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# 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, 2022**

**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**

# CYTOKINETICS, INCORPORATED
**(Exact name of registrant as specified in its charter)**

| **Delaware** | **94-3291317** |
|---|---|
| **(State or other jurisdiction of incorporation or organization)** | **(I.R.S. Employer Identification No.)** |
| **350 Oyster Point Blvd.<br>South San Francisco, California** | **94080** |
| **(Address of principal executive offices)** | **(Zip Code)** |

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

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

| **Title of each class** | **Trading symbol** | **Name of each exchange on which registered** |
|---|---|---|
| **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 | ☒ | Accelerated filer | ☐ |
| Non-accelerated filer | ☐ | Smaller reporting company | ☐ |
| Emerging growth company | ☐ | | |

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

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

Number of shares of common stock, $0.001 par value, outstanding as of November 2, 2022: 94,631,001

**CYTOKINETICS, INCORPORATED**
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**FOR THE THREE AND NINE MONTHS ENDED SEPTEMBER 30, 2022**

**PART I. FINANCIAL INFORMATION**

**ITEM 1. FINANCIAL STATEMENTS**

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

| | September 30, 2022 | December 31, 2021 |
|---|---|---|
| **ASSETS** | | |
| Current assets: | | |
| Cash and cash equivalents | $ 106,238 | $ 112,666 |
| Short-term investments | 761,426 | 358,972 |
| Accounts receivable | 2,294 | 51,819 |
| Prepaid expenses and other current assets | 14,317 | 12,215 |
| Total current assets | 884,275 | 535,672 |
| Long-term investments | 28,544 | 152,050 |
| Property and equipment, net | 80,302 | 73,271 |
| Operating lease right-of-use assets | 75,076 | 73,138 |
| Other assets | 7,764 | 7,188 |
| Total assets | $ 1,075,961 | $ 841,319 |
| **LIABILITIES AND STOCKHOLDERS' (DEFICIT) EQUITY** | | |
| Current liabilities: | | |
| Accounts payable | $ 14,429 | $ 21,087 |
| Accrued liabilities | 40,229 | 34,370 |
| Short-term operating lease liabilities | 16,056 | 14,863 |
| Other current liabilities | 5,782 | 1,540 |
| Total current liabilities | 76,496 | 71,860 |
| Term loan, net | 63,544 | 47,367 |
| Convertible notes, net | 544,986 | 95,471 |
| Liabilities related to revenue participation right purchase agreements, net | 291,260 | 179,072 |
| Long-term deferred revenue | — | 87,000 |
| Long-term operating lease liabilities | 114,405 | 112,229 |
| Other non-current liabilities | 1,247 | 4,457 |
| Total liabilities | 1,091,938 | 597,456 |
| Commitments and contingencies | | |
| Stockholders' equity: | | |
| Preferred stock, $0.001 par value | — | — |
| Common stock, $0.001 par value | 93 | 84 |
| Additional paid-in capital | 1,438,103 | 1,452,268 |
| Accumulated other comprehensive loss | (5,559) | (869) |
| Accumulated deficit | (1,448,614) | (1,207,620) |
| Total stockholders' (deficit) equity | (15,977) | 243,863 |
| Total liabilities and stockholders' (deficit) equity | $ 1,075,961 | $ 841,319 |

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, 2022 | September 30, 2021 | September 30, 2022 | September 30, 2021 |
| Revenues: | | | | |
| Research and development revenues | $ 2,515 | $ 437 | $ 4,631 | $ 9,828 |
| Milestone revenues | — | 5,000 | 1,000 | 5,000 |
| Realization of revenue participation right purchase agreement | — | — | 87,000 | — |
| Total revenues | 2,515 | 5,437 | 92,631 | 14,828 |
| Operating expenses: | | | | |
| Research and development | 62,734 | 48,436 | 165,795 | 116,440 |
| General and administrative | 48,222 | 26,202 | 124,008 | 62,997 |
| Total operating expenses | 110,956 | 74,638 | 289,803 | 179,437 |
| Operating loss | (108,441) | (69,201) | (197,172) | (164,609) |
| Interest expense | (6,804) | (4,161) | (12,357) | (12,222) |
| Loss on settlement of debt | (22,246) | — | (24,939) | — |
| Non-cash interest expense on liabilities related to revenue participation right purchase agreements | (8,963) | (2,955) | (22,530) | (8,621) |
| Interest and other income, net | 4,144 | 231 | 5,423 | 708 |
| Net loss | $ (142,310) | $ (76,086) | $ (251,575) | $ (184,744) |
| Net loss per share — basic and diluted | $ (1.52) | $ (0.95) | $ (2.85) | $ (2.48) |
| Weighted-average number of shares used in computing net loss per share — basic and diluted | 93,758 | 80,329 | 88,195 | 74,460 |
| Other comprehensive loss: | | | | |
| Unrealized loss on available-for-sale securities, net | (1,065) | (43) | (4,690) | (214) |
| Comprehensive loss | $ (143,375) | $ (76,129) | $ (256,265) | $ (184,958) |

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

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

| | Common Stock | | Additional Paid-In Capital | Accumulated Other Comprehensive Loss | Accumulated Deficit | Total Stockholders' (Deficit) Equity |
|---|---|---|---|---|---|---|
| | Shares | Amount | | | | |
| Balance, December 31, 2021 | 84,799,542 | $ 84 | $ 1,452,268 | $ (869) | $ (1,207,620) | $ 243,863 |
| ASU 2020-06 adoption | — | — | (49,476) | — | 10,581 | (38,895) |
| Exercise of stock options | 374,242 | 1 | 4,074 | — | — | 4,075 |
| Vesting of restricted stock units, net of taxes withheld | 403,169 | — | (9,602) | — | — | (9,602) |
| Stock-based compensation | — | | 8,985 | — | — | 8,985 |
| Other comprehensive loss | — | — | — | (2,720) | — | (2,720) |
| Net loss | — | — | — | — | (89,445) | (89,445) |
| Balance, March 31, 2022 | 85,576,953 | 85 | 1,406,249 | (3,589) | (1,286,484) | 116,261 |
| Exercise of stock options | 233,365 | — | 2,143 | — | — | 2,143 |
| Vesting of restricted stock units, net of taxes withheld | 41,628 | — | — | — | — | — |
| Issuance of common stock under Employee Stock Purchase Plan | 49,088 | — | 1,540 | — | — | 1,540 |
| Exercise of warrants | 14,136 | — | — | — | — | — |
| Stock-based compensation | — | — | 12,195 | — | — | 12,195 |
| Other comprehensive loss | — | — | — | (905) | — | (905) |
| Net loss | — | — | — | — | (19,820) | (19,820) |
| Balance, June 30, 2022 | 85,915,170 | 85 | 1,422,127 | (4,494) | (1,306,304) | 111,414 |
| Exercise of stock options | 577,369 | — | 6,187 | — | — | 6,187 |
| Induced conversion of convertible notes | 8,071,343 | 8 | (3,386) | — | — | (3,378) |
| Exercise of warrants | 14,170 | — | — | — | — | — |
| Stock-based compensation | — | — | 13,175 | — | — | 13,175 |
| Other comprehensive loss | — | — | — | (1,065) | — | (1,065) |
| Net loss | — | — | — | — | (142,310) | (142,310) |
| Balance, September 30, 2022 | 94,578,052 | $ 93 | $ 1,438,103 | $ (5,559) | $ (1,448,614) | $ (15,977) |

| | 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 |
| Issuance of common stock under Employee Stock Purchase Plan | 64,975 | — | 969 | — | — | 969 |
| Stock-based compensation | — | — | 7,093 | — | — | 7,093 |
| 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 |

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, 2022 | September 30, 2021 |
| **Cash flows from operating activities:** | | |
| Net loss | $ (251,575) | $ (184,744) |
| Adjustments to reconcile net loss to net cash used in operating activities: | | |
| Loss on investments | 107 | — |
| Non-cash interest expense on liabilities related to revenue participation right purchase agreements | 22,617 | 8,707 |
| Stock-based compensation expense | 34,355 | 20,121 |
| Non-cash lease expense | 1,502 | 5,407 |
| Depreciation of property and equipment | 4,156 | 1,542 |
| Interest receivable and amortization on investments | (492) | 3,440 |
| Non-cash interest expense related to debt | 4,609 | 5,250 |
| Loss on extinguishment of debt | 2,693 | — |
| Loss on inducement of convertible debt | 22,246 | — |
| Changes in operating assets and liabilities: | | |
| Accounts receivable | 54,525 | 3,776 |
| Prepaid and other assets | (8,942) | (11,244) |
| Accounts payable | (8,524) | (2,802) |
| Accrued and other liabilities | 11,195 | 13,821 |
| Operating lease liabilities | 1,057 | 33,466 |
| Other non-current liabilities | (3,855) | 5,475 |
| Deferred revenue | (87,000) | — |
| Net cash used in operating activities | (201,326) | (97,785) |
| **Cash flows from investing activities:** | | |
| Purchases of investments | (730,214) | (493,450) |
| Maturities of investments | 446,961 | 326,156 |
| Sales of investments | — | 3,300 |
| Purchases of property and equipment | (8,130) | (31,118) |
| Net cash used in investing activities | (291,383) | (195,112) |
| **Cash flows from financing activities:** | | |
| Repayment of finance lease liabilities | (839) | — |
| Repayment of term loan | (47,651) | — |
| Debt extinguishment costs | (2,409) | — |
| Repayment of convertible debt | (140,330) | — |
| Proceeds from issuance of convertible debt, net | 523,586 | — |
| Proceeds from public offerings of common stock, net of discounts, commissions and offering cost | — | 296,905 |
| Proceeds from 2020 RPI Transactions, net | 149,581 | — |
| Proceeds from and payments for stock-based award activities, net | 4,343 | 3,569 |
| Net cash provided by financing activities | 486,281 | 300,474 |
| Net (decrease) increase in cash and cash equivalents | (6,428) | 7,577 |
| Cash and cash equivalents, beginning of period | 112,666 | 82,985 |
| Cash and cash equivalents, end of period | $ 106,238 | $ 90,562 |
| **Supplemental cash flow disclosures:** | | |
| Cash paid for interest | $ 5,555 | $ 5,499 |
| **Non-cash investing and financing activities:** | | |
| Right-of-use assets recognized in exchange for operating lease obligations | $ 2,312 | $ 83,208 |
| Right-of-use assets recognized in exchange for finance lease obligations | $ 1,055 | $ — |
| Amounts unpaid for purchases of property and equipment | $ 1,866 | $ 10,974 |
| Issuance of common stock in connection with repurchase of convertible note | $ 317,123 | $ — |

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 $1,448.6 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, sales of future revenues and royalties, debt financing arrangements, government grants and interest income. Until we achieve profitable operations, we intend to continue to fund operations through payments from strategic collaborations, additional sales of equity securities, grants and debt financings. We have never generated revenues from commercial sales of our drugs and may not have drugs to market for 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 subsidiaries. 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, 2021 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, 2021, 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 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"). Under ASU 2020-06 the embedded conversion features are no longer separated from the host contract for convertible instruments with conversion features that are not required to be accounted for as derivatives under Topic 815, Derivatives and Hedging, or that do not result in substantial premiums accounted for as paid-in capital. Consequently, a convertible debt instrument will be accounted for as a single liability measured at its amortized cost and convertible preferred stock will be accounted for as a single equity instrument measured at its historical cost, as long as no other features require bifurcation and recognition as derivatives. By removing those separation models, the interest rate of convertible debt instruments typically will be closer to the coupon interest rate. ASU 2020-06 also provides for certain disclosures with regard to convertible instruments and associated fair values. ASU 2020-06 is effective for annual reporting periods after December 15, 2021 and interim periods within those annual periods and early adoption is permitted. ASU 2020-06 provides companies with the option to adopt the new standard using either the full retrospective or modified retrospective method.

We adopted this new guidance using the modified retrospective method as of January 1, 2022, with respect to our 4.00% Convertible Senior Notes due 2026 (the "2026 Notes"). The cumulative effect of initially applying the new standard was recognized as an adjustment to accumulated deficit. The following table summarizes the adjustments made to our condensed consolidated balance sheet as of January 1, 2022, upon adoption of the new standard:

| Balance sheet account description | Ending Balance as of December 31, 2021 | ASU 2020-06 Adjustments | Beginning Balance as of January 1, 2022 |
|---|---|---|---|
| Convertible notes, net | $ 95,471 | $ 38,895 | $ 134,366 |
| Additional paid-in capital | 1,452,268 | (49,476) | 1,402,792 |
| Accumulated deficit | (1,207,620) | 10,581 | (1,197,039) |

The adoption of this new guidance resulted in an increase in the carrying value of the 2026 Notes to reflect the full principal amount of the convertible notes outstanding, net of issuance costs, a decrease in additional paid-in capital to remove the equity component separately recorded for the conversion feature associated with the convertible notes, a cumulative-effect adjustment to the beginning balance of our accumulated deficit as of January 1, 2022 to reverse the accretion of discount that resulted from the bifurcation of the equity component of the 2026 Notes, and a reversal of the related deferred tax liability of $8.3 million with a corresponding increase in our deferred tax asset valuation allowance. The adoption of this new guidance has reduced non-cash interest expense for the year ending December 31, 2022 and will continue to do so until the 2026 Notes have been settled. The remaining debt issuance costs will continue to be amortized over the term of the notes.

We have recognized $0.3 million and $3.4 million of interest expense of the 2026 Notes for the three and nine months ended September 30, 2022, respectively, which is $0.2 million and $3.1 million less than under the previous accounting standards for the three and nine months ended September 30, 2022, respectively. Without the adoption of ASU 2020-06, our reported net loss would have increased by $0.2 million and $3.1 million for the three and nine months ended September 30, 2022, respectively. Without the adoption of ASU 2020-06, our reported net loss per share would have increased by $0.03 per share for the nine months ended September 30, 2022 and no material impact for the three months ended September 30, 2022.

On July 6, 2022, the Company issued 3.50% Convertible Senior Notes due 2027 (the "2027 Notes") and partially repurchased the 2026 Notes as further described in Note 7 – "Debt." The new guidance applied in respect of the 2027 Notes from the moment of issuance, and thus the above adjustments apply only in respect of the 2026 Notes.

**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, 2022 | September 30, 2021 |
|---|---|---|
| Options to purchase common stock | 10,838 | 9,511 |
| Warrants to purchase common stock | 13 | 48 |
| Restricted stock and performance units | 1,275 | 1,515 |
| Shares issuable related to the ESPP | 41 | 38 |
| Shares issuable upon conversion of 2026 Notes | 2,554 | 16,675 |
| Shares issuable upon conversion of 2027 Notes | 10,572 | — |
| Total shares | 25,293 | 27,787 |

**Note 3 — Research and Development Arrangements**

***2021 Ji Xing and RTW Transactions***

The Ji Xing OM License Agreement, as defined below, and the sales of common stock to the RTW Investors, as defined below, in December 2021, as described below, (together the "2021 RTW Transactions") were entered into with parties that were at the time of our entry into the 2021 RTW Transactions affiliated and in contemplation of one another and, accordingly, we have assessed the accounting for these transactions in the aggregate. Unconstrained arrangement consideration under the 2021 RTW Transactions totaled $70.0 million and was allocated in accordance with *ASC 820* and *ASC 606* as follows (in thousands):

| | Allocated Consideration |
|---|---|
| Units of Accounting: | |
| License and collaboration | $ 54,856 |
| Common stock (fair value) | 15,144 |
| Total consideration | $ 70,000 |

*Ji Xing Omecamtiv Mecarbil License and Collaboration Agreement*

On December 20, 2021, we entered into a License and Collaboration Agreement (the "Ji Xing OM License Agreement") with Ji Xing Pharmaceuticals Limited, pursuant to which we granted to Ji Xing an exclusive license to develop and commercialize omecamtiv mecarbil in the People's Republic of China (including the Hong Kong and Macau Special Administrative Districts) (together "China") and Taiwan, and which was subsequently assigned to Ji Xing Pharmaceuticals Hong Kong Limited (together with Ji Xing Pharmaceuticals Limited, "Ji Xing"). Under the terms of the Ji Xing OM License Agreement, we are the beneficiary of a nonrefundable $50.0 million payment obligation from Ji Xing comprised of a $40.0 million payment as consideration for the rights granted by us to Ji Xing and $10.0 million attributable to our having submitted to the U.S. Food and Drug Administration (the "FDA") a new drug application ("NDA") for omecamtiv mecarbil. The $50.0 million payment was received by the Company in January 2022. We may be eligible to receive from Ji Xing additional payments totaling up to $330.0 million for the achievement of certain commercial milestone events in connection to omecamtiv mecarbil. In addition, Ji Xing will pay us tiered royalties in the mid-teens to the low twenties range on the net sales of pharmaceutical products containing omecamtiv mecarbil in China and Taiwan, subject to certain reductions for generic competition, patent expiration and payments for licenses to third party patents.

Ji Xing will be responsible for the development and commercialization of omecamtiv mecarbil at its own cost and is required to use diligent efforts to develop and commercialize omecamtiv mecarbil in China and Taiwan. The development of omecamtiv mecarbil will be initially focused on heart failure with reduced ejection fraction ("HFrEF"), and Ji Xing will have the opportunity to participate in Cytokinetics' global clinical trials of omecamtiv mecarbil. Cytokinetics will supply omecamtiv mecarbil to Ji Xing either as a finished product or as an active pharmaceutical ingredient. Ji Xing may reimburse Cytokinetics for certain costs related to development and supply activities that we performed on their behalf.

The Ji Xing OM License Agreement, unless terminated earlier, will continue on a market-by-market basis until expiration of the relevant royalty term. Ji Xing has the right to terminate the Ji Xing OM License Agreement for convenience. Each party may terminate the Ji Xing OM License Agreement for the other party's uncured material breach, insolvency, or failure to perform due to extended force majeure events. Cytokinetics may also terminate the Ji Xing OM License Agreement if Ji Xing challenges Cytokinetics' patents or undergoes certain change of control transactions. Rights granted to Ji Xing in relation to omecamtiv mecarbil will revert to Cytokinetics upon termination, and, under certain circumstances, subject to a low single digit royalty payment by the Company to Ji Xing on the net sales of the products containing the compound omecamtiv mecarbil in China and Taiwan. We assessed this arrangement in accordance with *ASC 606* and concluded that there is one performance obligation relating to the license of functional intellectual property. The performance obligation was satisfied, and we recognized the residual allocation of arrangement consideration as revenue of $54.9 million for 2021. Due to the nature of development, including the inherent risk of development and approval by regulatory authorities, we are unable to estimate if and when the development milestone payments could be achieved or become due and, accordingly, we consider the milestone payments to be fully constrained and excluded any potential milestone payments from the initial transaction price.

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

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

*Common Stock Purchase Agreements*

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

***2020 Ji Xing and RTW Transactions***

On July 14, 2020, we entered into a series of transactions as described below with RTW Royalty Holdings Designated Activity Company ("RTW Royalty Holdings") and Ji Xing Pharmaceuticals Limited, related to aficamten, our proprietary small molecule cardiac myosin inhibitor product, a novel cardiac myosin inhibitor, and other assets (together, the "2020 RTW Transactions"). The 2020 RTW Transactions include entering into a licensing and collaboration agreement with Ji Xing, the sale of Cytokinetics common stock to the RTW Investors, an agreement to sell to RTW Royalty Holdings our interest in certain future royalties on net sales of products containing the compound mavacamten that are or may be developed or commercialized by Bristol-Myers Squibb Company (formerly by MyoKardia, Inc.), including Camzyos™ (mavacamten), 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 received and expect to receive a combination of license fees, milestone revenues and sale proceeds from the RTW Investors, RTW Royalty Holdings and Ji Xing.

The 2020 RTW Transactions were entered into with parties that were at the time of our entry into the 2020 RTW Transactions 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 2020 RTW Transactions as further described below. The Company allocated the total consideration in accordance with ASC 820, Fair Value Measurement, and ASC 606, Revenue from Contracts with Customers, as follows (in thousands):

| | Allocated Consideration |
|---|---|
| Units of Accounting: | |
| License and collaboration (residual) | $ 36,501 |
| Royalty (fair value) | 87,000 |
| Common stock (fair value) | 36,499 |
| Total consideration | $ 160,000 |

*Ji Xing Aficamten License and Collaboration Agreement*

On July 14, 2020, we entered into a License and Collaboration Agreement (the "Ji Xing Aficamten License Agreement") with Ji Xing Pharmaceuticals Limited, pursuant to which we granted to Ji Xing an exclusive license to develop and commercialize aficamten in China and Taiwan, and which was subsequently assigned to Ji Xing Pharmaceuticals Hong Kong Limited. Under the terms of the Ji Xing Aficamten License Agreement, we received from Ji Xing a nonrefundable upfront payment of $25.0 million. We may be eligible to receive from Ji Xing milestone payments totaling up to $200.0 million for the achievement of certain development and commercial milestone events in connection to aficamten in the field of 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 Aficamten License Agreement, unless terminated earlier, will continue on a market-by-market basis until expiration of the relevant royalty term. Ji Xing has the right to terminate the Ji Xing Aficamten License Agreement for convenience. Each party may terminate the Ji Xing Aficamten License Agreement for the other party's uncured material breach, insolvency, or failure to perform due to extended force majeure events. Cytokinetics may also terminate the Ji Xing Aficamten License Agreement if Ji Xing challenges Cytokinetics' patents or undergoes certain change of control transactions. Rights granted to Ji Xing in relation to aficamten will revert to Cytokinetics upon termination, and, under certain circumstances, subject to a low single digit royalty payment by the Company to Ji Xing on the net sales of the products containing the compound aficamten in China and Taiwan.

We assessed this arrangement in accordance with ASC 606 and concluded that there is one performance obligation relating to the license of functional intellectual property. The performance obligation was satisfied, and we recognized the residual allocation of arrangement consideration as revenue of $36.5 million for 2020. No license revenue was recognized in 2021 related to the Ji Xing Aficamten License Agreement. Due to the nature of development, including the inherent risk of development and approval by regulatory authorities, we are unable to estimate if and when the development milestone payments could be achieved or become due and, accordingly, we consider the milestone payments to be fully constrained and exclude the milestone payments from the initial transaction price.

The consideration related to sales-based milestone payments, including royalties, will be recognized when the related sales occur under the sales- and usage-based royalty exception of ASC 606 as these amounts have been determined to relate predominantly to the license.

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

We recognized a $5.0 million milestone from Ji Xing during the third quarter of 2021 for initiation of a phase 3 clinical trial for aficamten in oHCM. Although our contractual right to payment had not arisen under the Ji Xing Aficamten License Agreement, we determined recognition of the milestone in 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 oHCM and was recorded as a corresponding contract asset in other current assets in our consolidated balance sheet as of December 31, 2021. The $5.0 million was reclassed to accounts receivable since we had a contractual right to payment as of March 31, 2022 and received such payment during the quarter ended June 30, 2022.

*Royalty Purchase Agreement*

On July 14, 2020, 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 understand that on April 18, 2022, RTW ICAV and MyoKardia, Inc. entered into agreements, which purported to assign all of RTW ICAV's rights, title and interest to the Mavacamten Royalty to MyoKardia, Inc., and on April 25, 2022, we entered into a tripartite agreement with RTW ICAV and MyoKardia, Inc. acknowledging the release and discharge of any further obligations by us or MyoKardia, Inc. in connection to the Mavacamten Royalty.

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

*Common Stock Purchase Agreements*

On July 14, 2020, we entered into common stock purchase agreements with each of the RTW Investors. These common stock purchase agreements provided for the sale and issuance of an aggregate of 2.0 million shares of common stock of Cytokinetics 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 of common stock they purchased pursuant to these agreements, including a restriction on sales or other transfers of the shares, subject to certain exceptions, for a period of 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 of common stock purchased. 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*

During July 2020, we also entered into a Funding Agreement (the "Funding Agreement") with RTW Royalty Holdings. Pursuant to the Funding Agreement, RTW Royalty Holdings had committed to provide up to $90.0 million (the "RTW Funding Commitment") to fund our development and commercialization of aficamten in nHCM and oHCM.

On January 7, 2022, we announced that we had elected to unilaterally terminate the Funding Agreement in connection with our entry into the RP Aficamten RPA (as defined below). At the time of its termination, we had not exercised any rights to sell any revenue interest in aficamten under the Funding Agreement.

***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").

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 a 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. The termination of the Astellas OSSA Agreement was effective 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 $2.5 million and $0.4 million for the three months ended September 30, 2022 and 2021, respectively, and $4.6 million and $2.5 million for the nine months ended September 30, 2022 and 2021, respectively.

***Amgen Inc. ("Amgen")***

On November 23, 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.

We recognized research and development revenue for reimbursements from Amgen of both internal costs of certain full-time employee equivalents and other costs related to the Amgen Agreement, which terminated effective May 20, 2021. There was no research and development revenue from Amgen for the three months ended September 30, 2022 and 2021 and nine months ended September 30, 2022. Research and development revenue from Amgen was $7.4 million for the nine months ended September 30, 2021.

**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):

| | | September 30, 2022 | | | |
|---|---|---|---|---|---|
| | Fair Value Hierarchy Level | Amortized Cost | Unrealized Gains | Unrealized Losses | Fair Value |
| Money market funds | Level 1 | $ 95,463 | $ — | $ — | $ 95,463 |
| U.S. Treasury securities | Level 1 | 216,513 | — | (1,940) | 214,573 |
| U.S. and non-U.S. government agency bonds | Level 2 | 95,783 | 5 | (839) | 94,949 |
| Commercial paper | Level 2 | 356,570 | 1 | (741) | 355,830 |
| U.S. and non-U.S. corporate obligations | Level 2 | 136,659 | — | (2,045) | 134,614 |
| | | $ 900,988 | $ 6 | $ (5,565) | $ 895,429 |

| | | December 31, 2021 | | | |
|---|---|---|---|---|---|
| | Fair Value Hierarchy Level | Amortized Cost | Unrealized Gains | Unrealized Losses | Fair Value |
| Money market funds | Level 1 | $ 115,937 | $ — | $ — | $ 115,937 |
| U.S. Treasury securities | Level 1 | 133,498 | 1 | (268) | 133,231 |
| U.S. and non-U.S. government agency bonds | Level 2 | 33,489 | — | (53) | 33,436 |
| Commercial paper | Level 2 | 169,622 | 6 | (19) | 169,609 |
| U.S. and non-U.S. corporate obligations | Level 2 | 175,282 | — | (536) | 174,746 |
| | | $ 627,828 | $ 7 | $ (876) | $ 626,959 |

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

| | September 30, 2022 | December 31, 2021 |
|---|---|---|
| Cash equivalents | $ 105,459 | $ 115,937 |
| Short-term investments | 761,426 | 358,972 |
| Long-term investments | 28,544 | 152,050 |
| | $ 895,429 | $ 626,959 |

Interest income, net was $4.1 million and $0.2 million for the three months ended September 30, 2022 and 2021, respectively, and $5.4 million and 0.7 million for the nine months ended September 30, 2022 and 2021, respectively.

No credit losses on debt securities were recognized during the nine months ended September 30, 2022 or 2021. 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 approximate fair value due to the short-term nature of these instruments.

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):

| | September 30, 2022 | December 31, 2021 |
|---|---|---|
| Accrued liabilities: | | |
| Clinical and preclinical costs | $ 12,336 | $ 13,872 |
| Compensation related | 17,775 | 14,930 |
| Other accrued expenses | 10,118 | 5,568 |
| Total accrued liabilities | $ 40,229 | $ 34,370 |

**Note 6 — Agreements with Royalty Pharma**

On January 7, 2022, we announced that we had entered into the Development Funding Loan Agreement (the "RP Loan Agreement") and the Revenue Participation Right Purchase Agreement (the "RP Aficamten RPA") with Royalty Pharma Development Funding, LLC ("RPDF") and Royalty Pharma Investments 2019 ICAV ("RPI ICAV") ("2022 RPI Transactions") respectively, each of which are affiliated with Royalty Pharma International plc.

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

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

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

***2022 RP Loan Agreement***

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

- $50.0 million of tranche 2 term loans during the one year period following the receipt on or prior to December 31, 2022 of marketing approval from FDA of omecamtiv mecarbil;
- $25.0 million of tranche 3 term loans during the one year period following the commercial availability of a diagnostic test measuring levels of omecamtiv mecarbil to support the final FDA label language applicable to such drug, subject to such commercial availability and the conditions to the tranche 2 term loans having occurred on or prior to December 31, 2022;

- $75.0 million of tranche 4 term loans during the one year period following the receipt on or prior to September 30, 2024 of positive results from SEQUOIA-HCM, the Phase 3 trial for aficamten; and
- $100.0 million of tranche 5 term loans during the one year period following the acceptance by the FDA on or prior to March 31, 2025 of a new drug application ("NDA") for aficamten, subject to the conditions to the tranche 4 term loans having occurred on or prior to September 30, 2024.

Each term loan under the RP Loan Agreement matures on the 10 year anniversary of the funding date for such term loan and is repayable in quarterly installments of principal, interest and fees commencing on the last business day of the seventh full calendar quarter following the calendar quarter of the applicable funding date for such term loan, with the aggregate amount payable in respect of each term loan (including interest and other applicable fees) equal to 190% of the principal amount of the term loan (such amount with respect to each term loan, "Final Payment Amount"). We accounted for amounts drawn under the RP Loan Agreement using the effective interest method which resulted in an effective interest rate of 7.65% over the ten-year term. Upon the prepayment or maturity of the term loan (or upon the date such prepayment or repayment is required to be paid), we are required to pay an additional amount equal to $34.6 million.

We may prepay the term loans in full (but not in part) at any time at our option by paying an amount equal to the unpaid portion of Final Payment Amount for the outstanding term loans under the RP Loan Agreement; provided that if the conditions for either the tranche 4 term loans or the tranche 5 term loans have been met, we must have borrowed at least $50 million principal amount of the tranche 4 or 5 term loans. In addition, the term loans under the RP Loan Agreement are repayable in full at the option of either us or the lender in an amount equal to the unpaid portion of Final Payment Amount for the outstanding term loans upon a change of control of Cytokinetics. Given the new PDUFA target action date, it is likely that we will not be able to satisfy certain conditions and deadlines for the tranche 2 and tranche 3 loan disbursements as described above.

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

| **Years ending December 31:** | |
|---|---|
| 2022 remainder | $ — |
| 2023 | 1,440 |
| 2024 | 10,080 |
| 2025 | 11,520 |
| 2026 | 11,520 |
| Thereafter | 60,480 |
| Future minimum payments | 95,040 |
| Less: Unamortized interest and loan costs | (31,496) |
| Term Loan, net | $ 63,544 |

As of September 30, 2022, the fair value of our RP Loan approximated its carrying value of $63.5 million based upon a market observable interest rate, which is a Level 2 input.

Interest expense for the RP Loan Agreement was $1.2 million and $3.5 million for the three and nine months ended September 30, 2022, respectively.

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

***2022 RP Aficamten Royalty Purchase Agreement***

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

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

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

The carrying amount of the RP Aficamten Liability is based on our estimate of the future royalties to be paid to RPI ICAV over the life of the arrangement as discounted using an imputed rate of interest. The imputed rate of interest on the unamortized portion of the RP Aficamten Liability was approximately 11.7% as of the second quarter of 2022.

During the third quarter of 2022, we updated our analyses of the RP Aficamten RPA 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.

Our estimates regarding the amount of future royalty payments under the RP Aficamten RPA increased due to changes in management's estimates of unobservable inputs related to market conditions and timing. The adjustment is accounted for on a prospective basis in our liability calculation and resulted in an increase in our imputed interest rate and noncash interest expenses from 11.7% and $2.6 million in the second quarter of 2022 to 25.0% and $5.5 million in the third quarter of 2022, respectively. During the three and nine months ended September 30, 2022, the change in estimate had no impact on revenue and increased the net loss by $2.8 million. The change in accounting estimate increased the net loss per share by $0.03 in the three and nine months ended September 30, 2022.

***2017 RP Omecamtiv Mecarbil Royalty Purchase Agreement***

In February 2017, we entered into the RP OM RPA pursuant to which we sold a portion of our right to receive royalties from Amgen on future net sales of omecamtiv mecarbil to RPI Finance Trust ("RPFT") for a one-time payment of $90 million, which is non-refundable even if omecamtiv mecarbil is never commercialized. Concurrently, we entered into a common stock purchase agreement with RPFT through which RPFT purchased 875,656 shares of the Company's common stock for $10.0 million. We allocated the consideration and issuance costs on a relative fair value basis to our liability to RPFT related to sale of future royalties under the RP OM RPA (the "RP OM Liability") and the common stock sold to RPFT, which resulted in the RP OM Liability being initially recognized at $92.3 million. The RP OM RPA provides for the sale of a royalty to RPFT of 4.5% on worldwide net sales of omecamtiv mecarbil, subject to a potential increase of up to an additional 1% under certain circumstances.

As a result of the termination of the Amgen Agreement and pursuant to our obligations under the RP OM RPA, we and RPFT entered into Amendment No. 1 to Royalty Purchase Agreement, dated January 7, 2022 to preserve RPFT's rights under the RP OM RPA by providing for direct payments by us to RPFT of 4.5% of our and our affiliates and licensees worldwide net sales of omecamtiv mecarbil, subject to a potential increase of up to an additional 1% under certain circumstances (if the FDA approves omecamtiv mecarbil on its target PDUFA date of February 28, 2023, the royalty owed to RPFT will be 5.1% of worldwide net sales of omecamtiv mecarbil). Amendment No. 1 to the Royalty Purchase Agreement, dated January 7, 2022 had no impact on the original accounting for the $92.3 million associated with the RP OM Liability established in February 2017.

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

The carrying amount of the RP OM Liability is based on our estimate of the future royalties to be paid to RPFT over the life of the arrangement as discounted using an imputed rate of interest. The excess of future estimated royalty payments over the $92.3 million of allocated proceeds, less issuance costs, is recognized as non-cash interest expense using the effective interest method. The imputed rate of interest on the unamortized portion of the RP OM Liability was approximately 7.5% as of September 30, 2022 and 10.0% as of December 31, 2021.

Our estimates regarding the amount of future royalty payments under the RP OM RPA decreased and the time periods within which we anticipated that such payments will be due changed based on management's estimates. 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 10.0% and $4.4 million in the second quarter of 2022 to 7.5% and $3.4 million in in the third quarter of 2022, respectively. During the three and nine months ended September 30, 2022, the change in estimate had no impact on revenue and reduced the net loss by $1.1 million. The change in accounting estimate reduced the net loss per share by $0.01 in the three and nine months ended September 30, 2022.

***Accounting for the Royalty Pharma Royalty Purchase Agreements***

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

There are a number of factors that could materially affect the amount and timing of royalty payments, most of which are not within our control. The RP OM Liability and the RP Aficamten Liability are recognized using significant unobservable inputs. These inputs are derived using internal management estimates developed based on third party data, including competitor sales data, and reflect management’s judgements, current market conditions surrounding competing products, and forecasts. The significant unobservable inputs include the estimated patient population, estimated selling price, estimated peak sales and sales ramp, the expected term of the royalty stream, timing of the expected launch and its impact on the royalty rate 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 RP OM Liability and the RP Aficamten Liability.

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

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

| | 2022 | | 2021 |
|---|---|---|---|
| | RP Aficamten Liability | RP OM Liability | RP OM Liability |
| Beginning balance, January 1 | $ — | $ 179,072 | $ 166,068 |
| Initial carrying value | 89,571 | — | — |
| Interest accretion | 2,286 | 4,278 | 2,795 |
| Amortization of issuance costs | — | 28 | 27 |
| Ending balance, March 31 | 91,857 | 183,378 | 168,890 |
| Interest accretion | 2,574 | 4,429 | 2,871 |
| Amortization of issuance costs | — | 28 | 29 |
| Ending balance, June 30 | 94,431 | 187,835 | 171,790 |
| Interest accretion | 5,469 | 3,494 | 2,955 |
| Amortization of issuance costs | — | 31 | 30 |
| Ending balance, September 30 | $ 99,900 | $ 191,360 | $ 174,775 |

As of September 30, 2022, the fair value of the liabilities related to the sale of future royalties to RPFT and RPI ICAV are consistent with their carrying values of $99.9 million and $191.4 million, respectively, and is based on our current estimates of the amount and timing of future royalties expected to be paid to RPFT and RPI ICAV under the RP OM RPA and the RP Aficamten RPA agreements, respectively, as defined above, over the life of the arrangement, which are considered Level 3 inputs.

We recognized $9.0 million and $3.0 million in non-cash interest expense for the three months ended September 30, 2022 and 2021, respectively, and $22.5 million and $8.6 million for the nine months ended September 30, 2022 and 2021, respectively, related to the RP Aficamten RPA and the RP OM RPA.

**Note 7 — Debt**

***Silicon Valley Bank and Oxford Finance Term Loans***

Prior to January 7, 2022, we maintained a loan and security agreement dated as of October 19, 2015, as amended (the “Term Loan Agreement”), with Silicon Valley Bank and Oxford Finance LLC (“Oxford”) (the “Lenders”).

Both borrowings under the Term Loan Agreement were subject to 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 Term Loan Agreement was 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 oHCM and was 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 was to be followed by equal monthly payments of principal and interest to the maturity date in December 2023. We were required to make a final payment upon loan maturity of 6.00% of the notes payable, which we accreted over the life of the Term Loan Agreement. Our obligations under the Term Loan Agreement were secured by substantially all our current and future assets, other than our intellectual property.

The Term Loan Agreement was terminated and all amounts thereunder repaid in connection to our entry into that certain Development Funding Loan Agreement, dated January 7, 2022 (the "RP Loan Agreement"), between us and Royalty Pharma Development Funding, LLC ("RPDF"), as further described below. Amounts outstanding under the Term Loan Agreement were classified as non-current in our condensed consolidated balance sheet as of December 31, 2021, because short-term obligations expected to be refinanced on a long-term basis are not expected to require the use of working capital during the ensuing fiscal year.

As a result of the termination of the Term Loan Agreement and the repayment to the Lenders, during the nine months ended September 30, 2022, we recorded $2.7 million in loss on debt extinguishment in the condensed consolidated statements of operations and comprehensive loss, consisting of the premium on debt repayments and the write-off of the remaining term loan fees and debt issuance costs.

Interest expense for the Term Loan Agreement was immaterial for the three and nine months ended September 30, 2022 because it represented approximately one week of interest before extinguishment. Interest expense for the Term Loan Agreement was $1.2 million and $3.6 million for the three and nine months ended September 30, 2021.

***Convertible Notes***

On November 13, 2019, the Company issued $138.0 million aggregate principal amount of 2026 Notes. On July 6, 2022, the Company issued $540.0 million aggregate principal amount of 2027 Notes and used approximately $140.3 million of the net proceeds from the offering of 2027 Notes and issued 8,071,343 shares of common stock to repurchase approximately $116.9 million aggregate principal amount of the 2026 Notes pursuant to privately negotiated exchange agreements entered into with certain holders of the 2026 Notes concurrently with the pricing of the offering of the 2027 Notes. As a result of the partial repurchase of the 2026 Notes, the Company recorded an inducement loss of $22.2 million, consisting of the difference between the consideration to the holders pursuant to the exchange agreements and the if-converted value of the 2026 Notes under the original terms. As of September 30, 2022, there remain $21.1 million aggregate principal amount of 2026 Notes outstanding.

The 2026 Notes are unsecured obligations and bear interest at an annual rate of 4.0% per year, payable semi-annually on May 15 and December 15 of each year, beginning May 15, 2020. The 2026 Notes are governed by an indenture 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 agreement, dated November 13, 2019 between the Company and U.S. Bank National Association, as trustee, as supplemented by the first supplemental indenture dated as of November 13, 2019 between the Company and such trustee) 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.

As discussed in Note 1, effective January 1, 2022, the Company adopted ASU 2020-06 using the modified retrospective method and, as a result, it is no longer required to separately account for the liability and equity components of the 2026 Notes, and, instead, account for the 2026 Notes wholly as debt.

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

| | Three Months Ended September 30, 2022 | Three Months Ended September 30, 2021 | Nine Months Ended September 30, 2022 | Nine Months Ended September 30, 2021 |
|---|---|---|---|---|
| Contractual interest expense | $ 294 | $ 1,380 | $ 3,054 | $ 4,140 |
| Amortization of debt discount | — | 1,522 | — | 4,338 |
| Amortization of debt issuance costs | 19 | 15 | 328 | 43 |
| Total interest expense recognized | $ 313 | $ 2,917 | $ 3,382 | $ 8,521 |

The effective interest rate of the 2026 Notes was 4.6% for the three and nine months ended September 30, 2022. As of September 30, 2022, the unamortized debt issuance cost for the 2026 Notes was $0.5 million and will be amortized over approximately 4.2 years. If the 2026 Notes were to be converted on September 30, 2022, the holders of the 2026 Notes would receive common shares of 2.6 million with an aggregate value of $123.7 million based on the Company's closing stock price of $48.45 as of September 30, 2022. The if-converted value of the 2026 Notes exceeded its principal amount by $102.6 million as of September 30, 2022.

The 2027 Notes are the Company's senior, unsecured obligations and are (i) senior in right of payment to the Company's future indebtedness that is expressly subordinated to the 2027 Notes in right of payment; (ii) equal in right of payment with all of the Company's indebtedness that is not so subordinated (including the 2026 Notes); (iii) effectively subordinated to the Company's existing and future secured indebtedness, to the extent of the value of the collateral securing that indebtedness; and (iv) structurally subordinated to all existing and future indebtedness and other liabilities, including trade payables, and (to the extent the Company is not a holder thereof) preferred equity, if any, of the Company's subsidiaries. The net proceeds of the 2027 Notes were approximately $523.6 million after deducting issuance costs related to the 2027 Notes. The 2027 Notes bear interest at a rate of 3.50% per year, payable semiannually in arrears on January 1 and July 1 of each year, beginning on January 1, 2023. The 2027 Notes will mature on July 1, 2027, unless earlier converted, redeemed or repurchased.

The 2027 Notes are convertible into cash, shares of 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(s). The initial conversion rate for the 2027 Notes is 19.5783 shares of the Company's Common Stock per $1,000 principal amount of such Notes, which is equivalent to an initial conversion price of approximately $51.08 per share. Holders of the 2027 Notes may convert all or any portion of their convertible notes at their option only in the following circumstances: (i) during any calendar quarter (and only during such calendar quarter) commencing after the calendar quarter ending on September 30, 2022, if the last reported sale price per share of the Company's common stock, $0.001 par value per share, exceeds 130% of the conversion price for each of at least 20 trading days, whether or not consecutive, during the 30 consecutive trading days ending on, and including, the last trading day of the immediately preceding calendar quarter; (ii) during the five consecutive business days immediately after any 10 consecutive trading day period (such 10 consecutive trading day period, the "measurement period") if the trading price per $1,000 principal amount of 2027 Notes for each trading day of the measurement period was less than 98% of the product of the last reported sale price per share of the Company's common stock on such trading day and the conversion rate on such trading day; (iii) upon the occurrence of certain corporate events or distributions on the Company's common stock, as described in the indenture agreement, dated July 6, 2022, between the Company and U.S. Bank Trust Company, as trustee (the "2027 Indenture"); (iv) if the Company calls such 2027 Notes for redemption; and (v) at any time from, and including, March 1, 2027 until the close of business on the scheduled trading day immediately before the maturity date.

The Company may not redeem the 2027 Notes at its option at any time before July 7, 2025. The 2027 Notes will be redeemable, in whole or in part (subject to the "Partial Redemption Limitation" (as defined in the 2027 Indenture)), at the Company's option at any time, and from time to time, on or after July 7, 2025 and, in the case of a partial redemption, on or before the 60th scheduled trading day immediately before the maturity date, at a cash redemption price equal to the principal amount of the 2027 Notes to be redeemed, plus accrued and unpaid interest, if any, to, but excluding, the redemption date, but only if the last reported sale price per share of the Company's common stock exceeds 130% of the conversion price on (i) each of at least 20 trading days, whether or not consecutive, during the 30 consecutive trading days ending on, and including, the trading day immediately before the date the Company sends the related redemption notice; and (ii) the trading day immediately before the date the Company sends such notice. In addition, calling any of the 2027 Notes for redemption will constitute a Make-Whole Fundamental Change with respect to that convertible note, in which case the conversion rate applicable to the conversion of that Note will be increased in certain circumstances if it is converted after it is called for redemption. The conversion rate for the 2027 Notes shall not exceed 25.4517 shares per $1,000 principal amount of such Notes, subject to certain customary anti-dilution adjustments (as defined in the 2027 indenture). Pursuant to the Partial Redemption Limitation, the Company may not elect to redeem less than all of the outstanding 2027 Notes unless at least $75.0 million aggregate principal amount of 2027 Notes are outstanding and not subject to redemption as of the time the Company sends the related redemption notice.

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

In accounting for the Notes, issuance costs of $16.4 million for the 2027 Notes were deducted from the respective debt liability in the consolidated balance sheet. Issuance costs are amortized to interest expense using the straight-line method, which materially approximates the effective interest method, over five-year term for the 2027 Notes.

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

| | Three and Nine Months Ended September 30, 2022 |
|---|---|
| Contractual interest expense | $ 4,462 |
| Amortization of debt issuance costs | 749 |
| Total interest expense recognized | $ 5,211 |

The effective interest rate of the 2027 Notes was 4.17% for the three and nine months ended September 30, 2022. As of September 30, 2022, the unamortized debt issuance cost for the 2027 Notes was $15.7 million and will be amortized over approximately 4.8 years. If the 2027 Notes were to be converted on September 30, 2022, the holders of the 2027 Notes would receive common shares of 10.5 million with an aggregate value of $512.2 million based on the Company's closing stock price of $48.45 as of September 30, 2022. The if-converted value of the 2027 Notes was below the principal value of the Notes of $540.0 million as of September 30, 2022. In addition, during the three months ended September 30, 2022, the conditions allowing holders of the Notes to convert were not met. As a result, the Notes are not convertible during the three months ended September 30, 2022.

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

| Years ending December 31: | 2027 Notes | 2026 Notes |
|---|---|---|
| 2022 remainder | $ — | $ 423 |
| 2023 | 18,638 | 845 |
| 2024 | 18,900 | 845 |
| 2025 | 18,900 | 845 |
| 2026 | 18,900 | 21,978 |
| Thereafter | 558,900 | — |
| Future minimum payments | 634,238 | 24,936 |
| Less: Interest | (94,238) | (3,804) |
| Convertible notes, principal amount | 540,000 | 21,132 |
| Less: Debt costs on the convertible notes | (15,665) | (481) |
| Net carrying amount of the convertible notes | $ 524,335 | $ 20,651 |

As of September 30, 2022, the estimated fair value of the 2027 Notes and 2026 Notes was $659.9 million and $99.6 million, respectively, and was based upon observable, Level 2 inputs, including pricing information from recent trades of the convertible notes.

***Capped Call Transactions***

In connection with the offering of the 2026 Notes, the Company entered into privately-negotiated capped call transactions with one of the underwriters in the offering or its affiliate. 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, 2022, the Company had not purchased any shares under the convertible note capped call transactions.

**Note 8 — Stockholders' Equity**

***Equity Incentive Plan***

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

In May 2022, our stockholders approved an amendment to the 2004 Plan to increase the number of authorized shares reserved for issuance under the 2004 Plan by an additional 6.0 million shares. In May 2022, our board of directors approved an amendment to the 2004 Plan to increase the number of authorized shares reserved for issuance under the 2004 Plan by an additional 1.6 million shares for inducement grants to new employees. As of September 30, 2022, the total authorized shares under the 2004 Plan available for grant was 10.0 million.

***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 NDA for omecamtiv mecarbil has been filed and accepted by the FDA by December 31, 2021 or June 30, 2022 and the second tranche vests upon certification by the Compensation Committee that the FDA approval of the NDA is with an approved label that is consistent with the expectations underlying the Company's commercial launch plans for omecamtiv mecarbil in effect immediately prior to such approval by June 30, 2022 or December 31, 2022. As the FDA accepted our NDA for omecamtiv mecarbil subsequent to the year ended 2021, it resulted in a change of estimate of the probability of meeting the performance conditions for the PSU grants during the fourth quarter of 2021. The previous estimate was based on assumptions that were the best available information at the time. The change of estimate resulted in a cancellation of 91,250 PSUs and decrease of $0.5 million in stock-based compensation expense for the year ended December 31, 2021.

During the nine months ended September 30, 2022, the performance target for the first tranche of PSUs was met. As a result, the Company recognized expense of $0.2 million and $0.6 million for the three and nine months ended September 30, 2022, respectively, for the first tranche of PSUs. No expense has been recognized for the second tranche to date. It is unlikely that the performance target for the second tranche of PSUs will be met as the FDA recently extended the PDUFA target action date for omecamtiv mecarbil to February 28, 2023. As of September 30, 2022, there was $0.2 million of unamortized stock-based compensation which may vest and be recognized with respect to the achievement of the performance goals and service period. The Company will assess the likelihood of achieving the performance conditions quarterly and the expense recognized will be adjusted accordingly.

***Warrants***

In May 2022, Silicon Valley Bank exercised 16,901 warrants issued pursuant to the Term Loan Agreement with a strike price of $7.10 per share and elected the cashless settlement method. Accordingly, in May 2022, we issued to Silicon Valley Bank a total of 14,136 shares of our common stock. In June 2022, Silicon Valley Bank exercised additional 9,226 warrants and 8,638 warrants with a strike price of $9.76 per share and $10.42 per share, respectively.

As of September 30, 2022, we had outstanding warrants issued pursuant to the Term Loan Agreement with a weighted average exercise price of $10.42 per share to purchase 12,957 shares of our common stock.

**Note 9 — Commitments and Contingencies**

***Operating 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.

During the fourth quarter of 2021, we officially relocated from our existing headquarters located at 250, 256, and 280 East Grand Avenue, South San Francisco to our new facilities at Oyster Point. As a result of the relocation, we considered ceasing use of the existing headquarters, which triggered an impairment assessment. No expense was recognized for the nine months ended September 30, 2022 due to the impairment that was recorded in 2021. We were subject to the fixed rental fee payments for the existing headquarters until the lease expired in June 2022.

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, January 2021 and November 2021, we entered into first, second and third 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 had an initial expiration date of 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. During the third quarter of 2021, we amended the lease payment schedule and were required to start making rent payments in January 2022. The lease term is extended until October 31, 2033. The amendment was accounted for as a lease modification in accordance with Topic 842.

As of September 30, 2022, the remaining lease term of the Oyster Point Lease is 11.1 years and the discount rate used to determine the related lease liability was 10.1%. We paid a total security deposit of $5.1 million in December 2019 and December 2020. The landlord has provided 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, 2022, the total commitment of undiscounted lease payments for the Oyster Point Lease was $221.7 million.

In January 2022, we entered into a series of lease agreements with the sub-landlord and landlord and leased an approximately 14,887 square feet of office space at a facility located in Radnor, Pennsylvania (the "Radnor Lease"). The Radnor Lease commenced on September 1, 2022, when the leasehold improvements were substantially completed and we gained a control over the use of the underlying assets. Upon commencement, we recognized a right-of-use asset of $3.4 million, a short-term lease liability of $0.4 million and a long-term lease liability of $1.9 million. The right-of-use asset includes $1.1 million of lease prepayments made before the commencement date. The Radnor Lease had an initial expiration date of May 31, 2024 with the sub-landlord. We will then continue to lease the premises with the landlord through July 31, 2027 with one five-year option to extend the lease. The option 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.

Subject to rent abatement for the first three months of the lease, we will be required to pay the sub-landlord $31.50 per square foot for the entire leased square footage for the first twelve months of the lease term, which will increase at a rate of 2.0% per year. After May 31, 2024, the rent will be payable to the landlord with a rent abatement period for the first two months. Following the abatement period, we will be required to pay the landlord $45.50 per square foot, which will increase at a rate of 2.5% per year through the end of lease term on July 31, 2027. An advance payment of the first and last month of the sublease rent is also required as part of the lease. We paid the advance rent payment in the first half of 2022 which is included in the lease prepayments. We will pay certain operating costs of the facility and have certain rights to sublease under the agreement.

As of September 30, 2022, the remaining lease term of the Radnor Lease is 4.8 years and the discount rate used to determine the related lease liability was 8.3%. We have incurred a tenant improvement cost of $1.2 million relating to the initial design and construction of the improvements before the commencement date. The tenant improvement cost is offset by a tenant improvement allowance of $0.3 million from the landlord, and the net tenant improvement cost incurred before the commencement date is accounted for lease prepayment. The total commitment of undiscounted lease payments for the Radnor Lease was $2.8 million as of September 30, 2022.

Cash paid for amounts included in the measurement of operating lease liabilities was $18.1 million and $4.4 million for the nine months ended September 30, 2022 and 2021, respectively, and was included in net cash used in operating activities in our condensed consolidated statements of cash flows.

***Finance Leases***

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

Finance leases are accounted for on the condensed consolidated balance sheets with right-of-use assets and lease liabilities recognized in property and equipment, other current liabilities, and other non-current liabilities, respectively. The finance lease cost is recognized as a combination of the amortization expense for the right-of-use assets calculated on a straight-line basis over the five-year estimated useful life for laboratory equipment and interest expense for the outstanding lease liabilities using the determined discount rates. As of September 30, 2022, we have recognized finance lease right-of-use assets of $2.6 million, short-term finance lease liabilities of $1.0 million, and long-term finance lease liabilities of $1.2 million.

As of September 30, 2022, the weighted average remaining lease term for the finance leases is 4.2 years and the weighted average discount rate used to determine the finance lease liabilities is 9.47%.

The cash paid for amounts included in the measurement of finance lease liabilities for the nine months ended September 30, 2022 was $0.8 million and was included in financing activities in our condensed consolidated statement of cash flows.

Future minimum lease payments under non-cancellable leases as of September 30, 2022 are as follows (in thousands):

| Years ending December 31: | Operating Leases | Finance Leases |
|---|---|---|
| 2022 remainder | $ 3,917 | $ 247 |
| 2023 | 17,496 | 990 |
| 2024 | 18,062 | 990 |
| 2025 | 18,886 | 204 |
| 2026 | 19,503 | — |
| Thereafter | 146,611 | — |
| Total future minimum lease payments | 224,475 | 2,431 |
| Less: Imputed interest | (94,014) | (228) |
| Total lease liability | $ 130,461 | $ 2,203 |

Rent expense for operating and finance leases was $5.4 million for the three months ended September 30, 2022 and 2021, and $16.4 million and $12.2 million for the nine months ended September 30, 2022 and 2021, respectively.

**Note 10 — Subsequent Events**

On October 24, 2022, we entered into a termination agreement in connection to the capped call transactions described in Note 7 – Debt above related to the 2026 Notes. As a result, we received gross proceeds of $26.4 million.

## 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 2022 or any subsequent period;
- 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 2022 and in any subsequent period;
- the initiation, design, conduct, enrollment, progress, timing and scope of clinical trials and development activities for our drug candidates conducted by ourselves or our partners, including the anticipated timing for completion and announcement of results of our clinical trials, including SEQUOIA-HCM, our ongoing Phase 3 clinical trial of aficamten in patients with symptomatic obstructive hypertrophic cardiomyopathy and COURAGE-ALS, our ongoing Phase 3 clinical trial of reldesemtiv in patients with amyotrophic lateral sclerosis, 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, and revenue interest agreements 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 with respect to the timing, design and conduct of development and commercialization activities for aficamten or omecamtiv mecarbil in the People's Republic of China (including the Hong Kong SAR and Macau SAR) and Taiwan;
- our ability to meet any of the conditions for disbursement and our receipt of any loan disbursements under the Development Funding Loan Agreement, dated January 7, 2022, between us and Royalty Pharma Development Funding, LLC;
- our ability to meet any of the conditions for disbursement of additional sale proceeds under the Revenue Participation Right Purchase Agreement, dated January 7, 2022, between us and Royalty Pharma Investments 2019 ICAV;
- decisions by FDA or other regulatory authorities to approve our new drug application for omecamtiv mecarbil by February 28, 2023 (target PDUFA action date) or otherwise, or to condition such approval on the 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 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, contract manufacturing organizations, and other vendors;
- potential ownership changes under Internal Revenue Code Section 382; and
- the timeliness and accuracy of information filed with the U.S. Securities and Exchange Commission by third parties.

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

***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, a novel cardiac myosin inhibitor, and CK-3772271 ("CK-271"), our second novel cardiac myosin inhibitor.

Omecamtiv mecarbil is being evaluated for the potential treatment of heart failure. We previously announced positive results from GALACTIC-HF (**G**lobal **A**pproach to **L**owering **A**dverse **C**ardiac Outcomes **T**hrough **I**mproving **C**ontractility in **H**eart Failure), a Phase 3 cardiovascular outcomes clinical trial of omecamtiv mecarbil in heart failure. On February 4, 2022, we announced the United States Food and Drug Administration ("FDA") had accepted for filing our new drug application ("NDA") for omecamtiv mecarbil for treatment of heart failure with reduced ejection fraction ("HFrEF").

CK-136 was discovered under our joint research program with Amgen Inc. ("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 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 ("oHCM"). Following the results from Cohorts 1, 2 and 3 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 conducting SEQUOIA-HCM (Safety, Efficacy, and Quantitative Understanding of Obstruction Impact of Aficamten in HCM), the ongoing 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, and Cohort 4 of REDWOOD-HCM to, *inter alia*, determine the safety and tolerability of aficamten in patients with non-obstructive HCM ("nHCM").

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 is being evaluated for treatment in patients with amyotrophic lateral sclerosis ("ALS") in our ongoing Phase 3 clinical trial, COURAGE-ALS (Clinical Outcomes Using Reldesemtiv on ALSFRS-R in a Global Evaluation in 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, 2022 and 2021 were $62.7 million and $48.4 million, respectively, and $165.8 million and $116.4 million for the nine months ended September 30, 2022 and 2021, 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 now terminated 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 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 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 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.

As a result of the termination of the Amgen Agreement and Servier Agreement, 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 these terminations and to enhance our commercial capabilities.

In 2017, we entered into a Royalty Purchase Agreement (the "RP OM RPA") with RPI Finance Trust ("RPFT"). Under the RP OM RPA, Cytokinetics sold a portion of its right to receive royalties from Amgen on future net sales of omecamtiv mecarbil to RPFT for a one-time payment of $90 million. The RP OM RPA provides for the sale of a royalty to RPFT of 4.5% on worldwide net sales of omecamtiv mecarbil, subject to a potential increase of up to an additional 1% under certain circumstances. As a result of the termination of the Amgen Agreement and pursuant to our obligations under the RP OM RPA, we and RPFT entered into Amendment No. 1 to Royalty Purchase Agreement, dated January 7, 2022 to preserve RPFT's rights under the RP OM RPA by providing for direct payments by us to RPFT of 4.5% of our and our affiliates' and licensees' worldwide net sales of omecamtiv mecarbil, subject to a potential increase of up to an additional 1% under certain circumstances (if the FDA approves omecamtiv mecarbil on its target PDUFA date of February 28, 2023, the royalty owed to RPFT will be 5.1% of worldwide net sales of omecamtiv mecarbil).

*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.

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

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

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

The effect of omecamtiv mecarbil was consistent across most prespecified subgroups and with a potentially greater treatment effect suggested in patients with a lower left ventricular ejection fraction ("LVEF") (LVEF ≤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.

In December 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 LVEF (LVEF ≤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.

In May 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 ≤22%, EF 23-28%, EF 29-32% and EF ≥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 ≤22%) the incidence (35.6 per 100 patient-years) was almost 80% greater than in the highest EF quartile (EF ≥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.

In June 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.

In September 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.

In April 2022, we announced that additional data from GALACTIC-HF were presented at the American College of Cardiology 71st Annual Scientific Session, including a healthcare resource utilization analysis and an analysis of the effect of treatment with omecamtiv mecarbil in hospitalized patients compared outpatients. Specifically, an analysis was presented indicating that treatment with omecamtiv mecarbil led to a 19% cost reduction per patient among the patient subgroup with ejection fraction less than 30% and were without atrial fibrillation and being treated with digoxin. In addition, an analysis was presented indicating that the rate of the primary outcome in GALACTIC-HF was higher in hospitalized patients in the placebo group (38.3/100 person-years [PY]) than in outpatients (23.1/100 PY) with an adjusted hazard ratio (HR) of 1.21 (95% CI 1.12, 1.31). There was a stepwise gradient in risk, with those randomized as outpatients in the placebo group within 3 months of a heart failure event at the highest risk (26.6/100 patient years (PY)) as compared with those 9-12 months post-event (19.0/100 PY) with an adjusted hazard ratio (HR) of 1.20 (95% CI 1.01, 1.42), p for trend = 0.008). The effect of omecamtiv mecarbil versus placebo on the primary outcome was similar in hospitalized patients (HR 0.89, 95% CI 0.78, 1.01) and outpatients (HR 0.94, 95% CI 0.86, 1.02), indicating that omecamtiv mecarbil similarly reduced the risk of the primary outcome both when initiated in hospitalized patients and in outpatients. In both hospitalized patients and outpatients, the initiation of omecamtiv mecarbil was safe and well tolerated. Treatment-emergent serious adverse events occurred more frequently in patients randomized during hospitalization but did not differ significantly between the treatment groups.

In May 2022, we announced the results from two additional analyses of omecamtiv mecarbil from GALACTIC-HF were presented in Late-Breaking Science Sessions at Heart Failure 2022, an International Congress of the European Society of Cardiology. The analysis from GALACTIC-HF related to low blood pressure has been simultaneously published in the European Heart Journal.

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

The second analysis presented on the impact of tricuspid regurgitation (TR) on the effectiveness of omecamtiv mecarbil. The analysis indicated that patients with moderate/severe TR in GALACTIC-HF experienced higher rates of the primary composite endpoint, cardiovascular death, all-cause death and heart failure events. The impact of moderate/severe TR on heart failure events was more pronounced in outpatients and in patients with higher LVEF, lower NT-proBNP and lower eGFR. The treatment effect of omecamtiv mecarbil on the primary outcome was consistent across patients with no TR, mild TR and moderate/severe TR such that baseline TR did not modify the treatment effect (interaction p=0.91).

METEORIC-HF: On February 15, 2022, we announced topline results and on April 3, 2022, we announced the full results from METEORIC-HF (Multicenter Exercise Tolerance Evaluation of Omecamtiv Mecarbil Related to Increased Contractility in Heart Failure), a Phase 3 clinical trial of omecamtiv mecarbil in patients with HFrEF, were presented at the American College of Cardiology 71st Annual Scientific Session. METEORIC-HF evaluated the effect of treatment with omecamtiv mecarbil compared to placebo on exercise capacity as determined by cardiopulmonary exercise testing ("CPET") following 20 weeks of treatment in patients with HFrEF receiving standard of care therapy. The trial completed enrollment of 276 patients in June 2021. There was no effect on the primary endpoint, which was the change in peak oxygen uptake ($pVO_2$) on CPET from baseline to Week 20 in patients treated with omecamtiv mecarbil compared to placebo. Adverse events, including major cardiac events, were similar between the treatment arms and the safety profile of omecamtiv mecarbil in METEORIC-HF was consistent with prior clinical trials including GALACTIC-HF.

*Omecamtiv mecarbil: New Drug Application*

On February 4, 2022, we announced that the FDA had accepted and filed our NDA for omecamtiv mecarbil for the treatment of HFrEF. The FDA assigned the NDA a standard review with a Prescription Drug User Fee Act ("PDUFA") target action date of November 30, 2022. The FDA also indicated, at that time, that it was not currently planning to hold an advisory committee meeting to discuss the NDA. On May 17, 2022, we announced that the Company recently participated in a mid-cycle communication meeting with the FDA and was informed that the FDA was planning to convene an advisory committee meeting to discuss the NDA. On June 17, 2022, we announced that, in response to a request from the FDA, the Company provided additional pharmacokinetic analyses of omecamtiv mecarbil related to its NDA and after an initial review of the Company's submission, the FDA communicated that the additional data provided constituted a major amendment to the NDA and extended the PDUFA target action date by three (3) months to February 28, 2023 to provide time for a full review of the submission. On June 24, 2022, we announced that the FDA had informed the Company that the previously announced meeting of the Cardiovascular and Renal Drugs Advisory Committee to review the NDA for omecamtiv mecarbil is currently scheduled for December 13, 2022.

*Omecamtiv mecarbil: Microgenics Immunoassay Development*

Amgen and Microgenics Corporation ("Microgenics") were 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.

*Omecamtiv mecarbil: Ji Xing Strategic Alliance*

On December 20, 2021, we entered into License and Collaboration Agreement with Ji Xing (the "Ji Xing OM License Agreement"), pursuant to which we granted to Ji Xing an exclusive license to develop and commercialize omecamtiv mecarbil in the People's Republic of China (including the Hong Kong and Macau SARs) ("China") and Taiwan. Under the terms of the Ji Xing OM License Agreement, we are the beneficiary of a nonrefundable $50.0 million payment obligation from Ji Xing comprised of a $40.0 million payment as consideration for the rights granted by us to Ji Xing and $10.0 million attributable to our having submitted to FDA an NDA for omecamtiv mecarbil. We may be eligible to receive from Ji Xing additional payments totaling up to $330.0 million for the achievement of certain commercial milestone events in connection to omecamtiv mecarbil. In addition, Ji Xing will pay us tiered royalties in the mid-teens to the low twenties range on the net sales of pharmaceutical products containing omecamtiv mecarbil in China and Taiwan, subject to certain reductions for generic competition, patent expiration and payments for licenses to third party patents. The Ji Xing OM License Agreement, unless terminated earlier, will continue on a market-by-market basis until expiration of the relevant royalty term.

*CK-136*

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.

*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 program for CK-136 to Cytokinetics.

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.

In October 2021, we announced that preclinical data relating to the discovery and optimization of CK-136 were presented at the 2021 Medicinal Chemistry Gordon Research Conference in West Dover, VT. The data presented described the primary research objectives related to CK-136 including the identification of initial hit compounds and subsequent chemical optimization as well as preclinical characterization in biochemical assays, cardiac myocytes, and *in vivo* models of cardiac function. An initial cardiac troponin activator identified in screening was shown in a reconstituted sarcomere assay to selectively activate the cardiac troponin complex. Importantly, it did not inhibit phosphodiesterase 3 (PDE-3) and showed no effect on the cardiomyocyte calcium transient, indicating its selectivity. The optimization of the initial hit compound that led to CK-136 focused to maximizing the therapeutic window and its pharmacokinetic profile as could result in favorable increases in cardiac function. Preclinical studies demonstrated that the pharmacodynamic range for CK-136 was larger than that associated with omecamtiv mecarbil in similar preclinical models. Additionally, CK-136 demonstrated a pharmacokinetic profile and a projected human half-life that should enable once or twice daily dosing. These preclinical data suggest that CK-136 is a selective cardiac troponin activator with a favorable pharmacodynamic window associated with substantial increases in cardiac contractility, representing a potential approach to augmenting cardiac contractility in diseases characterized by reduced cardiac function.

*Aficamten*

Aficamten is a novel, oral, small molecule cardiac myosin inhibitor that our company scientists discovered. Aficamten arose from an extensive chemical optimization program conducted with attention to therapeutic index and pharmacokinetic properties that may translate into next-in-class potential in clinical development. Aficamten was purposely designed to reduce the hypercontractility that is associated with HCM. In preclinical models, aficamten reduces myocardial contractility by binding directly to cardiac myosin at a distinct and selective allosteric binding site, thereby preventing myosin from entering a force producing state. Aficamten reduces the number of active actin-myosin cross bridges during each cardiac cycle and consequently reduces myocardial contractility. This mechanism of action may be therapeutically effective in conditions characterized by excessive hypercontractility, such as HCM. The preclinical pharmacokinetics of aficamten were characterized evaluated and optimized for potential rapid onset, ease of titration and rapid symptom relief in the clinical setting. The initial focus of the development program for aficamten will include an extensive characterization of its pharmacokinetics/pharmacodynamic ("PK/PD") relationship as has been a hallmark of Cytokinetics' 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 aficamten 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 aficamten 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 aficamten 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 oHCM (REDWOOD-HCM), which started in the first quarter of 2020.

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

In May 2021, we announced that the first site had been activated to enroll patients in REDWOOD-HCM OLE, an open-label extension clinical study designed to assess the long-term safety and tolerability of aficamten in patients with symptomatic oHCM. Eligible patients have completed participation in REDWOOD-HCM, the Phase 2 clinical trial of aficamten.

In July 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.

In September 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).

In October 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 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 ≥1 class improvement in 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 open for enrollment and is expected 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 ≥30 mmHg, post-Valsalva peak LVOT-G ≥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 ≥30 mmHg and a biplane LVEF ≥55%. Patients who do not meet escalation criteria will continue to receive their current dose or may be down-titrated if appropriate.

In December 2021, we announced that the FDA granted Breakthrough Therapy Designation for aficamten for the treatment of oHCM.

On February 1, 2022, we announced positive topline results from Cohort 3 of REDWOOD-HCM and on April 2, 2022, we announced that the full results were presented at the American College of Cardiology 71st Annual Scientific Session. Cohort 3 of REDWOOD-HCM enrolled patients with symptomatic oHCM and a resting or post-Valsalva LVOT-G of ≥50 mmHg whose background therapy included disopyramide and in the majority a beta-adrenergic blocker. All patients received up to three escalating doses of aficamten once daily (5, 10, 15 mg), titrated based on echocardiographic guidance. The doses employed were the same as those used in Cohort 1 of REDWOOD-HCM. Overall treatment duration was 10 weeks with a 4-week follow up period after the last dose. In total, thirteen patients were enrolled and all patients completed the study on treatment.

Results from Cohort 3 demonstrated a substantial reduction in the mean (± SD) resting LVOT-G (from 50 ± 25 at baseline to 24 ± 17 mmHg at Week 10) and Valsalva LVOT-G (from 78 ± 27 to 50 ± 25 mmHg). For the resting LVOT-G, the least square mean difference (± SE) for the change from baseline to Week 10 was -28 ± 3.2 mmHg ($p < 0.0001$) and for the Valsalva LVOT-G was -27 ± 5.9 mmHg ($p = 0.0002$). The relief of obstruction was accompanied by a modest reduction in LVEF (from 74 ± 7% at baseline to 69 ± 7% at Week 10). For LVEF, the least square mean difference (± SE) for the change from baseline to Week 10 was -4.8 ± 1.9% ($p = 0.018$). There were no patients who experienced a reduction in LVEF below the prespecified safety threshold of 50%.

Treatment with aficamten resulted in 6 of the 13 patients (46%) experiencing a complete hemodynamic response by Week 10, with the remaining 7 (54%) still eligible for dose escalation to the highest dose of aficamten (20 mg) employed in SEQUOIA-HCM, the Phase 3 trial. Eleven of 13 patients (85%) experienced improvement in NYHA class by at least one class. In addition to hemodynamic and functional capacity improvements, patients also experienced a significant improvement in NT-proBNP and trended to lower hs-troponin I. The safety and tolerability of aficamten were consistent with prior experience in REDWOOD-HCM with no dose interruptions or treatment discontinuations and no serious adverse events. Coadministration of aficamten along with disopyramide and beta-blockers or calcium-channel blockers did not result in any significant electrocardiographic changes including in the QT-interval, or in blood pressure or heart rate.

On March 2, 2022, we announced the opening of enrollment in Cohort 4 of REDWOOD-HCM. Cohort 4 will enroll, in an open label fashion, 30-40 patients with symptomatic non-obstructive HCM ("nHCM") receiving background medical therapy. At screening, patients must have a LVEF of ≥60%, an elevated NT-proBNP >300 pg/mL, and must not have resting or post-Valsalva LVOT gradients (<30 mmHg in each case). The primary objective is to determine the safety and tolerability of aficamten in patients with nHCM. Other objectives include the effect of aficamten on LVEF, NYHA Functional Class and cardiac biomarkers. All patients will receive up to three escalating doses of aficamten, with doses being adjusted based on echocardiography according to LVEF alone. Cohort 4 will employ doses of 5, 10 and 15 mg once daily. Overall treatment duration will be 10 weeks with a 4-week follow up period after the last dose.

On May 23, 2022, we announced positive data relating to aficamten from REDWOOD-HCM OLE were presented in Late-Breaking Science Sessions at Heart Failure 2022, an International Congress of the European Society of Cardiology. Specifically, data from 38 patients enrolled in REDWOOD-HCM OLE were presented, including 30 patients treated for 12 weeks and 19 patients treated for 24 weeks. The data showed that treatment with aficamten was associated with substantial reductions in the average resting LVOT-G (mean change from baseline (SD) = -32.6 (28) mmHg, $p<0.0001$ at 12 weeks, -32.8 (32.3) mmHg, $p=0.0003$ at 24 weeks) and Valsalva LVOT-G (-42.7 (38.7) mmHg, $p<0.0001$ at 12 weeks, -51.1 (35.3) mmHg, $p<0.0001$ at 24 weeks). These reductions started to occur within two weeks of treatment, were sustained through 24 weeks of treatment, and were achieved with only modest decreases in the average LVEF (-3.2 (4.2) %, $p=0.0038$ at 24 weeks). Compared to baseline (47% Class II, 53% Class III), New York Heart Association (NYHA) Functional Class was improved in the majority of patients ($p<0.0001$ for improvement by one or more NYHA class), and no patients had a worsening of NYHA Class. At 12 weeks, 72% of patients improved by one class and 7% improved by two classes; at 24 weeks 61% of patients improved by one class and 17% improved by two classes. For patients reaching Week 24, 56% were Class I and 39% were Class II. There were also significant improvements in cardiac biomarkers including NTpro-BNP (reduction of 70% from baseline, $p<0.001$) and cardiac troponin (20% reduction, $p=0.002$). Treatment with aficamten was well-tolerated with one temporary discontinuation due to LVEF <50% and one temporary down-titration, neither related to drug. Both patients remain on treatment with aficamten.

On June 13, 2022, we announced that additional data from a new analysis of REDWOOD-HCM relating to the effect of treatment with aficamten on measures of cardiac structure and function were presented at the American Society of Echocardiography (ASE) 33rd Annual Scientific Sessions. Specifically, the new analysis investigated changes from baseline in echocardiographic measures of cardiac structure and function after 10 weeks of treatment with aficamten compared with placebo. At baseline, all patients (n=41) enrolled in Cohorts 1 and 2 of REDWOOD-HCM had severe left ventricular outflow tract (LVOT) obstruction, 88% had associated systolic anterior motion (SAM) of the mitral valve, and 90% had mitral regurgitation. SAM occurs when the mitral valve leaflet gets pushed against the interventricular septum during systole, resulting in obstruction of the LVOT and mitral regurgitation.

Measures of cardiac structure, diastolic and mitral valve function improved at Week 10 in patients treated with aficamten. There was a significant reduction in left atrial volume index ($p<0.01$) and a trend towards a reduction in left ventricular hypertrophy (left ventricular mass index; $p=0.06$). Treatment with aficamten also resulted in improved ventricular relaxation and filling, as indicated by a reduction in lateral E/e' ($p<0.01$) and an increase in lateral e' ($p<0.05$). Additionally, treatment with aficamten improved mitral valve dynamics as noted by a reduction in the proportion of patients with SAM (placebo: 92.3% at baseline to 75.0% at Week 10; aficamten: 85.7% at baseline to 35.7% at Week 10; $p=0.038$ for comparison to placebo) and a trend towards a reduction in those with eccentric mitral regurgitation (placebo: 25.0% at baseline to 33.3% at Week 10; aficamten: 42.9% at baseline to 7.1% at Week 10; $p=0.055$ for comparison to placebo) at Week 10. Together, these data point to evidence of early signs of improved cardiac function and structure and improved mitral valve dynamics after a 10-week treatment period with aficamten.

On September 30, 2022, we announced new data on the reduction and withdrawal of background standard of care medical therapy in patients treated with aficamten in REDWOOD-HCM OLE in a late breaking clinical trials session at the 2022 HCM Society Scientific Sessions. Patients in REDWOOD-HCM OLE were classified as receiving standard of care therapy if they were being treated with at least a beta-blocker, nondihydropyridine calcium channel blocker, or disopyramide. Patients were eligible for background therapy reduction/withdrawal (BTR/W) at the discretion of the site investigator, only after Week 12 and after having received a stable dose of aficamten for at least four weeks. Of 42 patients enrolled at the time of this analysis, 39 (93%) were taking ≥1 standard of care medication, and of those, 27 (69%) were receiving a beta-blocker only, 4 (10%) were receiving a calcium channel blocker only, 7 (18%) were receiving disopyramide and either a calcium channel blocker or beta-blocker, and 1 patient (3%) was receiving all three therapies. Of the 35 patients who had completed treatment with aficamten through Week 12, BTR/W was attempted in 20 patients. 17 patients (85%) achieved successful BTR/W, defined as at least one dose reduction of one medication to ≤50% of the baseline dose. Ten patients completely discontinued at least one medication, and 5 withdrew from all standard of care therapies. BTR/W was unsuccessful in three patients, who reinstituted a beta-blocker as a result of recurrence of symptoms or elevated left ventricular outflow tract gradients (LVOT-G). NYHA functional class and NT-proBNP and high-sensitivity troponin I levels remained stable before and after BTR/W. In 14 patients with an available assessment before and after BTR/W, BTR/W resulted in an increase in resting heart rate of 12 bpm (mean HR=74 ±10 bpm, p=0.0001) and Valsalva LVOT-G of 15 mmHg (mean Valsalva LVOT-G=42 ±26 mmHg, p=0.02). This data suggests that patients who achieved successful BTR/W experienced similar benefits from treatment with aficamten as those who remained on background standard of care therapy, and warrants further study.

On October 2, 2022, we announced new data on symptom improvement and quality of life related to treatment with aficamten in REDWOOD-HCM OLE in a late breaking clinical trials session at the HFSA Annual Scientific Meeting. This new analysis evaluated patients' self-reported health status using the Kansas City Cardiomyopathy Questionnaire (KCCQ) and compared baseline values to those collected at Week 12 and Week 24. The KCCQ is a validated patient reported outcomes tool 1 used to evaluate heart failure symptoms and their impact on social and physical limitations as well as quality of life. Higher scores indicate better health status. As early as Week 12, patients experienced substantial and significant symptom improvements as measured by the change in their KCCQ scores. The KCCQ Overall Summary Score (KCCQ-OSS) and all KCCQ sub-domain scores demonstrated these improvements, improvements which were also noted to be sustained through Week 24. At 12 and 24 weeks, the change from baseline (mean [SD]) change in KCCQ-OSS was 16.5 [16.7] (p<0.0001) and 17.6 [24.7] (p=0.0015). The proportion of patients with clinically important improvements (improvement ≥5 points on the KCCQ-OSS) was 72.7% at Week 12 and 72.0% at Week 24, and 36.4% of patients at Week 12 and 40.0% at Week 24 reported a very large clinical improvement (≥20 points).

We renamed the open-label extension clinical study of aficamten in patients with hypertrophic cardiomyopathy (HCM), previously known as REDWOOD-HCM OLE (Randomized Evaluation of Dosing With CK-274 in Obstructive Outflow Disease in HCM Open Label Extension) to FOREST-HCM (Five-Year, Open-Label, Research Evaluation of Sustained Treatment with Aficamten in HCM) to reflect the entry of patients from additional clinical trials of aficamten including SEQUOIA-HCM.

*Ji Xing Strategic Alliance*

On July 14, 2020, we entered into a certain License and Collaboration Agreement with Ji Xing (the "Ji Xing Aficamten License Agreement"), pursuant to which we granted to Ji Xing an exclusive license to develop and commercialize aficamten in China and Taiwan. Under the terms of the Ji Xing Aficamten License Agreement, we 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 oHCM, and/or nHCM and other indications. In addition, Ji Xing will pay us tiered royalties in the low-to-high teens range on the net sales of pharmaceutical products containing aficamten in China and Taiwan, subject to certain reductions for generic competition, patent expiration and payments for licenses to third party patents. The Ji Xing Aficamten License Agreement, unless terminated earlier, will continue on a market-by-market basis until expiration of the relevant royalty term.

*CK-271*

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. The primary objective of this Phase 1 placebo-controlled, single ascending dose clinical study in healthy adults was to assess the safety and tolerability of CK-271. The secondary objective was to evaluate the pharmacokinetic profile of CK-271 following single oral ascending doses. The study design included 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. 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, spinal muscular atrophy ("SMA"), chronic obstructive pulmonary disease ("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.

In April 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 Astellas 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' 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 that certain 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. The effective date of the termination of the Astellas OSSA Agreement was 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 advanced in clinical research, the Astellas OSSA 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 Astellas OSSA Agreement, upon the effective date of the termination, all licenses and other rights granted to Astellas under the Astellas OSSA Agreement terminated.

*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 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 Radicava® (edaravone) and/or Rilutek® (riluzole).

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

Also in December 2020, we announced the design of COURAGE-ALS, the Phase 3 clinical trial of reldesemtiv in patients with ALS, which is currently open for enrollment. 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 ≥65% predicted, and a screening ALSFRS-R ≤44. Patients currently taking stable doses of Radicava® (edaravone) and/or Rilutek® (riluzole) will be permitted and randomization stratified accordingly. The primary efficacy endpoint will be change from baseline to 24 weeks in ALSFRS-R. Secondary endpoints include combined assessment of ALSFRS-R total score; time to onset of respiratory insufficiency and survival time up to week 24 using a joint rank test; change from baseline to 24 weeks for vital capacity; ALSAQ-40; and bilateral handgrip strength. Two unblinded interim analyses by the Data Monitoring Committee are planned. The first will assess for futility, 12 weeks after approximately one-third or more of the planned sample size is randomized. A second interim analysis will also assess for futility, and there will be an option for a fixed increase in total enrollment if necessary to augment the statistical power of the trial. This Phase 3 clinical trial design builds on insights gained from FORTITUDE-ALS, further exploring the hypothesis that fast skeletal muscle activation with reldesemtiv may be an important therapeutic strategy in ALS.

In August 2021, we announced that COURAGE-ALS was opened to enrollment, and enrollment is currently ongoing.

In June 2022, we announced the start of COURAGE-ALS OLE, an open-label extension clinical study designed to assess the long-term safety and tolerability of reldesemtiv in people with ALS. Patients will be eligible for COURAGE-ALS OLE after completing their participation in COURAGE-ALS.

On October 10, 2022, we announced that the Data Monitoring Committee (DMC) for COURAGE-ALS, recently convened to conduct the first planned interim analysis of this ongoing Phase 3 clinical trial which assessed for the potential of futility. The DMC reviewed unblinded data from COURAGE-ALS and recommended that conduct of the clinical trial of reldesemtiv continue. The first interim analysis was triggered twelve (12) weeks after approximately one-third or more of the intended number of patients were randomized to participate in COURAGE-ALS. A second interim analysis, which is anticipated to occur in the first half of next year, will also assess for potential futility and will also allow for a fixed increase in total enrollment, if deemed necessary, to augment the statistical power of the trial.

*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.

**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, 2021.

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 now terminated collaboration agreements with Amgen and Astellas, namely the Amgen Agreement and the Astellas OSSA Agreement, 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.

Revenues for the three and nine months ended September 30, 2022 and 2021, were as follows (in thousands):

| | Three Months Ended | | | Nine Months Ended | | |
|---|---|---|---|---|---|---|
| | September 30, 2022 | September 30, 2021 | Increase (Decrease) | September 30, 2022 | September 30, 2021 | Increase (Decrease) |
| Research and development revenues | $ 2,515 | $ 437 | $ 2,078 | $ 4,631 | $ 9,828 | $ (5,197) |
| Milestone revenues | — | 5,000 | (5,000) | 1,000 | 5,000 | (4,000) |
| Realization of revenue participation right purchase agreement | — | — | — | 87,000 | — | 87,000 |
| Total revenues | $ 2,515 | $ 5,437 | $ (2,922) | $ 92,631 | $ 14,828 | $ 77,803 |

Research and development revenues for the three and nine months ended September 30, 2022 were from Astellas for reimbursements under the Astellas FSRA Agreement and in 2021 were from Astellas and Amgen under the Amgen Agreement.

Co-funding under the Astellas FSRA Agreement for the conduct of COURAGE-ALS will continue until the $12.0 million cap is reached.

During the nine months ended September 30, 2022, we recognized milestone revenues under the Research Collaboration Agreement, dated August 24, 2012, between us and MyoKardia, Inc.

During the nine months ended September 30, 2022, we recognized revenues of $87.0 million related to the 2020 RTW Royalty Purchase Agreement. In July 2020, 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. 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 understand that on April 18, 2022, RTW ICAV and MyoKardia, Inc. entered into agreements, which purported to assign all of RTW ICAV's rights, title and interest to the Mavacamten Royalty to MyoKardia, Inc., and on April 25, 2022, we entered into a tripartite agreement with RTW ICAV and MyoKardia, Inc. acknowledging the release and discharge of any further obligations by us or MyoKardia, Inc. in connection to the Mavacamten Royalty. As a result of the full extinguishment of the Mavacamten Royalty, we recognized revenue of $87.0 million.

***Research and Development Expenses***

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

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

Research and development expenses by program for the three and nine months ended September 30, 2022 and 2021, were as follows (in thousands):

| | Three Months Ended | | | Nine Months Ended | | |
|---|---|---|---|---|---|---|
| | September 30, 2022 | September 30, 2021 | Increase | September 30, 2022 | September 30, 2021 | Increase |
| Cardiac muscle contractility | $ 31,331 | $ 34,189 | $ (2,858) | $ 84,482 | $ 76,601 | $ 7,881 |
| Skeletal muscle contractility | 18,517 | 6,034 | 12,483 | 44,817 | 17,484 | 27,333 |
| All other research programs | 12,886 | 8,213 | 4,673 | 36,496 | 22,355 | 14,141 |
| Total research and development expenses | $ 62,734 | $ 48,436 | $ 14,298 | $ 165,795 | $ 116,440 | $ 49,355 |

Research and development expenses for the three and nine months ended September 30, 2022 increased by $14.3 million and $49.4 million from the three and nine months ended September 30, 2021, respectively, primarily due to higher expenses for our clinical development activities for COURAGE-ALS, for our cardiac muscle inhibitor programs, and for early research activities.

We continue to develop reldesemtiv to treat ALS and 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 now terminated strategic alliance with Amgen, Amgen was responsible for the development of omecamtiv mecarbil until the effective termination of the Amgen Agreement, which occurred on May 20, 2021. Following the effective termination of the Amgen Agreement, we continued 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 alliances with Ji Xing, Ji Xing is responsible for the development of aficamten and omecamtiv mecarbil 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 by program for the three and nine months ended September 30, 2022 and 2021, were as follows (in thousands):

| | Three Months Ended | | | Nine Months Ended | | |
|---|---|---|---|---|---|---|
| | September 30, 2022 | September 30, 2021 | Increase | September 30, 2022 | September 30, 2021 | Increase |
| Total general and administrative expenses | $ 48,222 | $ 26,202 | $ 22,020 | $ 124,008 | $ 62,997 | $ 61,011 |

General and administrative expenses for the three and nine months ended September 30, 2022 increased by $22.0 million and $61.0 million from the three and nine months ended September 30, 2021, respectively, primarily due to higher outside service spend in anticipation of the potential commercial launch of omecamtiv mecarbil and an increase in personnel related costs including stock-based compensation recorded in the nine months ended September 30, 2022.

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

| | Three Months Ended | | | Nine Months Ended | | |
|---|---|---|---|---|---|---|
| | September 30, 2022 | September 30, 2021 | Increase (Decrease) | September 30, 2022 | September 30, 2021 | Increase (Decrease) |
| Term loan | $ 1,199 | $ 1,214 | $ (15) | $ 3,524 | $ 3,615 | $ (91) |
| 2026 Notes | 313 | 2,917 | (2,604) | 3,382 | 8,521 | (5,139) |
| 2027 Notes | 5,211 | — | 5,211 | 5,211 | — | 5,211 |
| Warrants | — | — | — | — | — | — |
| Other | 81 | 30 | 51 | 240 | 86 | 154 |
| Total interest expense | $ 6,804 | $ 4,161 | $ 2,643 | $ 12,357 | $ 12,222 | $ 135 |

Interest expense for the three and nine months ended September 30, 2022 consists of interest expense related to the RP Loan Agreement between the Company and RPDF, dated January 7, 2022, interest expense related to the 2026 Notes and 2027 Notes, and interest expense related to the finance leases. Commensurate with our entry into the RP Loan Agreement, we terminated the Term Loan Agreement with Silicon Valley Bank and Oxford Finance LLC and repaid all amounts outstanding thereunder in January 2022. In July 2022, the Company issued the 2027 Notes and used the net proceeds and common stock to partially repurchase the 2026 Notes.

***Loss on settlement of debt***

As a result of the termination of the Term Loan Agreement and the repayment to the Lenders, during the nine months ended September 30, 2022, we recorded a loss of $2.7 million in loss on debt extinguishment in the condensed consolidated statements of operations and comprehensive loss, consisting of the premium on debt repayments and the write-off of the remaining term loan fees and debt issuance costs.

As a result of the partial repurchase of the 2026 Notes in the third quarter of 2022, during the three and nine months ended September 30, 2022, we recorded $22.2 million in loss on induced conversion, consisting of the difference between the consideration paid to the holders pursuant to the exchange agreements and the if-converted value of the 2026 Notes under the original terms.

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

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

On January 7, 2022, we entered into the RP Aficamten RPA with RPI ICAV. Pursuant to the RP Aficamten RPA, RPI ICAV purchased the right to receive a percentage of net sales equal to 4.5% for annual worldwide net sales of pharmaceutical products containing aficamten up to $1 billion and 3.5% for annual worldwide net sales of pharmaceutical products containing aficamten in excess of $1 billion, subject to reduction in certain circumstances (the "RP Aficamten Liability"). The carrying amount of the RP Aficamten Liability is based on our estimate of the future royalties to be paid to RPI ICAV over the life of the arrangement as discounted using an imputed rate of interest. The imputed rate of interest on the unamortized portion of the RP Aficamten Liability was approximately 11.7% as of the second quarter of 2022.

During the third quarter of 2022, we updated our analyses of the RP OM RPA and the RP Aficamten RPA 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.

Our estimates regarding the amount of future royalty payments under the RP Aficamten RPA increased due to changes in management's estimates of unobservable inputs related to market conditions and timing. The adjustment is accounted for on a prospective basis in our liability calculation and resulted in an increase in our imputed interest rate and noncash interest expenses from 11.7% and $2.6 million in the second quarter of 2022 to 25.0% and $5.5 million in the third quarter of 2022, respectively. During the three and nine months ended September 30, 2022, the change in estimate had no impact on revenue and increased the net loss by $2.8 million. The change in accounting estimate increased the net loss per share by $0.03 in the three and nine months ended September 30, 2022.

Our estimates regarding the amount of future royalty payments under the RP OM RPA decreased and the time periods within which we anticipated that such payments will be due changed based on management's estimates. 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 10% and $4.4 million in the second quarter of 2022 to 7.5% and $3.4 million in in the third quarter of 2022, respectively. During the three and nine months ended September 30, 2022, the change in estimate had no impact on revenue and reduced the net loss by $1.1 million. The change in accounting estimate reduced the net loss per share by $0.01 in the three and nine months ended September 30, 2022.

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

Non-cash interest expense on liability related to the RP OM RPA and the RP Aficamten RPA for the three and nine months ended September 30, 2022 and 2021, were as follows (in thousands):

| | Three Months Ended | | | Nine Months Ended | | |
|---|---|---|---|---|---|---|
| | September 30, 2022 | September 30, 2021 | Increase | September 30, 2022 | September 30, 2021 | Increase |
| RP OM Liability | $ 3,494 | $ 2,955 | $ 539 | $ 12,201 | $ 8,621 | $ 3,580 |
| RP Aficamten Liability | 5,469 | — | 5,469 | 10,329 | — | 10,329 |
| Total non-cash interest expense recognized | $ 8,963 | $ 2,955 | $ 6,008 | $ 22,530 | $ 8,621 | $ 13,909 |

***Interest and Other Income, net***

Interest and other income, net for the three and nine months ended September 30, 2022 and 2021 consisted primarily of interest income generated from our cash, cash equivalents and investments.

**Liquidity and Capital Resources**

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

| | September 30, 2022 | December 31, 2021 |
|---|---|---|
| Financial assets: | | |
| Cash and cash equivalents | $ 106,238 | $ 112,666 |
| Short-term investments | 761,426 | 358,972 |
| Long-term investments | 28,544 | 152,050 |
| Total cash, cash equivalents and marketable securities | $ 896,208 | $ 623,688 |
| Borrowings: | | |
| Term loan, net | $ 63,544 | $ 47,367 |
| Convertible notes, net | 544,986 | 95,471 |
| Total borrowings | $ 608,530 | $ 142,838 |
| Working capital: | | |
| Current assets | $ 884,275 | $ 535,672 |
| Current liabilities | 76,496 | 71,860 |
| Working capital | $ 807,779 | $ 463,812 |

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

| | Nine Months Ended | |
|---|---|---|
| | September 30, 2022 | September 30, 2021 |
| Net cash used in operating activities | $ (201,326) | $ (97,785) |
| Net cash used in investing activities | (291,383) | (195,112) |
| Net cash provided by financing activities | 486,281 | 300,474 |
| Net (decrease) increase in cash and cash equivalents | $ (6,428) | $ 7,577 |

***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 $201.3 million in the nine months ended September 30, 2022 which include a net loss of $251.6 million was largely due to ongoing research and development activities, general and administrative expenses to support those activities, offset by collection of receivables primarily from our 2021 RTW Transactions. Net loss for the nine months ended September 30, 2022 included, among other items: non-cash stock-based compensation, non-cash interest expense related to sale of future royalties, non-cash interest expense related to debt, and loss on settlement of debt.

Net cash used in investing activities of $291.4 million in the nine months ended September 30, 2022 was primarily due to purchases of investments and property and equipment offset by proceeds from maturity of investments.

Net cash provided by financing activities of $486.3 million in the nine months ended September 30, 2022 was primarily due to $540.0 million of proceeds related to 2027 Notes, the proceeds related to the RP Aficamten RPA and the RP Loan Agreement, offset by the repayment of amounts owed under our Term Loan Agreement and 2026 Notes, and stock-based activities.

*2021 Ji Xing and RTW Transactions*

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

In addition to the Ji Xing OM License Agreement, we entered into common stock purchase agreements with each of RTW Master Fund, Ltd., RTW Innovation Master Fund, Ltd. and RTW Venture Fund Limited (collectively, the "RTW Investors"), pursuant to which we sold and issued an aggregate of 0.5 million shares of our common stock at a price per share of $39.125 and an aggregate purchase price of $20.0 million.

*2022 Royalty Pharma Transactions*

On January 7, 2022, we announced that we had entered into that certain Development Funding Loan Agreement (the "RP Loan Agreement") and the Revenue Participation Right Purchase Agreement (the "RP Aficamten RPA") with Royalty Pharma Development Funding, LLC ("RPDF") and Royalty Pharma Investments 2019 ICAV ("RPI ICAV") respectively, each of which were at the time of our entry into such agreements affiliated with Royalty Pharma International plc.

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

- $50.0 million of tranche 2 term loans during the one year period following the receipt on or prior to December 31, 2022 of marketing approval from FDA of omecamtiv mecarbil;

- $25.0 million of tranche 3 term loans during the one year period following the commercial availability of a diagnostic test measuring levels of omecamtiv mecarbil to support the final FDA label language applicable to such drug, subject to such commercial availability and the conditions to the tranche 2 term loans having occurred on or prior to December 31, 2022;
- $75.0 million of tranche 4 term loans during the one year period following the receipt on or prior to September 30, 2024 of positive results from SEQUOIA-HCM, the Phase 3 trial for aficamten; and
- $100.0 million of tranche 5 term loans during the one year period following the acceptance by the FDA on or prior to March 31, 2025 of an NDA for aficamten, subject to the conditions to the tranche 4 term loans having occurred on or prior to September 30, 2024.

The FDA's recent postponement of the PDUFA target action date for our NDA for omecamtiv mecarbil to February 28, 2023 is likely to have an adverse impact on our ability to meet the tranche 2 and tranche 3 conditions for disbursement under the RP Loan Agreement.

Each term loan under the RP Loan Agreement matures on the 10 year anniversary of the funding date for such term loan and is repayable in quarterly installments of principal, interest and fees commencing on the last business day of the seventh full calendar quarter following the calendar quarter of the applicable funding date for such term loan, with the aggregate amount payable in respect of each term loan (including interest and other applicable fees) equal to 190% of the principal amount of the term loan (such amount with respect to each term loan, "Final Payment Amount").

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

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

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

Commensurate with our entry into the RP Loan Agreement and the RP Aficamten RPA, we terminated the Term Loan Agreement with the Lenders and repaid all amounts outstanding thereunder.

*Convertible Notes*

On November 13, 2019, the Company issued $138.0 million aggregate principal amount of 2026 Notes. On July 6, 2022, the Company issued $540.0 million aggregate principal amount of 2027 Notes and used approximately $140.3 million of the net proceeds from the offering of 2027 Notes and issued 8,071,343 shares of common stock to repurchase approximately $116.9 million aggregate principal amount of the 2026 Notes pursuant to privately negotiated exchange agreements entered into with certain holders of the 2026 Notes concurrently with the pricing of the offering of the 2027 Notes. As a result of the partial repurchase of the 2026 Notes, the Company recorded an inducement loss of $22.2 million, consisting of the difference between the consideration to the holders pursuant to the exchange agreements and the if-converted value of the 2026 Notes under the original terms. As of September 30, 2022, there remains $21.1 million aggregate principal amount of 2026 Notes outstanding and $540.0 million of aggregate principal amount of 2027 Notes outstanding.

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
- the cost of additional construction to expand our headquarters in South San Francisco and in relation to our newly leased office facilities in Radnor, Pennsylvania;
- 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 aficamten to us. Finally, notwithstanding the expansion of our collaboration with Ji Xing to include omecamtiv mecarbil in December 2021 and our recent financing transactions with entities affiliated with Royalty Pharma International plc in January 2022, we plan to continue 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.

We have incurred an accumulated deficit of $1,448.6 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.

**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, 2021.

## 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, 2022, 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, 2022, 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 as we expand our research and development activities and expand our organization to prepare for commercialization of any approved drug. We have funded our operations and capital expenditures with proceeds primarily from private and public sales of our equity securities, royalty monetization agreements, revenue interest agreements, strategic alliances, long-term debt, other financings, interest on investments and grants. We believe that our existing cash and cash equivalents, short-term investments and interest earned on investments should be sufficient to meet our projected operating requirements for at least the next 12 months. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect. Because of the numerous risks and uncertainties associated with the development of our drug candidates and other research and development activities, including risks and uncertainties that could impact the rate of progress of our development activities, we are unable to estimate with certainty the amounts of capital outlays and operating expenditures associated with these activities.

For the foreseeable future, our operations will require significant additional funding, in large part due to our research and development expenses, the organizational scale up and associated expenditures with commercial readiness activities to launch approved drugs combined with the absence of any revenues from product sales. 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 loans under the RP Loan Agreement with RPDF, potential additional revenue interest sale proceeds under the RP Aficamten RPA, and reimbursements, milestone and royalty payments that we may receive under our agreements with Astellas and Ji Xing. We may not receive any further funds under any of these 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, and if we cannot raise the funds we need to operate our business, we will need to delay or discontinue certain research and development activities, and our stock price may be negatively affected.

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

On January 7, 2022, we announced that we had entered into the RP Loan Agreement and the RP Aficamten RPA with each of RPDF and RPI ICAV respectively, each such entity being affiliated with Royalty Pharma International plc. Together these agreements make available to us up to $150.0 million in revenue interest sale proceeds under the RP Aficamten RPA and up to $300.0 million in loans, of which a $50.0 million loan and $50.0 million in revenue interest sale proceeds were paid to us at the closing of such transactions. In addition, on March 10, 2022, we received a further $50.0 million in revenue interest sale proceeds from RPI ICAV under the RP Aficamten RPA following the initiation of our first pivotal trial in oHCM for aficamten. However, additional loan disbursements and sale proceeds under the RP Aficamten RPA and the RP Loan Agreement are subject to our satisfaction of certain conditions related to the development of aficamten and omecamtiv mecarbil, in certain cases by specific deadlines. Should we not satisfy such conditions by the applicable deadlines, or in the event we fail to meet our obligations or default under these agreements, the actual amount of additional loan disbursements and/or sale proceeds could be substantially less than the maximum amounts available thereunder.

In June 2022, we announced that the FDA had extended the PDUFA target action date for our NDA for omecamtiv mecarbil to February 28, 2023. Given the new PDUFA target action date, it is likely that we will not be able to satisfy certain conditions and deadlines for the tranche 2 and tranche 3 loan disbursements under the RP Loan Agreement.

***We are subject to counterparty risk under the RP Aficamten RPA and the RP Loan Agreement***

We are subject to counterparty risk in the event that either RPDF or RP ICAV default on their respective obligations under the RP Loan Agreement or the RP Aficamten RPA respectively.

In respect of the RP Aficamten RPA, our ability to receive additional revenue interest sale proceeds is subject to the risk that RPI ICAV may default or otherwise fail to perform its obligations thereunder to pay us additional revenue interest sale proceeds that we would be entitled to upon satisfaction of certain conditions. In such event, subject to a cure right of RPI ICAV, we will have a limited right to reduce the amount of royalty payable by unless such obligation is contested in good faith, but otherwise our exposure to the credit risk of RPI ICAV will not be secured by any collateral. If RPI ICAV 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 and without any reversion of the revenue interest having been sold to RPI ICAV (other than the aforementioned reduction) and without any recourse against Royalty Pharma International plc or any of its other affiliated or controlled entities.

In respect of the RP Loan Agreement, our ability to receive additional loan disbursements is subject to the risk that RPDF may default or otherwise fail to perform its obligations thereunder to extend additional loan disbursement that we would be entitled to upon satisfaction of certain conditions. In such event, we have no recourse against Royalty Pharma International plc or any of its other affiliated or controlled entities, and in the event of an RPDF insolvency, we would have no rights to additional loan disbursements from RPDF.

***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 subsequently 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.

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

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

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

Separately, in response to the global COVID-19 pandemic, the FDA had a period during which manufacturing inspections were not conducted, leading to delay, and has resumed on-site inspections of domestic manufacturing facilities subject to a risk-based prioritization system. The FDA intends to use this risk-based assessment system to identify the categories of regulatory activity that can occur within a given geographic area, ranging from mission critical inspections to resumption of all regulatory activities. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

***Our indebtedness and liabilities could limit the cash flow available for our operations, expose us to risks that could adversely affect our business, financial condition and results of operations and impair our ability to satisfy our obligations under the 2026 Notes, the 2027 Notes and the RP Loan Agreement.***

As of September 30, 2022, we had $611.1 million aggregate principal amount of indebtedness, comprised of $50.0 million under the RP Loan Agreement, $21.1 million under our 4.00% convertible senior notes due 2026 (the “2026 Notes”) and $540.0 million under our 3.50% convertible senior notes due 2027 (the “2027 Notes”).

We may also incur additional indebtedness to meet future financing needs. Our indebtedness could have significant negative consequences for our security holders and our business, results of operations and financial condition by, among other things:

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

Our business may not generate sufficient funds, and we may otherwise be unable to maintain sufficient cash reserves, to pay amounts due under our indebtedness and our cash needs may increase in the future. In addition, any required repurchase of the 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 the RP Loan Agreement, the RP Aficamten RPA, the RP OM RPA, and the indentures related to our convertible notes restrict our business and operations in many ways and if we do not effectively manage our covenants, our financial conditions and results of operations could be adversely affected. Our operations may not provide sufficient cash to meet our debt repayment obligations.***

The RP Loan Agreement, the RP Aficamten RPA, the RP OM RPA, and the indenture related to the notes require that we comply with certain covenants applicable to us, including among other things, covenants restricting dispositions, changes in business, management, ownership or business locations, mergers or acquisitions, indebtedness, encumbrances, distributions, investments, transactions with affiliates and subordinated debt, any of which could restrict our business and operations, particularly our ability to respond to changes in our business or to take specified actions to take advantage of certain business opportunities that may be presented to us. In addition, the RP Aficamten RPA and the RP OM RPA contain certain covenants applicable to us, including among other things, development and commercialization diligence obligations in connection to aficamten and omecamtiv mecarbil and reporting obligations, which could also restrict our business and operations, particularly in connection to our development and commercialization of aficamten and omecamtiv mecarbil.

Our failure to comply with any of the covenants could result in a default under the RP Loan Agreement, the RP Aficamten RPA, the RP OM RPA, or the indenture related to the notes, which could permit the counterparties to declare all or part of any outstanding borrowings or other payment obligations to be immediately due and payable and/or enforce any outstanding liens against our assets.

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

In addition, certain provisions in the 2026 Notes, the 2027 Notes and the related indentures could make a third party attempt to acquire us more difficult or expensive. For example, if a takeover constitutes a fundamental change under our indenture, then noteholders will have the right to require us to repurchase their notes for cash. In addition, if a takeover constitutes a make-whole fundamental change under our indenture, then we may be required to temporarily increase the conversion rate. In either case, and in other cases, our obligations under the 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.

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

***The accounting method for our convertible notes could adversely affect our reported financial condition and results.***

The accounting method for reflecting the 2026 Notes and 2027 Notes (together, the "Convertible Notes") on our balance sheet, accruing interest expense for the Convertible 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.

In August 2020, the Financial Accounting Standards Board published an Accounting Standards Update, which we refer to as ASU 2020-06, which simplifies certain of the accounting standards that apply to convertible notes. In accordance with ASU 2020-06, we expect that the Convertible Notes will be reflected as a liability on our balance sheets, with the initial carrying amount equal to the principal amount of the notes, net of issuance costs. The issuance costs will be treated as a debt discount for accounting purposes, which will be amortized into interest expense over the term of the Convertible Notes. As a result of this amortization, the interest expense that we expect to recognize for the Convertible Notes for accounting purposes will be greater than the cash interest payments we will pay on the Convertible Notes, which will result in lower reported income.

In addition, we expect that the shares underlying the Convertible Notes will be reflected in our diluted earnings per share using the "if converted" method, in accordance with ASU 2020-06. Under that method, diluted earnings per share would generally be calculated assuming that all the Convertible 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, and accounting standards may change in the future in a manner that may adversely affect our diluted earnings per share.

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

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

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

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

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

GALACTIC-HF was conducted under a Special Protocol Assessment (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 dexpramipexole, known as EMPOWER, the National Institute of Neurological Disorders and Stroke's trial of ceftriaxone, and Trophos SA's trial of olesoxime. Reldesemtiv, like these compounds, may fail in clinical development if it does not show a statistically significant level of clinical efficacy or if the adverse event profile is too great compared to 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 and the FDA having accepted our NDA for filing, 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.

In February 2022, we announced that the FDA had accepted our NDA for omecamtiv mecarbil for the treatment of HFrEF for filing and assigned a PDUFA target action date of November 30, 2022. In June 2022, we announced that the FDA had extended the PDUFA target action date by three (3) months to February 28, 2023.

Although our supplemental analyses showed that omecamtiv mecarbil potentially has a greater treatment effect in certain subgroups of trial patients and the FDA has accepted our NDA for filing, 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 or that FDA will ultimately approve omecamtiv mecarbil for the treatment of HFrEF based on our NDA as filed by the FDA, whether by the PDUFA target action date of February 28, 2023 or subsequently.

***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, including COURAGE-ALS and SEQUOIA-HCM, our clinical development activities could be delayed or otherwise adversely affected.***

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

- the patient eligibility criteria defined in the protocol;
- the size of the patient population required for analysis of the trial's primary endpoints;
- the proximity of patients to study sites;
- the design of the trial;
- the ability to recruit clinical trial investigators with the appropriate competencies and experience;
- clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies or clinical trials, including any new drugs that may be approved for the indications we are investigating or clinical trial results;
- the ability to obtain and maintain patient consents;
- the risk that patients enrolled in clinical trials will drop out of the trials before completion;
- the effects of the COVID-19 pandemic, including governmental responses and restrictions on movement and the ability of patients to visit clinical trial sites and practicability and/or availability of virtual and/or home healthcare visits.

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 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 continue to 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 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 a dosage selection test for 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, the 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). Finally, any dosage selection test alternative to the Microgenics OM Assay would require that we enter into an agreement with a suitable partner to develop and operationalize the test, and no assurance can be given that we will identify a suitable partner with the necessary expertise and capabilities, agree to contractual terms that are advantageous to us, or that such partner will in fact commercialize the test in a manner that is supportive of our commercialization efforts for omecamtiv mecarbil.

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

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

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

***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 associated with any post approval commitments in connection with any drug regulatory approvals that are imposed on us by FDA or any other regulatory authority;
- 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 clinical research organizations ("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 contract manufacturers to produce our clinical trial materials, including our drug candidates, and will have continued reliance on contract manufacturers for the development and commercialization of our potential drugs.***

We do not currently operate manufacturing facilities for clinical or commercial production of our drug candidates and rely on contract manufacturing organizations ("CMOs") for the manufacture of finished drug product and active pharmaceutical ingredient. We have limited experience in drug formulation and manufacturing, and we lack the resources and the capabilities to manufacture any of our drug candidates on a clinical or commercial scale.

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 have engaged with Amgen's existing contract manufacturers for the manufacture and packaging of omecamtiv mecarbil to enter into supply agreements. In January 2022, we entered into a long-term commercial supply agreement for the supply of finished drug product for omecamtiv mecarbil, and in October 2022 we entered into a long-term commercial supply agreement for the supply of active pharmaceutical ingredient for omecamtiv mecarbil.

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

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

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

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

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

***We may not be able to successfully manufacture our drug candidates in sufficient quality and quantity, which would delay or prevent us from developing our drug candidates and commercializing 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 certain of our drug candidates are unproven, and we do not know whether we will be able to develop any drug of commercial value.***

We have discovered and develop drug candidates that have what we believe are novel mechanisms of action directed against cytoskeletal targets. 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 of our or our licensors' ownership of our owned, co-owned or in-licensed patents, trade secrets or other intellectual property. If we or our licensors fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, intellectual property that is important to our product candidates. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

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 and/or more effective than ours, which may diminish or eliminate the commercial success of any drugs that we may commercialize.***

We compete with companies that have developed drugs or are developing drug candidates for cardiovascular diseases, diseases and conditions associated with muscle weakness or wasting and other diseases for which our drug candidates may be useful treatments. 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), marketed by Mitsubishi Tanabe Pharma Corporation, and Relyvrio™ (AMX0035), marketed by Amylyx Pharmaceuticals. These are the first two FDA approved drugs for the treatment of ALS since riluzole in 1995. In addition, we may then also compete with other potential new therapies for ALS that are currently being developed by companies including, but not limited to, AB Science, Alexion Pharmaceuticals, BrainStorm Cell Therapeutics, Biogen, Biohaven Pharmaceuticals, Clene Nanomedicine, Ferrer, Ionis, Medicinova, Inc., Orphazyme, Prilenia, Revalesio Corporation and Seelos Therapeutics. 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 will compete with Camzyos™ (mavacamten). Aficamten and Camzyos™ (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 Camzyos™ (mavacamten) may have an impact on our ability to obtain regulatory approval for, or the commercial prospects of, aficamten. In addition to Camzyos™, other companies, including but not limited to Novartis AG, Eli Lilly, Boehringer Ingelheim, Gilead and Imbria are conducting clinical trials in HCM and could complete with 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 and/or more efficacious than our potential drugs, or that reach the market sooner than our potential drugs, we may not achieve commercial success. In addition, the life sciences industry is characterized by rapid technological change. If we fail to stay at the forefront of technological change, we may be unable to compete effectively. Our competitors may render our technologies obsolete by improving existing technological approaches or developing new or different approaches, potentially eliminating the advantages in our drug discovery process that we believe we derive from our research approach and proprietary technologies.

***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.

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

We have been granted Breakthrough Therapy Designation for aficamten for oHCM by the FDA and may seek these and/or additional special designations from regulatory authorities to expedite the review and approval process for our product candidates.

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

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

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

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

***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 do not possess all these 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 sell and 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 disproportionally larger share of Medicare patients relative to commercial and other payors. Overall coverage will likely be delayed given Medicare's defined bid timelines for inclusion in the Medicare Part D formulary. In addition, the rebate levels we may have to offer to PBMs and payors to be included in their formularies may also impact the profitability of omecamtiv mecarbil.

Moreover, pricing of our drug candidates, if approved by the FDA or other regulatory authorities for commercialization, may be impacted by cost-effectiveness and economic analyses by a Health Technology Assessment (HTA) organization such as the Institute for Clinical and Economic Review ("ICER"), an independent non-profit research institute that produces reports analyzing the evidence underlying the effectiveness and value of drugs and other medicinal services. ICER assessments and recommended pricing based on cost-effectiveness may affect our ability to obtain favorable pricing terms with Medicare, Medicaid, VA, DoD, Tri Care, and other commercial payors. For example, in November 2021, ICER published its final evidence report and policy recommendations related to Camzyos™ (mavacamten), a small molecule myosin inhibitor being developed by Bristol-Myers Squibb Company (formerly by MyoKardia, Inc.) that has a similar mechanism of action to aficamten. The report concluded that a majority of contributing panelists found that current evidence was not adequate to demonstrate a net health benefit for Camzyos™ (mavacamten) added to background therapy when compared to background therapy alone or a net health benefit of Camzyos™ (mavacamten) when compared to disopyramide. Moreover, ICER's final report concluded that modeling short-term clinical benefits of Camzyos™ (mavacamten) over a longer time period produces a health-benefit price benchmark index for Camzyos™ (mavacamten) between $12,000-$15,000 per year, significantly lower than the $89,500 annual price that Bristol-Myers Squibb Company has indicated. Whilst not binding on Medicare, Medicaid, VA, DoD, Tri Care, and other commercial payors, or indicative of the net health benefits, ICER could conclude for aficamten a similar conclusion that could adversely impact our ability to obtain favorable pricing.

***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.

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

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

***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.

**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.

***Failure to obtain regulatory approvals in foreign jurisdictions would prevent us from marketing our products internationally.***

In order to market any product in the EEA (which is composed of the 27 member states of the E.U. plus Norway, Iceland and Liechtenstein), and many other foreign jurisdictions, separate regulatory approvals are required. In the EEA, medicinal products can only be commercialized after obtaining a Marketing Authorization ("MA"). Before the MA is granted, the EMA or the competent authorities of the member states of the EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

The approval procedures vary among countries and can involve additional clinical testing, and the time required to obtain approval may differ from that required to obtain FDA approval. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries. Approval by the FDA does not ensure approval by regulatory authorities in other countries, and approval by one or more foreign regulatory authorities does not ensure approval by regulatory authorities in other foreign countries or by the FDA. However, a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in others. The foreign regulatory approval process may include all of the risks associated with obtaining FDA approval. We may not be able to file for regulatory approvals or to do so on a timely basis, and even if we do file we may not receive necessary approvals to commercialize our products in any market.

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

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

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 2031, except for a temporary suspension from May 1, 2020 through March 31, 2022 due to the COVID-19 pandemic, unless additional Congressional action is taken. Under current legislation, the actual reduction in Medicare payments will vary from 1% in 2022 to up to 3% in the final fiscal year of this sequester. In January 2013, the American Taxpayer Relief Act of 2012 was enacted which, among other things, further reduced Medicare payments to several providers, including hospitals and outpatient clinics, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Since its enactment, there have been executive, judicial and Congressional challenges to numerous elements of the ACA, as well as efforts to repeal or replace certain aspects of the ACA. For example, on June 17, 2021 the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Thus, the ACA will remain in effect in its current form. It is possible that the ACA will be subject to executive, judicial, and Congressional challenges in the future. It is unclear how any such challenges will impact the ACA and our business. 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.

In August 2022, the Inflation Reduction Act of 2022 was signed into law, which includes prescription drug provisions that may impact product pricing including the potential for net price reductions and/or the ability to increase price at level of inflation over the lifecycle of our products, and/or may increase our rebate obligation to Medicare. Provisions include a requirement that the Department of Health and Human Services (HHS) negotiate drug prices for single-source brand-name drugs and biologics that are among the 50 drugs with the highest total Medicare Part D spending. The law establishes a maximum fair price, outlines the process by which the Secretary of HHS will identify drugs for negotiations, and establishes non-compliance penalties for manufacturers. The Act implements inflation rebates in Medicare when a drug's Average Manufacturer Price (AMP, in Part D) or Average Sale Price (ASP, in Part B) rises faster than the inflation index (CPI-U). In addition, the Part D drug benefit caps beneficiary spending at $2,000, eliminates the coverage gap for patients, and modifies, beginning in 2025, liabilities for drug manufacturers by replacing the 70% discount in the Coverage gap with a 10% discount in the Initial Coverage phase and a 20% discount in the Catastrophic phase.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. However, we cannot predict the timing or substance of proposals that may be adopted in the future, particularly in light of the difficulty of advancing legislation through Congress. The continuing efforts of governments, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare, including by imposing price controls, may adversely affect the demand 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), other health care professionals (such as physician assistants and nurse practitioners), and teaching hospitals, as well as information regarding ownership and investment interests held by physicians and their immediate family members. Payments made to physicians and research institutions for clinical trials are included within the ambit of this law.
- Analogous state laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, and some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures and state and local laws that require the registration of sales representatives.

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

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

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

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

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

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

**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 Cuts and Jobs Act (the "Tax Act"), with unused NOLs expiring 20 years after we report a tax loss. These NOLs could expire unused and be unavailable to offset future taxable income. We cannot predict if and to what extent various states will conform to the Tax Act, as modified by additional tax legislation enacted in 2020.

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

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

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

In 2017, the U.S. government enacted the Tax Act that includes significant changes to the taxation of business entities, which was modified by additional federal tax legislation in 2020. 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). Furthermore, proposals have been made in Congress (which have not yet been enacted) to make further changes to the federal income tax laws applicable to corporations that could have an adverse impact on us. The impact of the 2017 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, including potential additional proposed federal tax law changes.

***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. 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. | | Incorporated by Reference | | | | Filed Herewith |
|---|---|---|---|---|---|---|
| | | Form | File No. | Filing Date | Exh. No. | |
| 3.1 | Amended and Restated Certificate of Incorporation | S-3 | 333-174869 | June 13, 2011 | 3.1 | |
| 3.2 | Certificate of Amendment of Amended and Restated Certificate of Incorporation | 8-K | 000-50633 | June 25, 2013 | 5.1 | |
| 3.3 | Certificate of Amendment of Amended and Restated Certificate of Incorporation | 8-K | 000-50633 | May 20, 2016 | 3.1 | |
| 3.4 | Amended and Restated Bylaws | S-1 | 333-112261 | January 27, 2004 | 3.2 | |
| 4.1 | Specimen Common Stock Certificate | 10-Q | 000-50633 | May 9, 2007 | 4.1 | |
| 10.1 | Description of Director Compensation | | | | | X |
| 31.1 | Certification of Principal Executive Officer pursuant to Rule 13a-14(a) and Rule 15d-14(a) of the Securities Exchange Act, as amended | | | | | X |
| 31.2 | Certification of Principal Financial Officer pursuant to Rule 13a-14(a) and Rule 15d-14(a) of the Securities Exchange Act, as amended | | | | | X |
| 31.3 | Certification of Principal Accounting Officer pursuant to Rule 13a-14(a) and Rule 15d-14(a) of the Securities Exchange Act, as amended | | | | | X |
| 32.1 | 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 (2) | | | | | 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 |

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

(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 4, 2022

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)

**Exhibit 10.1**

## DESCRIPTION OF DIRECTOR COMPENSATION

Our non-employee director compensation program consists of both a cash component and an equity component. Non-employee directors are also able to elect to receive their annual base retainers in equity, as further described below. We do not compensate members of the Board of Directors or committees on a per-meeting basis.

### Annual Retainers

Our non-employee directors received annual base retainers in the amounts set forth below.

| | | | |
|---|---|---|---|
| Base Retainer | Board of Directors Chair | $ | 75,000 |
| | Other directors | $ | 45,000 |
| Committee Chair Retainer | Audit Committee | $ | 20,000 |
| | Compliance Committee | $ | 15,000 |
| | Compensation and Talent Committee | $ | 15,000 |
| | Nominating and Governance Committee | $ | 10,000 |
| | Science and Technology Committee | $ | 25,000 |
| Committee Member Retainer | Audit Committee | $ | 10,000 |
| | Compliance Committee | $ | 7,500 |
| | Compensation and Talent Committee | $ | 7,500 |
| | Nominating and Governance Committee | $ | 5,000 |
| | Science and Technology Committee | $ | 7,500 |

We also reimburse our non-employee directors for out-of-pocket expenses incurred in connection with service on our Board of Directors.

### Election to Receive Retainers in Cash or Equity

Each non-employee director may make an annual election to receive his or her annual base retainer (but not committee retainers) either wholly in cash or to receive either 50% or 100% of that retainer in fully vested shares of Common Stock under our 2004 Equity Incentive Plan ("2004 EIP") of equal value. Non-employee directors electing to receive 50% or 100% of their annual base retainer in fully vested Common Stock will receive such shares on the first business day of each calendar quarter for which the election is in effect.

### Initial and Annual Equity Grants to Non-Employee Directors

Non-employee directors receive grants of stock awards under the 2004 EIP. Non-employee directors receive an initial option grant of 35,000 shares on joining the Board of Directors. Continuing directors receive an annual option grant of 10,000 shares and an annual restricted stock unit ("RSU") grant 5,000 shares. Generally, an initial option grant to a director vests monthly over three years. The annual option grants to continuing directors vest monthly over one year, and the annual RSU grants to continuing directors are subject to 100% cliff vesting on the one-year anniversary of the RSU grant. Our Board of Directors continues to have discretion to grant options to new and continuing non-employee directors. A non-employee director that resigns from the Board of Directors has one year following resignation to exercise vested options, but such one-year period may be extended at the discretion of the Compensation and Talent Committee.

**Exhibit 31.1**

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 4, 2022

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

**Exhibit 31.2**

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 4, 2022

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

**Exhibit 31.3**

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 4, 2022

By: /s/ Robert C. Wong

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

**Exhibit 32.1**

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, 2022 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 4, 2022

/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)