in its sole discretion. The Administrator shall amend this Policy as it deems necessary to comply with applicable law or any Listing Standard.

9. SUCCESSORS

This Policy shall be binding and enforceable against all Covered Officers and, to the extent required by Rule 10D-1 and/or the applicable Listing Standards, their beneficiaries, heirs, executors, administrators or other legal representatives.

10. REQUIRED FILINGS

The Company shall make any disclosures and filings with respect to this Policy that are required by law, including as required by the SEC.

* * * * *

CYTOKINETICS, INCORPORATED

INCENTIVE COMPENSATION RECOUPMENT POLICY

FORM OF EXECUTIVE ACKNOWLEDGMENT

I, the undersigned, agree and acknowledge that I am bound by, and subject to, the Cytokinetics, Incorporated Incentive Compensation Recoupment Policy, as may be amended, restated, supplemented or otherwise modified from time to time (the "**Policy**"). In the event of any inconsistency between the Policy and the terms of any employment agreement, offer letter or other individual agreement with Cytokinetics, Incorporated (the "**Company**") to which I am a party, or the terms of any compensation plan, program or agreement, whether or not written, under which any compensation has been granted, awarded, earned or paid to me, the terms of the Policy shall govern.

In the event that the Administrator (as defined in the Policy) determines that any compensation granted, awarded, earned or paid to me must be forfeited or reimbursed to the Company pursuant to the Policy, I will promptly take any action necessary to effectuate such forfeiture and/or reimbursement. I further agree and acknowledge that I am not entitled to indemnification, and hereby waive any right to advancement of expenses, in connection with any enforcement of the Policy by the Company.

Agreed and Acknowledged:

Name: _____

Title: _____

Date: _____
