

**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
Washington, D.C. 20549**

**FORM 10-Q**

(Mark One)

**QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the quarterly period ended September 30, 2021

or

**TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from \_\_\_\_\_ to \_\_\_\_\_

Commission file number: 000-50633

**CYTKINETICS, INCORPORATED**

(Exact name of registrant as specified in its charter)

Delaware  
(State or other jurisdiction of  
incorporation or organization)  
  
280 East Grand Avenue  
South San Francisco, California  
(Address of principal executive offices)

94-3291317  
(I.R.S. Employer  
Identification No.)

94080  
(Zip Code)

Registrant's telephone number, including area code: (650) 624-3000

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

<u>Title of each class</u>	<u>Trading symbol</u>	<u>Name of each exchange on which registered</u>
Common Stock, \$0.001 par value	CYTK	The Nasdaq Global Select Market

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 every 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	<input checked="" type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input type="checkbox"/>	Smaller reporting company	<input type="checkbox"/>
Emerging growth company	<input type="checkbox"/>		

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

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

Number of shares of common stock, \$0.001 par value, outstanding as of November 1, 2021: 83,882,953

**CYTOKINETICS, INCORPORATED**  
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**PART I. FINANCIAL INFORMATION****ITEM 1. FINANCIAL STATEMENTS**

**CYTOKINETICS, INCORPORATED**  
**CONDENSED CONSOLIDATED BALANCE SHEETS**  
(In thousands, except per share data) (Unaudited)

	September 30, 2021	December 31, 2020
<b>ASSETS</b>		
Current assets:		
Cash and cash equivalents	\$ 90,562	\$ 82,985
Short-term investments	387,074	381,075
Accounts receivable	644	4,420
Prepaid expenses and other current assets	16,661	5,741
Total current assets	494,941	474,221
Long-term investments	191,295	36,954
Property and equipment, net	53,896	13,346
Operating lease right-of-use assets	80,725	2,924
Other assets	6,682	6,358
Total assets	\$ 827,539	\$ 533,803
<b>LIABILITIES AND STOCKHOLDERS' EQUITY</b>		
Current liabilities:		
Accounts payable	\$ 16,222	\$ 8,050
Accrued liabilities	31,772	19,315
Current portion of long-term debt	16,875	—
Short-term lease liabilities	13,586	2,785
Other current liabilities	2,413	1,049
Total current liabilities	80,868	31,199
Term loan, net	30,203	46,209
Convertible notes, net	93,885	89,504
Liability related to the sale of future royalties, net	174,775	166,068
Long-term deferred revenue	87,000	87,000
Long-term lease and other non-current liabilities	111,788	440
Total liabilities	578,519	420,420
Commitments and contingencies		
Stockholders' equity:		
Preferred stock, \$0.001 par value	—	—
Common stock, \$0.001 par value	84	70
Additional paid-in capital	1,426,051	1,105,470
Accumulated other comprehensive (loss) income	(65)	149
Accumulated deficit	(1,177,050)	(992,306)
Total stockholders' equity	249,020	113,383
Total liabilities and stockholders' equity	\$ 827,539	\$ 533,803

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

**CYTOKINETICS, INCORPORATED**  
**CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS**  
(In thousands, except per share data) (Unaudited)

	Three Months Ended		Nine Months Ended	
	September 30, 2021	September 30, 2020	September 30, 2021	September 30, 2020
<b>Revenues:</b>				
Research and development revenues	\$ 437	\$ 5,187	\$ 9,828	\$ 12,605
License revenues	—	36,501	—	36,501
Milestone revenues	5,000	—	5,000	—
Total revenues	<u>5,437</u>	<u>41,688</u>	<u>14,828</u>	<u>49,106</u>
<b>Operating expenses:</b>				
Research and development	48,436	24,202	116,440	67,730
General and administrative	26,202	12,302	62,997	38,912
Total operating expenses	<u>74,638</u>	<u>36,504</u>	<u>179,437</u>	<u>106,642</u>
Operating (loss) income	(69,201)	5,184	(164,609)	(57,536)
Interest expense	(4,161)	(3,976)	(12,222)	(11,945)
Non-cash interest expense on liability related to the sale of future royalties	(2,955)	(5,461)	(8,621)	(17,062)
Interest and other income, net	231	1,078	708	3,183
Net loss	<u>\$ (76,086)</u>	<u>\$ (3,175)</u>	<u>\$ (184,744)</u>	<u>\$ (83,360)</u>
Net loss per share — basic and diluted	<u>\$ (0.95)</u>	<u>\$ (0.05)</u>	<u>\$ (2.48)</u>	<u>\$ (1.34)</u>
Weighted-average number of shares used in computing net loss per share — basic and diluted	<u>80,329</u>	<u>68,279</u>	<u>74,460</u>	<u>62,406</u>
<b>Other comprehensive loss:</b>				
Unrealized (loss) gain on available-for-sale securities, net	(43)	(379)	(214)	279
Comprehensive loss	<u>\$ (76,129)</u>	<u>\$ (3,554)</u>	<u>\$ (184,958)</u>	<u>\$ (83,081)</u>

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

**CYTOKINETICS, INCORPORATED**  
**CONDENSED CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY (DEFICIT)**  
(In thousands, except share data) (Unaudited)

	Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive (Loss) Income	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance, December 31, 2020	71,015,183	\$ 70	\$ 1,105,470	\$ 149	\$ (992,306)	\$ 113,383
Exercise of stock options	187,807	1	1,271	—	—	1,272
Vesting of restricted stock units, net of taxes withheld	360,050	—	(4,449)	—	—	(4,449)
Net share settlement	—	—	(418)	—	—	(418)
Stock-based compensation	—	—	5,261	—	—	5,261
Other comprehensive loss	—	—	—	(99)	—	(99)
Net loss	—	—	—	—	(47,104)	(47,104)
Balance, March 31, 2021	71,563,040	\$ 71	\$ 1,107,135	\$ 50	\$ (1,039,410)	\$ 67,846
Exercise of stock options	276,790	1	2,206	—	—	2,207
Stock-based compensation	—	—	7,093	—	—	7,093
Issuance of common stock under Employee Stock Purchase Plan	64,975	—	969	—	—	969
Other comprehensive loss	—	—	—	(72)	—	(72)
Net loss	—	—	—	—	(61,554)	(61,554)
Balance, June 30, 2021	71,904,805	\$ 72	\$ 1,117,403	\$ (22)	\$ (1,100,964)	\$ 16,489
Exercise of stock options	421,110	1	3,987	—	—	3,988
Stock-based compensation	—	—	7,767	—	—	7,767
Underwritten public offering of common stock, net of discounts, commissions and offering cost	11,500,000	11	296,894	—	—	296,905
Other comprehensive loss	—	—	—	(43)	—	(43)
Net loss	—	—	—	—	(76,086)	(76,086)
Balance, September 30, 2021	83,825,915	\$ 84	\$ 1,426,051	\$ (65)	\$ (1,177,050)	\$ 249,020

	Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Income	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount				
Balance, December 31, 2019	59,172,124	\$ 59	\$ 853,341	\$ 679	\$ (865,016)	\$ (10,937)
Exercise of stock options	12,165	—	93	—	—	93
Vesting of restricted stock units, net of taxes withheld	274,563	—	(2,255)	—	—	(2,255)
Claims settlement under Section 16(b)	—	—	2,151	—	—	2,151
Issuance of warrants	—	—	184	—	—	184
Stock-based compensation	—	—	3,524	—	—	3,524
Other comprehensive income	—	—	—	934	—	934
Net loss	—	—	—	—	(39,405)	(39,405)
Balance, March 31, 2020	59,458,852	\$ 59	\$ 857,038	\$ 1,613	\$ (904,421)	\$ (45,711)
Exercise of stock options	396,379	1	3,333	—	—	3,334
Stock-based compensation	—	—	4,527	—	—	4,527
Issuance of common stock under Employee Stock Purchase Plan	86,839	—	826	—	—	826
Other comprehensive loss	—	—	—	(276)	—	(276)
Net loss	—	—	—	—	(40,780)	(40,780)
Balance, June 30, 2020	59,942,070	\$ 60	\$ 865,724	\$ 1,337	\$ (945,201)	\$ (78,080)
Exercise of stock options	171,363	—	1,227	—	—	1,227
Exercise of warrants	95,932	—	—	—	—	—
Stock-based compensation	—	—	4,692	—	—	4,692
Underwritten public offering of common stock, net of discounts, commissions and offering cost	8,385,417	8	188,875	—	—	188,883
Issuance of common stock upon private placement	2,000,000	2	36,435	—	—	36,437
Other comprehensive loss	—	—	—	(379)	—	(379)
Net loss	—	—	—	—	(3,175)	(3,175)
Balance, September 30, 2020	70,594,782	\$ 70	\$ 1,096,953	\$ 958	\$ (948,376)	\$ 149,605

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

**CYTOKINETICS, INCORPORATED**  
**CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS**  
(In thousands) (Unaudited)

	Nine Months Ended	
	September 30, 2021	September 30, 2020
<b>Cash flows from operating activities:</b>		
Net loss	\$ (184,744)	\$ (83,360)
Adjustments to reconcile net loss to net cash used in operating activities:		
Non-cash interest expense on liability related to sale of future royalties	8,707	17,119
Non-cash stock-based compensation expense	20,121	12,743
Non-cash lease expense	5,407	3,126
Depreciation and amortization of property and equipment	1,542	1,360
Interest receivable and amortization on investments	3,440	(402)
Non-cash interest expense related to debt	5,250	4,949
Changes in operating assets and liabilities:		
Accounts receivable	3,776	198
Prepaid and other assets	(11,244)	294
Accounts payable	(2,802)	(1,422)
Accrued and other liabilities	13,821	5,645
Operating lease liabilities	33,466	(3,457)
Other non-current liabilities	5,475	—
Net cash used in operating activities	<u>(97,785)</u>	<u>(43,207)</u>
<b>Cash flows from investing activities:</b>		
Purchases of investments	(493,450)	(166,547)
Maturities of investments	326,156	148,147
Sales of investments	3,300	—
Purchases of property and equipment	(31,118)	(4,497)
Net cash used in investing activities	<u>(195,112)</u>	<u>(22,897)</u>
<b>Cash flows from financing activities:</b>		
Proceeds from public offerings of common stock, net of discounts, commissions and offering cost	296,905	188,883
Proceeds from private placement, net	—	36,225
Proceeds from and payments for stock-based award activities, net	3,569	3,224
Claims settlement under Section 16(b)	—	2,151
Net cash provided by financing activities	<u>300,474</u>	<u>230,483</u>
Net increase in cash and cash equivalents	7,577	164,379
Cash and cash equivalents, beginning of period	82,985	36,433
Cash and cash equivalents, end of period	<u>\$ 90,562</u>	<u>\$ 200,812</u>
<b>Non-cash investing and financing activities:</b>		
Right-of-use assets recognized in exchange for lease obligations	\$ 83,208	\$ 1,106
Amounts unpaid for purchases of property and equipment	10,974	—

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

**CYTOKINETICS, INCORPORATED**  
**NOTES TO UNAUDITED CONDENSED CONSOLIDATED FINANCIAL STATEMENTS**

**Note 1 — Organization and Significant Accounting Policies**

Cytokinetics, Incorporated (the “Company”, “we” or “our”) was incorporated under the laws of the state of Delaware on August 5, 1997. The Company is 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 \$1,177.1 million since inception and there can be no assurance that we will attain profitability. The Company anticipates that it will have operating losses and net cash outflows in future periods.

We are subject to risks common to late stage biopharmaceutical companies including, but not limited to, development of new drug candidates, dependence on key personnel, and the ability to obtain additional capital as needed to fund our future plans. Our liquidity will be impaired if sufficient additional capital is not available on terms acceptable to us. To date, we have funded operations primarily through sales of our common stock, contract payments under our collaboration agreements, sale of future royalties, debt financing arrangements, government grants and interest income. Until we achieve profitable operations, we intend to continue to fund operations through payments from strategic collaborations, additional sales of equity securities, grants and debt financings. We have never generated revenues from commercial sales of our drugs and may not have drugs to market for at least several years, if ever. Our success is dependent on our ability to enter into new strategic collaborations and/or raise additional capital and to successfully develop and market one or more of our drug candidates. 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 from the filing date of this Quarterly Report on Form 10-Q. 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.

***Basis of Presentation***

Our condensed consolidated financial statements include the accounts of Cytokinetics and our wholly owned subsidiary. The accompanying unaudited condensed consolidated financial statements have been prepared in accordance with generally accepted accounting principles in the United States of America (“GAAP”) for interim financial information and the instructions to Form 10-Q and Rule 10-01 of Regulation S-X. The financial statements include all adjustments (consisting only of normal recurring adjustments) that management believes are necessary for the fair statement of our financial information. These interim results are not necessarily indicative of results to be expected for the full fiscal year or any future interim period. The balance sheet as of December 31, 2020 has been derived from the audited financial statements at that date but does not include all of the information and footnotes required by GAAP for complete financial statements. The financial statements and related disclosures have been prepared with the presumption that users of the interim financial statements have read or have access to the audited financial statements for the preceding fiscal year. Accordingly, these financial statements should be read in conjunction with the audited financial statements and notes thereto contained in the Company’s Form 10-K for the year ended December 31, 2020, as filed with the Securities and Exchange Commission.

***Use of Estimates***

The preparation of condensed consolidated financial statements in conformity with GAAP requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosures of contingent assets and liabilities at the date of the condensed consolidated financial statements and 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.

### Recent Accounting Pronouncements

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

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

### Note 2 — Net Loss Per Share

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):

	September 30, 2021	September 30, 2020
Options to purchase common stock	9,511	8,805
Warrants to purchase common stock	48	62
Restricted stock and performance units	1,515	1,124
Shares issuable related to the ESPP	38	36
Shares issuable upon conversion of convertible notes	16,675	16,675
Total shares	<u>27,787</u>	<u>26,702</u>

### **Note 3 — Research and Development Arrangements**

#### ***Amgen Inc. (“Amgen”)***

On November 20, 2020, we received written notice of termination from Amgen of that certain Collaboration and Option Agreement, dated December 29, 2006, as amended (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.

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

We recognize research and development revenue for reimbursements from Amgen of both internal costs of certain full-time employee equivalents and other costs related to the Amgen Agreement, which terminated effective as of May 20, 2021. There was no research and development revenue from Amgen for the three months ended September 30, 2021. Research and development revenue from Amgen was \$3.8 million for the three months ended September 30, 2020, and \$7.4 million and \$8.3 million for the nine months ended September 30, 2021 and 2020, respectively, and consists of reimbursement of costs we incurred related to METEORIC-HF.

We had no accounts receivable from Amgen as of September 30, 2021. Accounts receivable from Amgen was \$1.7 million as of December 31, 2020.

#### ***Astellas Pharma Inc. (“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 License and Collaboration Agreement, dated June 21, 2013 between the parties (the “Astellas Agreement”).

In 2014, we and Astellas amended and restated the Astellas Agreement (the “2014 Astellas Amendment”) and expanded the objective of the collaboration to include spinal muscular atrophy (“SMA”) and potentially other neuromuscular indications for reldesemtiv and other fast skeletal muscle troponin activators (“FSTAs”). License revenues in 2018 related to our performance obligations under the 2014 Astellas Amendment. In 2018, we completed all our deliverables for the 2014 Astellas Amendment.

In 2016, we and Astellas amended the Astellas Agreement (the “2016 Astellas Amendment”) to expand the collaboration to include the development of reldesemtiv for the potential treatment of amyotrophic lateral sclerosis (“ALS”), as well as the possible development in ALS of other FSTAs previously licensed by us to Astellas, and Astellas paid us a \$35.0 million non-refundable upfront amendment fee and an accelerated \$15.0 million milestone payment for the initiation of the first Phase 2 clinical trial of reldesemtiv in ALS that was otherwise provided for in the Astellas Agreement, as if such milestone had been achieved upon the execution of the 2016 Astellas Amendment, and committed research and development consideration of \$44.2 million, for total consideration of \$94.2 million.

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

#### ***Fast Skeletal Regulatory Activator Agreement***

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

Under the Astellas FSRA Agreement, Astellas 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. In addition, Astellas agreed to non-cash contributions to the Company, which include the transfer of its existing inventories of active pharmaceutical ingredient of reldesemtiv and CK-601. Astellas has also agreed to the continued conduct of ongoing stability studies pertaining to such existing inventories of active pharmaceutical ingredient, at Astellas' cost. In exchange, the Company will pay Astellas a low- to mid- single digit royalty on sales of reldesemtiv in the United States, Canada, United Kingdom and the European Union until the later of (i) ten years following the first commercial sale of such product in a major market country, or (ii) December 31, 2034, subject to certain royalty reduction provisions. The Company will not owe Astellas royalties on sales of reldesemtiv in any other country, or on the sale of any FSRA compounds or related products other than reldesemtiv.

#### *License and Collaboration Agreement for Other Skeletal Sarcomere Activators*

The Company and Astellas also entered into that certain License and Collaboration Agreement for Other Skeletal Sarcomere Activators, dated April 23, 2020 (the "Astellas OSSA Agreement"), which is an amendment and restatement of the Astellas Agreement and removes the FSRA compounds and related products from the collaboration.

On April 27, 2021, we received written notice of termination from Astellas of the Astellas OSSA Agreement, which is effective as of November 1, 2021.

We recognized research revenue for reimbursements from Astellas of internal costs of certain full-time employee equivalents, supporting collaborative research and development programs, and of other costs related to those programs through March 31, 2021 when the research term of the Astellas OSSA Agreement expired.

Research and development revenue from Astellas was \$0.5 million and \$1.4 million for the three months ended September 30, 2021 and 2020 respectively, and \$2.5 million and \$4.0 million for the nine months ended September 30, 2021 and 2020, respectively.

We had accounts receivable from Astellas of \$0.6 million as of September 30, 2021 and \$2.7 million as of December 31, 2020.

#### **RTW Transactions**

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

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

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

### License and Collaboration Agreement

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

The Ji Xing License Agreement, unless terminated earlier, will continue on a market-by-market basis until expiration of the relevant royalty term. Ji Xing has the right to terminate the Ji Xing License Agreement for convenience. Each party may terminate the Ji Xing License Agreement for the other party’s uncured material breach, insolvency, or failure to perform due to extended force majeure events. Cytokinetics may also terminate the Ji Xing License Agreement if Ji Xing challenges Cytokinetics’ patents or undergoes certain change of control transactions. Rights granted to Ji Xing in relation to 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.

License revenues and milestone revenues for the three and nine months ended September 30, 2021 and 2020 were as follows (in thousands):

	Three Months Ended		Nine Months Ended	
	September 30, 2021	September 30, 2020	September 30, 2021	September 30, 2020
License revenues	\$ —	\$ 36,501	\$ —	\$ 36,501
Milestone revenues	5,000	—	5,000	—
	<u>\$ 5,000</u>	<u>\$ 36,501</u>	<u>\$ 5,000</u>	<u>\$ 36,501</u>

We assessed this arrangement in accordance with ASC 606 and concluded that there is one performance obligation relating to the license of functional intellectual property. The performance obligation was satisfied, and we recognized the residual allocation of arrangement consideration as revenue of \$36.5 million for 2020. No license revenue was recognized for the three and nine months ended September 30, 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 exclude the milestone payments from the initial transaction price.

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

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

We earned a \$2.5 million milestone from Ji Xing as of December 31, 2020 for the first patient dosed in Cohort 2 of REDWOOD-HCM (Randomized Evaluation of Dosing With CK-274 in Obstructive Outflow Disease in HCM). We determined recognition of the milestone during 2020 based on clinical trial progress. Our determination that we expected to earn the \$2.5 million milestone resulted in a change in the overall transaction price of the collaboration agreement, as it was probable that a significant reversal of cumulative revenue would not occur. A corresponding contract asset was recorded in other current assets in our condensed consolidated balance sheet as of December 31, 2020 and was released in the first quarter of 2021 upon receipt of cash.

We recognized a \$5.0 million milestone from Ji Xing as of September 30, 2021 for initiation of a phase 3 clinical trial for aficamten in obstructive HCM. Although our contractual right to payment has not yet arisen under the Ji Xing License Agreement, we determined recognition of the milestone in accordance with ASC 606 during the third quarter of 2021 was appropriate based on our expected initiation of a phase 3 clinical trial of aficamten in obstructive HCM and recorded a corresponding contract asset in other current assets in our condensed consolidated balance sheet as of September 30, 2021.

#### *Royalty Purchase Agreement*

We entered into a Royalty Purchase Agreement (the “RTW Royalty Purchase Agreement”) with RTW Royalty Holdings, pursuant to which we sold our right to receive certain payments on the net sales of products containing the compound mavacamten, a cardiac myosin inhibitor (the “Mavacamten Royalty”), under the Research Collaboration Agreement, dated August 24, 2012, between us and MyoKardia, Inc. to RTW Royalty Holdings for a one-time payment of \$85.0 million. The RTW Royalty Purchase Agreement transaction closed on November 13, 2020. On March 31, 2021, RTW Royalty Holdings assigned its rights and obligations under the RTW Royalty Purchase Agreement to its affiliate, RTW Investments ICAV for RTW Fund 1 (“RTW ICAV”).

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

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

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

#### *Common Stock Purchase Agreement*

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

#### *Funding Agreement*

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

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

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

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

On March 31, 2021, RTW Royalty Holdings assigned its rights and obligations under the Funding Agreement to its affiliate, RTW ICAV.

**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.

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):

	Fair Value Hierarchy Level	September 30, 2021			
		Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Money market funds	Level 1	\$ 68,688	\$ —	\$ —	\$ 68,688
U.S. Treasury securities	Level 1	161,122	13	(14)	161,121
Agency bonds	Level 2	34,584	5	(9)	34,580
Commercial paper	Level 2	204,097	14	(1)	204,110
Corporate obligations	Level 2	198,181	—	(73)	198,108
		<u>\$ 666,672</u>	<u>\$ 32</u>	<u>\$ (97)</u>	<u>\$ 666,607</u>
	Fair Value Hierarchy Level	December 31, 2020			
		Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Money market funds	Level 1	\$ 80,050	\$ —	\$ —	\$ 80,050
U.S. Treasury securities	Level 1	274,407	147	(8)	274,546
Agency bonds	Level 2	51,581	15	(3)	51,593
Commercial paper	Level 2	49,500	3	(1)	49,502
Corporate obligations	Level 2	42,392	7	(11)	42,388
		<u>\$ 497,930</u>	<u>\$ 172</u>	<u>\$ (23)</u>	<u>\$ 498,079</u>

The available-for-sale securities in our condensed consolidated balance sheet are as follows (in thousands):

	<b>September 30, 2021</b>	<b>December 31, 2020</b>
Cash equivalents	\$ 88,238	\$ 80,050
Short-term investments	387,074	381,075
Long-term investments	191,295	36,954
	<u>\$ 666,607</u>	<u>\$ 498,079</u>

Interest income, net was \$0.2 million and \$1.1 million for three months ended September 30, 2021 and 2020, respectively, and \$0.7 million and \$3.2 million for the nine months ended September 30, 2021 and 2020, respectively.

No credit losses on debt securities were recorded during the nine months ended September 30, 2021 or 2020. In its evaluation to determine expected credit losses, management considered all available historical and current information, expectations of future economic conditions, the type of security, the credit rating of the security, and the size of the loss position, as well as other relevant information. The Company does not intend to sell, and is unlikely to be required to sell, any of these available-for-sale investments before their effective maturity or market price recovery.

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

***Fair value of financial liabilities:***

As of September 30, 2021, the fair value of our term loan approximated its carrying value of \$47.1 million based upon a market observable interest rate, which is a Level 2 input (see Note 6 – “Debt”).

As of September 30, 2021, the estimated fair value of our convertible notes was \$458.6 million and was based upon observable, Level 2 inputs, including pricing information from recent trades of the convertible notes (see Note 6 – “Debt”).

As of September 30, 2021, the fair value of the liability related to the sale of future royalties to RPI Finance Trust (“RPI”) is consistent with its carrying value of \$174.8 million, and is based on our current estimates of future royalties expected to be paid to RPI under the Royalty Purchase Agreement dated February 1, 2017 between us and RPI (the “RPI Royalty Purchase Agreement”), over the life of the arrangement, which are considered Level 3 inputs (See Note 7 – “Liability Related to Sale of Future Royalties”).

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

**Note 5 — Balance Sheet Components**

Accrued liabilities were as follows (in thousands):

	<u>September 30, 2021</u>	<u>December 31, 2020</u>
Accrued liabilities:		
Clinical and preclinical costs	\$ 15,054	\$ 6,124
Compensation related	11,749	11,787
Other accrued expenses	4,969	1,404
Total accrued liabilities	<u>\$ 31,772</u>	<u>\$ 19,315</u>

**Note 6 — Debt*****Term Loan***

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

On May 17, 2019, we entered into a new loan and security agreement (the “Term Loan Agreement”) with the Lenders for \$45.0 million (the “Term Loan”) and terminated the Original Loan Agreement. The proceeds of the Term Loan were used in part to repay in full all of the outstanding term loans under the Original Loan Agreement in an aggregate principal amount of \$42.0 million. On November 6, 2019 and November 7, 2019, the Company entered into a First Amendment and a Second Amendment to the Term Loan Agreement. The Term Loan Agreement, as amended, permits the issuance of the Convertible Notes and Capped Call Transactions discussed below. On July 16, 2020, the Company and the Lenders entered into the Third Amendment to the Term Loan Agreement, which amended the Term Loan Agreement to permit (i) the sale of the Mavacamten Royalty under the RTW Royalty Purchase Agreement and (ii) subject to entry into an intercreditor agreement between Oxford (as security agent for the Lenders) and RTW Royalty Holdings in form and substance reasonably satisfactory to the Lenders and RTW Royalty Holdings, permits the draw of funding under the Funding Agreement and the grant of a security interest to RTW Royalty Holdings in the intellectual property located in the United States and accounts receivable related to aficamten. On June 30, 2021, the Company and the Lenders entered into the Fourth Amendment to the Term Loan Agreement, which amended the Term Loan Agreement to permit the draw of funding for the finance lease obligations and purchase money may incur in the future not to exceed \$3.0 million in the aggregate. As of September 30, 2021, no draw has been made under the Fourth Amendment of the Term Loan Amendment.

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

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

Interest expense for the Term Loan was \$1.2 million for the three months ended September 30, 2021 and 2020, and \$3.6 million and \$3.7 million for the nine months ended September 30, 2021 and 2020, respectively. As of September 30, 2021, the interest rate applicable to borrowings under the Term Loan was 8.05%.

The Term Loan Agreement contains customary representations and warranties and customary affirmative and negative covenants applicable to us and includes customary events of default, including but not limited to the nonpayment of principal or interest, violations of covenants and material adverse changes. Upon an event of default, the Lenders may, among other things, accelerate the loans and foreclose on the collateral. Our obligations under the Term Loan Agreement are secured by substantially all our current and future assets, other than our intellectual property. If the Term Loan becomes subject to mandatory prepayment under these provisions, we are subject to certain prepayment premiums of 3.00% in the first year, 2.00% in the second year and 1.00% in the third year and thereafter. We determined that these contingent prepayment provisions were an embedded component that qualified as a derivative which should be bifurcated from the Term Loan and accounted for separately from the host contract. As of September 30, 2021, the fair value of this embedded derivative was immaterial.

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

**Years ending December 31:**

2021 remainder	\$	915
2022		25,330
2023		28,080
Future minimum payments		54,325
Less: Interest and final payment		(9,325)
Term Loan, gross	\$	45,000

**Convertible Notes**

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

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

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

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

Debt issuance costs for the issuance of the 2026 Notes were approximately \$5.0 million, consisting of initial purchasers' discount and other issuance costs. In accounting for the transaction costs, the Company allocated the total amount incurred to the liability and equity components using the same proportions as the proceeds from the 2026 Notes. Transaction costs attributable to the liability component were approximately \$3.1 million, were recorded as debt issuance cost (presented as contra debt in the consolidated balance sheet) and are being amortized to interest expense over the term of the 2026 Notes. The transaction costs attributable to the equity component were approximately \$1.9 million and were netted with the equity component in stockholders' equity. As of September 30, 2021, the unamortized debt issuance cost for the 2026 Notes was \$2.5 million.

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

	<b>Three Months Ended September 30, 2021</b>	<b>Nine Months Ended September 30, 2021</b>
Contractual interest expense	\$ 1,380	\$ 4,140
Amortization of debt discount	1,522	4,338
Amortization of debt issuance costs	15	43
<b>Total interest costs recognized</b>	<b>\$ 2,917</b>	<b>\$ 8,521</b>

The effective interest rate on the liability component of the 2026 Notes was 12.5% for the period ended September 30, 2021, which remains unchanged from the date of issuance. The remaining unamortized debt discount was \$41.6 million as of September 30, 2021 and will be amortized over approximately 5.2 years. If the 2026 Notes were to be converted on September 30, 2021, the holders of the 2026 Notes would receive common shares of 16.7 million with an aggregate value of \$596.0 million based on the Company's closing stock price of \$35.74 as of September 30, 2021. The if-converted value of the 2026 Notes exceeded its principal amount by \$458.0 million as of September 30, 2021.

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

**Years ending December 31:**

2021 remainder	\$	2,760
2022		5,520
2023		5,520
2024		5,520
2025		5,520
Thereafter		143,520
Future minimum payments		168,360
Less: Interest		(30,360)
The 2026 Notes, principal amount		138,000
Less: Debt discount and debt issuance costs on the 2026 Notes		(44,115)
Net carrying amount of the 2026 Notes	\$	93,885

***Capped Call Transactions***

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

Given that the transactions meet certain accounting criteria, the convertible note capped call transactions are recorded in stockholders' equity, and they are not accounted for as derivatives and are not remeasured each reporting period. As of September 30, 2021, the Company had not purchased any shares under the convertible note capped call transactions.

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

In February 2017, we entered into the RPI Royalty Purchase Agreement under which we sold a portion of our right to receive royalties on potential net sales of omecamtiv mecarbil (and potentially other compounds with the same mechanism of action) under the Amgen Agreement to RPI for a payment of \$90.0 million, which is non-refundable even if omecamtiv mecarbil is never commercialized. Concurrently, we entered into a common stock purchase agreement with RPI through which RPI 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 the liability related to the sale of future royalties (the "RPI Liability") and the common stock, which resulted in the RPI Liability being initially recognized at \$92.3 million.

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

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

The carrying amount of the RPI Liability is based on our estimate of the future royalties to be paid to RPI over the life of the arrangement as discounted using an imputed rate of interest. The excess of future estimated royalty payments over the \$92.3 million of allocated proceeds, less issuance costs, is recognized as non-cash interest expense using the effective interest method. The imputed rate of interest on the unamortized portion of the RPI Liability was approximately 7% as of September 30, 2021 and 15% as of December 31, 2020.

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

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

In the first quarter ended March 31, 2021, we updated our analyses to reflect current assumptions resulting from ongoing market research in the U.S. and to reflect other adjustments in connection with our anticipated commercialization plans in other key markets outside of the U.S. Our estimates regarding the amount of future royalty payments decreased and the time periods within which we anticipated that such payments will be due changed. Each of these adjustments was accounted for on a prospective basis in our liability calculation and resulted in a decline in our imputed interest rate and noncash interest expenses from 15% and \$5.7 million for the three months ended December 31, 2020 to 7% and \$2.8 million for the three months ended March 31, 2021, respectively. During the three months ended March 31, 2021, the change in estimate had no impact on revenue and reduced the net loss by \$2.9 million. The change in accounting estimate reduced the net loss per share by \$0.04 during the three months ended March 31, 2021. We review our assumptions on a quarterly basis and there were no other changes to the significant unobservable inputs since March 31, 2021. Our estimates may change in the future as we refine and reassess our assumptions.

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

	<b>2021</b>	<b>2020</b>
Beginning balance, January 1	\$ 166,068	\$ 143,276
Interest accretion	2,795	5,689
Amortization of issuance costs	27	18
Ending balance, March 31	168,890	148,983
Interest accretion	2,871	5,912
Amortization of issuance costs	29	19
Ending balance, June 30	171,790	154,914
Interest accretion	2,955	5,461
Amortization of issuance costs	30	20
Ending balance, September 30	<u>\$ 174,775</u>	<u>\$ 160,395</u>

We recognized \$3.0 million and \$5.5 million in non-cash interest expense for the three months ended September 30, 2021 and 2020, respectively, and \$8.6 million and \$17.1 million for the nine months ended September 30, 2021 and 2020, respectively, related to the RPI Agreement.

## **Note 8 — Stockholders' Equity**

### ***Warrants***

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

### ***Claims settlement***

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

### ***Performance Stock Units***

In May 2021, the Compensation and Talent Committee of the Company's Board of Directors ("the Compensation Committee") granted a total of 375,000 Performance Stock Units ("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 new drug application ("NDA") for omecamtiv mecarbil has been filed and accepted by the U.S. Food and Drug Administration ("FDA") 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 omecamtiv mecarbil in effect immediately prior to such approval. During the three and nine months ended September 30, 2021, the Company recognized expense of \$1.2 million and \$1.9 million, respectively, for the first tranche of PSUs. No expense has been recognized for the second tranche. The Company will assess the likelihood of achieving the performance conditions quarterly and the expense recognized will be adjusted accordingly.

### ***Public Offering of Common Stock***

In July 2021, we closed an underwritten public offering of 11,500,000 shares of our common stock at a public offering price of \$27.50, which included the exercise in full by the underwriters of their option to purchase up to 1,500,000 shares of our common stock at the same price. The gross proceeds were \$316.3 million and net proceeds were approximately \$296.9 million, after deducting the applicable underwriting discounts and commissions.

### ***Equity Incentive Plan***

In May 2019, the Company's stockholders approved an amendment to the Amended and Restated 2004 Equity Incentive Plan (the "2004 Plan") to increase the number of authorized shares reserved for issuance under the 2004 Plan by 4.1 million shares. In May 2020, the Company's board of directors approved an amendment to the 2004 Plan to increase the number of authorized shares reserved for issuance under the 2004 Plan by 0.8 million shares for inducement grants to new employees. In August 2021, the Company's board of directors approved another amendment to the 2004 plan and increased the number of shares reserved for issuance for inducement grants to new employees from the 0.8 million to 1.9 million. We started granting inducement grants in September 2020. As of September 30, 2021, 5.8 million authorized shares were available for grant under the 2004 Plan.

**Note 9 — Commitments and Contingencies****Leases**

In May 2021, we amended the lease agreement for buildings 250, 256 and 280 East Grand Avenue, South San Francisco, California for our existing facilities and extended the lease term until June 30, 2022, which was accounted for as a lease modification in accordance with Topic 842. Pursuant to such guidance, the Company remeasured the modified lease using the revised term as of the modification date. Adjustments were made to reflect the remeasured liability with the offset to the right-of-use asset. The lease includes rental payments and payment of certain operating expenses. Under the lease terms, we have minimum rental fee payment obligations of \$0.5 million per month through the remaining term. As of September 30, 2021, the remaining lease term is 0.8 years and the weighted average discount rate used to determine the operating lease liability was 11.5% for building 250 East Grand Avenue, South San Francisco and 6.8% for buildings 256 and 280 East Grand Avenue, South San Francisco.

In July 2019, we entered into a lease agreement for approximately 234,892 square feet of office and laboratory space at a facility located in South San Francisco, California and in May 2020 and January 2021, we entered into first and second amendments to the lease (collectively the “Oyster Point Lease”). The Oyster Point Lease commenced on March 31, 2021 and upon commencement, we recognized a right-of-use asset of \$77.9 million, a short-term lease liability of \$3.7 million and a long-term lease liability of \$85.3 million. The long-term lease liability includes \$11.1 million of tenant improvement reimbursements as of March 31, 2021. The Oyster Point Lease expires on September 30, 2033 and we have two consecutive five-year options to extend the lease. The options to extend the lease term were not included as part of the right-of-use asset or lease liability as the exercise of the options were not reasonably assured at the inception of the lease. We will be required to start making rent payments in October 2021. As of September 30, 2021, the remaining lease term of the Oyster Point Lease is 12.0 years and the discount rate used to determine the related lease liability was 9.8%. We paid a total security deposit of \$5.1 million in December 2019 and December 2020. The landlord will provide a tenant improvement allowance of \$43.6 million in aggregate for costs relating to the initial design and construction of the improvements. As of September 30, 2021, we had \$48.3 million in construction in progress related to the Oyster Point Lease and the total commitment of undiscounted lease payments for the Oyster Point Lease was \$230.5 million.

The undiscounted future non-cancellable lease payments under all our lease agreements as of September 30, 2021 is as follows (in thousands):

**Years ending December 31:**

2021 remainder	\$	2,635
2022		15,887
2023		17,107
2024		17,668
2025		18,249
Thereafter		163,434
Total undiscounted future lease payments		234,980
Less: Present value adjustments		(115,081)
Total lease liability	\$	119,899

As of September 30, 2021, the weighted average remaining lease term is 11.8 years and the weighted average discount rate used to determine the operating lease liability is 9.8%.

Cash paid for amounts included in the measurement of lease liabilities for the nine months ended September 30, 2021 and 2020 was \$4.4 million and \$5.2 million, respectively, and was included in net cash used in operating activities in our condensed consolidated statements of cash flows.

Rent expense was \$5.4 million and \$1.4 million for the three months ended September 30, 2021 and 2020, respectively, and \$12.2 million and \$4.2 million for the nine months ended September 30, 2021 and 2020, respectively.

As of September 30, 2021, we entered into a master lease agreement for equipment leases that have not yet commenced. The leases have an initial term of 3 years and are expected to commence between the fourth quarter of 2021 and the second quarter of 2022. The master lease agreement provides an option to extend the lease for one year, a purchase option with a bargain purchase price, and an option to return the leased equipment by entering a new equipment lease at the end of the term. The estimated aggregate lease obligation is approximately \$3.4 million, which is not included in the table above. We will pay certain operating costs of the leased equipment.

**ITEM 2. 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.

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

- guidance concerning revenues, research and development expenses and general and administrative expenses for 2021;
- the sufficiency of existing resources to fund our operations for at least the next 12 months;
- our capital requirements and needs for additional financing;
- our expectations as to our cash utilization for 2021 and afterwards;
- the initiation, design, conduct, enrollment, progress, timing and scope of clinical trials and development activities for our drug candidates conducted by ourselves or our partners, including the anticipated timing for initiation of clinical trials, including SEQUOIA-HCM, our planned Phase 3 clinical trial of aficamten (also known as CK-274) in patients with oHCM and COURAGE-ALS, our Phase 3 clinical trial of reldesemtiv in patients with ALS, anticipated rates of enrollment for clinical trials and anticipated timing of results becoming available or being announced from clinical trials;
- the results from the clinical trials, the non-clinical studies and chemistry, manufacturing, and controls activities of our drug candidates and other compounds, and the significance and utility of such results; anticipated interactions with regulatory authorities;
- our and our partners' plans or ability to conduct the continued research and development of our drug candidates and other compounds;
- the timing and likelihood of regulatory approval for omecamtiv mecarbil or any of our other drug candidates;
- 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;
- the sufficiency of the clinical trials conducted with our drug candidates to demonstrate that they are safe and efficacious;
- our receipt of milestone payments, royalties, reimbursements and other funds from current or future partners under strategic alliances;
- our ability to continue to identify additional potential drug candidates that may be suitable for clinical development;
- market acceptance of our drugs;
- changes in third party healthcare coverage and reimbursement policies;
- our plans or ability to commercialize drugs, with or without a partner, including our intention to develop sales and marketing capabilities;
- the focus, scope and size of our research and development activities and programs;
- the utility of our focus on the biology of muscle function, and our ability to leverage our experience in muscle contractility to other muscle functions;
- our ability to protect our intellectual property and to avoid infringing the intellectual property rights of others;
- future payments and other obligations under loan, lease agreements, and revenue interest agreement and the convertible notes;

- potential competitors and competitive products;
- retaining key personnel and recruiting additional key personnel; the potential impact of recent accounting pronouncements on our financial position or results of operations; and
- the continuing impact of the COVID-19 pandemic on our research and development activities and business operations.

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

- decisions by Ji Xing Pharmaceuticals Limited (“Ji Xing”) with respect to the timing, design and conduct of development and commercialization activities for aficanten in the People’s Republic of China (including the Hong Kong SAR and Macau SAR) (together “China”) and Taiwan;
- our ability to receive funds under the Funding Agreement, dated July 14, 2020 (the “Funding Agreement”) between us and RTW Royalty Holdings Designated Activity Company (“RTW Royalty Holdings”) or its assignee, RTW Investments ICAV for RTW Fund 1 (“RTW ICAV”), which is subject to certain conditions;
- decisions by the FDA or other regulatory authorities to condition our approval of omecamtiv mecarbil on the need or approval of a dosage selection test for the personalized dose optimization of omecamtiv mecarbil in patients, our ability or the ability of any third party to develop or commercialize such a dosage selection test, or the timing, prospects, process or likelihood of the approval of such a dosage selection test;
- 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 of our drug candidates and other compounds;
- the possibility that the U.S. Food and Drug Administration (the “FDA”) or foreign regulatory agencies may delay or limit our or our partners’ ability to conduct clinical trials or may delay or withhold approvals for the manufacture and sale of our products;
- changing standards of care and the introduction of products by competitors or alternative therapies for the treatment of indications we target that may limit the commercial potential of our drug candidates;
- difficulties or delays in achieving market access, reimbursement and favorable drug pricing for our drug candidates and the potential impacts of health care reform;
- changes in laws and regulations applicable to drug development, commercialization or reimbursement;
- the uncertainty of protection for our intellectual property, whether in the form of patents, trade secrets or otherwise;
- potential infringement or misuse by us of the intellectual property rights of third parties;
- activities and decisions of, and market conditions affecting, current and future strategic partners;
- accrual information provided by and performance of our contract research organizations (“CROs”), contract manufacturing organizations (“CMOs”), and other vendors;
- potential ownership changes under Internal Revenue Code Section 382; and
- the timeliness and accuracy of information filed with the U.S. Securities and Exchange Commission (the “SEC”) by third parties.

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

### **Business**

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

### **Overview**

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

Our clinical-stage drug candidates are: omecamtiv mecarbil, a novel cardiac myosin activator, CK-136 (formerly known as AMG 594), a novel cardiac troponin activator, reldesemtiv, a novel fast skeletal muscle troponin activator (“FSTA”), aficamten (also known as CK-3773274 or CK-274), a novel cardiac myosin inhibitor, and CK-3772271 (“CK-271”), our second novel cardiac myosin inhibitor.

Omecamtiv mecarbil was developed under a strategic alliance with Amgen Inc. (“Amgen”) and is being evaluated for the potential treatment of heart failure. We previously announced positive results from GALACTIC-HF (Global Approach to Lowering Adverse Cardiac Outcomes Through Improving Contractility in Heart Failure), a Phase 3 cardiovascular outcomes clinical trial of omecamtiv mecarbil in heart failure. Currently, we are conducting METEORIC-HF (Multicenter Exercise Tolerance Evaluation of Omecamtiv Mecarbil Related to Increased Contractility in Heart Failure), a second Phase 3 clinical trial intended to evaluate its potential to increase exercise performance.

CK-136 (formerly known as AMG 594) was discovered under our joint research program with Amgen. In collaboration with us, Amgen conducted a randomized, placebo-controlled, double-blind, single and multiple ascending dose, single-center Phase 1 study to assess the safety and tolerability, pharmacokinetics and pharmacodynamics of CK-136 in healthy subjects.

Aficamten (also known as CK-274) is a novel, oral, small molecule cardiac myosin inhibitor. 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 designed to reduce the hypercontractility that is associated with hypertrophic cardiomyopathy (“HCM”).

Aficamten is being evaluated in patients with symptomatic, obstructive HCM. Following the results of REDWOOD-HCM (Randomized Evaluation of Dosing With CK-274 in Obstructive Outflow Disease in HCM), a Phase 2 multicenter, randomized, placebo-controlled, double-blind, dose-finding clinical trial of aficamten, we are planning to commence SEQUOIA-HCM (Safety, Efficacy, and Quantitative Understanding of Obstruction Impact of Aficamten in HCM), the planned Phase 3 randomized, placebo-controlled, double-blind, multi-center clinical trial designed to evaluate *aficamten* in patients with symptomatic obstructive HCM on background medical therapy for 24 weeks.

CK-271 is our second novel, oral, small molecule cardiac myosin inhibitor. CK-271 produces reversible dose and plasma concentration-dependent reductions in cardiac contractility without affecting heart rate in preclinical models. CK-271 reduces compensatory cardiac hypertrophy and cardiac fibrosis in preclinical models of HCM and heart failure with preserved ejection fraction.

Reldesemtiv selectively activates the fast skeletal muscle troponin complex in the sarcomere by increasing its sensitivity to calcium, leading to an increase in skeletal muscle contractility. Reldesemtiv was developed under our joint development program with Astellas Pharma Inc. (“Astellas”).

In collaboration with Astellas, we conducted a Phase 2 clinical trial of reldesemtiv in patients with spinal muscular atrophy (“SMA”) and a Phase 2 clinical trial of reldesemtiv in patients with amyotrophic lateral sclerosis (“ALS”), called FORTITUDE-ALS (Functional Outcomes in a Randomized Trial of Investigational Treatment with CK-2127107 to Understand Decline in Endpoints – in ALS). Astellas, in collaboration with us, conducted a Phase 2 clinical trial of reldesemtiv in patients with chronic obstructive pulmonary disease (“COPD”) and a Phase 1b clinical trial of reldesemtiv in elderly subjects with limited mobility. COURAGE-ALS (Clinical Outcomes Using Reldesemtiv on ALSFRS-R in a Global Evaluation in ALS) is our Phase 3 clinical trial of reldesemtiv in patients with ALS.

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

## **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 for the three months ended September 30, 2021 and 2020 were \$48.4 million and \$24.2 million, respectively, and \$116.4 million and \$67.7 million for the nine months ended September 30, 2021 and 2020, respectively.

### ***Cardiac Muscle Program***

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

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

#### Amgen Strategic Alliance

Our strategic alliance with Amgen to discover, develop, and commercialize novel small molecule therapeutics designed to activate cardiac muscle, including omecamtiv mecarbil, for the potential treatment of heart failure was governed by the collaboration and option agreement dated December 29, 2006, as amended (the “Amgen Agreement”). Prior to the effective termination of the Amgen Agreement, Amgen had exclusive, worldwide rights to develop and commercialize omecamtiv mecarbil and related compounds subject to our specified development and commercial participation rights. Amgen also entered an alliance with Les Laboratoires Servier and Institut de Recherches Internationales Servier (“Servier”) for exclusive commercialization rights for omecamtiv mecarbil in Europe as well as the Commonwealth of Independent States (“CIS”), including Russia; Servier has contributed funding for development and provides strategic support to the program.

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

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

On December 23, 2020, we announced that Amgen notified us that Servier elected to terminate the sublicense agreement between Amgen and Servier for the development and commercialization of omecamtiv mecarbil in Europe and the Commonwealth of Independent States, including Russia (the “Servier Agreement”). The termination was effective as of March 18, 2021, at which time all development, commercialization and other rights with respect to omecamtiv mecarbil previously granted by Amgen to Servier reverted to Amgen.

The termination of the Amgen Agreement was effective May 20, 2021, at which time worldwide rights related to the development and commercialization of omecamtiv mecarbil and CK-136 (formerly AMG 594) reverted to Cytokinetics. Cytokinetics and Amgen have entered into several agreements to facilitate the transition of the programs for omecamtiv mecarbil and CK-136 to Cytokinetics, including an agreement for the sale and purchase of approximately 2.0 tons of active pharmaceutical ingredient of omecamtiv mecarbil.

We have engaged and will continue to engage with regulatory authorities in 2021 regarding the results of GALACTIC-HF with the objective to assess potential regulatory paths for new drug application (“NDA”) submission for omecamtiv mecarbil and concurrently we are continuing our commercial planning activities. Finally, we are evaluating a wide range of corporate development strategies for potential co-development, co-commercialization and licensing deals in relation to omecamtiv mecarbil and our other drug candidates in order to mitigate the cost effects of the termination of the Amgen Agreement and Servier Agreement and enhance our commercial capabilities.

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

### Omecamtiv mecarbil

Our lead drug candidate from our cardiac contractility program is omecamtiv mecarbil, a novel cardiac myosin activator. We are developing omecamtiv mecarbil as a potential treatment across the continuum of care in heart failure both for use in the hospital setting and for use in the outpatient setting.

#### *Omecamtiv mecarbil: Clinical Development*

**GALACTIC-HF:** GALACTIC-HF is a Phase 3 cardiovascular outcomes clinical trial of omecamtiv mecarbil which was conducted by Amgen, in collaboration with Cytokinetics. The primary objective of this double-blind, randomized, placebo-controlled multicenter clinical trial is to determine if treatment with omecamtiv mecarbil when added to standard of care is superior to standard of care plus placebo in reducing the risk of cardiovascular death or heart failure events in patients with high risk chronic heart failure and reduced ejection fraction. GALACTIC-HF was conducted under a Special Protocol Assessment (“SPA”) with the FDA. GALACTIC-HF completed enrollment in mid-2019, having enrolled 8,256 symptomatic chronic heart failure patients with reduced ejection fraction in over 1,000 sites in 35 countries who were either currently hospitalized for a primary reason of heart failure or had had a hospitalization or admission to an emergency room for heart failure within one year prior to screening. Patients were randomized to either placebo or omecamtiv mecarbil with dose titration up to a maximum dose of 50 mg twice daily based on the plasma concentration of omecamtiv mecarbil after initiation of drug therapy. The primary endpoint is a composite of time to cardiovascular death or first heart failure event, whichever occurs first, with heart failure event defined as hospitalization, emergency room visit, or urgent unscheduled clinic visit for heart failure. Secondary endpoints include time to cardiovascular death; patient reported outcomes as measured by the Kansas City Cardiomyopathy Questionnaire Total Symptom Score; time to first heart failure hospitalization; and time to all-cause death.

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

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

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

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

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

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

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

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

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

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

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

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

On May 17, 2021, at the American College of Cardiology 70th Annual Scientific Session, we announced data from a secondary analysis of GALACTIC-HF assessing the effect of omecamtiv mecarbil on clinical outcomes in relationship to patient baseline ejection fraction. The analysis evaluated 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.

On June 30, 2021, at the European Society of Cardiology-Heart Failure Congress, we announced additional analyses from GALACTIC-HF demonstrating patients with atrial fibrillation or flutter have increased treatment effect with omecamtiv mecarbil; patients with higher baseline NT-proBNP have increased treatment effect with omecamtiv mecarbil; and patients with severe heart failure have increased treatment effect with omecamtiv mecarbil.

We are continuing to review prespecified analyses and supplemental analyses of results of GALACTIC-HF. In addition, we have engaged and will continue engaging regulatory authorities in 2021 with the objective to assess potential regulatory paths and continuing our commercial planning activities.

On September 12, 2021, we announced that additional results from GALACTIC-HF assessing the effect of omecamtiv mecarbil in Black patients with HFrEF were presented in a late breaking clinical trial session at the HFSA Annual Scientific Meeting. Specifically, it was presented that of the 8,256 patients enrolled in the trial, 562 were Black (6.8%) and 285 were randomized to receive treatment with omecamtiv mecarbil. Among Black patients, 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.

**METEORIC-HF:** We are conducting METEORIC-HF, a second Phase 3 clinical trial intended to evaluate its potential to increase exercise performance. Patients are being randomized in a 2:1 fashion to omecamtiv mecarbil, which is started at 25 mg twice daily and titrated to 25, 37.5 or 50 mg twice daily based on the same pharmacokinetics-guided dosing regimen as is used in GALACTIC-HF, or to placebo. METEORIC-HF is planned to enroll approximately 270 symptomatic chronic heart failure patients in nine countries. The primary endpoint of METEORIC-HF is change in peak oxygen uptake on Cardio-Pulmonary Exercise Testing (“CPET”) from baseline to Week 20. Secondary endpoints include change in total workload during CPET from baseline to Week 20, change in ventilatory efficiency during CPET from baseline to Week 20 and change in the average daily activity units measured over 2 weeks from baseline to Week 18-20. After temporarily suspending enrollment in METEORIC-HF due to the COVID-19 pandemic earlier this year, we resumed enrollment in June 2020. On June 15, 2021 we announced that patient enrollment had been completed for METEORIC-HF.

#### *Omecamtiv mecarbil: Microgenics Immunoassay Development*

Amgen and Microgenics Corporation (“Microgenics”) are parties to that certain Collaborative Development and Commercialization Agreement, dated July 26, 2012 (as amended from time to time, the “Assay Agreement”), for the development of an antibody-based immunoassay (the “Microgenics OM Assay”) used for the in vitro measurement of concentrations of omecamtiv mecarbil in human blood and other bodily fluids, as well as related calibrator and controls, based on immunoassay technologies developed by Microgenics and its affiliates suitable for application on automated chemistry analyzers. The Microgenics OM Assay was intended to ensure personalized dose optimization of omecamtiv mecarbil in patients being treated. The Microgenics OM Assay was utilized in both GALACTIC-HF and METEORIC-HF to enable optimal dose titration in patients. We have been informed by Amgen that the Assay Agreement terminated contemporaneously with the termination of the Amgen Agreement. Consequently, we are pursuing the development and/or usage of alternative dosage selection tests to the Microgenics OM Assay to be used for personalized dose optimization of omecamtiv mecarbil if required by FDA or other regulatory authorities in order to obtain marketing approval of omecamtiv mecarbil.

#### *CK-136 (formerly known as AMG 594)*

CK-136 is a novel, selective, oral, small molecule cardiac troponin activator which was discovered under our joint research program with Amgen. In preclinical models, CK-136 increases myocardial contractility by binding to cardiac troponin through an allosteric mechanism that sensitizes the cardiac sarcomere to calcium, facilitating more actin-myosin cross bridge formation during each cardiac cycle thereby resulting in increased myocardial contractility. Similar to cardiac myosin activation, preclinical research has shown that cardiac troponin activation does not change the calcium transient of cardiac myocytes.

In 2020, we announced that preclinical data were presented at the Keystone Symposium “Charting a New Course for Heart Failure: From Discovery to Data,” demonstrating that CK-136 selectively increases calcium sensitivity of cardiac muscle fibers and increases cardiac contractility.

### *CK-136: Clinical Development*

In collaboration with Cytokinetics, Amgen conducted a randomized, placebo-controlled, double-blind, single and multiple ascending dose, single-center Phase 1 study to assess the safety and tolerability, pharmacokinetics and pharmacodynamics of CK-136 in healthy subjects. As a result of the effective termination of the Amgen Agreement on May 20, 2021, worldwide rights related to the development and commercialization of CK-136 reverted to Cytokinetics, and Cytokinetics and Amgen have entered into several agreements to facilitate the transition of the CK-136 program to Cytokinetics.

### *Aficamten (also known as CK-274)*

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’ industry-leading 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.

### *Aficamten: Clinical Development*

We conducted a Phase 1 double-blind, randomized, placebo-controlled, multi-part, single and multiple ascending dose clinical trial of CK-274 to assess the safety and tolerability, pharmacokinetics and pharmacodynamics of aficamten in healthy subjects. In September 2019 we presented data from the Phase 1 study of CK-274 at the HFSA 23rd Annual Scientific Meeting in Philadelphia. The study met its primary and secondary objectives to assess the safety and tolerability of single and multiple oral doses of aficamten, describe the pharmacokinetics of CK-274 and its pharmacodynamic effects as measured by echocardiography, as well as to characterize the PK/PD relationship with regards to cardiac function. These data support the advancement of aficamten into a Phase 2 clinical trial in patients with obstructive HCM (REDWOOD-HCM), which started in the first quarter of 2020 and will continue to be conducted in 2021.

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

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

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

Based on the interim analysis of data from Cohort 1 of REDWOOD-HCM, the steering committee and the data monitoring committee of REDWOOD-HCM recommended that the trial proceed to Cohort 2. Enrollment in Cohort 2 of REDWOOD-HCM completed in the first quarter of 2021. Full results from REDWOOD-HCM across both Cohort 1 and Cohort 2 are expected in mid-2021.

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

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

On April 12, 2021, we announced that data related to the optimization of aficamten, including the first disclosure of its chemical structure, were presented at the American Chemical Society Spring 2021 Virtual Meeting.

On May 4, 2021, we announced the opening of enrollment in Cohort 3 of REDWOOD-HCM. Cohort 3 will enroll 8-12 patients whose background therapy includes disopyramide to assess the safety, tolerability and pharmacokinetic effects of aficamten in patients taking disopyramide.

On May 6, 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 CK-274 in patients with symptomatic obstructive HCM (“oHCM”). Eligible patients have completed participation in REDWOOD-HCM, the Phase 2 clinical trial of aficamten.

On July 19, 2021, we announced positive topline results of Cohorts 1 and 2 of REDWOOD-HCM. Specifically, results from Cohorts 1 and 2 of REDWOOD-HCM demonstrated that treatment with aficamten for 10 weeks resulted in statistically significant reductions from baseline compared to placebo in the average resting left ventricular outflow tract pressure gradient (“LVOT-G”) ( $p=0.0003$ ,  $p=0.0004$ , Cohort 1 and Cohort 2, respectively) and the average post-Valsalva LVOT-G ( $p=0.001$ ,  $p<0.0001$ , Cohort 1 and Cohort 2, respectively). The majority of patients treated with aficamten (78.6% in Cohort 1 and 92.9% in Cohort 2) achieved the target goal of treatment, defined as resting gradient  $<30$  mmHg and post-Valsalva gradient  $<50$  mmHg at Week 10 compared to placebo (7.7%). Reductions in LVOT-G occurred within two weeks of initiating treatment with aficamten, were maximized within two to six weeks of the start of dose titration, and were sustained until the end of treatment at 10 weeks. The observed reductions in LVOT-G were dose dependent, with patients achieving greater reductions of LVOT-G with increasing doses of aficamten. Treatment with aficamten in REDWOOD-HCM was generally well tolerated. The incidence of adverse events was similar between treatment arms. No serious adverse events were attributed to aficamten and no treatment interruptions occurred on aficamten. No new cases of atrial fibrillation in patients treated with aficamten were reported. In this dose-range finding trial, one patient experienced a transient decrease in LVEF that required dose adjustment but not dose interruption. LVEF returned to baseline within two weeks after the end of treatment in both cohorts, which was consistent with the reversibility of LVEF decreases that were similarly observed in healthy participants in the Phase 1 study of aficamten.

On September 12, 2021, we announced that the primary results of REDWOOD-HCM were presented in a late breaking clinical trial session at the HFSA Annual Scientific Meeting.

Reductions in LVOT-G occurred within two weeks of initiating treatment with *aficamten*, were maximized within two to six weeks of the start of dose titration and were sustained until the end of treatment at 10 weeks. Reversibility of the pharmacodynamic effect of *aficamten* was seen after a two-week washout, with resting LVOT-G, post-Valsalva LVOT-G, NT-proBNP and LVEF returning to baseline values. The observed reductions in LVOT-G were dose dependent, with patients achieving greater reductions of LVOT-G with increasing doses of *aficamten*. Over the 10-week study period, patients treated with *aficamten* in both Cohort 1 and Cohort 2 also experienced statistically significant reductions in NT-proBNP ( $p=0.003$ ). Treatment with *aficamten* was also associated with an improvement in heart failure functional class as measured by New York Heart Association (NYHA) class. Improvement by at least one class was achieved by 31% in the placebo group, 43% of patients in Cohort 1 ( $p>0.1$ ) and 64% of patients in Cohort 2 ( $p=0.08$ ).

On October 7, 2021, we announced the design of SEQUOIA-HCM. SEQUOIA-HCM is 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 is to assess the effect of *aficamten* on change in peak oxygen uptake ( $pVO_2$ ) measured by cardiopulmonary exercise testing (CPET) from baseline to week 24. Secondary objectives include change in Kansas City Cardiomyopathy Questionnaire (KCCQ) score from baseline to week 12 and week 24, the proportion of patients with  $\geq 1$  class improvement in New York Heart Association (NYHA) functional class from baseline to week 12 and week 24, change in post-Valsalva left ventricular outflow tract gradient (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.

SEQUOIA-HCM is planned to enroll 270 patients, randomized on a 1:1 basis to receive *aficamten* or placebo in addition to standard-of-care treatment. Each patient will receive up to four escalating doses of *aficamten* or placebo based on echocardiographic guidance alone. At screening, patients enrolled in SEQUOIA-HCM must have a resting LVOT-G  $\geq 30$  mmHg, post-Valsalva peak LVOT-G  $\geq 50$  mmHg, and be NYHA Class II or III. Patients receiving *aficamten* will begin with 5 mg dosed once daily. At weeks 2, 4 and 6 patients will receive an echocardiogram to determine if they will be up-titrated to escalating doses of 10, 15 or 20 mg. Dose escalation will occur only if a patient has a post-Valsalva LVOT-G  $\geq 30$  mmHg and a biplane left ventricular ejection fraction (LVEF)  $\geq 55\%$ . Patients who do not meet escalation criteria will continue to receive their current dose or may be down-titrated if appropriate. Study start up, regulatory filings, and IRB submissions are underway, with the first site initiations already completed. Drug product availability in early 2022 will enable the commencement of screening and enrollment of the first patients in this trial at that time.

#### *Ji Xing Strategic Alliance*

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

#### *CK-271*

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

#### ***Skeletal Muscle Contractility Program***

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

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

### *Astellas Strategic Alliance*

Our strategic alliance with Astellas to advance novel therapies for diseases and medical conditions associated with muscle impairment and weakness commenced in 2013 under the License and Collaboration Agreement, dated June 21, 2013 between the parties (the “Astellas Agreement”). Initially we exclusively licensed to Astellas rights to co-develop and potentially co-commercialize reldesemtiv and other FSTAs in non-neuromuscular indications and to develop and commercialize other novel mechanism skeletal muscle activators in all indications, subject to certain Cytokinetics’ development and commercialization rights. Subsequently, in 2014, we and Astellas expanded the strategic alliance to include certain neuromuscular indications, including SMA, for reldesemtiv and other FSTAs and to advance reldesemtiv into Phase 2 clinical development, initially in SMA. In 2016, we and Astellas further expanded the strategic alliance to include the development of reldesemtiv for the potential treatment of ALS, as well as the possible development in ALS of other FSTAs previously licensed by us to Astellas.

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

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

Cytokinetics and Astellas also signed a License and Collaboration Agreement for Other Skeletal Sarcomere Activators, dated April 23, 2020 (the “Astellas OSSA Agreement”). The Astellas OSSA Agreement is an amendment and restatement of the Astellas Agreement and removes the FSRA compounds and related products from the collaboration.

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

On April 27, 2021, we received written notice of termination from Astellas of the Astellas OSSA Agreement, which is effective as of November 1, 2021.

Under the terms of the Astellas OSSA Agreement, Astellas received exclusive rights to co-develop and commercialize skeletal sarcomere activators (other than FSRA compounds and products) in all indications, subject to certain development and commercialization rights of Cytokinetics; Cytokinetics had the right to co-promote and conduct certain commercial activities in the U.S., Canada and/or Europe under agreed scenarios. If development candidates were identified and advance in clinical research, the Agreement contained provisions related to shared development roles between Cytokinetics and Astellas, and opportunities for Cytokinetics to co-invest and/or co-promote under certain conditions. In the case of development candidates taken forward solely by Astellas, Cytokinetics would have received development and regulatory milestones of \$25 to \$35 million per product, up to \$250 million for all products, except under certain scenarios, commercial milestones of up to \$200 million, and royalties that ranged from a mid-single digit level to low double-digits. In the event of co-investment by Cytokinetics and approvals in certain indications, Cytokinetics would have received royalties ranging from mid-to-high double digits (not to exceed an incremental rate in the mid-twenties).

Pursuant to the terms of the Agreement, upon the effective date of the termination, all licenses and other rights granted to Astellas under the Astellas OSSA Agreement will terminate.

### Reldesemtiv

Reldesemtiv selectively activates the fast skeletal muscle troponin complex in the sarcomere by increasing its sensitivity to calcium, leading to an increase in skeletal muscle contractility. Reldesemtiv has demonstrated pharmacological activity in preclinical models and evidence of potentially clinically relevant pharmacodynamic effects in humans. The FDA granted reldesemtiv orphan drug designation for the potential treatment of SMA in 2017 and for the potential treatment of ALS in 2019. The European Medicines Agency (“EMA”) granted orphan medicinal product designation to reldesemtiv for the potential treatment of SMA in July 2019 and for the potential treatment of ALS in March 2020.

#### *Reldesemtiv: Clinical Development*

**SMA:** In 2018, we announced data from a hypothesis-generating, Phase 2 double-blind, randomized, placebo-controlled clinical study in patients with SMA which was designed to determine potential pharmacodynamic effects of a suspension formulation of reldesemtiv following 8 weeks of oral dosing in each of two cohorts of 36 patients with Type II, Type III, or Type IV disease. Secondary objectives were to evaluate the safety, tolerability and pharmacokinetics of reldesemtiv. The study showed statistically significant concentration-dependent increases in changes from baseline in Six Minute Walk Distance (“6MWD”), a sub-maximal exercise test of aerobic capacity and endurance. The study also showed statistically significant increases for Maximal Expiratory Pressure (“MEP”), a measure of strength of respiratory muscles. Other assessments, including the Hammersmith Functional Motor Score – Extended, Revised Upper Limb Module, Timed Up-and-Go, Forced Vital Capacity, and the SMA Health Index (“SMA-HI”), a patient reported outcome measure (“PROM”) developed to comply with FDA standards for PROMs, did not demonstrate differences between reldesemtiv versus placebo. Adverse events were similar between groups receiving reldesemtiv and placebo.

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

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

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

**ALS:** In collaboration with Astellas, we conducted FORTITUDE-ALS (Functional Outcomes in a Randomized Trial of Investigational Treatment with CK-2127107 to Understand Decline in Endpoints – in ALS). This Phase 2 trial enrolled 458 eligible ALS patients who were randomized (1:1:1:1) to receive either 150 mg, 300 mg or 450 mg of reldesemtiv or placebo dosed orally twice daily for 12 weeks. The primary efficacy endpoint of FORTITUDE-ALS was the change from baseline in the percent predicted slow vital capacity (“SVC”) at 12 weeks. Secondary endpoints included slope of the change from baseline in the mega-score of muscle strength measured by hand held dynamometry and handgrip dynamometry in patients on reldesemtiv; change from baseline in the ALS Functional Rating Scale – Revised (“ALSFRS-R”); incidence and severity of treatment-emergent adverse events; and plasma concentrations of reldesemtiv at the sampled time points during the study. Exploratory endpoints measured included the effect of reldesemtiv versus placebo on self-assessments of respiratory function made at home by the patient with help as needed by the caregiver; disease progression through quantitative measurement of speech production characteristics over time; disease progression through quantitative measurement of handwriting abilities over time; and the change from baseline in quality of life (as measured by the ALS Assessment Questionnaire-5) in patients on reldesemtiv.

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

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

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

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

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

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

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

On August 2, 2021 we announced that COURAGE-ALS is open to enrollment.

### *Next Generation Fast Skeletal Muscle Troponin Activators*

In 2018, we announced the advancement of CK-601, a next-generation FSTA, into IND-enabling studies, which triggered a \$2.0 million milestone payment from Astellas to us. CK-601 was designed in a joint research program conducted by the companies' scientists to have different pharmacokinetics and physicochemical properties than reldesemtiv which may inform its development for the treatment of diseases and conditions associated with both neuromuscular and non-neuromuscular etiology and pathogenesis.

### *Ongoing Research in Skeletal Muscle Activators*

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 skeletal or cardiac muscle contractility and to apply those findings to the further evaluation of our drug candidates in clinical populations. In addition to contractility, other major functions of muscle play a role in certain diseases that could benefit from novel mechanism treatments. Accordingly, our knowledge of muscle contractility may serve as an entry point to the discovery of novel treatments for disorders involving muscle functions other than muscle contractility. We are leveraging our current understandings of muscle biology to investigate new ways of modulating these other aspects of muscle function for other potential therapeutic applications.

### **COVID-19 Business Update**

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

Based on guidance issued by federal, state and local authorities, we transitioned to a remote work model for a vast majority of our employees effective March 16, 2020, while maintaining certain essential in-person laboratory functions in order to advance key research and development initiatives, supported by the implementation of updated onsite procedures. We have since implemented a voluntary return to work for our employees subject to precautionary measures such as mandatory temperature checks for those employees that do work on site from time to time. We are currently accommodating both our employees who wish to work onsite on a several days per week basis and those employees who wish to work entirely remotely. We expect our employees to be returning to onsite work in larger numbers over the next few months and that the vast majority will have chosen to be vaccinated against COVID-19. We will continue to monitor the evolution of the pandemic and take appropriate precautionary actions in accordance with applicable laws and guidelines.

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

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

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

## Critical Accounting Policies and Significant Estimates

The accounting policies that we consider to be our most critical (i.e., those that are most important to the portrayal of our financial condition and results of operations and that require our most difficult, subjective or complex judgments), the effects of those accounting policies applied and the judgments made in their application are summarized in “Item 7 — Management’s Discussion and Analysis of Financial Condition and Results of Operations — Critical Accounting Policies and Significant Estimates” in our Annual Report on Form 10-K for the fiscal year ended December 31, 2020.

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.

## Recent Accounting Pronouncements

See Note 1, “Recent Accounting Pronouncements” in the Notes to Unaudited Condensed Consolidated Financial Statements for a discussion of recently adopted accounting pronouncements and accounting pronouncements not yet adopted, and their expected impact on our financial position and results of operations.

## Results of Operations

### Revenues

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

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

Revenues for the three and nine months ended September 30, 2021 and 2020, were as follows (in thousands):

	Three Months Ended			Nine Months Ended		
	September 30, 2021	September 30, 2020	Increase (Decrease)	September 30, 2021	September 30, 2020	Increase (Decrease)
Research and development revenues	\$ 437	\$ 5,187	\$ (4,750)	\$ 9,828	\$ 12,605	\$ (2,777)
License revenues	—	36,501	(36,501)	—	36,501	(36,501)
Milestone revenues	5,000	—	5,000	5,000	—	5,000
Total revenues	\$ 5,437	\$ 41,688	\$ (36,251)	\$ 14,828	\$ 49,106	\$ (34,278)

Research and development revenues were \$0.4 million and \$5.2 million for the three months ended September 30, 2021 and 2020, respectively, and \$9.8 million and \$12.6 million for the nine months ended September 30, 2021 and 2020, respectively. Research and development revenues primarily consisted of research and development revenue from our collaborations with Amgen of zero and \$3.8 million for the three months ended September 30, 2020, and \$7.4 million and \$8.3 million for the nine months ended September 30, 2021 and 2020, respectively, and Astellas of \$0.5 million and \$1.4 million for the three months ended September 30, 2021 and 2020, respectively, and \$2.5 million and \$4.0 million for the nine months ended September 30, 2021 and 2020, respectively.

We recognized a \$5.0 million milestone from Ji Xing as of September 30, 2021 for initiation of a phase 3 clinical trial for aficamten in obstructive HCM. Although our contractual right to payment has not yet arisen under the Ji Xing License Agreement, we determined recognition of the milestone in accordance with ASC 606 during the third quarter of 2021 was appropriate based on our expected initiation of a phase 3 clinical trial of aficamten in obstructive HCM.

There were no license revenues for the three and nine months ended September 30, 2021. License revenues for the three and nine months ended September 30, 2020 was the result of the Ji Xing License Agreement, pursuant to which we granted to Ji Xing an exclusive license to develop and commercialize CK-274 in the greater China region. Under the terms of the Ji Xing License Agreement, we received from Ji Xing a nonrefundable upfront payment of \$25.0 million. License revenues for the three and nine months ended September 30, 2020 was \$36.5 million and consisted of the residual allocation of consideration from the RTW transactions.

We expect future revenues from Amgen and Astellas to decline due to the termination of the Amgen Agreement effective May 20, 2021, and Astellas OSSA Agreement effective November 1, 2021.

### **Research and Development Expenses**

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

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

Research and development expenses for the three and nine months ended September 30, 2021 and 2020, were as follows (in thousands):

	<b>Three Months Ended</b>			<b>Nine Months Ended</b>		
	<b>September 30, 2021</b>	<b>September 30, 2020</b>	<b>Increase</b>	<b>September 30, 2021</b>	<b>September 30, 2020</b>	<b>Increase</b>
Cardiac muscle contractility	\$ 34,189	\$ 14,167	\$ 20,022	\$ 76,601	\$ 39,048	\$ 37,553
Skeletal muscle contractility	6,034	3,247	2,787	17,484	8,309	9,175
All other research programs	8,213	6,788	1,425	22,355	20,373	1,982
Total research and development expenses	<u>\$ 48,436</u>	<u>\$ 24,202</u>	<u>\$ 24,234</u>	<u>\$ 116,440</u>	<u>\$ 67,730</u>	<u>\$ 48,710</u>

Research and development expenses for the three and nine months ended September 30, 2021 increased by \$24.2 million and \$48.7 million from the three and nine months ended September 30, 2020, respectively, primarily due to higher expenses for our clinical development activities for our cardiac muscle inhibitor programs and COURAGE-ALS. In addition, for the three and nine months ended September 30, 2021, we incurred transition costs related to the termination of our collaboration with Amgen and our purchase from Amgen of approximately \$7.3 million and \$14.6 million, respectively, of materials including manufactured quantities of the active pharmaceutical ingredient for omecamtiv mecarbil.

We continue to develop reldesemtiv to treat ALS and we recently announced that COURAGE-ALS, the Phase 3 clinical trial of reldesemtiv in patients with ALS, is open to enrollment. We may also continue to develop reldesemtiv to treat SMA. Under the Astellas FSRA Agreement, Astellas has agreed to pay one-third of the out-of-pocket clinical development costs which may be incurred in connection with Cytokinetics' Phase 3 clinical trial, COURAGE-ALS, of reldesemtiv in ALS up to a maximum contribution by Astellas of \$12.0 million.

Under our strategic alliance with Amgen, Amgen was responsible for the development of omecamtiv mecarbil until the effective termination of the Amgen Agreement (May 20, 2021). Following the effective termination of the Amgen Agreement, we expect to continue the Phase 3 development of omecamtiv mecarbil for the potential treatment of heart failure, at our own cost. We expect to continue the development of aficamten to assess the potential of aficamten to improve exercise capacity and relieve symptoms in patients with hyperdynamic ventricular contraction due to HCM. Under our strategic alliance with Ji Xing, Ji Xing is responsible for the development of aficamten in China and Taiwan, and we may be entitled to receive milestone payments upon the achievement of certain development and commercial milestones.

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

**General and Administrative Expenses**

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

General and administrative expenses for the three and nine months ended September 30, 2021 and 2020, were as follows (in thousands):

	Three Months Ended			Nine Months Ended		
	September 30, 2021	September 30, 2020	Increase	September 30, 2021	September 30, 2020	Increase
Total general and administrative expenses	\$ 26,202	\$ 12,302	\$ 13,900	\$ 62,997	\$ 38,912	\$ 24,085

General and administrative expenses for the three and nine months ended September 30, 2021 increased by \$13.9 million and \$24.1 million, from the three and nine months ended September 30, 2020, respectively, primarily due to higher outside service spend in anticipation of the potential commercial launch of omecantiv mecarbil, an increase in personnel related costs including stock-based compensation and facilities expense due to the Oyster Point Lease recorded at the end of the first quarter of 2021.

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

**Interest expense**

Interest expense for the three and nine months ended September 30, 2021 and 2020, were as follows (in thousands):

	Three Months Ended			Nine Months Ended		
	September 30, 2021	September 30, 2020	Increase (Decrease)	September 30, 2021	September 30, 2020	Increase (Decrease)
Term loan	\$ 1,214	\$ 1,217	\$ (3)	\$ 3,615	\$ 3,667	\$ (52)
Convertible notes	2,917	2,739	178	8,521	8,037	484
Warrants	—	—	—	—	184	(184)
Other	30	20	10	86	57	29
Total interest expense	\$ 4,161	\$ 3,976	\$ 185	\$ 12,222	\$ 11,945	\$ 277

Interest expense for the three and nine months ended September 30, 2021 and 2020 consists of interest expense related to the Term Loan Agreement and respective warrants by and among the Company, Oxford and Silicon Valley Bank and interest expense related to our 4.0% convertible senior notes due 2026 (the "2026 Notes"). Approximately half of the 2026 Notes' interest expense is due to the amortization of the discount associated with the equity component of the 2026 Notes.

Interest expense for the three and nine months ended September 30, 2021 increased from the three and nine months ended September 30, 2020 due to the convertible notes that were issued in November 2019 offset slightly due to the lack of warrant expense in 2021.

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

Non-cash interest expense related to our liability to RPI related to the sale of future royalties under the RPI Royalty Purchase Agreement (the “RPI Liability”) related to sale of future royalties for the three and nine months ended September 30, 2021 and 2020 results from accretion of the liability related to sale of future royalties. In the first quarter ended March 31, 2021, we updated our analyses in the first quarter of 2021 to reflect our current assumptions resulting from ongoing market research in the U.S. and to reflect other adjustments in connection with our anticipated commercialization plans in other key markets outside of the U.S. Our estimates regarding the amount of future royalty payments decreased and the time periods within which we anticipated that such payments will be due changed. Each of these adjustments is accounted for on a prospective basis in our liability calculation and resulted in a decline in our imputed interest rate and noncash interest expenses from 15% and \$5.7 million for the three months ended December 31, 2020 to 7% and \$8.6 million for the nine months ended September 30, 2021, respectively. During the nine months ended September 30, 2021, the change in estimate had no impact on revenue and reduced the net loss by \$2.9 million. The change in accounting estimate reduced the net loss per share by \$0.04 during the nine months ended September 30, 2021. We review our assumptions on a quarterly basis and there were no other changes to the significant unobservable inputs since March 31, 2021. Our estimates may change in the future as we refine and reassess our assumptions.

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

Non-cash interest expense on liability related to the RPI Agreement for the three and nine months ended September 30, 2021 and 2020, were as follows (in thousands):

	Three Months Ended			Nine Months Ended		
	September 30, 2021	September 30, 2020	Decrease	September 30, 2021	September 30, 2020	Decrease
Non-cash interest expense recognized	\$ 2,955	\$ 5,461	\$ (2,506)	\$ 8,621	\$ 17,062	\$ (8,441)

### Interest and Other Income, net

Interest and other income, net for the three and nine months ended September 30, 2021 and 2020 primarily consisted 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:

	September 30, 2021	December 31, 2020
<b>Financial assets:</b>		
Cash and cash equivalents	\$ 90,562	\$ 82,985
Short-term investments	387,074	381,075
Long-term investments	191,295	36,954
Total cash, cash equivalents and marketable securities	<u>\$ 668,931</u>	<u>\$ 501,014</u>
<b>Borrowings:</b>		
Term loan, net	\$ 47,078	\$ 46,209
Convertible notes, net	93,885	89,504
Total borrowings	<u>\$ 140,963</u>	<u>\$ 135,713</u>
<b>Working capital:</b>		
Current assets	\$ 494,941	\$ 474,221
Current liabilities	80,868	31,199
Working capital	<u>\$ 414,073</u>	<u>\$ 443,022</u>

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

	<b>Nine Months Ended</b>	
	<b>September 30, 2021</b>	<b>September 30, 2020</b>
Net cash used in operating activities	\$ (97,785)	\$ (43,207)
Net cash used in investing activities	(195,112)	(22,897)
Net cash provided by financing activities	300,474	230,483
	<u>\$ 7,577</u>	<u>\$ 164,379</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.

Net cash used in operating activities of \$97.8 million in the nine months ended September 30, 2021 was largely due to ongoing research and development activities, general and administrative expenses to support those activities, and operating lease liability related to the existing and new leases. Net loss for the nine months ended September 30, 2021 included, among other items: non-cash stock-based compensation, non-cash interest expense related to sale of future royalties and non-cash interest expense related to debt.

Net cash used in investing activities of \$195.1 million in the nine months ended September 30, 2021 was primarily due to purchases of investments offset by proceeds from maturity of investments.

Net cash provided by financing activities of \$300.5 million in the nine months ended September 30, 2021 was preliminary due to \$296.9 million of proceeds related to issuance of common stock in an underwritten public offering and stock-based activities.

### ***Future Sources and Uses of Cash***

In July 2021, we closed an underwritten public offering of 11,500,000 shares of our common stock at a public offering price of \$27.50, which included the exercise in full by the underwriters of their option to purchase up to 1,500,000 shares of our common stock at the same price. The gross proceeds were \$316.3 million and net proceeds were approximately \$296.9 million, after deducting the applicable underwriting discounts and commissions.

In 2021, in addition to the costs and expenses of our research and development activities, we expect to incur an increase in costs and expenses as compared to previous annual periods as a result of advancement of our pipeline, and our commercial planning activities in view of the potential commercial launch of omeamtiv mecarbil in the U.S. and potentially elsewhere. Such costs and expenses are likely to include an increase in headcount, particularly in our sales and marketing functions, and the procurement of omeamtiv mecarbil drug product for commercial launch. These costs and expenses will be greater than what they would have been had Amgen not elected to terminate the Amgen Agreement and Servier not elected to terminate the Servier Agreement. We may explore potential strategic partnerships and/or structured financing transactions to finance the increased costs and expenses. We will also incur expenses in connection to our relocation from our existing headquarters to our new facilities at Oyster Point in 2021.

In future periods, we expect to incur substantial costs as we continue to expand our research programs and related research and development activities. We expect to incur significant research and development expenses as we advance the research and development of compounds from our other muscle biology programs through research to candidate selection to clinical development. We may also incur significant sales and marketing expenses if and when one or more of our drug candidates receive regulatory approvals, and 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, chemistry, manufacturing, and controls (“CMC”), and clinical trials for our drug candidates and other compounds;
- the time and costs involved in obtaining regulatory approvals;
- the jurisdictions in which we are granted regulatory approvals and thus are able to successfully launch our products for commercial sale;
- delays that may be caused by requirements of regulatory agencies;

- our level of funding for the development of current or future drug candidates;
- the number of drug candidates we pursue and the stage of development that they are in;
- the costs involved in filing and prosecuting patent applications and enforcing or defending patent claims;
- our ability to establish and maintain selected strategic alliances required for the development of drug candidates and commercialization of our potential drugs;
- our plans or ability to expand our drug development capabilities, including our capabilities to conduct clinical trials for our drug candidates;
- our plans or ability to engage third-party manufacturers for our drug candidates and potential drugs;
- our plans or ability to build or access sales and marketing capabilities and to achieve market acceptance for potential drugs;
- the expansion and advancement of our research programs;
- the hiring of additional employees and consultants;
- the acquisition of technologies, products and other business opportunities that require financial commitments; and
- our revenues, if any, from successful development of our drug candidates and commercialization of potential drugs
- As we advance commercialization plans for omecamtiv mecarbil, which we believe will importantly lay a strong foundation for commercialization of aficamten and the expansion of our cardiovascular franchise, we anticipate that our spending would increase, but we are also studying comparable company best practices and building a fit-for-purpose commercial organization.

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

Future uses of cash also include capital purchases of equipment and tenant improvements to build out the Oyster Point Lease totaling approximately \$35.0 million. We intend to occupy the Oyster Point building late 2021 or early 2022.

We have incurred an accumulated deficit of \$1,177.1 million since inception and there can be no assurance that we will attain profitability. We are subject to risks common to clinical-stage companies including, but not limited to, development of new drug candidates, dependence on key personnel, and the ability to obtain additional capital as needed to fund our future plans. Our liquidity will be impaired if sufficient additional capital is not available on terms acceptable to us, if at all. Until we achieve profitable operations, we intend to continue to fund operations through payments from strategic collaborations, additional sales of equity securities, grants and other financings. We have never generated revenues from commercial sales of our drugs and may not have drugs to market for at least several years, if ever. Our success is dependent on our ability to obtain additional capital by entering into new strategic collaborations and/or through financings, and ultimately on our and our collaborators' ability to successfully develop and market one or more of our drug candidates. We cannot be certain that sufficient funds will be available from such collaborators or financings when needed or on satisfactory terms. Additionally, there can be no assurance that any of our drug candidates will be accepted in the marketplace or that any future products can be developed or manufactured at an acceptable cost. These factors could have a material adverse effect on our future financial results, financial position and cash flows.

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

### Contractual Obligations and Other Commitments

The following table summarizes our contractual obligations as of September 30, 2021:

	Payment Due by Period		
	Total	Less than 1 Year	More than 1 year
	(In millions)		
Operating lease obligations(1)	\$ 235.0	\$ 14.3	\$ 220.7
Long-term debt obligations(2)	54.3	20.1	34.2
Convertible notes(3)	30.3	5.5	24.8
Purchase obligations(4)	15.4	9.6	5.8
Total contractual obligations	<u>\$ 335.0</u>	<u>\$ 49.5</u>	<u>\$ 285.5</u>

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

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

(3) Represents interest payable for our convertible notes.

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

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

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

The obligations in the above table are as of September 30, 2021. We expect the amount of these obligations to change materially over time as new contracts are initiated and existing contracts are completed, terminated, or modified.

### Off-Balance Sheet Arrangements

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

### ITEM 3. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Our exposure to market risk has not changed materially since our disclosures in Item 7A, “Quantitative and Qualitative Disclosures About Market Risk” in our Annual Report on Form 10-K for the year ended December 31, 2020.

### ITEM 4. CONTROLS AND PROCEDURES

#### (a) 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 Exchange Act, and the rules and regulations thereunder, 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 principal executive officer and principal financial officer, or persons performing similar functions, as appropriate, to allow for timely decisions regarding required or necessary disclosure. In designing and evaluating the disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable, not absolute, assurance of achieving the desired control objectives, and we are required to apply judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of September 30, 2021, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

#### (b) Changes in internal control over financial reporting

There were no changes in our internal control over financial reporting that occurred during the quarter ended September 30, 2021, that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

#### (c) Limitations on the effectiveness of controls

A control system, no matter how well-conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the controls are met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues, if any, within a company have been detected. Accordingly, our disclosure controls and procedures are designed to provide reasonable, not absolute, assurance that the objectives of our disclosure control system are met.

## PART II. OTHER INFORMATION

### ITEM 1. LEGAL PROCEEDINGS

None.

### ITEM 1A. RISK FACTORS

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

#### Risks Related to Our Business

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

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

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

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

For the foreseeable future, our operations will require significant additional funding, in large part due to our research and development expenses, 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. For example, we are preparing for a launch of omecamtiv mecarbil in the U.S. requiring additional hiring and investment, and we will also require significant additional funding to enable us to conduct further development of our product candidates. Until we can generate a sufficient amount of product revenue, we expect to raise future capital through strategic alliance and licensing arrangements, public or private equity offerings and debt financings. We do not currently have any commitments for future funding other than through our Funding Agreement with RTW ICAV (as assignee of RTW Royalty Holdings), and reimbursements, milestone and royalty payments that we may receive under our collaboration agreement with Ji Xing. We may not receive any further funds under those agreements. Our ability to raise funds may be adversely impacted by current economic conditions. As a result of these and other factors, we do not know whether additional financing will be available when needed, or that, if available, such financing would be on terms favorable to our stockholders or us.

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

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

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

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

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

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

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

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

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

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

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

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

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

***Covenants in our Term Loan Agreement, the indenture related to the 2026 Notes and the Funding Agreement restrict our business and operations in many ways and if we do not effectively manage our covenants, our financial conditions and results of operations could be adversely affected. Our operations may not provide sufficient cash to meet the repayment obligations of our debt incurred under the Term Loan Agreement.***

The Term Loan Agreement and the indenture related to the 2026 Notes requires that we comply with certain covenants applicable to us, including among other things, covenants restricting dispositions, changes in business, management, ownership or business locations, mergers or acquisitions, indebtedness, encumbrances, distributions, investments, transactions with affiliates and subordinated debt, any of which could restrict our business and operations, particularly our ability to respond to changes in our business or to take specified actions to take advantage of certain business opportunities that may be presented to us. In addition, should we exercise our option pursuant to the Funding Agreement, such agreement contains certain covenants applicable to us, including among other things, development and commercialization diligence obligations in connection to aficamten, use of proceeds, reporting and encumbrances, which could also restrict our business and operations, particularly in connection to our development and commercialization of aficamten.

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

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

If we are unable to repay those amounts, the relevant creditors could proceed against the collateral granted to them to secure that debt (if any), which would seriously harm our business. In addition, should we be unable to comply with these covenants or if we default on any portion of our outstanding borrowings, the Lenders in connection to the Term Loan can also impose a 5.0% penalty. In addition, the Term Loan has interest only payments through December 31, 2021.

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

We currently have no drugs for sale and we cannot guarantee that we will ever develop or obtain approval to market any drugs. To receive marketing approval for any drug candidate, we must demonstrate that the drug candidate satisfies rigorous standards of safety and efficacy to the FDA in the United States and other regulatory authorities abroad. We and our partners will need to conduct significant research and preclinical and clinical testing before we or our partners can file applications with the FDA or other regulatory authorities for approval of any of our drug candidates. In addition, to compete effectively, our drugs must be easy to use, cost-effective, covered by insurance or government sponsored medical plans, and economical to manufacture on a commercial scale, compared to other therapies available for the treatment of the same conditions. We may not achieve any of these objectives. Currently, our clinical-stage drug candidates include omecamtiv mecarbil for the potential treatment of heart failure, reldesemtiv for the potential treatment of ALS and potentially other indications associated with muscle weakness, and 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. 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.

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

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

All of our drug candidates, including aficamten and reldesemtiv, are prone to the risks of failure inherent in drug development. Preclinical studies may not yield results that would adequately support the filing of an IND (or a foreign equivalent) with respect to our potential drug candidates. Even if the results of preclinical studies for a drug candidate are sufficient to support such a filing, the results of preclinical studies do not necessarily predict the results of clinical trials. As an example, because the physiology of animal species used in preclinical studies may vary substantially from other animal species and from humans, it may be difficult to assess with certainty whether a finding from a study in a particular animal species will result in similar findings in other animal species or in humans. For any of our drug candidates, the results from Phase 1 clinical trials in healthy volunteers and clinical results from Phase 1 and 2 trials in patients are not necessarily indicative of the results of later and larger clinical trials that are necessary to establish whether the drug candidate is safe and effective for the applicable indication. Likewise, interim results from a clinical trial may not be indicative of the final results from that trial, and results from early Phase 2 clinical trials may not be indicative of the results from later clinical trials. For example, early Phase 2 clinical trials of our first-generation FSTA, tirasemtiv, in patients with ALS showed encouraging dose-related trends in measurements of the ALSFRS-R, a clinically validated instrument designed to measure disease progression and changes in functional status, for patients receiving tirasemtiv compared to those receiving placebo. However, BENEFIT-ALS, a Phase 2b clinical trial of tirasemtiv in patients with ALS, did not achieve its primary efficacy endpoint, the mean change from baseline in the ALSFRS-R for patients receiving tirasemtiv compared to those receiving placebo, and in November 2017, we announced that VITALITY-ALS did not achieve its primary endpoint or secondary endpoints. Following the results of VITALITY-ALS, we suspended development of tirasemtiv.

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

In addition, while the clinical trials of our drug candidates are designed based on the available relevant information, such information may not accurately predict what actually occurs during the course of the trial itself, which may have consequences for the conduct of an ongoing clinical trial or for the eventual results of that trial. For example, the number of patients planned to be enrolled in a placebo-controlled clinical trial is determined in part by estimates relating to expected treatment effect and variability about the primary endpoint. These estimates are based upon earlier non-clinical and clinical studies of the drug candidate itself and clinical trials of other drugs thought to have similar effects in a similar patient population. If information gained during the conduct of the trial shows these estimates to be inaccurate, we may elect to adjust the enrollment accordingly, which may cause delays in completing the trial, additional expense or a statistical penalty to apply to the evaluation of the trial results.

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

Furthermore, while planned interim analyses in clinical trials can enable early terminations for futility or for overwhelming efficacy, the timing, which can be based on accrual of events, enrollment or other factors, and the results of such analyses, is unpredictable.

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

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

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

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

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

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

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

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

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

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

In May 2021, we announced data from a secondary analysis of GALACTIC-HF assessing the effect of omecamtiv mecarbil on clinical outcomes in relationship to patient baseline ejection fraction. Analysis of ejection fraction as a continuous variable demonstrated a progressively larger treatment effect of omecamtiv mecarbil with decreasing ejection fraction.

In June 2021, we announced additional analyses from GALACTIC-HF demonstrating patients with atrial fibrillation or flutter have increased treatment effect with omecamtiv mecarbil; patients with higher baseline NT-proBNP have increased treatment effect with omecamtiv mecarbil; and patients with severe heart failure have increased treatment effect with omecamtiv mecarbil.

In September 2021, we announced that additional results from GALACTIC-HF assessing the effect of omecamtiv mecarbil in Black patients with HFrEF. Among Black patients, 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.

Although our supplemental analyses showed that omecamtiv mecarbil potentially has a greater treatment effect in certain subgroups of trial patients, no assurance can be given that the FDA or any other regulatory authority will consider any such subgroup analysis as the basis for an approval of omecamtiv mecarbil without requiring additional clinical trials.

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

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

- delays in obtaining, or inability to obtain, regulatory or other approvals to commence and conduct clinical trials in the manner we or our partners deem necessary for the appropriate and timely development of our drug candidates and commercialization of any resulting drugs;
- delays in identifying and reaching agreement, or inability to identify and reach agreement, on acceptable terms, with prospective clinical trial sites and other entities involved in the conduct of our or our partners' clinical trials;
- delays or additional costs in developing, or inability to develop, appropriate formulations of our drug candidates for clinical trial use;
- slower than expected rates of patient recruitment and enrollment;
- for those drug candidates that are the subject of a strategic alliance, delays in reaching agreement with our partner as to appropriate development strategies;
- a regulatory authority may require changes to a protocol for a clinical trial that then may require approval from regulatory agencies in other jurisdictions where the trial is being conducted;
- a regulatory authority in one jurisdiction may not accept a clinical trial design that is acceptable in another jurisdiction;
- an institutional review board ("IRB") or its foreign equivalent may require changes to a protocol that then require approval from regulatory agencies and other IRBs and their foreign equivalents, or regulatory authorities may require changes to a protocol that then require approval from the IRBs or their foreign equivalents;
- for clinical trials conducted in foreign countries, the time and resources required to identify, interpret and comply with foreign regulatory requirements or changes in those requirements, and political instability or natural disasters occurring in those countries;
- lack of effectiveness of our drug candidates during clinical trials;
- unforeseen safety issues;
- inadequate supply, or delays in the manufacture or supply, of clinical trial materials;
- uncertain dosing issues;
- failure by us, our partners, or clinical research organizations, investigators or site personnel engaged by us or our partners to comply with good clinical practices and other applicable laws and regulations, including those concerning informed consent;
- inability or unwillingness of investigators or their staffs to follow clinical protocols;
- failure by our clinical research organizations, clinical manufacturing organizations and other third parties supporting our or our partners' clinical trials to fulfill their obligations;
- inability to monitor patients adequately during or after treatment;

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

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

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

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

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

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

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

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

On November 23, 2020, we announced that Amgen elected to terminate the Amgen Agreement and thereby end its collaboration with Cytokinetics, and that it intended to transition development and commercialization rights for omecamtiv mecarbil and CK-136 to us. The termination of the Amgen Agreement was effective May 20, 2021. Pursuant to the terms of the Amgen Agreement, upon the effective date of Amgen's termination, research, development and commercialization rights for compounds, including omecamtiv mecarbil and CK-136, have reverted to us. Under the Amgen Agreement, Amgen has certain obligations that survive its termination, including: cooperating with us and our designee(s) to facilitate a reasonably smooth, orderly and prompt transition of the programs, including transfer and assignment to us of specified regulatory filings, data and other information; if requested by us, transferring inventory of compounds to us at our expense; to the extent possible and requested by us, assigning relevant third-party manufacturing agreements to us; and granting to us exclusive and non-exclusive licenses to certain intellectual property rights. In addition, we and Amgen have entered into several agreements to facilitate the transition of the programs for omecamtiv mecarbil and CK-136 to us, including an agreement for the sale and purchase of approximately 2.0 tons of materials including active pharmaceutical ingredient of omecamtiv mecarbil to enable our launch supply of drug product.

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

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

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

Finally, no assurance can be made that we will have or be able to mobilize the capital, personnel, systems or other recourses required by the effective termination of the Amgen Agreement to ensure our ability to meet our legal or regulatory responsibilities and obligations, to continue the development of the omecamtiv mecarbil and/or CK-136 programs, including the design and conduct of clinical trials of omecamtiv mecarbil and/or CK-136, without substantial delays to the timelines previously anticipated prior to Amgen's decision to terminate the Amgen Agreement or without significant costs as compared to our anticipated costs prior to Amgen's decision to terminate the Amgen Agreement, or to ensure commercial preparedness for a potential product launch of omecamtiv mecarbil. In such cases, we would have to seek a new partner for development or commercialization, curtail or abandon that development or commercialization, or undertake and fund the development of omecamtiv mecarbil or CK-136 or commercialization of the resulting drugs ourselves. If we seek a new partner but are unable to do so on acceptable terms, or at all, or do not have sufficient funds to conduct the development or commercialization of omecamtiv mecarbil ourselves, we would have to curtail or abandon that development or commercialization of omecamtiv mecarbil and/or CK-136, which could harm our business.

***The failure to successfully develop, validate and obtain regulatory clearance or approval of an assay for plasma concentrations of omecamtiv mecarbil could delay or harm our development and commercialization strategy for omecamtiv mecarbil.***

An important element of our development and commercialization strategy for omecamtiv mecarbil has been the development of an assay used for the in vitro measurement of concentrations of omecamtiv mecarbil in human blood, which is intended to enable personalized dose optimization of omecamtiv mecarbil. In COSMIC-HF, a liquid chromatography-tandem mass spectrometry assay was used for such measurements. Thereafter, an antibody-based immunoassay, Microgenics OM Assay, was developed under the Assay Agreement between Amgen and Microgenics Corporation and was utilized in both GALACTIC-HF and METEORIC-HF. We have been informed by Amgen that the Assay Agreement terminated contemporaneously with the termination of the Amgen Agreement. Consequently, we are pursuing the development and/or usage of alternative dosage selection tests to the Microgenics OM Assay to be used for personalized dose optimization of omecamtiv mecarbil and, if required by FDA or other regulatory authorities, in order to obtain marketing approval of omecamtiv mecarbil. In the event we do not develop an assay acceptable to the FDA or other regulatory authorities and any such authorities require a dosage selection test as a condition to regulatory approval of omecamtiv mecarbil, our ability to obtain or receive marketing approval for omecamtiv mecarbil may be significantly delayed or may not be obtainable at all. Moreover, the development of a dosage selection test alternative to the Microgenics OM Assay may be complex from an operational and regulatory perspective, particularly in the event a dosage selection test is deemed a companion diagnostic, a Class III device, requiring the most stringent device application process. If deemed by FDA to be a Class III device, the approval of the dosage selection test will require a pre-market application approval to establish the safety and efficacy of the dosage selection test. If there is a need for both omecamtiv mecarbil and the dosage selection test to receive regulatory clearance or approval, such approval may not be obtainable in all territories where omecamtiv mecarbil could ultimately be commercialized. In the US specifically, CDER (Center for Drug Evaluation and Research) could require an FDA cleared or approved assay for the approval of omecamtiv mecarbil such that their approval may be conditioned on the approval or clearance of our proposed dosage selection test by CDRH (Center for Devices and Radiologic Health).

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

Under the terms of the Ji Xing License Agreement, Ji Xing will be responsible for the development and commercialization of aficamten in China and Taiwan. The timing and amount of any milestone and royalty payments we may receive under the Ji Xing License Agreement will depend in part on the efforts and successful commercialization of aficamten 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 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 in China and Taiwan. If Ji Xing were to violate, or was alleged to have violated, any laws or regulations during the performance of its obligations for us, it is possible that we could suffer financial and reputational harm or other negative outcomes, including possible legal consequences.

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

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

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

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

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

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

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

- fund clinical trials and seek regulatory approvals;
- expand our development capabilities;
- engage third-party manufacturers for such drug candidate or drug;
- build or access commercialization capabilities;
- significantly scale up the number of commercial employees;
- implement additional internal systems and infrastructure;
- maintain, defend and expand the scope of our intellectual property; and
- hire and support additional management and scientific personnel.

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

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

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

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

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

Our CROs' failure to carry out development activities on our behalf as agreed and in accordance with our and the FDA's or other regulatory agencies' requirements and applicable U.S. and foreign laws, or our failure to properly coordinate and manage these activities, could increase the cost of our operations and delay or prevent the development, approval and commercialization of our drug candidates. For example, in June 2013, we learned from our data management vendor for our Phase 2b clinical trial of tirasemtiv in patients with ALS, BENEFIT-ALS, that a programming error in the electronic data capture system controlling study drug assignment caused 58 patients initially randomized to and treated with tirasemtiv to receive placebo instead at a certain trial visit and for the remainder of the trial. In order to maintain the originally intended statistical power of the trial, we amended the protocol to permit enrollment of approximately 680 patients, or 180 patients in addition to the 500 patients allowed under the existing protocol. This protocol amendment resulted in additional costs and delays in conducting BENEFIT-ALS. Further, for the quarter ended September 30, 2016, we determined that there was an error in the accounting for the recognition of clinical research and development expenses related to the information received from one of our CROs, which resulted in a restatement of our clinical research and development expenses, related clinical accrual accounts and related financial disclosures as of and for the three and nine month periods ended September 30, 2016. In addition, if a CRO fails to perform as agreed, our ability to collect damages may be contractually limited. If we fail to effectively manage the CROs carrying out the development of our drug candidates or if our CROs fail to perform as agreed, the commercialization of our drug candidates will be delayed or prevented. In many cases, our CROs have the right to terminate their agreements with us in the event of an uncured material breach. Identifying, qualifying and managing performance of third-party service providers can be difficult, time consuming and cause delays in our development programs. In addition, there is a natural transition period when a new CRO commences work and the new CRO may not provide the same type or level of services as the original provider. If any of our relationships with our third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs or to do so timely or on commercially reasonable terms.

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

We do not currently operate manufacturing facilities for clinical or commercial production of our drug candidates. We have limited experience in drug formulation and manufacturing, and we lack the resources and the capabilities to manufacture any of our drug candidates on a clinical or commercial scale.

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

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

Under the Ji Xing License Agreement, we have committed to providing Ji Xing with supply of aficamten for development and commercialization of aficamten in China and Taiwan, which we will have to source from our contract manufacturers. We expect to rely on contract manufacturers to supply all future drug candidates for which we conduct development, as well as other materials required to conduct our clinical trials, and to fulfil our obligations under the Ji Xing License Agreement.

If any of our existing or future contract manufacturers fail to perform satisfactorily, it could delay development or regulatory approval of our drug candidates or commercialization of our drugs, producing additional losses and depriving us of potential product revenues, and also lead to our breach of the Ji Xing License Agreement, giving rise to the ability to terminate such agreement and other adverse consequences as stipulated in the Ji Xing License Agreement. In addition, if a contract manufacturer fails to perform as agreed, our ability to collect damages may be contractually limited.

Our drug candidates require precise high-quality manufacturing. The failure to achieve and maintain high manufacturing standards, including failure to detect or control anticipated or unanticipated manufacturing errors or the frequent occurrence of such errors, could result in patient injury or death, discontinuance or delay of ongoing or planned clinical trials, delays or failures in product testing or delivery, cost overruns, product recalls or withdrawals and other problems that could seriously hurt our business. Contract drug manufacturers often encounter difficulties involving production yields, quality control and quality assurance and shortages of qualified personnel. These manufacturers are subject to stringent regulatory requirements, including the FDA's current good manufacturing practices regulations and similar foreign laws and standards. Each contract manufacturer must pass a pre-approval inspection before we can obtain marketing approval for any of our drug candidates and following approval will be subject to ongoing periodic unannounced inspections by the FDA, the U.S. Drug Enforcement Agency and other regulatory agencies, to ensure strict compliance with current good manufacturing practices and other applicable government regulations and corresponding foreign laws and standards. We seek to ensure that our contract manufacturers comply fully with all applicable regulations, laws and standards. However, we do not have control over our contract manufacturers' compliance with these regulations, laws and standards. If one of our contract manufacturers fails to pass its pre-approval inspection or maintain ongoing compliance at any time, the production of our drug candidates could be interrupted, resulting in delays or discontinuance of our clinical trials, additional costs and potentially lost revenues. In addition, failure of any third-party manufacturers or us to comply with applicable regulations, including pre- or post-approval inspections and the current good manufacturing practice requirements of the FDA or other comparable regulatory agencies, could result in sanctions being imposed on us. These sanctions could include fines, injunctions, civil penalties, failure of regulatory authorities to grant marketing approval of our products, delay, suspension or withdrawal of approvals, license revocation, product seizures or recalls, operational restrictions and criminal prosecutions, any of which could significantly and adversely affect our business.

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

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

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

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

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

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

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

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

We own, co-own or hold exclusive licenses to a number of U.S. and foreign patents and patent applications directed to our drug candidates, compounds and research technologies. Our success depends on our ability to obtain patent protection both in the United States and in other countries for our drug candidates, their methods of manufacture and use, and our technologies. Our ability to protect our drug candidates, compounds and technologies from unauthorized or infringing use by third parties depends substantially on our ability to obtain and enforce our patents. If our issued patents and patent applications, if granted, do not adequately describe, enable or otherwise provide coverage of our technologies and drug candidates, we, our licensors or our licensees would not be able to exclude others from developing or commercializing these drug candidates. Furthermore, the degree of future protection of our proprietary rights is uncertain because legal means may not adequately protect our rights or permit us to gain or keep our competitive advantage. If we are unable to obtain and maintain sufficient intellectual property protection for our technologies and drug candidates, or if the scope of the intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize drug candidates similar or identical to ours, and our ability to successfully commercialize product candidates that we may pursue may be impaired.

Obtaining and enforcing biopharmaceutical patents is costly, time consuming and complex, and we may not be able to file and prosecute all necessary or desirable patent applications, or maintain, enforce and license any patents that may issue from such patent applications, at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. We may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the rights to patents licensed to third parties. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

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

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

We may not be able to protect our intellectual property rights throughout the world. Patent protection is afforded on a country-by-country basis. Filing, prosecuting and defending patents on our product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. Many companies have encountered significant difficulties in protecting and defending intellectual property rights in foreign jurisdictions. Some of our development efforts are performed in countries outside of the United States through third-party contractors. We may not be able to effectively monitor and assess intellectual property developed by these contractors. We therefore may not be able to effectively protect this intellectual property and could lose potentially valuable intellectual property rights. In addition, the legal protection afforded to inventors and owners of intellectual property in countries outside of the United States may not be as protective of intellectual property rights as in the United States. Therefore, we may be unable to acquire and protect intellectual property developed by these contractors to the same extent as if these development activities were being conducted in the United States. If we encounter difficulties in protecting our intellectual property rights in foreign jurisdictions, our business prospects could be substantially harmed.

Patent terms may be inadequate to protect our competitive position on our technologies and drug candidates for an adequate amount of time. Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our technologies and drug candidates are obtained, once the patent life has expired, we may be open to competition from competitive products, including generics or biosimilars. Given the amount of time required for the development, testing and regulatory review of new drug candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned, co-owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours or our partners.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements. Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to be paid to the USPTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents and/or applications. Non-compliance could result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, our competitors might be able to enter the market and this circumstance would have a material adverse effect on our business.

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

We or our licensors may be subject to claims that former employees, collaborators, consultants or other third parties have an interest in our owned, co-owned or in-licensed patents, trade secrets, or other intellectual property as an inventor or co-inventor. For example, we or our licensors may have inventorship disputes arise from conflicting obligations of employees, collaborators, consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship or our or our licensors' ownership of our owned, co-owned or in-licensed patents, trade secrets or other intellectual property. If we or our licensors fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, intellectual property that is important to our product candidates. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

The uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to conduct clinical trials, continue our research programs, license necessary technology from third parties, or enter into development partnerships that would help us bring our drug candidates or other product candidates that we may identify to market. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions, or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock.

***We may become involved in disputes with our strategic partners over intellectual property ownership, and publications by our research collaborators and clinical investigators could impair our ability to obtain patent protection or protect our proprietary information, either of which would have a significant impact on our business.***

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

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

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

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

We compete with companies that have developed drugs or are developing drug candidates for cardiovascular diseases, diseases and conditions associated with muscle weakness or wasting and other diseases for which our drug candidates may be useful treatments. For example, if omecamtiv mecarbil is approved for marketing by the FDA or other regulatory authorities for the treatment of heart failure, it would compete against other drugs used for the treatment of acute and chronic heart failure. These include generic drugs, such as milrinone, dobutamine or digoxin and branded drugs such as Corlanor® (ivabradine), Entresto® (sacubitril/valsartan) and Verquvo® (vericiguat). Omecamtiv mecarbil could also potentially compete against other novel drug candidates and therapies in development, such as those being developed by, but not limited to, Novartis AG, Merck & Co., Inc., Bayer AG, AstraZeneca PLC and Bristol-Myers Squibb Company. Omecamtiv mecarbil may also compete with currently approved drugs, such as in the SGLT2 class, that 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). In addition, there are a number of medical devices both marketed and in development for the potential treatment of heart failure.

If reldesemtiv is approved for marketing by the FDA or other regulatory authorities for the treatment of ALS, it will then compete with RADICAVA™ (edaravone), the first FDA approved drug for the treatment of ALS since riluzole in 1995, and may then compete with other potential new therapies for ALS that are currently being developed by companies including, but not limited to, AB Science, Alexion Pharmaceuticals, Amylyx Pharmaceuticals Inc, BrainStorm Cell Therapeutics, Medicinova, Inc., Mitsubishi Tanabe Pharma Corporation, Orphazyme, and Revalesio Corporation. Also, if reldesemtiv is approved by the FDA or other regulatory authorities for the treatment of SMA, it may be used in combination with or compete with SPINRAZA® (nusinersen), Zolgensma® (onasemnogene abeparvovec-xioi) and/or Evrysdi™ (risdiplam) or any other potential new therapies being developed by companies including, but not limited to, F. Hoffman-La Roche Ltd. (in collaboration with PTC Therapeutics, Inc.). If reldesemtiv is approved by the FDA or other regulatory authorities for the treatment of non-neuromuscular indications associated with muscle weakness, it may then compete with other potential new therapies being developed by companies including, but not limited to, Regeneron Pharmaceuticals, Inc. (in collaboration with Sanofi), Eli Lilly and Company, Stealth BioTherapeutics, and Novartis (in collaboration with MorphoSys AG).

If aficamten is approved for marketing by the FDA or other regulatory authorities for the treatment of HCM, it may compete with mavacamten, a drug candidate being developed by Bristol-Myers Squibb Company for which a new drug application is currently pending with the FDA. Aficamten and mavacamten are both drugs that affect cardiac muscle contractility and any adverse regulatory action or other fact, matter or circumstance in connection to the development or commercialization of mavacamten may have an impact on our ability to obtain regulatory approval for, or the commercial prospects of, aficamten.

Our competitors may:

- develop drug candidates and market drugs that are less expensive or more effective than our future drugs;
- commercialize competing drugs before we or our partners can launch any drugs developed from our drug candidates;
- hold or obtain proprietary rights that could prevent us from commercializing our products;
- initiate or withstand substantial price competition more successfully than we can;
- more successfully recruit skilled scientific workers and management from the limited pool of available talent;
- more effectively negotiate third-party licenses and strategic alliances;
- take advantage of acquisition or other opportunities more readily than we can;
- develop drug candidates and market drugs that increase the levels of safety or efficacy that our drug candidates will need to show in order to obtain regulatory approval; or
- introduce therapies or market drugs that render the market opportunity for our potential drugs obsolete.

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

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

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

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

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

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

We are not guaranteed to maintain orphan status for reldesemtiv or aficamten or to receive orphan status for reldesemtiv or 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.

***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. For example, our management concluded that our internal controls over financial reporting were not effective as of December 31, 2018 because an unremediated material weakness existed in our internal control over financial reporting related to employee turnover resulting in a temporary lack of resources in financial reporting roles with the appropriate skills to perform effective review during our financial statement close process. We also rely on consultants and advisors to assist us in formulating our research and development strategy. All of our consultants and advisors are either self-employed or employed by other organizations, and they may have conflicts of interest or other commitments, such as consulting or advisory contracts with other organizations, that may affect their ability to contribute to us. In addition, if and as our business grows, we will need to recruit additional executive management and scientific, technical and financial reporting personnel. There is intense competition for skilled executives and employees with relevant scientific and technical expertise, and this competition is likely to continue. Our inability to attract and retain sufficient scientific, technical, 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.

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

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

***We currently are building sales and marketing capabilities but don't possess all of the people or capabilities at this time. If we are unable to enter into or maintain strategic alliances with marketing partners or to fully develop our own sales and marketing capabilities, we may not be successful in commercializing omecamtiv mecarbil or our other potential drugs.***

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

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

***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 ("PBMs") and payors in the U.S. These major PBMs and payors include Medicare, Medicaid, VA, DoD, Tri Care, and other commercial payors with whom we have had limited interactions. The process to achieve coverage with PBMs 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 omecamtiv mecarbil, even if such drug candidate is approved by the FDA or other regulatory authorities for commercialization, it may not become a guideline-directed medical therapy for heart failure or it 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 bid timelines for inclusion in the Medicare Part-D formulary. In addition, the rebate levels we may have to offer to PBMs and payors to be included in their formularies may also impact the profitability of omecamtiv mecarbil.

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

Despite the implementation of security measures, our internal computer systems and those of our third-party CROs, CMOs, supply chain partners, collaboration partners and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our drug development programs. For example, the loss of clinical study data from completed or ongoing clinical studies for any of our drug candidates could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our operations could be compromised and the further development of our product candidates could be delayed.

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

Our business is increasingly dependent on complex and interdependent information technology systems, including internet-based systems, databases and programs, to support our business processes as well as internal and external communications. As use of information technology systems has increased, deliberate attacks and attempts to gain unauthorized access to computer systems and networks have increased in frequency and sophistication. Our information technology, systems and networks are potentially vulnerable to breakdown, malicious intrusion and computer viruses which may result in the impairment of production and key business processes or loss of data or information. We are also potentially vulnerable to data security breaches—whether by employees or others—which may expose sensitive data to unauthorized persons. We have in the past and may in the future be subject to security breaches. For example, in February 2018, we discovered that our e-mail server suffered unauthorized intrusions in which proprietary business information was accessed. In addition, in December 2019, one of our employee’s email account suffered an unauthorized intrusion, leading to the submission and inadvertent payment of a fraudulent invoice in the amount of approximately one hundred thousand dollars. In December 2019, our IT systems were exposed to a ransomware attack, which partially impaired certain IT systems for a short period of time. Finally, in September 2020, one of our employees’ email account suffered unauthorized access as result of a phishing incident, but the Company believes no sensitive information was accessed. Although we do not believe that we have experienced any material losses related to security breaches, including in three recent email “phishing” incidents or the ransomware attack, there can be no assurance that we will not suffer such losses in the future. Breaches and other inappropriate access can be difficult to detect and any delay in identifying them could increase their harm. While we have implemented measures to protect our data security and information technology systems, such measures may not prevent these events. Any such breaches of security and inappropriate access could disrupt our operations, harm our reputation or otherwise have a material adverse effect on our business, financial condition and results of operations.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

On July 24, 2019, we entered into a lease agreement with KR Oyster Point 1, LLC (“Kilroy”), a subsidiary of Kilroy Realty Corporation, relating to the lease of approximately 234,892 square feet of office and laboratory space at a facility (currently under construction) located in South San Francisco, California (the “New Facility”). Kilroy is expected to deliver possession of the New Facility in the fourth quarter of 2021, while the lease (the “Current Lease”) to our existing facility at 280 E Grand Avenue, South San Francisco (the “Old Facility”) expires on June 30, 2022. However, under our Current Lease, notwithstanding the general expiration date of June 30, 2022, our landlord has an early termination right whereby landlord may terminate all or a portion of our lease to the Old Facility at any time on or after January 31, 2022 on 30 days’ prior written notice. In the event that the New Facility is not delivered to us in sufficient time to allow us to move our operations to the New Facility as anticipated, whether as a result of potential construction delays attributable to the COVID 19 pandemic or otherwise, we may be required to holdover the Old Facility past expiry of its term, leading to: (i) additional costs (including holdover rent at 150% of our current rent); (ii) liability under our indemnification obligations owed to our current landlord under the Current Lease; and (iii) disruption to our business.

In addition, our relocation to the New Facility will require the transportation and installation of precision laboratory equipment, laboratory materials, IT hardware and networks, business records, and other equipment and materials that are important to the conduct of our business. If certain of our equipment and materials are damaged during the relocation or installed improperly at the New Facility, certain aspects of the conduct of our business may be adversely affected in the form of operational delays and/or financial losses.

## Risks Related to Our Industry

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

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

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

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

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

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

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

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

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

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

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

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

***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.

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

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

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

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

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

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by the U.S. Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least \$1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation’s automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect in April 2013, and, due to subsequent legislative amendments, will remain in effect through 2030, except for a temporary suspension from May 1, 2020 through March 31, 2021 due to the COVID-19 pandemic, unless additional Congressional action is taken. In January 2013, the American Taxpayer Relief Act of 2012 was enacted which, among other things, further reduced Medicare payments to several providers, including hospitals and outpatient clinics, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Since its enactment, there have been judicial and Congressional challenges to numerous elements of the ACA, as well as efforts to repeal or replace certain aspects of the ACA. In addition, there is ongoing litigation challenging the constitutionality of the ACA. It is unclear how such litigation will impact the ACA and our business. The U.S. Congress may consider and adopt other legislation to repeal and replace all or certain elements of the ACA. Policy changes, including potential modification or repeal of all or parts of the ACA or the implementation of new health care legislation, could result in significant changes to the health care system which may adversely affect our business in unpredictable ways.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. For example, there is proposed legislation that would require (i) the Department of Health and Human Services to directly negotiate drug prices with manufacturers and require rebates for drugs covered under Medicare Part B whose price rises above inflation and (ii) restructuring the Medicare Part D benefit, imposing more financial responsibility on certain drug manufacturers. 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 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. Furthermore, the increased emphasis on managed healthcare in the United States and on country and regional pricing and reimbursement controls in the E.U. will put additional pressure on product pricing, reimbursement and usage, which may adversely affect our future product sales. These pressures can arise from rules and practices of managed care groups, judicial decisions and governmental laws and regulations related to Medicare, Medicaid and healthcare reform, pharmaceutical reimbursement policies and pricing in general.

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

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

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

In addition, if we commercially launch drugs based on our drug candidates, we will face even greater exposure to product liability claims. This risk exists even with respect to those drugs that are approved for commercial sale by the FDA and foreign regulatory agencies and manufactured in licensed and regulated facilities. We intend to secure additional limited product liability insurance coverage for drugs that we commercialize, but may not be able to obtain such insurance on acceptable terms with adequate coverage, or at reasonable costs. Even if we are ultimately successful in product liability litigation, the litigation would consume substantial amounts of our financial and managerial resources and may create adverse publicity, all of which would impair our ability to generate sales of the affected product and our other potential drugs. Moreover, product recalls may be issued at our discretion or at the direction of the FDA and foreign regulatory agencies, other governmental agencies or companies having regulatory control for drug sales. Product recalls are generally expensive and often have an adverse effect on the reputation of the drugs being recalled and of the drug's developer or manufacturer.

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

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

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

- The federal healthcare anti-kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federally funded healthcare programs such as Medicare and Medicaid. This statute has been broadly interpreted to apply to manufacturer arrangements with prescribers, purchasers and formulary managers, among others. Several other countries, including the United Kingdom, have enacted similar anti-kickback, fraud and abuse, and healthcare laws and regulations.
- The federal false claims laws, including the False Claims Act, which can be enforced through whistleblower or qui tam actions, imposes penalties against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. The government and qui tam relators have brought False Claims Act actions against pharmaceutical companies on the theory that their practices have caused false claims to be submitted to the government.
- The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program. HIPAA also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information. HIPAA also imposes criminal liability for knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services.
- The federal Physician Payments Sunshine Act requires manufacturers of drugs, devices, biologics and medical supplies to report to the HHS information related to payments and other transfers of value made to or at the request of physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, and physician ownership and investment interests in such manufacturers. Payments made to physicians and research institutions for clinical trials are included within the ambit of this law. Beginning January 1, 2022, applicable manufacturers will also be required to report information regarding payments and other transfers of value provided during the previous year to physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified nurse anesthetists, and certified nurse-midwives.
- Analogous state laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, and some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures and state and local laws that require the registration of sales representatives.

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

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

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

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

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

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

## Generic Risk Factors

***We are obligated to develop and maintain proper and effective internal control over financial reporting. In the future, we may not complete our execution of our internal control over financial reporting in a timely manner, or these internal controls may not be determined to be effective, which may result in additional material misstatements in our consolidated financial statements and may adversely affect investor confidence in our company and, as a result, the value of our common stock.***

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

Complying with Section 404 requires a rigorous compliance program as well as adequate time and resources. We may not be able to complete our internal control evaluation, testing and any required remediation in a timely fashion. Additionally, if we identify one or more material weaknesses in our internal control over financial reporting, we will not be able to assert that our internal controls are effective. A material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of the Company's annual or interim financial statements will not be prevented or detected on a timely basis. As of December 31, 2019, we have remediated the material weakness related to our internal controls over financial reporting that were determined to be ineffective as of December 31, 2018. As of December 31, 2018, we identified a material weakness related to the ineffective review and verification of internally prepared reports and analyses utilized in our financial statement closing process. The material weakness related to employee turnover resulting in a temporary lack of resources in financial reporting roles with the appropriate skills to perform effective review during our financial statement close process. This material weakness did not result in the restatement of prior quarterly or annually filed financial statements. During 2019, management conducted a remediation plan to address its material weakness, which included increasing the quality and level of resources with the accounting department and other enhancements and design improvements to our processes to improve the level of review of financial information.

Even though we remediated this material weakness as of December 31, 2019, we cannot be certain that other material weaknesses and control deficiencies will not be discovered in the future. If our efforts are not successful or other material weaknesses are identified in the future or we are not able to comply with the requirements of Section 404 in a timely manner, our reported financial results could be materially misstated, we would receive an adverse opinion regarding our internal controls over financial reporting from our independent registered public accounting firm, and we could be subject to investigations or sanctions by regulatory authorities, which would require additional financial and management resources, and the value of our common stock could decline. To the extent we identify future weaknesses or deficiencies, there could be material misstatements in our consolidated financial statements and we could fail to meet our financial reporting obligations. As a result, our ability to obtain additional financing, or obtain additional financing on favorable terms, could be materially and adversely affected which, in turn, could materially and adversely affect our business, our financial condition and the value of our common stock. If we are unable to assert that our internal control over financial reporting is effective in the future, or if our independent registered public accounting firm is unable to express an opinion or expresses an adverse opinion on the effectiveness of our internal controls in the future, investor confidence in the accuracy and completeness of our financial reports could be further eroded, which would have a material adverse effect on the price of our common stock.

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

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

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

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

Our federal NOLs generated in taxable years beginning prior to 2018 will continue to be governed by tax rules in effect prior to the Tax Act, with unused NOLs expiring 20 years after we report a tax loss. These NOLs could expire unused and be unavailable to offset future taxable income. We cannot predict if and to what extent various states will conform to the Tax Act, as modified by additional tax legislation enacted in 2020.

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

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

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

In 2017, the U.S. government enacted the Tax Act that includes significant changes to the taxation of business entities, which was modified by additional federal tax legislation in 2020. These changes include, among others, (i) a permanent reduction to the corporate income tax rate, (ii) a partial limitation on the deductibility of business interest expense and net operating loss carryforwards, (iii) a shift of the U.S. taxation of multinational corporations from a tax on worldwide income to a territorial system (along with certain rules designed to prevent erosion of the U.S. income tax base) and (iv) a one-time tax on accumulated offshore earnings held in cash and illiquid assets, with the latter taxed at a lower rate. Further, the comprehensive tax legislation, among other things, reduces the orphan drug tax credit from 50% to 25% of qualifying expenditures. When and if we become profitable, this reduction in tax credits may result in an increased federal income tax burden on our orphan drug programs as it may cause us to pay federal income taxes earlier under the revised tax law than under the prior law and, despite being partially off-set by a reduction in the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, may increase our total federal tax liability attributable to such programs.

Notwithstanding the reduction in the corporate income tax rate, the overall impact of this comprehensive tax legislation resulted in an overall reduction in our deferred tax assets, and our business and financial condition could still be adversely affected as additional guidance and regulations are issued with respect to the original tax law change. In addition, it is uncertain if and to what extent various states will conform to this comprehensive tax legislation, and states may enact suspensions or limitations on the use of net operating losses and tax credits (including, without limitation, California legislation enacted in 2020 that suspends the use of California NOLs and limits the use of certain California tax credits for certain periods). The impact of this comprehensive tax legislation on holders of our common stock is also uncertain and could be adverse. Investors should consult with their legal and tax advisors with respect to this comprehensive tax legislation and the potential tax consequences of investing in or holding our common stock.

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

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

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

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

- announcements concerning any of the clinical trials for our drug candidates (including, but not limited to, the timing of initiation or completion of such trials and the results of such trials, and delays or discontinuations of such trials, including delays resulting from slower than expected or suspended patient enrollment or discontinuations resulting from a failure to meet pre-defined clinical end points);
- announcements concerning our strategic alliances;
- failure or delays in entering additional drug candidates into clinical trials;

- failure or discontinuation of any of our research programs;
- issuance of new or changed securities analysts' reports or recommendations;
- failure or delay in establishing new strategic alliances, or the terms of those alliances;
- market conditions in the pharmaceutical, biotechnology and other healthcare-related sectors;
- actual or anticipated fluctuations in our quarterly financial and operating results;
- developments or disputes concerning our intellectual property or other proprietary rights;
- introduction of technological innovations or new products by us or our competitors;
- issues in manufacturing, packaging, labeling and distribution of our drug candidates or drugs;
- market acceptance of our drugs;
- third-party healthcare coverage and reimbursement policies;
- FDA or other U.S. or foreign regulatory actions affecting us or our industry;
- litigation or public concern about the safety of our drug candidates or drugs;
- additions or departures of key personnel;
- substantial sales of our common stock by our existing stockholders, whether or not related to our performance;
- automated trading activity by algorithmic and high-frequency trading programs;
- volatility in the stock prices of other companies in our industry or in the stock market generally; and
- other factors described in this "Risk Factors" section.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

**ITEM 2.UNREGISTERED SALES OF EQUITY SECURITIES AND USE OF PROCEEDS**

None.

**ITEM 3.DEFAULTS UPON SENIOR SECURITIES**

None.

**ITEM 4.MINE SAFETY DISCLOSURES**

None.

**ITEM 5.OTHER INFORMATION**

None.

**ITEM 6.EXHIBITS**

A list of exhibits filed with this Quarterly Report on Form 10-Q or incorporated herein by reference is found in the Index to Exhibits immediately following the signature page of this report and is incorporated into this Item 6 by reference.

Exhibit No.	Exhibits	Form	Incorporated by Reference File No.	Reference Filing Date	Exh. No.	Filed Herewith
3.1	<a href="#">Amended and Restated Certificate of Incorporation</a>	S-3	333-174869	June 13, 2011	3.1	
3.2	<a href="#">Certificate of Amendment of Amended and Restated Certificate of Incorporation</a>	8-K	000-50633	June 25, 2013	5.1	
3.3	<a href="#">Certificate of Amendment of Amended and Restated Certificate of Incorporation</a>	8-K	000-50633	May 20, 2016	3.1	
3.4	<a href="#">Amended and Restated Bylaws</a>	S-1	333-112261	January 27, 2004	3.2	
4.1	<a href="#">Specimen Common Stock Certificate</a>	10-Q	000-50633	May 9, 2007	4.1	
10.1	<a href="#">Fourth Amendment to Loan and Security Agreement, dated June 30, 2021, by and among the Company, Oxford Finance LLC and Silicon Valley Bank</a>					X
10.2	<a href="#">Amended and Restated 2004 Equity Incentive Plan<sup>(1)</sup></a>					X
31.1	<a href="#">Certification of Principal Executive Officer pursuant to Rule 13a-14(a) and Rule 15d-14(a) of the Securities Exchange Act, as amended</a>					X
31.2	<a href="#">Certification of Principal Financial Officer pursuant to Rule 13a-14(a) and Rule 15d-14(a) of the Securities Exchange Act, as amended</a>					X
31.3	<a href="#">Certification of Principal Accounting Officer pursuant to Rule 13a-14(a) and Rule 15d-14(a) of the Securities Exchange Act, as amended</a>					X
32.1	<a href="#">Certifications of the Principal Executive Officer, Principal Financial Officer, and Principal Accounting Officer pursuant to 18 U.S.C 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 <sup>(2)</sup></a>					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 and contained in Exhibit 101)					X

(1) Management contract or compensatory plan or arrangement.

(2) This certification accompanies the Form 10-Q 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-Q), irrespective of any general incorporation language contained in such filing.

## SIGNATURES

Pursuant to the requirements of the Securities Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Dated: November 5, 2021

CYTOKINETICS, INCORPORATED  
(Registrant)

/s/ Robert I. Blum

Robert I. Blum  
President and Chief Executive Officer  
(Principal Executive Officer)

/s/ Ching W. Jaw

Ching W. Jaw  
Senior Vice President, Chief Financial Officer  
(Principal Financial Officer)

/s/ Robert C. Wong

Robert C. Wong  
Vice President, Chief Accounting Officer  
(Principal Accounting Officer)

**FOURTH AMENDMENT TO  
LOAN AND SECURITY AGREEMENT**

THIS **FOURTH AMENDMENT** to Loan and Security Agreement (this “**Amendment**”) is entered into as of June 30, 2021, by and between **OXFORD FINANCE LLC**, a Delaware limited liability company with an office located at 133 North Fairfax Street, Alexandria, Virginia 22314 (“**Oxford**”), as collateral agent (in such capacity, “**Collateral Agent**”), the Lenders listed on Schedule 1.1 of the Loan Agreement (as defined below) or otherwise party thereto from time to time (each a “**Lender**” and collectively, the “**Lenders**”) including Oxford in its capacity as a Lender and **SILICON VALLEY BANK**, a California corporation with an office located at 3003 Tasman Drive, Santa Clara, CA 95054 (“**Bank**” or “**SVB**”) (each a “**Lender**” and collectively, the “**Lenders**”), and **CYTOKINETICS, INCORPORATED**, a Delaware corporation with offices located at 280 East Grand Avenue, South San Francisco, CA 94080 (“**Borrower**”).

**RECITALS**

**A.** Collateral Agent, Lenders and Borrower have entered into that certain Loan and Security Agreement dated as of May 17, 2019 (as amended by that certain First Amendment to Loan and Security Agreement, dated as of November 6, 2019, as further amended by that certain Second Amendment to Loan and Security Agreement, dated as of November 7, 2019, as further amended by that certain Third Amendment to Loan and Security Agreement, dated as of July 16, 2020, and as may be further amended from time to time, the “**Loan Agreement**”).

**B.** Lenders have extended credit to Borrower for the purposes permitted in the Loan Agreement.

**C.** Borrower has requested that Collateral Agent and Lenders (i) modify the definition of Permitted Liens and (ii) make certain other revisions to the Loan Agreement as more fully set forth herein.

**D.** Collateral Agent and Lenders have agreed to amend certain provisions of the Loan Agreement, but only to the extent, and subject to the terms and conditions and in reliance upon the representations and warranties, set forth below.

**AGREEMENT**

**Now, THEREFORE**, in consideration of the foregoing recitals and other good and valuable consideration, the receipt and adequacy of which is hereby acknowledged, and intending to be legally bound, the parties hereto agree as follows:

**1. Definitions.** Capitalized terms used but not defined in this Amendment shall have the meanings given to them in the Loan Agreement.

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## 2. Amendments to Loan Agreement.

**2.1 Section 13.1 (Definitions).** The defined term “Permitted Indebtedness” in Section 13.1 of the Loan Agreement is hereby amended by amending and restating subsection (e) thereof to read in its entirety as follows:

“(e) Indebtedness consisting of capitalized lease obligations and purchase money Indebtedness, in each case incurred by Borrower or any of its Subsidiaries to finance the acquisition, repair, improvement or construction of fixed or capital assets of such person, provided that (i) the aggregate outstanding principal amount of all such Indebtedness does not exceed Three Million Dollars (\$3,000,000.00) at any time and (ii) the principal amount of such Indebtedness does not exceed the lower of the cost or fair market value of the property so acquired or built or of such repairs or improvements financed with such Indebtedness (each measured at the time of such acquisition, repair, improvement or construction is made); furthermore, notwithstanding anything to the contrary herein and strictly for the purposes of this clause (e) of the definition of Permitted Indebtedness and for no other purpose, any obligations of a Person that are or would have been treated as operating leases or capital leases for purposes of GAAP prior to the issuance by the Financial Accounting Standards Board on February 25, 2016 of an Accounting Standards Update (the “ASU”) shall continue to be accounted for as operating leases or capital leases (whether or not such operating lease obligations or capital lease obligations, as applicable, were in effect on such date) notwithstanding the fact that such obligations are required in accordance with the ASU (on a prospective or retroactive basis or otherwise) to be treated as capitalized lease obligations in accordance with GAAP;”

## 3. Limitation of Amendment.

**3.1** The amendments set forth in **Section 2** are effective for the purposes set forth herein and shall be limited precisely as written and shall not be deemed to (a) be a consent to any amendment, waiver or modification of any other term or condition of any Loan Document, or (b) otherwise prejudice any right or remedy which Collateral Agent or any Lender may now have or may have in the future under or in connection with any Loan Document.

**3.2** This Amendment shall be construed in connection with and as part of the Loan Documents and all terms, conditions, representations, warranties, covenants and agreements set forth in the Loan Documents, except as herein amended, are hereby ratified and confirmed and shall remain in full force and effect.

**4. Representations and Warranties.** To induce Collateral Agent and Lenders to enter into this Amendment, Borrower hereby represents and warrants to Collateral Agent and Lenders as follows:

**4.1** Immediately after giving effect to this Amendment (a) the representations and warranties contained in the Loan Documents are true, accurate and complete in all material respects as of the date hereof (except to the extent such representations and warranties relate to an earlier date, in which case they are true and correct as of such date), and (b) no Event of Default has occurred and is continuing;

**4.2** Borrower has the power and authority to execute and deliver this Amendment and to perform its obligations under the Loan Agreement, as amended by this Amendment;

**4.3** The organizational documents of Borrower delivered to Collateral Agent and Lenders on the Effective Date, or subsequent thereto, remain true, accurate and complete and have not been amended, supplemented or restated and are and continue to be in full force and effect;

**4.4** The execution and delivery by Borrower of this Amendment and the performance by Borrower of its obligations under the Loan Agreement, as amended by this Amendment, have been duly authorized;

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**4.5** The execution and delivery by Borrower of this Amendment and the performance by Borrower of its obligations under the Loan Agreement, as amended by this Amendment, do not and will not contravene (a) any law or regulation binding on or affecting Borrower, (b) any contractual restriction with a Person binding on Borrower, (c) any order, judgment or decree of any court or other governmental or public body or authority, or subdivision thereof, binding on Borrower, or (d) the organizational documents of Borrower;

**4.6** The execution and delivery by Borrower of this Amendment and the performance by Borrower of its obligations under the Loan Agreement, as amended by this Amendment, do not require any order, consent, approval, license, authorization or validation of, or filing, recording or registration with, or exemption by any governmental or public body or authority, or subdivision thereof, binding on Borrower; and

**4.7** This Amendment has been duly executed and delivered by Borrower and is the binding obligation of Borrower, enforceable against Borrower in accordance with its terms, except as such enforceability may be limited by bankruptcy, insolvency, reorganization, liquidation, moratorium or other similar laws of general application and equitable principles relating to or affecting creditors' rights.

**5. Release.** The Borrower hereby remises, releases, acquits, satisfies and forever discharges the Lenders and Collateral Agent, their agents, employees, officers, directors, predecessors, attorneys and all others acting or purporting to act on behalf of or at the direction of the Lenders and Collateral Agent ("Releasees"), of and from any and all manner of actions, causes of action, suit, debts, accounts, covenants, contracts, controversies, agreements, variances, damages, judgments, claims and demands whatsoever, in law or in equity, which any of such parties ever had, now has or, to the extent arising from or in connection with any act, omission or state of facts taken or existing on or prior to the date hereof, may have after the date hereof against the Releasees, for, upon or by reason of any matter, cause or thing whatsoever relating to or arising out of the Loan Agreement or the other Loan Documents on or prior to the date hereof and through the date hereof. Without limiting the generality of the foregoing, the Borrower waives and affirmatively agrees not to allege or otherwise pursue any defenses, affirmative defenses, counterclaims, claims, causes of action, setoffs or other rights they do, shall or may have as of the date hereof, including the rights to contest: (a) the right of Collateral Agent and each Lender to exercise its rights and remedies described in the Loan Documents; (b) any provision of this Amendment or the Loan Documents; or (c) any conduct of the Lenders or other Releasees relating to or arising out of the Loan Agreement or the other Loan Documents on or prior to the date hereof.

**6. Counterparts.** This Amendment may be executed in any number of counterparts and all of such counterparts taken together shall be deemed to constitute one and the same instrument. Delivery by electronic transmission (e.g. ".pdf") of an executed counterpart of this Amendment shall be effective as a manually executed counterpart signature thereof.

**7. Effectiveness.** This Amendment shall be deemed effective upon the due execution and delivery to Collateral Agent and Lenders of this Amendment by each party hereto.

**8. Condition Subsequent.** As a condition subsequent to this Amendment, Borrower agrees to promptly pay all of Lenders' Expenses incurred in connection with this Amendment and that Collateral Agent and each Lender may debit (or ACH) any deposit accounts, maintained by Borrower or any Loan Party, including the Designated Deposit Account for such Lenders' Expenses in accordance with Section 2.3(d) of the Loan Agreement.

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IN WITNESS WHEREOF, the parties hereto have caused this Amendment to be duly executed and delivered as of the date first written above.

**COLLATERAL AGENT AND LENDER:**

OXFORD FINANCE LLC  
By: /s/ Collette H. Featherly  
Name: Collette H. Featherly  
Title: Senior Vice President

**LENDER:**

SILICON VALLEY BANK  
By: /s/ Kristina Peralta  
Name: Kristina Peralta  
Title: Vice President

**BORROWER:**

CYTOKINETICS, INCORPORATED  
By: /s/ Ching W. Jaw  
Name: Ching W. Jaw  
Title: Chief Financial Officer

*[Signature Page to Fourth Amendment to Loan and Security Agreement]*

**CYTOKINETICS, INCORPORATED**  
**AMENDED AND RESTATED 2004 EQUITY INCENTIVE PLAN**

**AMENDED BY THE BOARD OF DIRECTORS: FEBRUARY 6, 2013**

**APPROVED BY STOCKHOLDERS: MAY 22, 2013**

**AMENDED TO REFLECT THE REVERSE STOCK SPLIT: JUNE 25, 2013**

**AMENDED AND RESTATED BY THE BOARD OF DIRECTORS: FEBRUARY 3, 2015**

**APPROVED BY STOCKHOLDERS: MAY 20, 2015**

**AMENDED AND RESTATED BY THE BOARD OF DIRECTORS: FEBRUARY 10, 2017**

**APPROVED BY STOCKHOLDERS: MAY 18, 2017**

**AMENDED AND RESTATED BY THE BOARD OF DIRECTORS: FEBRUARY 7, 2019**

**APPROVED BY STOCKHOLDERS: MAY 15, 2019**

**AMENDED TO REFLECT SEPARATE INDUCEMENT POOL: MAY 14, 2020**

**AMENDED AND RESTATED BY THE BOARD OF DIRECTORS: FEBRUARY 18, 2021**

**APPROVED BY STOCKHOLDERS: MAY 12, 2021**

**AMENDED AND RESTATED TO INCREASE SEPARATE INDUCEMENT POOL: AUGUST 13, 2021**

**1. PURPOSES OF THE PLAN AND PERMITTED AWARDS.**

The purposes of this Plan are to attract and retain the best available personnel for positions of substantial responsibility, to provide additional incentive to Employees, Directors and Consultants, and to promote the success of the Company's business. The Plan permits the grant of Incentive Stock Options, Nonstatutory Stock Options, Restricted Stock, Restricted Stock Units, Stock Appreciation Rights, Performance Units, Performance Shares, and Inducement Awards.

**2. SHARES SUBJECT TO THE PLAN.**

**(a) Shares Subject to the Plan.** Subject to adjustments as specified in Section 12 of the Plan, the maximum aggregate number of Shares that may be issued pursuant to Awards other than Inducement Awards under the Plan is 20,956,190 Shares. Notwithstanding the foregoing, an additional 1,850,000 Shares may be issued pursuant to Inducement Awards as provided in Section 2(e) of the Plan. The Shares may be authorized, but unissued or reacquired Stock.

**(b) Treatment of Lapsed Awards.** To the extent that an Award terminates, expires, or lapses for any reason, any Shares subject to the Award shall again be available for the grant of an Award pursuant to the Plan. Any shares of Stock tendered or withheld to satisfy the grant or exercise price or tax withholding obligation pursuant to any Award shall be treated as issued under this Plan and shall be deducted from the aggregate number of Shares which may be issued under Section 2(a). Shares of Stock repurchased on the open market with the proceeds of an exercise price shall not again be available for the grant of an Award pursuant to the Plan. Notwithstanding that a Stock Appreciation Right may be settled by the delivery of a net number of Shares, the full number of Shares underlying such Stock Appreciation Right shall not again be available for the grant of an Award pursuant to the Plan. In addition, no Shares may again be optioned, granted or awarded if such action would cause an Incentive Stock Option to fail to qualify as such under Section 422 of the Code. Notwithstanding the foregoing, any Inducement Shares that become available for issuance under the Plan pursuant to this Section 2(b) will only become available for issuance pursuant to Inducement Awards.

**(c) Calculation of Share Reserve Under the Fungible Ratio.** For purposes of determining the number of Shares issuable or transferred pursuant to Section 2(a) and except with respect to Inducement Awards, each Share which is issued or transferred pursuant to a Full Value Award (i) prior to May 20, 2015, shall be treated as if two Shares had been so issued or transferred, and (ii) on and after May 20, 2015, shall be treated as if 1.17 Shares had been so issued or transferred. To the extent there is issued a Share pursuant to a Full Value Award that counted as more than one Share against the number of Shares available for issuance under this Section and such Share again becomes available for issuance under the Plan pursuant to this Section, then the number of Shares available for issuance under the Plan shall increase by (A) two Shares for Shares returning prior to May 20, 2015, and (B) 1.17 Shares for Shares returning on and after May 20, 2015. To the extent permitted by Applicable Law or any exchange rule, Shares issued in assumption of, or in substitution for, any outstanding awards of any entity acquired in any form of combination by the Company or any Subsidiary of the Company shall not be counted against Shares available for grant pursuant to this Plan. The settlement of any Award in cash shall not be counted against the Shares available for issuance under the Plan.

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**(d) Incentive Stock Option Limit.** Subject to the provisions of Section 12 relating to capitalization adjustments, the aggregate maximum number of Shares that may be issued pursuant to the exercise of Incentive Stock Options will be 15,737,190 Shares.

**(e) Inducement Shares.** This Section 2(e) will apply with respect to the 1,850,000 Shares reserved under this Plan by action of the Board (or the Inducement Committee) to be used exclusively for the grant of Inducement Awards in compliance with NASDAQ Listing Rule 5635(c)(4) (the “**Inducement Shares**”). Notwithstanding anything to the contrary in this Plan, an Inducement Award (i) may only be granted with the prior written approval of the Inducement Committee and (ii) may be granted only to an Employee who has not previously been an Employee or a Director of the Company or any of its Affiliates, or following a bona fide period of non-employment, as an inducement material to the individual’s entering into employment with the Company within the meaning of Rule 5635(c)(4) of the NASDAQ Listing Rules. Incentive Stock Options may not be issued as part of an Inducement Award.

**(f) Share Reserve.** The Company, during the term of this Plan, will at all times reserve and keep available such number of Shares as will be sufficient to satisfy the requirements of the Plan.

### 3. ADMINISTRATION OF THE PLAN.

**(a) Procedure.** Unless and until the Board delegates administration to a Committee as set forth below, and subject to Section 2(e), the Plan shall be administered by the Board. The Board may delegate administration of the Plan to a Committee or Committees of one or more members of the Board. If administration is delegated to a Committee, the Committee shall have the powers theretofore possessed by the Board, including the power to delegate to a subcommittee any of the administrative powers the Committee is authorized to exercise. The Board may designate different Committees to administer the Plan with respect to different groups of Service Providers. Notwithstanding anything to the contrary set forth herein, only an Inducement Committee has the power to grant Inducement Awards.

**(b) Powers of the Administrator.** Subject to the provisions of the Plan, and in the case of a Committee, subject to the specific duties delegated by the Board to such Committee, the Administrator will have the authority, in its discretion:

**(i)** to determine the Fair Market Value;

**(ii)** to select the Service Providers to whom Awards may be granted hereunder, provided Inducement Awards can only be granted to certain Employees pursuant to Section 2(e) hereof;

**(iii)** to determine the number of Shares to be covered by each Award granted hereunder and the date of grant; the date of grant of an Award will be, for all purposes, the date on which the Administrator makes the determination granting such Award, or such later date as is determined by the Administrator;

**(iv)** to approve forms of agreement for use under the Plan;

**(v)** to determine the terms and conditions, not inconsistent with the terms of the Plan, of any Award granted hereunder. Such terms and conditions include, but are not limited to, the exercise price, the time or times when Awards may be exercised (which may be based on performance criteria), any vesting acceleration or waiver of forfeiture restrictions, and any restriction or limitation regarding any Award or the Shares relating thereto, based in each case on such factors as the Administrator will determine;

**(vi)** to construe and interpret the terms of the Plan and Awards granted pursuant to the Plan;

**(vii)** to prescribe, amend and rescind rules and regulations relating to the Plan, including rules and regulations relating to sub-plans established for the purpose of satisfying applicable foreign laws;

**(viii)** to modify or amend each Award (subject to Section 3(c) of the Plan); *provided, however*, that Administrator may amend the terms of an Award without the affected Participant’s consent if necessary (A) to maintain the qualified status of the Award as an Incentive Stock Option, (B) to clarify the manner of exemption from, or to bring the Award into compliance with, Section 409A of the Code, or (C) to comply with other Applicable Law;

**(ix)** to determine the terms and conditions of any, and with the approval of the Company’s stockholders, to institute an Exchange Program;

**(x)** to authorize any person to execute on behalf of the Company any instrument required to effect the grant of an Award previously granted by the Administrator;

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(xi) to allow a Participant to defer the receipt of the payment of cash or the delivery of Shares that would otherwise be due to such Participant under an Award; and

(xii) to make all other determinations deemed necessary or advisable for administering the Plan.

**(c) Prohibition Against Repricing.** Subject to adjustments made pursuant to Section 12, in no event shall the Administrator have the right to amend the terms of any Award to reduce the exercise price of such outstanding Award or cancel an outstanding Award in exchange for cash or other Awards with an exercise price that is less than the exercise price of the original Award without stockholder approval.

**(d) Effect of Administrator's Decision.** The Administrator's decisions, determinations and interpretations will be final and binding on all Participants and any other holders of Awards.

#### 4. ELIGIBILITY.

Nonstatutory Stock Options, Restricted Stock, Restricted Stock Units, Stock Appreciation Rights, Performance Units and Performance Shares may be granted to Service Providers. Incentive Stock Options may be granted only to Employees and Inducement Awards of any Nonstatutory Stock Options, Restricted Stock, Restricted Stock Units, Stock Appreciation Rights, Performance Units and Performance Shares may be granted only to Employees who meet the criteria set forth in Section 2(e).

#### 5. TERMS RELATING TO STOCK OPTIONS AND STOCK APPRECIATION RIGHTS.

Each Option or SAR will be in such form and will contain such terms and conditions as the Board deems appropriate. All Options will be separately designated Incentive Stock Options or Nonstatutory Stock Options at the time of grant, and, if certificates are issued, a separate certificate or certificates will be issued for Shares purchased on exercise of each type of Option. If an Option is not specifically designated as an Incentive Stock Option, or if an Option is designated as an Incentive Stock Option but some portion or all of the Option fails to qualify as an Incentive Stock Option under the applicable rules, then the Option (or portion thereof) will be a Nonstatutory Stock Option. The provisions of separate Options or SARs need not be identical; *provided, however*, that each Award Agreement will conform to (through incorporation of provisions hereof by reference in the applicable Award Agreement or otherwise) the substance of each of the following provisions:

**(a) Term of Option.** The term of each Option or SAR will be stated in the Award Agreement and will not exceed ten years from the date of grant, except that in the case of an Incentive Stock Option granted to a Participant who is a Ten Percent Stockholder, the term of the Incentive Stock Option may not be more than five years from the date of grant.

**(b) Exercise Price.** The exercise or strike price of each Option or SAR will be not less than 100% of the Fair Market Value of the Stock on the date the Award is granted, except that for Options or SARs granted to a Ten Percent Stockholder, the exercise or strike price of each Option or SAR will not be less than 110% of the Fair Market Value of the Stock on the date of grant. Notwithstanding the foregoing, an Option or SAR may be granted with an exercise or strike price lower than 100% of the Fair Market Value of the Stock subject to the Award if such Award is granted pursuant to an assumption of or substitution for another option or stock appreciation right pursuant to a Corporate Transaction and in a manner consistent with the provisions of Section 409A and, if applicable, Section 424(a) of the Code. Each SAR will be denominated in shares of Stock equivalents.

**(c) Waiting Period and Exercise Dates.** At the time an Option or SAR is granted, the Administrator will fix the period within which the Option or SAR may be exercised and will determine the vesting requirements and any other conditions that must be satisfied before the Option or SAR may be exercised.

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**(d) Exercise of an Option.** The Administrator will determine the acceptable method (which may be electronic) and form of consideration for exercising an Option, including the method of payment. Such consideration may include: (i) cash; (ii) check; (iii) promissory note, to the extent permitted by Applicable Laws; (iv) other shares of Stock provided that such shares have a Fair Market Value on the date of surrender equal to the aggregate exercise price of the Shares as to which said Option will be exercised and provided that accepting such shares of Stock, in the sole discretion of the Administrator, shall not result in any adverse accounting consequences to the Company; (v) consideration received by the Company under a cashless exercise program implemented by the Company in connection with the Plan; (vi) such other consideration and method of payment for the issuance of Shares to the extent permitted by Applicable Laws; or (vii) any combination of the foregoing methods of payment. In the case of an Incentive Stock Option, the Administrator will specify in the Award Agreement the acceptable forms of consideration.

**(e) Exercise and Payment of a SAR.** The Administrator will determine the acceptable method (which may be electronic) to exercise any outstanding SAR. The appreciation distribution payable on the exercise of a SAR will be not greater than an amount equal to the excess of (i) the aggregate Fair Market Value (on the date of the exercise of the SAR) of a number of shares of Stock equal to the number of Stock equivalents in which the Participant is vested under such SAR, and with respect to which the Participant is exercising the SAR on such date, over (ii) the strike price. The appreciation distribution may be paid in Stock, in cash, in any combination of the two or in any other form of consideration, as determined by the Board and contained in the Award Agreement evidencing such SAR.

**(f) Termination of Relationship as a Service Provider.** Except as otherwise provided in the applicable Award Agreement, if a Participant ceases to be a Service Provider, other than for Cause or upon the Participant's death or Disability, any unvested portion of the Option or SAR shall terminate and will revert to the Plan, and the Participant may exercise the vested portion of his or her Option or SAR until the earlier of three months following the Participant's termination, or expiration of the Option or SAR. If the Participant does not exercise his or her Option or SAR within the time specified, the Option or SAR will terminate, and the Shares covered by such Option or SAR will revert to the Plan. In the case of a Participant terminated for Cause, the Option or SAR will terminate immediately upon such Participant's termination as a Service Provider, and the Participant will be prohibited from exercising his or her Option or SAR from and after the date of such termination for Cause.

**(g) Disability of Participant.** Except as otherwise provided in the applicable Award Agreement, if a Participant ceases to be a Service Provider as a result of the Participant's Disability, any unvested portion of the Option or SAR shall terminate and will revert to the Plan, and the Participant may exercise the vested portion of his or her Option or SAR until the earlier of 12 months following the Participant's termination, or expiration of the Option or SAR. If the Participant does not exercise his or her Option or SAR within the time specified, the Option or SAR will terminate, and the Shares covered by such Option or SAR will revert to the Plan.

**(h) Death of Participant.** Except as otherwise provided in the applicable Award Agreement, if a Participant dies while a Service Provider, any unvested portion of the Option or SAR shall terminate and will revert to the Plan, and the Participant's properly designated beneficiary may exercise the Option or SAR until the earlier of 12 months following Participant's death, or until expiration of the term of such Option or SAR. If no such beneficiary has been designated by the Participant, then such Option or SAR may be exercised by the personal representative of the Participant's estate or by the person(s) to whom the Option or SAR is transferred pursuant to the Participant's will or in accordance with the laws of descent and distribution. If the Option or SAR is not so exercised within the time specified herein, the Award will terminate, and the Shares covered by such Option or SAR will revert to the Plan.

**(i) Rights of Holder of Option.** Unless otherwise stated in the applicable Award Agreement, an individual holding or exercising an Option or SAR shall have none of the rights of a stockholder (for example, the right to receive cash or dividend payments or distributions attributable to the subject Shares or to direct the voting of the subject Shares) until the Shares covered thereby are fully paid and issued to him. In no case shall an individual holding an Option receive cash or dividend payments or distributions or dividend equivalents attributable to unvested Shares underlying an Option. Except as provided in Section 12(a) hereof, no adjustment shall be made for dividends, distributions or other rights for which the record date is prior to the date of such issuance.

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## 6. RESTRICTED STOCK.

**(a) Grant of Restricted Stock.** The Administrator may grant Shares of Restricted Stock to Service Providers in such amounts as the Administrator, in its sole discretion, will determine, provided Inducement Awards of Restricted Stock can only be granted to certain Employees pursuant to Section 2(e) hereof.

**(b) Restricted Stock Agreement.** Each Restricted Stock Award will be evidenced by an Award Agreement that will specify the Period of Restriction, the number of Shares subject to such Restricted Stock Award, and such other terms and conditions as the Administrator will determine. Unless the Administrator determines otherwise, Restricted Stock will be held by the Company as escrow agent until the restrictions on such Shares have lapsed. The Administrator may impose such other restrictions on Restricted Stock as it may deem advisable or appropriate.

**(c) Transferability.** Except as provided in this Section 6, Restricted Stock may not be sold, transferred, pledged, assigned, or otherwise alienated or hypothecated until the end of the applicable Period of Restriction.

**(d) Removal of Restrictions.** Except as otherwise provided in this Section 6, Shares underlying each Restricted Stock Award made under the Plan will be released from escrow as soon as practicable after the last day of the Period of Restriction. The Administrator, in its discretion, may accelerate the time at which any restrictions will lapse or be removed.

**(e) Voting Rights.** During the Period of Restriction, Service Providers holding Restricted Stock granted hereunder may exercise full voting rights with respect to such Stock, unless the Administrator determines otherwise.

**(f) Dividends and Other Distributions.** During the Period of Restriction, Service Providers holding Restricted Stock will be entitled to receive all dividends and other distributions paid with respect to such Stock unless otherwise provided in the Award Agreement. Any such dividends will be subject to the same restrictions on transferability and forfeitability as the Restricted Stock with respect to which they were paid. For clarity, Service Providers holding Restricted Stock shall have the right to vote such Stock and the right to receive any dividends declared or paid with respect to such Stock provided that any such dividends shall be subject to the same vesting restrictions as the underlying Shares subject to the Restricted Stock Award during the Period of Restriction. Such dividends so accrued with respect to the Shares subject to any Restricted Stock Award, whether subject to time-based and/or performance-based vesting criteria, shall become payable no earlier than the date the applicable vesting criteria have been satisfied and the Period of Restriction with respect to such Restricted Stock has lapsed.

**(g) Return of Restricted Stock to Company.** On the date set forth in the Award Agreement, the Restricted Stock for which restrictions have not lapsed will revert to the Company and again will become available for grant under the Plan.

## 7. RESTRICTED STOCK UNITS.

**(a) Grant of Restricted Stock Units; Vesting and Other Terms.** Restricted Stock Units may be granted to Service Providers at any time with the number of Units to be determined by the Administrator, provided Inducement Awards of Restricted Stock Units can only be granted to certain Employees pursuant to Section 2(e) hereof. The Administrator will set service-based or other vesting provisions in its discretion which, depending on the extent to which they are met, will determine the number of Units to be issued to the Service Providers. Each Award of Restricted Stock Units will be evidenced by an Award Agreement that will specify the vesting schedule, and such other terms and conditions as the Administrator, in its sole discretion, will determine.

**(b) Earning of Restricted Stock Units; Form and Timing of Payment.** Upon vesting of Restricted Stock Units, the holder thereof will be issued that number of Shares equal to the number of Units that have vested. Issuance of Shares upon the vesting of Restricted Stock Units will be made as soon as practicable after vesting, but in no event later than the time required to avoid adverse tax consequences under Section 409A of the Code.

**(c) Cancellation of Restricted Stock Units.** If a holder of Restricted Stock Units terminates service prior to the vesting of all Units or as otherwise provided in an Award Agreement, all unvested Restricted Stock Units will be forfeited and will again be available for grant under the Plan.

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**(d) Dividend Equivalents.** Dividend equivalents may be credited in respect of Shares covered by an Award Agreement covering a Restricted Stock Unit, as determined by the Board and contained in such Award Agreement. At the sole discretion of the Board, such dividend equivalents may be converted into additional Shares covered by the Restricted Stock Unit in such manner as determined by the Board. Any additional Shares covered by the Restricted Stock Unit credited by reason of such dividend equivalents will be subject to all of the same terms and conditions (including forfeiture restrictions) of the underlying Restricted Stock Unit to which they relate, and such dividend equivalent shall not be paid unless and until the time that the Shares underlying the Restricted Stock Unit are vested and are distributed to the Service Provider.

## **8. PERFORMANCE UNITS AND PERFORMANCE SHARES.**

**(a) Grant of Performance Units and Performance Shares.** Performance Units and Performance Shares may be granted to Service Providers at any time as determined by the Administrator, in such numbers and subject to such other terms and conditions as determined by the Administrator, in its discretion, provided Inducement Awards of Performance Units and Performance Shares can only be granted to certain Employees pursuant to Section 2(e) hereof.

**(b) Value of Performance Units/Shares.** Each Performance Unit will have an initial value that is established by the Administrator on or before the date of grant. Each Performance Share will have an initial value equal to the Fair Market Value of a Share on the date of grant.

**(c) Performance Objectives and Other Terms.** The Administrator will set performance objectives or other vesting provisions in its discretion which, depending on the extent to which they are met, will determine the number or value of Performance Units/Shares that will be paid out to the Service Providers. Each Award of Performance Units/Shares will be evidenced by an Award Agreement that will specify the Performance Period, and such other terms and conditions as the Administrator will determine. The Administrator may set performance objectives based upon the achievement of Company-wide, divisional, or individual goals, applicable federal or state securities laws, or any other basis determined by the Administrator in its discretion.

**(d) Earning of Performance Units/Shares.** After the applicable Performance Period has ended, the holder of Performance Units/Shares will be entitled to receive a payout of the number of Performance Units/Shares earned by the Participant over the Performance Period, to be determined as a function of the extent to which the corresponding performance objectives or other vesting provisions have been achieved. After the grant of a Performance Unit/Share, the Administrator, in its sole discretion, may reduce or waive any performance objectives or other vesting provisions for such Performance Unit/Share.

**(e) Form and Timing of Payment of Performance Units/Shares.** Payment of earned Performance Units/Shares will be made as soon as practicable after the expiration of the applicable Performance Period. The Administrator may pay earned Performance Units/Shares in the form of cash, in Shares (which have an aggregate Fair Market Value equal to the value of the earned Performance Units/Shares at the close of the applicable Performance Period) or in a combination thereof.

**(f) Cancellation of Performance Units/Shares.** On the date set forth in the Award Agreement, all unearned or unvested Performance Units/Shares will be forfeited and will again be available for grant under the Plan.

**(g) Dividends and Other Distributions.** No cash dividends or distributions declared with respect to Shares subject to the Performance Units/Shares shall be paid to any Participant unless and until the Participant vests in such underlying Performance Units/Shares. Upon the vesting of a Performance Units/Shares, any cash dividends or distributions declared but not paid during the vesting period with respect to such Performance Units/Shares shall be paid to the Participant at the same time or times as the Shares underlying the Performance Units/Shares. Any stock dividends declared on Shares subject to a Performance Units/Shares shall be subject to the same restrictions and shall vest at the same time as the Performance Units/Shares from which said dividends were derived. All unvested dividends shall be forfeited by the Participants to the extent their underlying Performance Units/Shares are forfeited.

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## **9. PERFORMANCE GOALS.**

The granting and/or vesting of Awards of Restricted Stock, Restricted Stock Units, Performance Shares and Performance Units and other incentives under the Plan may be made subject to the attainment of performance goals relating to one or more business criteria and may provide for a targeted level or levels of achievement (“**Performance Goals**”) including, with respect to the Company or any business unit: (a) cash position, (b) clinical progression, (c) collaboration arrangements, (d) collaboration progression, (e) earnings per share, (f) a financing event, (g) net income, (h) operating cash flow, (i) market share, (j) operating expenses, (k) operating income, (l) product approval, (m) product revenues, (n) profit after tax, (o) projects in development, (p) regulatory filings, (q) return on assets, (r) return on equity, (s) revenue growth, and (t) total stockholder return, (u) implementation of, progression in or completion of projects or processes (including, without limitation, progress in research or development programs, progress in regulatory or compliance initiatives, clinical trial initiation, clinical trial enrollment, clinical trial results, new or supplemental indications for existing products, regulatory filing submissions, regulatory filing acceptances, regulatory or advisory committee interactions, regulatory approvals, product supply and systems development and implementation), (v) completion of a joint venture or other corporate transaction, (w) employee retention, (x) budget management and (y) any other measures of performance selected by the Board. The Administrator will determine whether any significant element(s) will be included in or excluded from the calculation of any Performance Goal with respect to any Participant. Any Performance Goals may be used to measure the performance of the Company as a whole or a business unit of the Company and may be measured relative to a peer group or index or to another Performance Goal. With respect to any Award, Performance Goals may be used alone or in combination. The Performance Goals may differ from Participant to Participant and from Award to Award. The Administrator will determine whether any significant element(s) will be included in or excluded from the calculation of any Performance Goal with respect to any Participant. In all other respects, Performance Goals will be calculated in accordance with the Company’s financial statements, generally accepted accounting principles, or under a methodology established by the Administrator prior to the issuance of an Award.

## **10. LEAVES OF ABSENCE.**

Unless the Administrator provides otherwise, vesting of Awards granted hereunder will be suspended during any unpaid leave of absence. A Service Provider will not cease to be an Employee in the case of (a) any leave of absence approved by the Company or (b) transfers between locations of the Company or between the Company, its Parent, or any of its Subsidiaries. For purposes of Incentive Stock Options, no such leave may exceed 90 days, unless reemployment upon expiration of such leave is guaranteed by statute or contract. If reemployment upon expiration of a leave of absence approved by the Company is not so guaranteed, then six months and a day following the 1st day of such leave any Incentive Stock Option held by the Participant will cease to be treated as an Incentive Stock Option and will be treated for tax purposes as a Nonstatutory Stock Option.

## **11. TRANSFERABILITY OF AWARDS.**

Unless determined otherwise by the Administrator, an Award may not be sold, pledged, assigned, hypothecated, transferred, or disposed of in any manner other than by will or by the laws of descent or distribution and may be exercised, during the lifetime of the Participant, only by the Participant. If the Administrator makes an Award transferable, such Award will contain such additional terms and conditions as the Administrator deems appropriate; provided, however, that the Administrator may only make an Award transferable to one or more of the following: (a) a “family member” (as defined pursuant to Rule 701 of the Securities Act of 1933, as amended) of the Participant; (b) a trust for the benefit of one or more of the Participant or the persons referred to in clause (a); (c) a partnership, limited liability company or corporation in which the Participant or the persons referred to in clause (a) are the only partners, members or stockholders; or (d) charitable donations.

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## 12. ADJUSTMENTS; DISSOLUTION OR LIQUIDATION; MERGER OR CHANGE IN CONTROL.

**(a) Adjustments.** In order to prevent diminution or enlargement of the benefits or potential benefits intended to be made available under the Plan, in the event that any dividend or other distribution (whether in the form of cash, shares of Stock, other securities, or other property), recapitalization, stock split, reverse stock split, reorganization, merger, consolidation, split-up, spin-off, combination, repurchase, or exchange of shares of Stock or other securities of the Company, or other change in the corporate structure of the Company affecting the shares of Stock occurs, the Administrator shall appropriately adjust the number and class of Shares that may be delivered under the Plan and/or the number, class, and price of Shares covered by each outstanding Award, the numerical Share limits as specified throughout the Plan.

**(b) Dissolution or Liquidation.** In the event of the proposed dissolution or liquidation of the Company, the Administrator will notify each Participant as soon as practicable prior to the effective date of such proposed transaction. To the extent it has not been previously exercised, an Award will terminate immediately prior to the consummation of such proposed action.

**(c) Change in Control.** In the event of a Change in Control, each outstanding Award will be assumed or an equivalent option or right substituted by the successor corporation or a Parent or Subsidiary of the successor corporation. In the event that the successor corporation refuses to assume or substitute for the Award, the Participant will fully vest in and have the right to exercise all of his or her outstanding time-based Options and SARs, including Shares as to which such Awards would not otherwise be vested or exercisable, all time-based restrictions on Restricted Stock shall lapse, and, with respect to Performance Shares, Restricted Stock Units and Performance Units, all Performance Goals or other vesting criteria will be deemed achieved at target levels and all other terms and conditions met.

**(i)** For the purposes of this Section (c), an Award will be considered assumed if, following the Change in Control, the Award confers the right to purchase or receive, for each Share subject to the Award immediately prior to the Change in Control, the Fair Market Value of the consideration received in the merger or Change in Control by holders of Stock for each Share held on the effective date of the transaction; provided, however, that if such consideration received in the Change in Control is not solely stock of the successor corporation or its Parent, the Administrator may, with the consent of the successor corporation, provide for the consideration to be received to be solely stock of the successor corporation or its Parent equal in Fair Market Value to the per share consideration received by holders of Stock in the Change in Control. The continuation or imposition of vesting terms or other restrictions on Awards in connection with a Change of Control shall not prevent such Awards from being considered assumed for purposes of this Section.

**(ii)** Notwithstanding the above, an Award that vests, is earned or paid-out upon the satisfaction of one or more Performance Goals will not be considered assumed if the Company or its successor modifies any of such Performance Goals without the Participant's consent; *provided, however*, a modification to such Performance Goals only to reflect the successor corporation's post-Change in Control corporate structure will not be deemed to invalidate an otherwise valid Award assumption.

**(iii)** If an Option or SAR is not assumed or substituted for in the event of a Change in Control, the Administrator will notify the Participant that the Option or SAR will be fully vested and exercisable for a stated period of time prior to the Change of Control, as determined by the Administrator, and the Option or SAR will terminate upon the expiration of such period.

**(iv)** With respect to Awards granted to an Outside Director that are assumed or substituted for, if on the date of or following such assumption or substitution the Participant's status as a Director or a director of the successor corporation, as applicable, is terminated other than upon a voluntary resignation by the Participant not at the request of the successor, then the Participant will fully vest in all Awards, and shall have the right to exercise Options and SARs for such periods as provided in the applicable Award Agreement.

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### 13. TAX WITHHOLDING.

**(a) Withholding Requirements.** Prior to the delivery of any Shares or cash pursuant to an Award (or exercise thereof), the Company will have the power and the right to deduct or withhold, or require a Participant to remit to the Company, an amount sufficient to satisfy federal, state, local, foreign or other taxes (including the Participant's FICA obligation) required to be withheld with respect to such Award (or exercise thereof).

**(b) Withholding Arrangements.** The Administrator, in its sole discretion and pursuant to such procedures as it may specify from time to time, may permit a Participant to satisfy such tax withholding obligation, in whole or in part by (without limitation) (i) paying cash, (ii) electing to have the Company withhold otherwise deliverable cash or shares of Stock having a Fair Market Value equal to the amount required to be withheld, (iii) delivering to the Company already-owned shares of Stock having a Fair Market Value equal to the amount required to be withheld, or (iv) selling a sufficient number of shares of Stock otherwise deliverable to the Participant through such means as the Administrator may determine in its sole discretion (whether through a broker or otherwise) equal to the amount required to be withheld. The amount of the withholding requirement will be deemed to include any amount which the Administrator agrees may be withheld at the time the election is made, not to exceed the amount determined by using the maximum federal, state or local marginal income tax rates applicable to the Participant with respect to the Award on the date that the amount of tax to be withheld is to be determined. The Fair Market Value of the shares of Stock to be withheld or delivered will be determined as of the date that the taxes are required to be withheld.

### 14. CLAWBACK AND RECOVERY OF AWARDS.

All Awards granted under the Plan will be subject to recoupment in accordance with any clawback policy that the Company is required to adopt pursuant to the listing standards of any national securities exchange or association on which the Company's securities are listed or as is otherwise required by the Dodd-Frank Wall Street Reform and Consumer Protection Act or other applicable law. In addition, the Board has adopted a clawback policy that allows the Company to seek repayment of incentive compensation that was erroneously paid. The policy provides that if the Board, or Compensation Committee as applicable, determines that there has been a material misstatement of publicly issued financial results from those previously issued to the public due to a knowing violation of rules and regulations of the Securities and Exchange Commission or Company policy, or the willful commission of an act of fraud, dishonesty, gross recklessness or gross negligence, our Board or Compensation Committee will review all incentive compensation made to our named executive officers during the three year period prior to the restatement on the basis of having met or exceeded specific Performance Goals. If such payments would have been lower had they been calculated based on such restated results, our Board or Compensation Committee will (to the extent permitted by governing law) seek to recoup the payments in excess of the amount that would have been paid based on the restated results.

### 15. CONDITIONS UPON ISSUANCE OF SHARES.

**(a) Legal Compliance.** Shares will not be issued pursuant to the exercise of an Award unless the exercise of such Award and the issuance and delivery of such Shares will comply with Applicable Laws and will be further subject to the approval of counsel for the Company with respect to such compliance.

**(b) Investment Representations.** As a condition to the exercise of an Award, the Company may require the person exercising such Award to represent and warrant at the time of any such exercise that the Shares are being purchased only for investment and without any present intention to sell or distribute such Shares if, in the opinion of counsel for the Company, such a representation is required.

### 16. AMENDMENT AND TERMINATION OF THE PLAN.

**(a) Amendment and Termination.** The Administrator may at any time amend, alter, suspend or terminate the Plan. The Company will obtain stockholder approval of any Plan amendment to the extent necessary and desirable to comply with Applicable Laws. Unless earlier terminated or extended, the Plan will continue in effect until February 6, 2029, at which time it shall terminate without further action on the part of the Board or the Company.

**(b) Effect of Amendment or Termination.** No amendment, alteration, suspension or termination of the Plan will impair the rights of any Participant, without the consent of the Participant. Termination of the Plan will not affect the Administrator's ability to exercise the powers granted to it hereunder with respect to Awards granted under the Plan prior to the date of such termination.

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## 17. MISCELLANEOUS

**(a) Not an Employment or Service Contract.** Neither the Plan nor any Award will confer upon a Participant any right with respect to continuing the Participant's relationship as a Service Provider with the Company, nor will they interfere in any way with the Participant's right or the Company's right to terminate such relationship at any time, with or without cause, to the extent permitted by Applicable Laws.

**(b) Inability to Obtain Authority.** The inability of the Company to obtain authority from any regulatory body having jurisdiction, which authority is deemed by the Company's counsel to be necessary to the lawful issuance and sale of any Shares hereunder, will relieve the Company of any liability in respect of the failure to issue or sell such Shares as to which such requisite authority will not have been obtained.

**(c) Electronic Delivery.** Any reference herein to a "written" agreement or document will include any agreement or document delivered electronically, filed publicly at [www.sec.gov](http://www.sec.gov) (or any successor website thereto) or posted on the Company's intranet (or other shared electronic medium controlled by the Company to which the Participant has access).

**(d) Compliance with Section 409A of the Code.** Unless otherwise expressly provided for in an Award Agreement, the Plan and Award Agreements will be interpreted to the greatest extent possible in a manner that makes the Plan and the Awards granted hereunder exempt from Section 409A of the Code, and, to the extent not so exempt, in compliance with Section 409A of the Code. If the Board determines that any Award granted hereunder is not exempt from and is therefore subject to Section 409A of the Code, the Award Agreement evidencing such Award will incorporate the terms and conditions necessary to avoid the consequences specified in Section 409A(a)(1) of the Code, and to the extent an Award Agreement is silent on terms necessary for compliance, such terms are hereby incorporated by reference into the Award Agreement. Notwithstanding anything to the contrary in this Plan (and unless the Award Agreement specifically provides otherwise), if the shares of Stock are publicly traded, and if a Participant holding an Award that constitutes "deferred compensation" under Section 409A of the Code is a "specified employee" for purposes of Section 409A of the Code, no distribution or payment of any amount that is due because of a "separation from service" (as defined in Section 409A of the Code without regard to alternative definitions thereunder) will be issued or paid before the date that is six months following the date of such Participant's "separation from service" (as defined in Section 409A of the Code without regard to alternative definitions thereunder) or, if earlier, the date of the Participant's death, unless such distribution or payment can be made in a manner that complies with Section 409A of the Code, and any amounts so deferred will be paid in a lump sum on the day after such six month period elapses, with the balance paid thereafter on the original schedule.

**(e) Choice of Law.** The law of the State of Delaware will govern all questions concerning the construction, validity and interpretation of this Plan, without regard to that state's conflict of laws rules.

## 18. DEFINITIONS.

As used herein, the following definitions will apply:

**(a) "Administrator"** means the Board or any of its Committees as will be administering the Plan, in accordance with Section 3 of the Plan. With respect to Inducement Awards, the term "Administrator" shall mean the Board or the Inducement Committee.

**(b) "Affiliate"** means, at the time of determination, any "parent" or "subsidiary" of the Company as such terms are defined in Rule 405 of the Securities Act. The Board will have the authority to determine the time or times at which "parent" or "subsidiary" status is determined within the foregoing definition.

**(c) "Applicable Law"** means the requirements relating to the administration of equity-based awards under U.S. federal and state corporate laws, U.S. federal and state securities laws, the Code, any stock exchange or quotation system on which the Stock is listed or quoted and the applicable laws of any foreign country or jurisdiction where Awards are, or will be, granted under the Plan.

**(d) "Award"** means, individually or collectively, a grant under the Plan of Options, SARs, Restricted Stock, Restricted Stock Units, Performance Units or Performance Shares and shall include Inducement Awards.

**(e) "Award Agreement"** means the written or electronic agreement setting forth the terms and provisions applicable to each Award granted under the Plan. The Award Agreement is subject to the terms and conditions of the Plan.

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(f) **“Board”** means the Board of Directors of the Company.

(g) **“Cause”** means, in respect of a Participant, the meaning ascribed to such term in the written employment agreement between a Participant and the Company then in effect, and in the absence of any written agreement between the Participant and the Company defining such term, with respect to a Participant, the occurrence of any of the following events: (i) such Participant’s commission of any felony or any crime involving fraud, dishonesty or moral turpitude under the laws of the United States or any state thereof; (ii) such Participant’s attempted commission of, or participation in, a fraud or act of dishonesty against the Company; (iii) such Participant’s intentional, material violation of any contract or agreement between the Participant and the Company or of any statutory duty owed to the Company; (iv) such Participant’s unauthorized use or disclosure of the Company’s confidential information or trade secrets; or (v) such Participant’s gross misconduct. The determination that a termination of the Participant is either for Cause or without Cause will be made by the Company, in its sole discretion. Any determination by the Company that the service of a Participant was terminated with or without Cause for the purposes of outstanding Awards held by such Participant under the Plan will have no effect upon any determination of the rights or obligations of the Company or such Participant for any other purpose.

(h) **“Change in Control”** means the occurrence of any of the following events:

(i) Any **“person”** (as such term is used in Sections 13(d) and 14(d) of the Exchange Act) becomes the **“beneficial owner”** (as defined in Rule 13d-3 of the Exchange Act), directly or indirectly, of securities of the Company representing fifty percent (50%) or more of the total voting power represented by the Company’s then outstanding voting securities; or

(ii) The consummation of the sale or disposition by the Company of all or substantially all of the Company’s assets;

(iii) A change in the composition of the Board occurring within a two-year period, as a result of which less than a majority of the directors are Incumbent Directors. **“Incumbent Directors”** means directors who either (A) are Directors as of the effective date of the Plan, or (B) are elected, or nominated for election, to the Board with the affirmative votes of at least a majority of the Incumbent Directors at the time of such election or nomination (but will not include an individual whose election or nomination is in connection with an actual or threatened proxy contest relating to the election of directors to the Company); or

(iv) The consummation of a merger or consolidation of the Company with any other corporation, other than a merger or consolidation which would result in the voting securities of the Company outstanding immediately prior thereto continuing to represent (either by remaining outstanding or by being converted into voting securities of the surviving entity or its parent) at least fifty percent (50%) of the total voting power represented by the voting securities of the Company or such surviving entity or its parent outstanding immediately after such merger or consolidation.

(i) **“Code”** means the Internal Revenue Code of 1986, as amended. Any reference to a section of the Code will be a reference to any successor or amended section of the Code.

(j) **“Committee”** means a committee of Directors appointed by the Board in accordance with Section 3 of the Plan.

(k) **“Company”** means Cytokinetics, Incorporated, a Delaware corporation, or any successor thereto.

(l) **“Consultant”** means any person, including an advisor, engaged by the Company or a Parent or Subsidiary of the Company to render services to such entity.

(m) **“Director”** means a member of the Board.

(n) **“Disability”** means total and permanent disability as defined in Section 22(e)(3) of the Code, provided that in the case of Awards other than Incentive Stock Options, the Administrator in its discretion may determine whether a permanent and total disability exists in accordance with non-discriminatory standards.

(o) **“Employee”** means any person employed by the Company or any Parent or Subsidiary of the Company.

(p) **“Exchange Act”** means the Securities Exchange Act of 1934, as amended.

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**(q) “Exchange Program”** means a program under which (i) outstanding Awards are surrendered or cancelled in exchange for Awards of the same type (which may have lower exercise prices and different terms), Awards of a different type, and/or cash, (ii) Participants would have the opportunity to transfer any outstanding Awards to a financial institution or other person or entity selected by the Administrator, and/or (iii) the exercise price of an outstanding Award is reduced. The Administrator will determine the terms and conditions of any Exchange Program in its sole discretion, subject to the provisions of Section 3(c).

**(r) “Fair Market Value”** means, as of any date, the value of Stock determined as follows:

**(i)** If the Stock is listed on any established stock exchange or a national market system, including without limitation the NASDAQ Global Market, the NASDAQ Global Select Market or the NASDAQ Capital Market, its Fair Market Value will be the closing sales price for such stock (or the closing bid, if no sales were reported) as quoted on such exchange or system on the day of determination, as reported in The Wall Street Journal or such other source as the Administrator deems reliable;

**(ii)** If the Stock is regularly quoted by a recognized securities dealer but selling prices are not reported, the Fair Market Value of a share of Stock will be the mean between the high bid and low asked prices for the Stock on the day of determination, as reported in The Wall Street Journal or such other source as the Administrator deems reliable; or

**(iii)** In the absence of an established market for the Stock, the Fair Market Value will be determined in good faith by the Administrator.

**(s) “Fiscal Year”** means the fiscal year of the Company.

**(t) “Full Value Award”** means any Award other than an Option, SAR or other Award for which the Participant pays the intrinsic value (whether directly or by forgoing a right to receive a payment from the Company).

**(u) “Incentive Stock Option”** means an Option intended to qualify as an incentive stock option within the meaning of Section 422 of the Code and the regulations thereunder.

**(v) “Inducement Award”** means an Award granted pursuant to Section 2(e) of the Plan.

**(w) “Inducement Committee”** means a Committee consisting of the majority of the Company’s independent directors or the Company’s independent Compensation Committee, in each case in accordance with NASDAQ Listing Rule 5635(c)(4).

**(x) “Nonstatutory Stock Option”** means an Option that by its terms does not qualify or is not intended to qualify as an Incentive Stock Option.

**(y) “Officer”** means a person who is an officer of the Company within the meaning of Section 16 of the Exchange Act and the rules thereunder.

**(z) “Option”** means a stock option granted pursuant to the Plan.

**(aa) “Outside Director”** means a Director who is not an Employee.

**(bb) “Parent”** means a “parent corporation,” whether now or hereafter existing, as defined in Section 424(e) of the Code.

**(cc) “Participant”** means the holder of an outstanding Award.

**(dd) “Performance Goals”** is defined in Section 9 of the Plan.

**(ee) “Performance Period”** means any Fiscal Year or such other period as determined by the Administrator in its sole discretion.

**(ff) “Performance Share” or “Performance Unit”** means an Award granted to a Participant pursuant to Section 8.

**(gg) “Period of Restriction”** means the period during which the transfer of shares of Restricted Stock are subject to restrictions and therefore, the shares of Restricted Stock are subject to a substantial risk of forfeiture. Such restrictions may be based on the passage of time, the achievement of target levels of performance, or the occurrence of other events as determined by the Administrator.

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**(hh) "Plan"** means this Amended and Restated 2004 Equity Incentive Plan.

**(ii) "Restricted Stock"** means Shares issued pursuant to a Restricted Stock Award under Section 6 of the Plan, or issued pursuant to the early exercise of an Option.

**(jj) "Restricted Stock Unit"** shall mean a bookkeeping entry representing an amount equal to the Fair Market Value of one Share, granted pursuant to Section 7. Each Restricted Stock Unit represents an unfunded and unsecured obligation of the Company.

**(kk) "Service Provider"** means an Employee, Director or Consultant.

**(ll) "Share"** means a share of the Stock, as adjusted in accordance with Section 12 of the Plan.

**(mm) "Stock"** means the Common Stock of the Company.

**(nn) "Stock Appreciation Right" or "SAR"** means an Award, granted alone or in connection with an Option, that pursuant to Section 5 is designated as a SAR.

**(oo) "Subsidiary"** means a "*subsidiary corporation*", whether now or hereafter existing, as defined in Section 424(f) of the Code.

**(pp) "Ten Percent Stockholder"** means a person who Owns (or is deemed to Own pursuant to Section 424(d) of the Code) stock possessing more than 10% of the total combined voting power of all classes of stock of the Company or any Affiliate.

CERTIFICATION OF THE CHIEF EXECUTIVE OFFICER  
Pursuant to Rule 13a-14(a) and Rule 15d-14(a) of the Securities Exchange Act, as amended

I, Robert I. Blum, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q 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 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 the 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 officers 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 that 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.

Dated: November 5, 2021

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

CERTIFICATION OF THE CHIEF FINANCIAL OFFICER  
Pursuant to Rule 13a-14(a) and Rule 15d-14(a) of the Securities Exchange Act, as amended

I, Ching W. Jaw, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q 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 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 the 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 officers 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 that 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.

Dated: November 5, 2021

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

CERTIFICATION OF THE CHIEF ACCOUNTING OFFICER  
Pursuant to Rule 13a-14(a) and Rule 15d-14(a) of the Securities Exchange Act, as amended

I, Robert C. Wong, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q 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 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 the 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 officers 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 that 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.

Dated: November 5, 2021

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

CERTIFICATION OF CHIEF EXECUTIVE OFFICER, CHIEF FINANCIAL OFFICER, AND CHIEF ACCOUNTING OFFICER  
Pursuant to 18. U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

I certify, pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, 18 U.S.C. Section 1350, that the Quarterly Report of Cytokinetics, Incorporated on Form 10-Q for the quarterly period ended September 30, 2021 fully complies with the requirements of Section 13(a) of the Securities Exchange Act of 1934 (15 U.S.C. 78m) and the information contained in such Form 10-Q fairly presents, in all material respects, the financial condition and results of operations of Cytokinetics, Incorporated.

Dated: November 5, 2021

/s/ Robert I. Blum

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Robert I. Blum  
President and Chief Executive Officer  
(Principal Executive Officer)

/s/ Ching W. Jaw

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Ching W. Jaw  
Senior Vice President, Chief Financial Officer  
(Principal Financial Officer)

/s/ Robert C. Wong

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Robert C. Wong  
Vice President, Chief Accounting Officer  
(Principal Accounting Officer)