UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 10-Q

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

For the quarterly period ended March 31, 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: 001-35945

EPIZYME, INC.

(Exact name of registrant as specified in its charter)

Delaware	**26-1349956**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
400 Technology Square, 4th Floor Cambridge, Massachusetts	**02139**
(Address of principal executive offices)	**(Zip code)**

617-229-5872
(Registrant's telephone number, including area code)

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

Title of each class	Trading symbol(s)	Name of each exchange on which registered
Common stock, $0.0001 par value	**EPZM**	**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 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 definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

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

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

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

The number of shares outstanding of the registrant's common stock as of May 4, 2022: 164,874,549 shares.

Forward-looking Information

This Quarterly Report on Form 10-Q contains forward-looking statements that involve substantial risks and uncertainties. These statements may be identified by such forward-looking terminology as "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," and similar statements or variations of such terms. Our forward-looking statements are based on a series of expectations, assumptions, estimates and projections about our company, are not guarantees of future results or performance and involve substantial risks and uncertainty. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in these forward-looking statements. Our business and our forward-looking statements involve substantial known and unknown risks and uncertainties, including the risks and uncertainties inherent in our statements regarding:

- our plans to research, develop and commercialize novel epigenetic therapies for patients with cancer;
- the ongoing commercialization of TAZVERIK;
- our sales, marketing and distribution capabilities and strategies, including for the commercialization and manufacturing of TAZVERIK and any future products;
- the rate and degree of market acceptance and clinical utility of TAZVERIK and any future products;
- our ongoing and planned clinical trials, including the timing of initiation and enrollment in the trials, the timing of availability of data from the trials and the anticipated results of the trials;
- the timing of and our ability to apply for, obtain and maintain regulatory approvals for tazemetostat in epithelioid sarcoma, follicular lymphoma and other indications, EZM0414 and any future product candidates;
- our ability to achieve anticipated milestones under our collaborations or to enter into additional collaborations;
- the impact of the COVID-19 pandemic on our business, results of operations, and financial condition;
- our intellectual property position;
- our ability to successfully implement and execute on our changes to our commercial strategy and organization, adjustments to our operating plans, including operating expense reductions, and leadership transitions; and
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing.

All of our forward-looking statements are made as of the date of this Quarterly Report on Form 10-Q only. In each case, actual results may differ materially from such forward-looking information as a result of various important factors. We can give no assurance that such expectations or forward-looking statements will prove to be correct. An occurrence of or any material adverse change in one or more of the risk factors or risks and uncertainties referred to in this Quarterly Report on Form 10-Q or our Annual Report on Form 10-K for the fiscal year ended December 31, 2021, or our Annual Report, or included in our other public disclosures or our other periodic reports or other documents or filings filed with or furnished to the Securities and Exchange Commission, or the SEC, could materially and adversely affect our business, prospects, financial condition and results of operations. Except as required by law, we do not undertake or plan to update or revise any such forward-looking statements to reflect actual results, changes in plans, assumptions, estimates or projections or other circumstances affecting such forward-looking statements occurring after the date of this Quarterly Report on Form 10-Q, even if such results, changes or circumstances make it clear that any forward-looking information will not be realized. Any public statements or disclosures by us following this Quarterly Report on Form 10-Q which modify or impact any of the forward-looking statements contained in this Quarterly Report on Form 10-Q will be deemed to modify or supersede such statements in this Quarterly Report on Form 10-Q.

Our management's discussion and analysis of our financial condition and results of operations are based upon our unaudited condensed consolidated financial statements included in this Quarterly Report on Form 10-Q, which have been prepared by us in accordance with accounting principles generally accepted in the United States of America, or GAAP, for interim periods and with Regulation S-X promulgated under the Securities Exchange Act of 1934, as amended, or the Exchange Act. Our management's discussion and analysis should be read in conjunction with these unaudited condensed consolidated financial statements and the notes thereto as well as in conjunction with the audited consolidated financial statements and notes thereto included in our Annual Report. The three months ended March 31, 2022 and 2021 are referred to as the first quarter of 2022 and 2021, respectively.

Note regarding certain references in this Quarterly Report on Form 10-Q

Unless otherwise stated or the context indicates otherwise, all references herein to "Epizyme," "Epizyme, Inc.," "we," "us," "our," "our company," "the Company" and similar references refer to Epizyme, Inc. and its wholly owned subsidiary, Epizyme Securities Corporation.

In addition, unless otherwise stated or the context indicates otherwise, all references in this Quarterly Report on Form 10-Q to "TAZVERIK (tazemetostat)" and "TAZVERIK" refer to tazemetostat in the context of the commercially-available product for which we received accelerated approval from the United States Food and Drug Administration in January 2020 for epithelioid sarcoma and in June 2020 for follicular lymphoma, as more fully described herein; whereas, unless otherwise stated or the context indicates otherwise, all references herein to "tazemetostat" refer to tazemetostat in the context of the product candidate for which we are exploring further applications and indications, as more fully described herein.

PART I – FINANCIAL INFORMATION

Item 1. Financial Statements

EPIZYME, INC.
CONDENSED CONSOLIDATED BALANCE SHEETS (UNAUDITED)
(Amounts in thousands, except per share data)

	March 31, 2022	December 31, 2021
ASSETS		
Current assets:		
Cash and cash equivalents	$ 77,421	$ 98,336
Marketable securities	122,309	78,454
Accounts receivable, net	5,902	6,572
Inventory	4,594	3,216
Prepaid expenses and other current assets	18,480	19,465
Total current assets	228,706	206,043
Property and equipment, net	1,295	1,545
Operating lease assets	19,286	20,054
Intangible assets, net	41,811	42,849
Restricted cash and other assets	21,088	18,509
Total assets	$ 312,186	$ 289,000
LIABILITIES AND STOCKHOLDERS' EQUITY (DEFICIT)		
Current liabilities:		
Accounts payable	$ 7,907	$ 10,265
Accrued expenses	26,190	30,777
Current portion of operating lease obligation	4,870	4,154
Total current liabilities	38,967	45,196
Operating lease obligation, net of current portion	17,074	18,497
Deferred revenue	11,950	11,950
Related party long-term debt, net of debt discount	216,670	216,461
Related party liability related to sale of future royalties, net of current portion	15,824	15,654
Warrants to purchase common stock	580	1,930
Commitments and contingencies		
Stockholders' equity:		
Preferred stock, $0.0001 par value; 5,000 shares authorized; 338 shares issued and outstanding (equivalent to 3,378 shares of common stock upon conversion at a 10:1 ratio)	36,127	36,127
Common stock, $0.0001 par value; 225,000 shares and 150,000 shares authorized, respectively; 164,868 shares and 106,098 shares issued and outstanding, respectively	17	11
Additional paid-in capital	1,270,508	1,183,006
Accumulated other comprehensive (loss) income	(191)	3
Accumulated deficit	(1,295,340)	(1,239,835)
Total stockholders' equity	11,121	(20,688)
Total liabilities and stockholders' equity (deficit)	$ 312,186	$ 289,000

See notes to condensed consolidated financial statements.

EPIZYME, INC.
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(UNAUDITED)
(Amounts in thousands, except per share data)

	Three Months Ended March 31,	
	2022	2021
Revenue:		
Product revenue, net	$ 8,656	$ 6,191
Collaboration and other revenue	40	1,440
Total revenue	8,696	7,631
Operating expenses:		
Cost of revenue	2,637	2,853
Research and development	29,781	32,704
Selling, general and administrative	27,204	36,411
Total operating expenses	59,622	71,968
Operating loss	(50,926)	(64,337)
Other (expense) income, net:		
Interest expense, net	(5,480)	(5,476)
Other expense (income), net	(48)	9
Change in fair value of warrants to purchase common stock	1,350	-
Related party non-cash interest expense related to sale of future royalties	(370)	(470)
Other expense, net	(4,548)	(5,937)
Loss before income taxes	(55,474)	(70,274)
Income tax provision	(31)	-
Net loss	$ (55,505)	$ (70,274)
Other comprehensive income (loss):		
Unrealized (loss) gain on available-for-sale securities	(194)	3
Comprehensive loss	$ (55,699)	$ (70,271)
Net loss per share attributable to common stockholders:		
Basic	$ (0.38)	$ (0.69)
Diluted	$ (0.38)	$ (0.69)
Weighted-average common shares outstanding used in net loss per share attributable to common stockholders:		
Basic	144,201	101,790
Diluted	144,201	101,790

See notes to condensed consolidated financial statements.

EPIZYME, INC.
CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS (UNAUDITED)
(Amounts in thousands)

	Three Months Ended March 31,	
	2022	**2021**
CASH FLOWS FROM OPERATING ACTIVITIES:		
Net loss	$ (55,505)	$ (70,274)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	1,298	1,282
Stock-based compensation	5,289	7,015
Amortization of discount on investments	131	363
Amortization of debt discount	208	188
Change in fair value of warrant liability	(1,350)	—
Non-cash royalty revenue associated with the sale of future royalties	(40)	—
Non-cash interest expense associated with the sale of future royalties	370	470
Changes in operating assets and liabilities:		
Accounts receivable	670	(6,659)
Inventory, current and noncurrent	(4,141)	(4,356)
Prepaid expenses and other current assets	1,498	1,028
Accounts payable	(2,566)	(4,816)
Accrued expenses	(4,750)	(4,719)
Deferred revenue	—	5,000
Operating lease assets	767	1,033
Operating lease liabilities	(707)	(1,128)
Other assets and liabilities	(362)	(2)
Net cash used in operating activities	(59,190)	(75,575)
CASH FLOWS FROM INVESTING ACTIVITIES:		
Purchases of available-for-sale securities	(91,978)	(120,589)
Maturities of available-for-sale securities	47,800	100,389
Purchases of property and equipment	(10)	(119)
Net cash used in investing activities	(44,188)	(20,319)
CASH FLOWS FROM FINANCING ACTIVITIES:		
Proceeds from issuance of common stock, net of commissions	82,257	—
Payment of offering costs	(185)	—
Proceeds from stock options exercised	—	199
Proceeds from the issuance of shares under employee stock purchase plan	391	1,191
Net cash provided by financing activities	82,463	1,390
Net decrease in cash, cash equivalents and restricted cash	(20,915)	(94,504)
Cash, cash equivalents and restricted cash, beginning of period	99,845	169,724
Cash, cash equivalents and restricted cash, end of period	$ 78,930	$ 75,220
SUPPLEMENTAL CASH FLOW INFORMATION:		
Interest paid	$ 5,363	$ 5,368
Cash paid for income taxes	$ 31	$ —
Unpaid offering costs	$ 208	$ —
Property and equipment included in accounts payable or accruals	$ —	$ 10

See notes to condensed consolidated financial statements

EPIZYME, INC.
CONDENSED CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
(Amounts in thousands, except share amounts)

	Common Stock		Preferred Stock		Additional Paid-In Capital	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Total Stockholders' Equity
	Shares	Amount	Shares	Amount				
Balance at December 31, 2020	101,627,070	$ 10	337,800	$ 36,127	$ 1,137,470	$ (988,713)	$ 3	$ 184,897
Exercise of stock options and vesting of restricted stock units	188,000	—	—	—	199	—	—	199
Stock-based compensation	—	—	—	—	6,943	—	—	6,943
Issuance of shares under employee stock purchase plan	146,049	—	—	—	1,191	—	—	1,191
Issuance of shares of common stock in lieu of board fees	7,632	—	—	—	72	—	—	72
Unrealized gain on available for sale securities	—	—	—	—	—	—	3	3
Net loss	—	—	—	—	—	(70,274)	—	(70,274)
Balance at March 31, 2021	101,968,751	$ 10	$ 337,800	$ 36,127	$ 1,145,875	$ (1,058,987)	$ 6	$ 123,031
Balance at December 31, 2021	106,097,528	$ 11	337,800	$ 36,127	$ 1,183,006	$ (1,239,835)	$ 3	$ (20,688)
Issuance of common stock (net of commissions and offering costs of $507)	58,139,825	6	—	—	81,822	—	—	81,828
Vesting of restricted stock units	276,761	—	—	—	—	—	—	-
Stock-based compensation	—	—	—	—	5,238	—	—	5,238
Issuance of shares under employee stock purchase plan	308,473				391	—	—	391
Issuance of shares of common stock in lieu of board fees	45,109	—	—	—	51	—	—	51
Unrealized gain on available for sale securities	—	—	—	—	—	—	(194)	(194)
Net loss	—	—	—	—	—	(55,505)	—	(55,505)
Balance at March 31, 2022	164,867,696	17	337,800	36,127	1,270,508	(1,295,340)	(191)	11,121

See notes to condensed consolidated financial statements.

1. The Company

Epizyme, Inc. (collectively referred to with its wholly owned, controlled subsidiary, Epizyme Securities Corporation, as “Epizyme” or the “Company”) is a commercial-stage biopharmaceutical company that is committed to rewriting treatment for people with cancer through the discovery, development, and commercialization of novel epigenetic medicines. The Company aspires to change the standard of care for patients and physicians by developing targeted medicines with fundamentally new mechanisms of action directed at specific causes of hematological malignancies and solid tumors.

Through March 31, 2022, in addition to revenues from product sales, the Company has raised an aggregate of $1,650.2 million to fund its operations. This includes $268.8 million of non-equity funding through its collaboration agreements, $368.1 million of funding, consisting of $150.0 million in equity funding received through agreements with RPI Finance Trust ("RPI"), and $218.1 million in debt financing received through a loan agreement with BioPharma Credit Investments V (Master) LP and BPCR Limited Partnership (as transferee of BioPharma Credit Investments V (Master) LP’s interest as a lender) (the "Lenders"), $937.3 million from the sale of common stock and series A convertible preferred stock (the “Series A Preferred Stock”) in the Company’s public offerings and at-the-market offerings and $76.0 million from the sale of redeemable convertible preferred stock in private financings prior to the Company’s initial public offering in May 2013. As of March 31, 2022, the Company had $199.7 million in cash, cash equivalents and marketable securities.

In 2020, the Company’s EZH2 inhibitor, tazemetostat, was approved in the United States as TAZVERIK for the treatment of epithelioid sarcoma ("ES"), and follicular lymphoma ("FL"). Commercial sales of TAZVERIK for the treatment of ES commenced in the first quarter of 2020 and commercial sales of TAZVERIK for the treatment of FL commenced in the end of the second quarter of 2020.

The Company commenced active operations in early 2008. Since its inception, the Company has generated an accumulated deficit of $1,295.3 million through March 31, 2022 and will require substantial additional capital to fund its research, development, and commercialization efforts. The Company is subject to risks common to companies in the biotechnology industry, including, but not limited to, risks of failure of commercialization, clinical trials and preclinical studies, the need to obtain additional financing to fund the future development and commercialization of tazemetostat and the rest of its pipeline, the need to obtain marketing approval for its product candidates, the need to successfully commercialize and gain market acceptance of TAZVERIK and of any product candidates that may be approved in the future, the impact of the COVID-19 pandemic on the Company’s business, results of operations, and financial condition, dependence on key personnel, protection of proprietary technology, compliance with government regulations, development by competitors of technological innovations and ability to transition from clinical-stage manufacturing to commercial-stage production, marketing, and sale of products.

Operating Cost Reduction

In August 2021, the Company implemented a cross-functional reduction of approximately 11% of its then current workforce under a cost reduction plan. Affected employees were offered separation benefits, including severance payments along with temporary healthcare coverage assistance. The severance and termination-related costs totaled approximately $2.0 million, $1.6 million of which were recorded as selling general and administrative expenses and $0.4 million of which was recorded as research and development expenses in the third quarter of 2021. The Company expects that payments of these costs will be made through August 2022.

In March 2022, the Company implemented further reductions of its expenses, including a pipeline reprioritization. Given the breadth of the Company's then-current tazemetostat clinical development program, the Company decided to discontinued enrollment in its Phase 2 study of tazemetostat in combination with rituximab with FL in the third-line or later treatment settings (SYMPHONY-2, EZH-1401), as well as in its Phase 1/1b basket study evaluating tazemetostat combinations in patients with solid tumors (EZH-1301). The Company has enrolled five patients in the EZH-1401 study and one patient in the EZH-1301 study and plans to continue to follow the patients currently enrolled in each of these two studies. The decision to discontinue these studies was based on evolving market dynamics and a continued focus on optimizing the Company's investments and eliminating potentially overlapping studies. The Company continues to study tazemetostat in combination with other therapies for both hematologic and solid tumor malignancies, both in ongoing Company-sponsored studies as well as investigator-initiated studies. In addition, as part of the cost reduction plan, the Company implemented a cross-functional workforce reduction of approximately 12% of the Company's then-current employees. The severance and termination related costs totaled approximately $2.5 million, $1.7 million of which were recorded as selling general and administrative expenses and $0.8 million of which were recorded as research and development expenses in the first quarter of 2022. The Company expects that payments of these costs will be made through December 2022.

2. Summary of Significant Accounting Policies

Basis of Presentation and Principles of Consolidation

The condensed consolidated financial statements of the Company included herein have been prepared, without audit, pursuant to the rules and regulations of the Securities and Exchange Commission, or the SEC. Certain information and footnote disclosures normally included in financial statements prepared in accordance with accounting principles generally accepted in the United States have been condensed or omitted from this report, as is permitted by such rules and regulations. Accordingly, these condensed consolidated financial statements should be read in conjunction with the financial statements and notes thereto included in the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2021, or the Annual Report.

The unaudited condensed consolidated financial statements include the accounts of Epizyme, Inc. and its wholly owned, controlled subsidiary, Epizyme Securities Corporation. All intercompany transactions and balances of subsidiaries have been eliminated in consolidation. In the opinion of management, the information furnished reflects all adjustments, all of which are of a normal and recurring nature, necessary for a fair presentation of the results for the reported interim periods. The Company considers events or transactions that occur after the balance sheet date but before the condensed consolidated financial statements are issued to provide additional evidence relative to certain estimates or to identify matters that require additional disclosure. The three months ended March 31, 2022 and 2021 are referred to as the first quarter of 2022 and 2021, respectively. The results of operations for interim periods are not necessarily indicative of results to be expected for the full year or any other interim period.

Use of Estimates

The preparation of these condensed consolidated financial statements in accordance with accounting principles generally accepted in the United States requires management to make estimates, judgments and assumptions that affect the reported amounts of assets and liabilities and disclosures of contingent assets and liabilities, as of the date of the condensed consolidated financial statements, and the reported amounts of revenue and expenses during the reporting period. Actual results and outcomes may differ materially from management's estimates, judgments and assumptions.

Significant Accounting Policies

The significant accounting policies used in preparation of these condensed consolidated financial statements for the three months ended March 31, 2022 are consistent with those discussed in Note 2 to the consolidated financial statements in the Annual Report and are updated below as necessary.

Going Concern

At each reporting period, the Company evaluates whether there are conditions or events that raise substantial doubt about the Company's ability to continue as a going concern within one year after the date that the financial statements are issued. The Company is required to make certain additional disclosures if it concludes substantial doubt exists about the Company's ability to continue as a going concern within one year after the date that the financial statements are issued and such doubt is not alleviated by the Company's plans or when the Company's plans alleviate substantial doubt about the Company's ability to continue as a going concern. The Company's evaluation entails analyzing prospective operating budgets and forecasts for expectations of the Company's cash needs, and comparing those needs to its available cash, cash equivalents and marketable securities.

The Company has recurring losses and expects to have recurring losses for the foreseeable future with the continued commercialization of TAZVERIK in ES and FL, the development of tazemetostat in other indications, and the development of the Company's other product candidates. In addition, the Company has experienced and continues to experience challenges in the continued commercialization of TAZVERIK resulting from the ongoing COVID-19 pandemic, which the Company believes has had an adverse impact on TAZVERIK revenues. In response to the challenges that the Company has continued to face since the Company commenced its launch of TAZVERIK in FL in June 2020, the Company implemented an operational cost reduction plan in August 2021, implemented further expense reductions in March 2022, and continues to evaluate its costs on an ongoing basis with the intention to streamline such costs.

The analysis of the Company's ability to continue as a going concern for the first quarter of 2022 included consideration of the Company's current cash needs, including its research and development plans, commercialization activities associated with the continued commercialization of TAZVERIK in the ES and FL indications, its existing debt service obligations, anticipated cost savings resulting from its operational cost reduction plans, including ongoing efforts to eliminate costs not related to the Company's strategic focus. The analysis included forecasted product revenues from sales of TAZVERIK. Such estimates of future sales contain significant judgment as TAZVERIK was first launched in the first half of 2020 and there is little history with which to base such estimates. In addition, the Company's ongoing efforts to eliminate costs not related to the Company's strategic focus contains uncertainties as to whether the Company can attain such benefits. Based on the analysis, the Company concluded that its available cash, cash equivalents and marketable securities as of March 31, 2022 will be sufficient to fund current planned operations and capital expenditure requirements and pay our debt service obligations as they become due into the third quarter of 2023, which is at least 12 months from the filing date of this Quarterly Report on Form 10-Q with the SEC. As a result, the Company concluded that it did not identify conditions or events that raise substantial doubt about the Company's ability to continue as a going concern within one year from the date these financial statements were issued. The Company's current operating plan is based on assumptions that may prove to be wrong, and the Company could use its capital resources sooner than it expects, in which case the Company would evaluate further reductions in its expenses or obtaining additional financing sooner than it otherwise would, which additional financing may not be available or may only be available on terms that are not acceptable to the Company.

Recently Adopted Accounting Pronouncements

In August 2020, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("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) ("ASU 2020-06") to simplify accounting for certain financial instruments. ASU 2020-06 eliminates the current models that require separation of beneficial conversion and cash conversion features from convertible instruments and simplifies the derivative scope exception guidance pertaining to equity classification of contracts in an entity's own equity. The new standard also introduces additional disclosures for convertible debt and freestanding instruments that are indexed to and settled in an entity's own equity. ASU 2020-06 amends the diluted earnings per share guidance, including the requirement to use the if-converted method for all convertible instruments. The Company adopted ASU 2020-06 effective as of January 1, 2022. The adoption of ASU 2020-06 did not have an impact on the Company's financial statements.

Revenue Recognition

The Company recognizes revenue when a customer obtains control of promised goods or services, in an amount that reflects the consideration which the Company expects to receive in exchange for those goods or services. To determine revenue recognition, the Company performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the Company satisfies a performance obligation. The Company only applies the five-step model to contracts when it is probable that the Company will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. For a further discussion of accounting for net product revenue see Note 3, *Product Revenue, Net*.

Other Revenue

Other revenue consists of revenue from the sales of tazemetostat active pharmaceutical ingredient ("API"), drug product to the Company's licensees or collaborators and non-cash royalty revenue related to sale of future royalties. The Company recognizes revenue on tazemetostat API and drug product when control has transferred under the terms of each agreement.

Cost of Revenues

Cost of revenues primarily consists of costs related to the sales of TAZVERIK and sales of tazemetostat API and drug product to the Company's licensees or collaborators. These costs include materials, labor, manufacturing overhead, amortization of milestone payments, and royalties payable on net sales of TAZVERIK. Cost of revenues for the three months ended March 31, 2021 included approximately $0.8 million related to sales of tazemetostat drug product. There were no sales of tazemetostat drug product during the three months ended March 31, 2022.

Accounts Receivable

The Company extends credit to customers based on its evaluation of the customer's financial condition. The Company records receivables for all billings when amounts are due under standard terms. Accounts receivable are stated at amounts due net of applicable prompt pay discounts and other contractual adjustments as well as an allowance for doubtful accounts. The Company assesses the need for an allowance for doubtful accounts by considering a number of factors, including the length of time trade accounts receivable are past due, the customer's ability to pay its obligation and the condition of the general economy and the industry as a whole. The Company will write off accounts receivable when the Company determines that they are uncollectible. In general, the Company has experienced no significant collection issues with its customers.

Inventory

The Company outsources the manufacturing of TAZVERIK and uses contract manufacturers to produce the raw and intermediate materials used in the production of TAZVERIK as well as the finished product. The Company currently has one supplier qualified for each step in the manufacturing process and is in the process of qualifying additional suppliers.

Inventory is composed of raw materials, intermediate materials, which are classified as work-in-process, and finished goods, which are goods that are available for sale. The Company states inventory at the lower of cost or net realizable value with the cost based on the first-in, first-out method. Inventory is classified as long-term when it is expected to be utilized beyond the Company's normal operating cycle and is included in restricted cash and other assets on the Company's condensed consolidated balance sheets. If the Company identifies excess, obsolete or unsalable items, it writes down its inventory to its net realizable value in the period in which the impairment is identified. These adjustments are recorded based upon various factors related to the product, including the level of product manufactured by the Company, the level of product in the distribution channel, current and projected demand, the expected shelf-life of the product and firm inventory purchase commitments. Shipping and handling costs incurred for inventory purchases are included in inventory costs and costs incurred for product shipments are recorded as incurred in cost of revenue.

Intangible Assets, Net

Intangible assets consist of capitalized milestone payments made to third parties under an in-license of patent rights upon receiving regulatory approval of TAZVERIK. The finite-lived intangible assets are being amortized on a straight-line basis over the expected time period the Company will benefit from the in-licensed rights, which is generally the patent life. Intangible assets are recorded at cost at the time of their acquisition and are stated in the Company's condensed consolidated balance sheets net of accumulated amortization and impairments, if applicable. The amortization expense is recognized as cost of revenue in the Company's condensed consolidated statement of operations and comprehensive loss. During 2020 the Company paid a total of $50.0 million in milestone payments under its agreement with Eisai, Co., Ltd. ("Eisai") following regulatory approval of tazemetostat for ES and FL. These regulatory milestones have been capitalized as intangible assets.

The following table presents intangible assets as of March 31, 2022 (in thousands):

	March 31, 2022	Estimated useful life (years)
In-licensed rights	$ 50,000	12.2
Less: accumulated amortization	(8,189)	
Total intangible asset, net	$ 41,811	

The Company recorded approximately $1.0 million in amortization expense related to intangible assets, using the straight-line methodology, during the three months ended March 31, 2022 and March 31, 2021. Estimated future amortization expense for intangible assets for the remainder of the year ended December 31, 2022 is $3.2 million and approximately $4.2 million per year thereafter.

The Company assesses its intangible assets for impairment if indicators are present or changes in circumstance suggest that impairment may exist. Events that could result in an impairment, or trigger an interim impairment assessment, include the receipt of additional clinical or nonclinical data regarding one of the Company's drug candidates or a potentially competitive drug candidate, changes in the clinical development program for a drug candidate, or new information regarding potential sales for the drug. If impairment indicators are present or changes in circumstance suggest that impairment may exist, the Company performs a recoverability test by comparing the sum of the estimated undiscounted cash flows of each intangible asset to its carrying value on the Company's condensed consolidated balance sheets. If the undiscounted cash flows used in the recoverability test are less than the carrying value, the Company would determine the fair value of the intangible asset and recognize an impairment loss if the carrying value of the intangible asset exceeds its fair value.

During the three months ended June 30, 2021, the Company concluded the lower than anticipated current and projected future revenue, due to the impact of the COVID-19 pandemic as well as other factors, was an indicator that impairment may exist related to its finite-lived intangible assets. As a result, the Company performed a recoverability test and determined that the finite-lived intangible assets were recoverable. The Company's quantitative assessment considered significant assumptions related to estimates of future TAZVERIK sales, offset by direct costs to derive the sales. The estimates of future TAZVERIK sales and associated costs include estimates of significant growth, however, these estimates are uncertain as the product was first launched in the first half of 2020 and due to the uncertainties associated with the ongoing COVID-19 pandemic. Given the limited history of sales and the inherent difficulty in making a long-range forecast, such estimates contain significant uncertainty. If the assumptions regarding forecasted revenue or the costs to derive such revenues prove to be inaccurate, the Company may be required to perform future impairment analyses and record an impairment charge for its intangible assets in future periods.

3. Product Revenue, Net

The Company sells TAZVERIK in the United States principally to a limited number of specialty pharmacies, which dispense the product directly to patients, and specialty distributors, which in turn sell the product to hospital pharmacies and community practice pharmacies (collectively, healthcare providers) for the treatment of patients. The specialty pharmacies and specialty distributors are referred to as the Company's customers.

Product revenue is recognized by the Company in an amount that reflects the consideration which the Company expects to receive in exchange for those goods or services when the customer obtains control of the product, which occurs at a point in time, typically when the product is received by the Company's customers. The Company provides a right of return to its customers for unopened product for a limited time before and after its expiration date, which right of return lapses upon shipment to a patient. Healthcare providers to whom specialty distributors sell TAZVERIK hold limited inventory that is designated for patients, and the Company monitors inventory levels in the distribution channel to limit the risk of return.

Reserves for Variable Consideration

Revenues from product sales are recorded as product revenue at the net sales price (transaction price), which includes estimates of variable consideration for which reserves are established and which result from discounts, returns, chargebacks, rebates, co-pay assistance and other allowances that are offered within contracts between the Company and its customers, health care providers, payors and other indirect customers relating to the Company's product sales. These reserves are based on the amounts earned or to be claimed on the related sales and are classified as reductions of accounts receivable (if the amount is payable to the customer) or a current liability (if the amount is payable to a party other than a customer). Where appropriate, these estimates take into consideration a range of possible outcomes that are probability-weighted for relevant factors such as the Company's historical experience, current contractual and statutory requirements, specific known market events and trends, industry data and forecasted customer buying and payment patterns. Overall, these reserves reflect the Company's best estimates of the amount of consideration to which the Company is entitled based on the terms of the contract(s). The amount of variable consideration that is included in the transaction price may be constrained, and is included in the net sales price only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period. Actual amounts of consideration ultimately received may differ from the Company's estimates. If actual results in the future vary from the Company's estimates, the Company will adjust these estimates, which would affect net product revenue and earnings in the period such variances become known.

Trade Discounts and Allowances: The Company generally provides customers with discounts that include incentive fees that are explicitly stated in customer contracts and are recorded as a reduction of revenue in the period the related product revenue is recognized. In addition, the Company receives sales order management, data and distribution services from certain customers. To the extent the services received are distinct from the Company's sale of products to the customer, these payments are classified in selling, general and administrative expenses in the Company's condensed consolidated statements of operations and comprehensive loss.

Product Returns: Consistent with industry practice, the Company generally offers customers a limited right of return based on the product's expiration date for product that has been purchased from the Company, which lapses upon shipment to a patient. The Company estimates the amount of product sales that may be returned by customers and records this estimate as a reduction of revenue in the period in which the related product revenue is recognized. The Company currently estimates product return liabilities using available industry data and the Company's own historical sales information, including its visibility into the product remaining in the distribution channel.

Provider Chargebacks and Discounts: Chargebacks for fees and discounts to healthcare providers represent the estimated obligations resulting from contractual commitments to sell products to qualified healthcare providers at prices lower than the list prices charged to customers who directly purchase the product from the Company. Customers charge the Company for the difference between what they pay for the product and the ultimate selling price to the qualified healthcare providers. These reserves are established in the same period that the related revenue is recognized, resulting in a reduction of product revenue and accounts receivable. Chargeback amounts are generally determined at the time of resale to the qualified healthcare provider by customers, and the Company generally issues credits for such amounts within a few weeks of the customer's notification to the Company of the resale. Reserves for chargebacks consist of credits that the Company expects to issue for units that remain in the distribution channel at each reporting period end that the Company expects will be sold to qualified healthcare providers, and chargebacks that customers have claimed but for which the Company has not yet issued a credit.

Government Rebates: The Company is subject to discount obligations under state Medicaid programs and Medicare. The Company estimates its Medicaid and Medicare rebates based upon a range of possible outcomes that are probability-weighted for the estimated payor mix. These reserves are recorded in the same period in which the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability that is included in accrued expenses on the Company's condensed consolidated balance sheets. For Medicare, the Company also estimates the number of patients in the prescription drug coverage gap for whom the Company will owe an additional liability under the Medicare Part D program. The Company's liability for these rebates consists of invoices received for claims from prior quarters that have not been paid or for which an invoice has not yet been received, estimates of claims for the current quarter, and estimated future claims that will be made for product that has been recognized as revenue, but remains in the distribution channel inventories at period end.

Payor Rebates: The Company may contract with various private payor organizations, primarily insurance companies and pharmacy benefit managers, for the payment of rebates with respect to utilization of the Company's products. The Company estimates these rebates and records such estimates in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability.

Other Incentives/Patient Assistance Programs: The Company also offers voluntary patient assistance programs such as co-pay assistance. Co-pay assistance programs are intended to provide financial assistance to qualified commercially insured patients with prescription drug co-payments required by payors. The calculation of the accrual for co-pay assistance is based on an estimate of claims and the cost per claim that the Company expects to receive associated with product that has been recognized as revenue, but remains in the distribution channel inventories at period end.

The following table summarizes activity in each of the above product revenue allowances and reserve categories for the three months ended March 31, 2022:

	Chargebacks, Discounts, and Fees	Government and Other Rebates	Returns	Total
	(In thousands)			
Balance, January 1, 2022	$ 244	$ 586	$ 109	$ 939
Provision	558	1,245	(5)	1,798
Payments or credits	(530)	(1,062)	—	(1,592)
Balance, March 31, 2022	$ 272	$ 769	$ 104	$ 1,145

Concentration of Credit Risk

Financial instruments which potentially subject the Company to concentrations of credit risk consist of accounts receivable from customers and cash held at financial institutions. The Company believes that such customers and financial institutions are of high credit quality.

For the three months ended March 31, 2022 and 2021, net product revenue was primarily generated from four individual customers. Revenue earned from each customer as a percentage of net product revenue is as follows:

	Three Months Ended March 31,	
	2022	2021
Customer 1	45%	42%
Customer 2	11%	14%
Customer 3	21%	25%
Customer 4	18%	19%

As of March 31, 2022 and December 31, 2021, the five individual customers represented as a percentage of accounts receivable as follows:

	March 31, 2022	December 31, 2021
Customer 1	25%	15%
Customer 2	16%	10%
Customer 3	28%	22%
Customer 4	22%	29%
Customer 5	9%	24%

No other customer represented more than 10 percent of net product revenue or accounts receivable.

4. Cash

A reconciliation of cash, cash equivalents, and restricted cash reported within the Company's condensed consolidated balance sheets that sum to the total of the same such amounts shown in the Company's condensed consolidated statements of cash flows, is as follows:

	As of March 31,	
	2022	2021
	(In thousands)	
Cash and cash equivalents	$ 77,421	$ 73,711
Restricted cash, as part of other assets	1,509	1,509
Total cash, cash equivalents, and restricted cash shown in the condensed consolidated statements of cash flows	$ 78,930	$ 75,220

The $1.5 million in restricted cash as of both March 31, 2022 and 2021 is comprised of $0.5 million in a letter of credit as a security deposit for the Company’s office and laboratory lease at Technology Square in Cambridge, Massachusetts and $1.0 million in a letter of credit as a security deposit for the Company’s office lease at Hampshire Street in Cambridge, Massachusetts. The Company has recorded cash held to secure these letters of credit as restricted cash in restricted cash and other assets on its condensed consolidated balance sheets. The restricted cash is classified as non-current based on the related lease terms.

5. Marketable Securities

The following table summarizes the available-for-sale securities held at March 31, 2022 (in thousands):

Description	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Commercial paper	$ 46,621	$ —	$ (30)	$ 46,591
U.S. government agency securities and U.S. Treasuries	75,877	—	(159)	75,718
Total	$ 122,498	$ —	$ (189)	$ 122,309

The following table summarizes the available-for-sale securities held at December 31, 2021 (in thousands):

Description	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Commercial paper	$ 68,427	$ 7	$ (3)	$ 68,431
U.S. government agency securities and U.S. Treasuries	10,025	—	(1)	10,024
Total	$ 78,452	$ 7	$ (4)	$ 78,455

Certain short-term debt securities with original maturities of less than 90 days are included in cash and cash equivalents within the Company's condensed consolidated balance sheets and are not included in the tables above.

The amortized cost of available-for-sale securities is adjusted for amortization of premiums and accretion of discounts to maturity. At March 31, 2022, the balance in the Company's accumulated other comprehensive loss was composed solely of activity related to the Company's available-for-sale marketable securities. There were no realized gains or losses recognized on the sale or maturity of available-for-sale securities during the three months ended March 31, 2022, and as a result, the Company did not reclassify any amounts out of accumulated other comprehensive loss for the same period.

The aggregate fair value of available-for-sale securities held by the Company in an unrealized loss position for less than twelve months as of March 31, 2022 was $119.3 million, which consisted of 12 commercial paper securities and 18 United States Treasury securities. The aggregate unrealized loss for those securities in an unrealized loss position for less than twelve months as of March 31, 2022 was less than $0.2 million.

The Company does not intend to sell and it is unlikely that the Company will be required to sell the above investments before recovery of their amortized cost bases, which may be maturity. The Company has determined that there has been no material change in the credit risk of any of its investments. As a result, the Company determined it did not hold any investments that were impaired as of March 31, 2022. The Company reviews its portfolio of available-for-sale debt securities, using both quantitative and qualitative factors, to determine if declines in fair value below cost have resulted from a credit-related loss or other factors. If the decline in fair value is due to credit-related factors, a loss is recognized in net income, whereas if the decline in fair value is not due to credit-related factors, the loss is recorded in other comprehensive income (loss). The weighted-average maturity of the Company's portfolio was approximately five months at March 31, 2022.

6. Fair Value Measurements

The Company's financial instruments as of March 31, 2022 and December 31, 2021 consisted primarily of cash and cash equivalents, marketable securities and accounts receivable and accounts payable. As of March 31, 2022 and December 31, 2021, the Company's financial assets recognized at fair value consisted of the following:

	Fair Value as of March 31, 2022			
	Total	Level 1	Level 2	Level 3
	(In thousands)			
Cash equivalents	$ 67,329	$ 32,611	$ 34,718	$ —
Marketable securities:				
Commercial paper	46,591	—	46,591	—
U.S. government agency securities and treasuries	75,718	—	75,718	—
Total	$ 189,638	$ 32,611	$ 157,027	$ —

	Fair Value as of December 31, 2021			
	Total	Level 1	Level 2	Level 3
	(In thousands)			
Cash equivalents	$ 88,637	$ 67,209	$ 21,428	$ —
Marketable securities:				
Commercial paper	68,431	—	68,431	—
U.S. government agency securities and treasuries	10,024	—	10,024	—
Total	$ 167,092	$ 67,209	$ 99,883	$ —

Cash equivalents and marketable securities have been initially valued at the transaction price and subsequently valued, at the end of each reporting period, utilizing third-party pricing services or other market observable data.

The Company measures its cash equivalents at fair value on a recurring basis, which approximates the net asset value per share. The Company classifies some of its cash equivalents within Level 1 of the fair value hierarchy because they are valued using observable inputs that reflect quoted prices for identical assets in active markets. The Company measures its marketable securities at fair value on a recurring basis and classifies those instruments and some cash equivalents within Level 2 of the fair value hierarchy. The pricing services used by management utilize industry standard valuation models, including both income- and market- based approaches and observable market inputs to determine the fair value of marketable securities and those cash equivalents classified within Level 2 of the fair value hierarchy.

7. Inventory

All of the Company's inventory relates to the manufacturing of TAZVERIK. The following table sets forth the Company's inventory as of March 31, 2022 and December 31, 2021:

	March 31, 2022	December 31, 2021
	(In thousands)	
Raw materials	$ 2,059	$ 3,227
Work in process	19,402	13,748
Finished goods	1,362	1,710
Total	$ 22,823	$ 18,685
Balance sheet classification		
Inventory	$ 4,594	$ 3,216
Restricted cash and other assets	18,229	15,469
Total	$ 22,823	$ 18,685

The Company's active pharmaceutical ingredient has a long shelf life and the Company's finished drug product has a three-year expiry, however the realizability of the inventory is subject to forecasted future sales of TAZVERIK. The Company's forecasted sales currently support the realizability of the Company's inventory but are uncertain and could change in the future, which would require the Company to write down the value of such inventory.

As of March 31, 2022 the Company has not capitalized inventory costs related to its other drug development programs.

8. Supplemental Balance Sheet Information

Accrued expenses consisted of the following:

	March 31, 2022	December 31, 2021
	(In thousands)	
Employee compensation and benefits	$ 7,750	$ 11,737
Research and development expenses	12,975	13,744
Current portion of liability related to the sale of future royalties	433	273
Professional services and other	5,032	5,023
Accrued expenses	$ 26,190	$ 30,777

9. Income Taxes

The Company recorded less than $0.1 million of federal or state income tax provision for the three months ended March 31, 2022 due to the expected and known loss before income taxes to be incurred, or incurred, as applicable, for the year ended December 31, 2022, as well as the Company's continued maintenance of a full valuation allowance against its net deferred tax assets. The Company did not record a federal or state income tax provision or benefit for the three months ended March 31, 2021 due to the expected and known loss before income taxes to be incurred, or incurred, as applicable, for the year ended December 31, 2021, as well as the Company's continued maintenance of a full valuation allowance against its net deferred tax assets.

10. Commitments and Contingencies

There have been no significant changes to the Company's commitments and contingencies, other than the minimum lease payments as disclosed in Note 11, *Leases*, in the three months ended March 31, 2022, as compared to those disclosed in Note 9, *Commitments and Contingencies*, included in the Annual Report.

11. Leases

The Company enters into lease arrangements for its facilities as well as certain equipment. A summary of the arrangements is as follows:

Operating Leases

The Company leases office and laboratory space at Technology Square in Cambridge, Massachusetts under a Lease Agreement, dated as of June 15, 2012, as amended (the "Technology Square Lease") with ARE-TECH Square, LLC, a Delaware limited liability company.

In May 2017, the Company exercised its option to extend the term of the Technology Square Lease to November 30, 2022. Under the Technology Square Lease as amended, the Company agreed to pay a monthly base rent of approximately $0.2 million for the period commencing December 1, 2017 through May 31, 2018, with an increase on June 1, 2018 of approximately $33,000 and annual increases of approximately $9,000 on December 1 of each subsequent year until the last increase, which will occur on December 1, 2021.

On August 11, 2021, the Company, entered into a fifth amendment to the Technology Square Lease (the "Fifth Amendment") with ARE-TECH Square, LLC. Under the Fifth Amendment, the Company extended the term of the Technology Square Lease through November 30, 2024. Under the Fifth Amendment, the Company will continue to pay the landlord the current monthly base rent amount contemplated by the Technology Square Lease through November 30, 2022, with an increase commencing on December 1, 2022 and adjusting the monthly base rent amount to approximately $377,000 and an increase commencing on December 1, 2023 and adjusting the monthly base rent amount to approximately $388,000 through November 30, 2024. In addition, under the Fifth Amendment, the landlord agreed to provide the Company with a tenant improvement allowance of up to approximately $430,000 if requested by the Company by August 11, 2022, subject to specified terms and conditions. In accordance with ASU 2016-02, Leases, or ASC 842, the Company accounted for the Fifth Amendment as a lease modification and remeasured the operating lease liability, resulting in an additional $7.0 million operating lease liability and right of use asset. Under the current terms of the Technology Square Lease, the Company does not have any further right to extend the term beyond November 30, 2024.

The Company has a $0.5 million letter of credit as a security deposit for the Technology Square Lease and has recorded cash held to secure this letter of credit as restricted cash and other assets on the Company's condensed consolidated balance sheets.

On August 16, 2019, the Company entered into a lease (the "Hampshire Street Lease") with BMR-Hampshire LLC ("BMR"). The Hampshire Street Lease is for 33,525 rentable square feet of office space in Cambridge, Massachusetts. The Hampshire Street Lease commenced as of December 1, 2019. The Hampshire Street Lease has an initial term of seven years and four months from the commencement date and provides the Company with an option to extend the lease term for one additional five-year period. After a four-month period during which base rent was not payable, the Hampshire Street Lease provides for monthly rent payments starting at approximately $0.2 million and increasing 2.5% per year. In the event that the Company exercises its option to extend the lease term, the Hampshire Street Lease provides for monthly rent payments during the additional five-year period at the greater of the base rent rate at the end of the initial term or the then-current market rent.

The Company has a $1.0 million letter of credit in favor of BMR as a security deposit for the Hampshire Street Lease and has recorded cash held to secure this letter of credit as restricted cash and other assets on the Company's condensed consolidated balance sheets. In applying ASC 842, the Company determined the classification of the Hampshire Street Lease to be operating and recorded a lease liability and a right-of-use asset as of December 31, 2019.

The Company is required to pay certain variable costs to its landlords in addition to fixed rent. These costs include common area maintenance, real estate taxes, and parking and are included in lease expense.

The following table contains a summary of the lease costs recognized under ASC 842 and other information pertaining to the Company's operating leases for the three months ended March 31, 2022 and 2021:

	Three Months Ended March 31,	
	2022	2021
	(in thousands)	
Lease cost		
Operating lease cost	$ 1,689	$ 1,515
Variable lease cost	491	480
Total lease cost	$ 2,180	$ 1,995
Other information		
Operating cash flows used for operating leases	$ 1,627	$ 1,605
Weighted average remaining lease term	3.9 years	4.7 years
Weighted average discount rate	9.74%	9.81%

Future minimum lease payments under the Company's non-cancelable operating leases as of March 31, 2022, are as follows:

	(In thousands)
2022	$ 4,950
2023	7,517
2024	7,322
2025	3,057
Thereafter	3,909
Total lease payments	$ 26,755
Less: imputed interest	(4,811)
Total operating lease liabilities at March 31, 2022	$ 21,944

12. Collaborations and Licensing Agreements

HutchMed

On August 7, 2021 (the "HutchMed Effective Date"), the Company entered into a strategic collaboration pursuant to a license agreement (the "HutchMed License Agreement") with Hutchmed Group Investment Limited (formerly known as Hutchison China MediTech Investment Limited) ("HutchMed") for the development, manufacture and commercialization of tazemetostat, either as a monotherapy or as a part of combinations with other therapies, including HutchMed proprietary compounds, agreed by the parties under the HutchMed License Agreement ("Licensed Products") for the treatment of ES, FL, diffuse large B-cell lymphoma in humans, and any additional indications agreed by the parties in accordance with the terms of the HutchMed License Agreement (the "Field") in mainland China, Taiwan, Hong Kong and Macau (each, a "Jurisdiction", and collectively, the "Territory").

Agreement Structure

The Company has granted HutchMed licenses under patent rights and know-how controlled by the Company to enable HutchMed to develop and commercialize Licensed Products in the Field in the Territory. The licenses granted to HutchMed are co-exclusive with the Company with respect to the development of Licensed Products in the Field in the Territory and exclusive with respect to the commercialization of Licensed Products in the Field in the Territory. The Company also granted HutchMed a license under patent rights and know-how controlled by the Company to enable HutchMed to manufacture tazemetostat drug substance and drug product for the purpose of developing and commercializing Licensed Products in the Field in the Territory. The Company retains development and commercialization rights with respect to Licensed Products in the rest of the world outside of the Territory except for Japan.

On May 6, 2022, as contemplated by the HutchMed License Agreement, the Company, Hutchmed Limited (formerly known as Hutchison MediPharma Limited) and Hutchmed (Hong Kong) Limited entered into a manufacturing technology transfer and supply agreement under which the Company has agreed to conduct a technology transfer of manufacturing technology to HutchMed to enable HutchMed to manufacture clinical and commercial quantities of tazemetostat drug substance and drug product to carry out its obligations and exercise its rights under the HutchMed License Agreement. Until the completion of the technology transfer to

HutchMed, the Company has agreed to manufacture and supply HutchMed with tazemetostat drug substance and drug product in sufficient quantities for HutchMed's development and commercialization activities for Licensed Products in the Field in the Territory.

HutchMed has agreed to use commercially reasonable efforts to carry out development activities in the Territory as agreed by the parties and to seek to obtain and maintain regulatory approval of the Licensed Products in the Territory. HutchMed agreed to use commercially reasonable efforts to commercialize Licensed Products in the Field in the Territory. HutchMed is responsible for all costs it incurs in developing, obtaining regulatory approval of, and commercializing Licensed Products in the Field in the Territory, including costs incurred by HutchMed in conducting clinical trials that only include clinical sites in the Territory. For global studies conducted by the Company that HutchMed elects to participate in by conducting any such study in the Territory, HutchMed will be responsible for enrolling and treating in the Territory 20% of the total number of study patients of such global study and will be responsible for costs for those patients enrolled and treated in such trials. HutchMed will also be responsible for 20% of the costs of such global studies that are not specific to any territory and the Company will be responsible for all other costs of such global studies. HutchMed has agreed to participate in the Company's EZH-301 and SYMPHONY-1 (EZH-302) global studies. Under an amendment to the HutchMed License Agreement executed by the parties on May 6, 2022, HutchMed has responsibility for the SYMPHONY-1 trial in the Territory at HutchMed's expense, except the Company is responsible for regulatory interactions and filings in mainland China and for the conduct of the SYMPHONY-1 trial in Taiwan, in each case subject to HutchMed's reimbursement of the Company's expenses commencing as of the HutchMed Effective Date, and Epizyme has oversight of the conduct of the SYMPHONY-1 trial to ensure consistency with the conduct of the trial globally.

Pursuant to the HutchMed License Agreement, the Company received a nonrefundable upfront payment of $25.0 million in September 2021. The Company is also entitled to milestone payments of up to $110.0 million in the aggregate for achievement of specified development and regulatory milestones with respect to Licensed Products in the Territory, and up to $175.0 million in the aggregate for achievement of specified sales milestones in the Territory with respect to the Licensed Products. The Company will also be entitled to receive tiered royalties, ranging from a mid-teens percentage to a low twenties percentage based on HutchMed's cumulative annual net sales, if any, of Licensed Products in the Territory. Royalties are payable for each Licensed Product commencing on the first commercial sale of the applicable Licensed Product and ending, on a Jurisdiction-by-Jurisdiction basis, on the latest of expiration of specified patent coverage, expiration of specified regulatory exclusivity or a specified period following the first commercial sale in such Jurisdiction and may be reduced in various circumstances.

Under the HutchMed License Agreement, the Company issued a warrant to HutchMed (the "HutchMed Warrant") , exercisable at any time prior to August 7, 2025 for up to 5,653,000 shares of the Company's common stock at an exercise price of $11.50 per share. On September 21, 2021 the Company filed with the SEC a registration statement on Form S-3 registering for resale the shares of the Company's common stock issuable upon exercise of the HutchMed Warrant in accordance with the HutchMed Warrant. Such registration statement on Form S-3 was declared effective by the SEC on September 29, 2021.

Unless earlier terminated, the HutchMed License Agreement will expire upon the expiration of the last royalty term for the last Licensed Product in the Field in the Territory. HutchMed may terminate the HutchMed License Agreement in its entirety for any or no reason upon 12 months' prior written notice to the Company. Either party may, subject to specified cure periods, terminate the HutchMed License Agreement in the event of the other party's uncured material breach, and under specified circumstances relating to the other party's insolvency or if the other party or its affiliates challenges the validity, patentability, or enforceability of patent rights that are owned by or licensed to such party or its affiliates and that are subject to the licenses granted in the HutchMed License Agreement.

License Revenue

The Company evaluated the terms of the HutchMed License Agreement and first determined that the HutchMed Warrant should be accounted for pursuant to ASC 815, Derivatives and Hedging, with the HutchMed Warrant's fair value of approximately $13.0 million (Note 15) at execution considered outside of the revenue arrangement.

The Company identified the following performance obligations at the inception of the HutchMed License Agreement: (1) exclusive license with rights to develop, manufacture and commercialize tazemetostat in the Territory, (2) research and development services related to global trials, and (3) a material right related to the Company's obligation to provide clinical supply of tazemetostat. In addition, the Company may also provide certain technology transfer services related to providing HutchMed with the capability to manufacture tazemetostat, for which the Company will receive reimbursement that approximates stand-alone selling price.

The Company evaluated the HutchMed License Agreement under ASC 606, *Revenue from Contracts with Customers*. Based on that evaluation, the $12.0 million of the up-front fee remaining after allocation to the HutchMed Warrant and the reimbursement to be received for its research and development services constituted the amount of the consideration to be included in the transaction price. Prior to the May 6, 2022 amendment to the HutchMed License Agreement, had the EZH-302 global trial not been deemed a confirmatory trial for purposes of regulatory approval in China, the Company would be responsible for reimbursing HutchMed for the costs of the portion of the EZH-302 global trial that would be performed in China. The Company had concluded that this potential repayment provision represented variable consideration under the arrangement. Due to the uncertainty of potential repayment, which was based solely on the decision of a regulatory authority, the Company could not assert that it was probable that a significant reversal of revenue would not occur. As a result, the Company determined that the transaction price should be fully constrained. Under the May 6, 2022 amendment to the HutchMed License Agreement, this potential repayment provision was removed. The Company will evaluate the amendment and the application of the constraint in the second quarter of 2022 and determine if the contingency has been resolved and whether the full upfront fee (or any portion thereof) and any reimbursement of research and development services will be included in the transaction price.

None of the development or regulatory milestones have been included in the transaction price, as all such milestone amounts were fully constrained. As part of the Company's evaluation of the constraint, the Company considered numerous factors, including that receipt of the milestones is outside the control of the Company and contingent upon success in future clinical trials and the licensee's efforts. Any consideration related to sales-based milestones (including royalties) will be recognized when the related sales occur as these amounts have been determined to relate predominantly to the license granted to HutchMed and therefore are recognized at the later of when the performance obligation is satisfied or the related sales occur.

The Company delivered the license during the third quarter of 2021 and expects that based on the estimated standalone selling price of the license, that the majority of the consideration in the arrangement will be allocated to the license performance obligation, once such consideration is no longer constrained. As the Company performs research and development services, it will recognize revenue as such services are performed, upon the transaction price no longer being fully constrained.

GSK

In January 2011, the Company entered into a collaboration and license agreement (the "GSK Collaboration and License Agreement") with Glaxo Group Limited (an affiliate of GlaxoSmithKline plc) ("GSK"), to discover, develop and commercialize novel small molecule HMT inhibitors directed to available targets from the Company's platform. Under the terms of the agreement, the Company granted GSK exclusive worldwide license rights to HMT inhibitors directed to three targets. In March 2014, the Company and GSK amended certain terms of this agreement for the third licensed target, revising the license terms with respect to candidate compounds and amending the corresponding financial terms, including reallocating milestone payments and increasing royalty rates as to the third target. Subsequent to a GSK strategic portfolio prioritization, the Company received notice in October 2017 that GSK terminated the agreement with respect to the third target, effective December 31, 2017, which returned all rights to that target to the Company. On December 16, 2021, the Company received written notice from GSK that GSK elected to terminate the GSK Collaboration and License Agreement without cause, and in accordance with the terms of the agreement and the notice of termination, the termination became effective as of March 16, 2022. As a result of the termination of the agreement, as of the termination effective date, the license rights granted by the Company to GSK terminated, and GSK ceased to accrue any financial obligations to the Company and the Company is entitled to pursue PRMT5 and PRMT1 targets in all fields worldwide without further obligation to GSK. The Company substantially completed all of its obligations under this agreement by the end of 2015. The termination of the agreement had no impact on the Company's financial statements.

Eisai

In April 2011, the Company entered into a collaboration and license agreement with Eisai, under which the Company granted Eisai an exclusive worldwide license to its small molecule HMT inhibitors directed to the EZH2 HMT, including the Company's product candidate tazemetostat, while retaining an opt-in right to co-develop, co-commercialize and share profits with Eisai as to licensed products in the United States. In March 2015, the Company entered into an amended and restated collaboration and license agreement with Eisai (the "Eisai License Agreement"), under which the Company reacquired worldwide rights, excluding Japan, to its EZH2 program, including tazemetostat. Under the Eisai License Agreement, the Company is responsible for global development, manufacturing and commercialization outside of Japan of tazemetostat and any other EZH2 product candidates, with Eisai retaining development and commercialization rights in Japan, as well as a right to elect to manufacture tazemetostat and any other EZH2 product candidates in Japan, and a right of first negotiation for the rest of Asia. Eisai waived its right of first negotiation for the rest of Asia in 2018.

In March 2021, the Company and Eisai entered into a supply agreement providing for the manufacture and supply to Eisai of tazemetostat drug product. Under the terms of the supply agreement, the Company also agreed to waive its right of exclusive supply of tazemetostat drug substance from the Company's drug substance manufacturer. During the three months ended March 31, 2021, the Company recognized $1.3 million related to the delivery of tazemetostat drug product in collaboration and other revenue. The Company deferred $5.0 million of revenue allocated to the Company's waiver of its exclusive right to supply of tazemetostat drug substance as of March 31, 2021, which was recognized in April 2021 upon delivery of the Company's waiver to the drug substance manufacture. No such revenue was recognized in the three months ended March 31, 2022.

During the three months ended March 31, 2021, Eisai purchased $0.4 million, of drug product from the Company at cost to facilitate development within Japan under the Eisai License Agreement which was recognized as a reduction to research and development expense.

As of March 31, 2022 and December 31, 2021, the Company had accounts receivable of less than $0.1 million for both periods, due from Eisai.

During the three months ended March 31, 2022 and 2021, the Company recorded $1.3 million and $0.9 million, respectively, related to the worldwide royalties due under the Eisai License Agreement in cost of revenue based on U.S. sales of TAZVERIK. As of March 31, 2022 and 2021, $1.3 million and $0.9 million, respectively, in royalties were payable under the Eisai License Agreement. For additional information regarding certain of the Eisai royalties, see Note 13, *Sale of Future Royalties*.

Roche

In December 2012, Eisai and the Company entered into a companion diagnostics agreement with Roche Molecular, under which Eisai and the Company engaged Roche Molecular to develop a companion diagnostic to identify patients who possess certain activating mutations of EZH2. In October 2013, this agreement was amended to include additional mutations in EZH2. The development costs due under the amended agreement with Roche Molecular were the responsibility of Eisai until the execution of the amended and restated collaboration and license agreement with Eisai in March 2015, at which time the Company assumed responsibility for the remaining development costs due under the agreement. In December 2015, the Company and Eisai entered into a second amendment to the companion diagnostics agreement with Roche Molecular. The agreement was further amended in March 2018. Under the amended agreement, the Company was responsible for remaining development costs of $10.4 million due under the agreement as of March 2018 and Eisai agreed to reimburse the Company $0.9 million of this amount related to a regulatory milestone for Japan. In July 2019, the Company entered into a fourth amendment to the companion diagnostics agreement. Under the amended agreement, the Company and Roche Molecular agreed to divide a $1.0 million regulatory milestone for the United States into two separate milestone payments, of which $0.5 million was paid by the Company as part of the signed amendment, and the remaining $0.5 million was paid by the Company in December 2019 upon the satisfaction of certain conditions set forth in the fourth amendment to the companion diagnostics agreement. As part of this fourth amendment, Roche Molecular also assigned all of its rights and obligations under the companion diagnostics agreement to Roche Sequencing due to a reorganization at the Roche group, and this assignment became effective as of January 1, 2020. As of March 31, 2022, the Company is responsible for the remaining development costs of $1.0 million due under the agreement. The $0.9 million that Eisai agreed to reimburse the Company related to a regulatory milestone for Japan was achieved as of June 30, 2020 and the payment was received in the fourth quarter of 2020. In addition, the Company paid $1.0 million for the achievement of a development milestone in the fourth quarter of 2020.

Under the agreement with Roche Sequencing, Roche Sequencing is obligated to use commercially reasonable efforts to develop and to make commercially available the companion diagnostic. Roche Sequencing has exclusive rights to commercialize the companion diagnostic. On June 18, 2020 the FDA approved the companion diagnostic that is intended to identify FL patients with an EZH2 mutation for treatment with tazemetostat.

The agreement with Roche Sequencing will expire when the Company and Eisai are no longer developing or commercializing tazemetostat. The Company and Eisai may terminate the agreement by giving Roche Sequencing 90 days' written notice if the Company and Eisai discontinue development and commercialization of tazemetostat or determine, in conjunction with Roche Sequencing, that the companion diagnostic is not needed for use with tazemetostat. Any party may also terminate the agreement in the event of a material breach by any party, in the event of material changes in circumstances that are contrary to key assumptions specified in the agreement or in the event of specified bankruptcy or similar circumstances. Under specified termination circumstances, Roche Sequencing may become entitled to specified termination fees.

13. Sale of Future Royalties

On November 4, 2019, the Company entered into a loan agreement with BioPharma Credit PLC (the "Collateral Agent"), and the Lenders, providing for up to $70.0 million in secured term loans to be advanced in up to three tranches (the "Loan Agreement"). As of June 30, 2020, the Company had borrowed an aggregate principal amount under the first tranche of $25.0 million (the "Tranche A Note Payable"), the second tranche of $25.0 million (the "Tranche B Note Payable"), and the third tranche of $20.0 million (the "Tranche C Note Payable") under the Loan Agreement. On November 3, 2020, the Company, the Collateral Agent and the Lenders amended and restated the Loan Agreement, (as amended and restated, the "Amended and Restated Loan Agreement"), to provide for, among other things, an additional secured term loan of $150.0 million, or the Tranche D Loan. On November 18, 2020, the Company borrowed the Tranche D Loan (see Note 14, *Long-Term Debt*). The Company paid a commitment fee of 2.00% of the original $70.0 million committed facility amount in November 2019 and 2% of the $150.0 million Tranche D Loan in November 2020, as well as expenses incurred by the Lender in executing the agreements. The interest rate for the Tranche D Loan will be determined by reference to a Eurodollar rate plus 7.75% above such Eurodollar rate. The Eurodollar rate will have a 2.00% floor. The Tranche D Loan will be due in eight equal quarterly principal payments commencing on the 51st month anniversary of the date on which the Lenders fund the Tranche D Loan. All unpaid principal and interest under the Tranche D Loan will be due and payable on the 72nd month anniversary of the date on which the Lenders funded the Tranche D Loan.

On November 4, 2019, the Company also executed a purchase agreement (the "RPI Purchase Agreement") with RPI. Pursuant to the RPI Purchase Agreement, the Company agreed to sell to RPI 6,666,667 shares of its common stock, a warrant to purchase up to 2,500,000 shares of common stock at an exercise price of $20.00 per share (the "Common Stock Warrant"), and all of the Company's rights to receive royalties from Eisai with respect to net sales by Eisai of tazemetostat products in Japan pursuant to the Eisai License Agreement and any successor arrangement for Japan sales (the "Japan Royalty", and collectively, the "Transaction"). In consideration for the sale of shares of common stock, the Common Stock Warrant and the Japan Royalty, RPI paid the Company $100.0 million upon the closing of the RPI Purchase Agreement. In addition, RPI agreed, in connection with RPI's acquisition from Eisai of the right to receive royalties from the Company under the Eisai License Agreement, to reduce the Company's royalty obligation by low single digits upon the achievement of specified annual net sales levels over $1.5 billion. In addition, under the RPI Purchase Agreement, the Company had the right to sell, and RPI had the obligation to purchase, subject to certain conditions, including a maximum purchase price of $20.00 per share, $50.0 million of shares of common stock at the Company's option for an 18-month period from the date of execution of the RPI Purchase Agreement (the "Put Option"). In February 2020, the Company sold 2.5 million shares of its common stock to RPI, for an aggregate of $50.0 million in proceeds pursuant to the Put Option. Additionally, under the terms of the RPI Purchase Agreement, the founder and chief executive officer of RP Management, an affiliate of RPI, and a co-founder of Pharmakon Advisors LP, an affiliate of the Lenders, was elected as a director of the Company. As of March 31, 2022 and December 31, 2021, RPI and its affiliates owned approximately 19.3% and 8.6% of the Company's common stock, respectively.

The Company accounted for the Loan Agreement and RPI Purchase Agreement as a single arrangement as RPI and the Lenders are related parties and the agreements were negotiated together. The aggregate proceeds of $125.0 million were allocated on a relative fair value basis, which approximated their respective actual fair values, to the four units of accounting pursuant to the transaction as follows: (1) $79.0 million to the common stock issued to RPI based on the closing price of the Company's common stock on the date of the transaction, (2) $8.4 million to the Common Stock Warrant to purchase shares of common stock, based on the Black-Scholes option pricing model, (3) $12.6 million to the liability related to the sale of future royalties based on a discounted cash flow model and (4) $25.0 million to the Tranche A Note Payable based on the terms of the Loan Agreement. Transaction costs of $2.0 million were allocated directly to the units of accounting it relates to.

Although the Company sold all of its rights to receive the Japan Royalty, under the terms of the RPI Agreement, the Company continues to own all tazemetostat intellectual property rights and at execution had significant continuing involvement in the generation of these royalties. Due to the Company's continuing involvement, the Company will continue to account for any royalties due as revenue and recorded the proceeds from this transaction as a liability ("Royalty Obligation") that will be accreted using the effective interest method over the estimated life of the RPI Purchase Agreement.

As royalties are remitted to RPI from Eisai, the balance of the Royalty Obligation will be effectively repaid over the life of the Eisai License Agreement. In order to determine the accretion of the Royalty Obligation, the Company is required to estimate the total amount of future royalty payments to RPI over the life of the Eisai License Agreement. The $12.6 million recorded at execution will be accreted to the total of these royalty payments as interest expense over the life of the Royalty Obligation. At execution, the Company's estimate of this total interest expense resulted in an effective annual interest rate of approximately 9.01%. This estimate contains significant assumptions that impact both the amount recorded at execution and the interest expense that will be recognized over the royalty period. The Company periodically assesses the estimated royalty payments to RPI from Eisai and to the extent the amount or timing of such payments is materially different than the original estimates, an adjustment is made to the effective interest

rate, which will be recorded prospectively to increase or decrease interest expense. There are a number of factors that could materially affect the amount and timing of royalty payments to RPI from Eisai, and correspondingly, the amount of interest expense recorded by the Company, most of which are not within the Company's control. Such factors include, but are not limited to, delays or discontinuation of development of tazemetostat in Japan, regulatory approval, changing standards of care, the introduction of competing products, manufacturing or other delays, generic competition, intellectual property matters, adverse events that result in governmental health authority imposed restrictions on the use of the drug products, significant changes in foreign exchange rates as the royalties remitted to RPI are made in U.S. dollars (USD) while the underlying Japan sales of tazemetostat will be made in currencies other than USD, and other events or circumstances that are not currently foreseen as tazemetostat is still under development in Japan and subject to regulatory approval. Changes to any of these factors could result in increases or decreases to both royalty revenues and interest expense. On June 23, 2021, Eisai announced that it had obtained manufacturing and marketing approval for the EZH2 inhibitor "Tazverik® Tablets 200 mg" (tazemetostat hydrobromide) in Japan with the indication of relapsed or refractory EZH2 gene mutation-positive FL (only when standard treatment is not applicable), which caused the Company to reassess the estimated future royalty payments to RPI. As of March 31, 2022, the Company's assessment of the estimated future royalty payments to RPI resulted in a current effective interest rate of approximately 9.2%.

The following table shows the activity of the Royalty Obligation since the transaction inception through March 31, 2022:

	As of March 31, 2022
	(In thousands)
Proceeds from sale of future royalties	$ 12,601
Non-cash royalty revenue	(71)
Non-cash interest expense recognized	3,727
Liability related to the sale of future royalties - ending balance	$ 16,257
Less current portion	(433)
Related party liability related to sale of future royalties, net of current portion	$ 15,824

During the three months ended March 31, 2022 and 2021, the Company recorded $40.0 thousand and $0, respectively, in non-cash royalties from net sales of tazemetostat in Japan. During the three months ended March 31, 2022 and 2021, the Company recorded $0.4 and $0.5 million, respectively, of related non-cash interest expense.

14. Long-Term Debt

On November 4, 2019, the Company entered into the Loan Agreement, which provided for up to $70.0 million in secured term loans to be advanced in up to three tranches. The Company borrowed $70.0 million in the aggregate under the three tranches pursuant to the Loan Agreement. With the FDA's June 2020 approval of tazemetostat for the treatment of FL in the United States, the Company also had the right, but not the obligation, to request up to an additional $300.0 million in secured term loans, subject to the approval of the Lenders, provided the Company had not prepaid any outstanding term loans at the time of such request and such request was made before November 18, 2021. On November 3, 2020, the Company entered into the Amended and Restated Loan Agreement with the Lenders. The Amended and Restated Loan Agreement provides for, among other things, an additional secured term loan of $150.0 million, or the Tranche D Loan. On November 3, 2020, the Company also delivered written notice to the Lenders to draw down the Tranche D Loan, which was funded on November 18, 2020. The Company paid a commitment fee of 2.00% of the original $70.0 million committed facility amount in November 2019 and 2% of the $150.0 million Tranche D Loan in November 2020, as well as expenses incurred by the Lender in executing the agreements.

The interest rate for the Tranche D Loan will be determined by reference to a Eurodollar rate plus 7.75% above such Eurodollar rate. The Eurodollar rate will have a 2.00% floor. The Tranche D Loan will be due in eight equal quarterly principal payments commencing on the 51st month anniversary of the date on which the Lenders fund the Tranche D Loan. All unpaid principal and interest under the Tranche D Loan will be due and payable on the 72nd month anniversary of the date on which the Lenders funded the Tranche D Loan.

The Amended and Restated Loan Agreement also amended the payment period principal and interest for the first three tranches of term loans. Under the original terms, the Company was required to make interest only payments on the outstanding obligation through February 28, 2023, and thereafter eight quarterly payments of principal and interest. Under the amended and restated terms, the Company is required to make interest only payments on the $70.0 million outstanding obligation through November 2023, and thereafter four quarterly payments of principal and interest. All unpaid principal and interest on the $70.0 million borrowed under the original Loan Agreement is due and payable in November 2024, the 60th month anniversary of the date on which the Lenders funded the first tranche of term loans. The interest rates for the existing tranches of term loans remain unchanged and will continue to be determined by reference to a Eurodollar rate plus 7.75% above such Eurodollar rate. The Eurodollar rate will have a 2.00% floor.

Each of the four term loans may be prepaid before maturity in whole or in part, however there is a $50.0 million minimum prepayment for any prepayment of the loans. If the Company prepays any tranche of term loans, in whole or in part, during the first 36 months from the date on which the Lenders funded such tranche of term loans, then the Company must pay a prepayment premium equal to the greater of (x) a make-whole amount equal to the interest that would have accrued on the principal amount to be prepaid and (y) a premium equal to 0.03 multiplied by the principal amount to be prepaid. If the Company prepays a tranche of term loan, in whole or in part, between the 36th month and 48th month from the date on which the Lenders funded such tranche of term loans, then the Company must pay a prepayment premium equal to 0.02 multiplied by the principal amount to be prepaid. If the Company prepays a tranche of term loans, in whole or in part, between the 48th month and 60th month from the date on which the Lenders funded such tranche of term loans, then the Company must pay a prepayment premium equal to 0.01 multiplied by the principal amount to be prepaid.

The Amended and Restated Loan Agreement was accounted for as a debt modification based on a comparison of the present value of the cash flows under the terms of the debt immediately before and after the effective date of The Amended and Restated Loan Agreement, which resulted in a change of less than 10%. As a result, issuance costs paid to the Lenders in connection with The Amended and Restated Loan Agreement were recorded as a reduction of the carrying amount of the debt liability and unamortized issuance costs as of the date of the modification are amortized to interest expense over the repayment term of The Amended and Restated Loan Agreement.

The obligations under the Amended and Restated Loan Agreement, including the Company’s payment obligations in respect of the Tranche D Loan are secured by the first priority security interest in and a lien on substantially all of the assets of the Company, subject to certain exceptions, that the Company granted to the Lenders in connection with the first tranche of term loans under the Loan Agreement.

The Amended and Restated Loan Agreement contains certain customary representations and warranties, affirmative and negative covenants and events of default applicable to the Company and its subsidiaries. If an event of default occurs and is continuing, the Collateral Agent may, among other things, accelerate the loans and foreclose on the collateral. The Company has determined that the risk of subjective acceleration under the material adverse events clause is not probable and therefore has classified the outstanding principal in non-current liabilities based on scheduled principal payments.

The Company has the following minimum aggregate future loan payments at March 31, 2022 :

	As of March 31, 2022 (In thousands)
2022	$ —
2023	—
2024	70,000
2025	75,000
2026	75,000
Total minimum payments	220,000
Less amounts representing interest and discount	(3,330)
Less current portion	—
Long-term debt, net of current portion	$ 216,670

For the three months ended March 31, 2022 and 2021, interest expense related to the Company's Amended and Restated Loan Agreement was approximately $5.4 million in both periods. The total carrying value of debt is classified as long-term on the Company's condensed consolidated balance sheet as of March 31, 2022 and December 31, 2021.

15. Stockholders’ (Deficit) Equity

Common Stock

On April 8, 2021, the Company’s board of directors adopted, subject to stockholder approval, an amendment to the Company’s Restated Certificate of Incorporation to increase the number of authorized shares of common stock from 150,000,000 to 225,000,000 (the "2021 Charter Amendment"). At the Company’s 2021 Annual Meeting of Stockholders, the stockholders of the Company approved the 2021 Charter Amendment, which was filed with the Secretary of State of the State of Delaware on June 11, 2021. The number of authorized shares of preferred stock was not affected by the 2021 Charter Amendment. On March 16, 2022, the Company’s board of directors adopted, subject to stockholder approval, a proposed amendment to the Company’s Restated Certificate of

Incorporation to increase the number of authorized shares of common stock from 225,000,000 to 450,000,000. The number of authorized shares of preferred stock would not be affected by the proposed amendment.

Each share of common stock entitles the holder to one vote on all matters submitted to a vote of the Company's stockholders. Common stockholders are entitled to dividends when and if declared by the board of directors.

In January 2022, the Company raised approximately $79.5 million in net proceeds (after deducting underwriting discounts and commissions and estimated offering costs, but excluding any expenses and other costs reimbursed by the underwriters) from the sale of 56,666,667 shares of its common stock in a public offering at a price of $1.50 per share.

2021 At-the-Market Offering Program

On May 6, 2021, the Company entered into an Open Market Sale Agreement℠ ("ATM Sale Agreement"), with Jefferies LLC ("Jefferies") to sell, from time to time, shares of the Company's common stock having an aggregate offering price of up to $200.0 million through an "at the market offering" as defined in Rule 415 under the Securities Act of 1933, as amended, under which Jefferies would act as sales agent (the "ATM Offering"). The shares that may be sold under the ATM Sale Agreement, if any, are issued and sold pursuant to the Company's shelf registration statement on Form S -3 that was declared effective by the Securities and Exchange Commission on May 13, 2021. The Company agreed to compensate Jefferies at a fixed commission rate equal to 3.0% of the gross sales proceeds of such shares.

From the initiation of the ATM Offering through March 31, 2022, the Company has issued and sold 5,314,135 shares under the ATM Offering, resulting in aggregate net proceeds of $18.3 million after deducting issuance costs of $0.6 million.

During the three months ended March 31, 2022, the Company sold a total of 1,473,158 shares of the Company's common stock under the ATM Sale Agreement, at a volume weighted average gross selling price of approximately $1.82 per share for net proceeds of approximately $2.4 million.

Convertible Preferred Stock

The Company has 337,800 shares of Series A Preferred Stock outstanding as of March 31, 2022 and as of December 31, 2021.

Voting Rights

Shares of Series A Preferred Stock will generally have no voting rights except as required by law and except that the consent of the holders of a majority of the outstanding shares of Series A Preferred Stock will be required to amend the terms of the Series A Preferred Stock or take certain other actions with respect to the Series A Preferred Stock.

Dividends

Shares of Series A Preferred Stock will be entitled to receive dividends equal to (on an as-if-converted-to-common stock basis), and in the same form and manner as, dividends actually paid on shares of the Company's common stock.

Liquidation Rights

Subject to the prior and superior rights of the holders of any senior securities of the Company, upon liquidation, dissolution or winding up of the Company, whether voluntary or involuntary, each holder of shares of Series A Preferred Stock shall be entitled to receive, in preference to any distributions of any of the assets or surplus funds of the Company to the holders of common stock, an amount equal to $0.001 per share of Series A Preferred Stock, plus an additional amount equal to any dividends declared but unpaid on such shares, before any payments shall be made or any assets distributed to holders of any class of common stock.

If, upon any such liquidation, dissolution or winding up of the Company, the assets of the Company shall be insufficient to pay the holders of shares of the Series A Preferred Stock the amount required under the preceding sentence, then all remaining assets of the Company shall be distributed ratably to holders of the shares of the Series A Preferred Stock in proportion to the respective amounts which would otherwise be payable in respect of the shares held by them upon such distribution if all amounts payable on or with respect to such shares were paid in full.

Conversion

Each share of Series A Preferred Stock shall be convertible, at any time and from time to time from and after the issuance date, at the option of the holder thereof, into a number of shares of common stock equal to 10 shares of common stock, provided that the holder will be prohibited from converting Series A Preferred Stock into shares of the Company's common stock if, as a result of such conversion, the holder, together with its affiliates and attribution parties, would own more than 9.99% of the total number of shares of common stock then issued and outstanding. The holder can change this requirement to a higher or lower percentage, not to exceed 9.99% of the number of shares of common stock outstanding, upon 61 days' notice to the Company.

In February 2020, 12,200 shares of Series A Preferred Stock were converted to 122,000 shares of common stock.

Redemption

The Company is not obligated to redeem or repurchase any shares of Series A Preferred Stock. Shares of Series A Preferred Stock are not entitled to any redemption rights or mandatory sinking fund or analogous fund provisions.

Warrants

In November 2019, the Company issued the Common Stock Warrant for the purchase of up to 2,500,000 shares of Common Stock at an exercise price of $20.00 per share to RPI pursuant to the RPI Purchase Agreement (for additional information see Note 13, *Sale of Future Royalties*), which was classified as equity and recorded at its relative fair value of $8.4 million to additional paid-in capital on the Company's condensed consolidated balance sheets. The Common Stock Warrant remains outstanding as of March 31, 2022.

In August 2021, the Company issued the HutchMed Warrant to HutchMed under the HutchMed License Agreement, exercisable at any time prior to August 7, 2025 for up to 5,653,000 shares of the Company's common stock at an exercise price of $11.50 per share. Under the HutchMed Warrant, the number of shares issuable under the warrant is reduced from 5,653,000 to 2,826,500 in the event that the HutchMed License Agreement is terminated for certain reasons as more fully described in the HutchMed License Agreement. Due to this provision in the HutchMed Warrant, the Company concluded that the warrant does not meet the exception from derivative accounting pursuant to ASC 815, Derivatives and Hedging, which requires that the warrant be accounted for as a derivative. Accordingly, the Company recorded a warrant liability in the amount of approximately $13.0 million upon issuance of the HutchMed Warrant. The fair value of the HutchMed Warrant was determined using a Black-Scholes and Monte Carlo pricing model.

The HutchMed Warrant is subject to revaluation at each balance sheet date and any changes in fair value are recorded as a non-cash gain or (loss) in the Company's condensed consolidated statement of operations and comprehensive loss as a component of other income (expense), net until the earlier of the exercise or expiration of the HutchMed Warrant or upon the completion of a liquidation event. Upon exercise, the HutchMed Warrant is subject to revaluation just prior to the date of the warrant exercise and any changes in fair value are recorded as a non-cash gain or (loss).

The Company recorded non-cash gains of approximately $1.4 million during the three months ended March 31, 2022 in its condensed consolidated statement of operations and comprehensive loss attributable to the decreases in the fair value of the warrant liability that resulted from a reduction in the Company's stock price as of March 31, 2022.

The following table rolls forward the fair value of the HutchMed Warrant liability, the fair value of which is determined by Level 3 inputs at inception on August 7, 2021, and as of March 31, 2022:

		(In thousands)
Fair value at January 1, 2022	$	1,930
Decrease in fair value		(1,350)
Fair value at March 31, 2022	$	580

The key assumptions used to value the HutchMed Warrant were as follows:

	Inception	As of March 31, 2022
Risk-free interest rate	0.6%	2.42%
Expected term (in years)	4.0 years	3.36 years
Expected volatility of underlying stock	70.0%	80.0%
Expected dividend yield	-	-
Stock price	$ 6.47	$ 1.15

16. Stock-Based Compensation

The Company maintains one stock incentive plan, the 2013 Stock Incentive Plan, as well as the 2013 Employee Stock Purchase Plan.

In addition, during the year ended December 31, 2021, the Company granted options to purchase an aggregate of 248,366 shares of the Company's common stock and 106,955 restricted stock units (RSUs) to four new employees as equity inducement awards outside of the Company's 2013 Stock Incentive Plan and material to the employees' acceptance of employment with the Company. These equity awards were approved in accordance with Nasdaq Listing Rule 5635(c)(4), and these equity awards remained outstanding as of March 31, 2022. No additional equity inducement awards were granted during the three months ended March 31, 2022. These options have a weighted average exercise price of $5.12 per share, and the RSUs have a weighted average grant date fair value of $5.08 per unit. These inducement awards are included in stock-based compensation expense and the following tables.

Total stock-based compensation expense related to stock options, restricted stock units, shares issued under the employee stock purchase plan, and shares granted to non-employee directors in lieu of board fees was $5.3 million and $7.0 million for the three months ended March 31, 2022 and 2021, respectively.

Stock-based compensation expense is classified in the condensed consolidated statements of operations and comprehensive loss as follows:

	Three Months Ended March 31,	
	2022	2021
	(In thousands)	
Research and development	$ 1,792	$ 2,230
General and administrative	3,497	4,785
Total	$ 5,289	$ 7,015

Stock Options

The weighted-average grant date fair value of options, estimated as of the grant date using the Black-Scholes option pricing model, was $0.91 and $6.75 per option for those options granted during the three months ended March 31, 2022 and 2021, respectively.

Key assumptions used to apply this pricing model were as follows:

	Three Months Ended March 31,	
	2022	2021
Risk-free interest rate	2.1%	0.4%
Expected life of options	5.96 years	6.0 years
Expected volatility of underlying stock	72.8%	70.5%
Expected dividend yield	0.0%	0.0%

The following is a summary of stock option activity for the three months ended March 31, 2022:

	Number of Options	Weighted Average Exercise Price per Share	Weighted Average Remaining Contractual Term	Aggregate Intrinsic Value
	(In thousands)		(In years)	(In thousands)
Outstanding at December 31, 2021	12,946	$ 11.61		
Granted	4,284	1.41		
Exercised	-	-		
Forfeited	(1,583)	10.82		
Outstanding at March 31, 2022	15,647	$ 8.89	7.61	$ -
Exercisable at March 31, 2022	5,923	$ 14.14	5.02	$ -

As of March 31, 2022, there was $29.0 million of unrecognized compensation cost related to stock options that are expected to vest. These costs are expected to be recognized over a weighted average remaining vesting period of 2.74 years.

Restricted Stock Units

During the three months ended March 31, 2022, 87,500 RSUs were granted to an executive. The awards were service-based. Assuming all service conditions are achieved, 25% of the RSUs would vest annually for four years.

	Number of Service Based RSU Shares (in thousands)	Weighted Average Grant Date Fair Value
Outstanding at December 31, 2021	2,222	$ 8.70
Granted	88	1.41
Vested	(277)	13.58
Forfeited	(345)	7.98
Outstanding at March 31, 2022	1,688	$ 7.67

Compensation expense totaling $1.3 million and $1.1 million was recognized for the service-based RSUs for the three months ended March 31, 2022 and 2021, respectively.

As of March 31, 2022, there was $10.3 million of unrecognized compensation cost related to service-based RSUs that are expected to vest. These costs are expected to be recognized over a weighted average remaining vesting period of 1.92 years.

17. Loss Per Share

Basic and diluted loss per share allocable to common stockholders are computed as follows:

	Three Months Ended March 31,	
	2022	2021
	(In thousands except per share data)	
Net loss	$ (55,505)	$ (70,274)
Weighted average shares outstanding	144,201	101,790
Basic and diluted loss per share allocable to common stockholders	$ (0.38)	$ (0.69)

The following common stock equivalents were excluded from the calculation of diluted loss per share allocable to common stockholders because their inclusion would have been anti-dilutive:

	As of March 31,	
	2022	2021
	(In thousands)	
Stock options	15,647	12,316
Restricted stock units	1,688	1,424
Shares issuable under employee stock purchase plan	122	31
Series A Preferred Stock (if converted)	3,378	3,378
Warrants	8,153	2,500
	28,988	19,649

18. Subsequent Events

Amendment of HutchMed License Agreement

On May 6, 2022 HutchMed and the Company executed an amendment to the HutchMed License Agreement and entered into a manufacturing technology transfer and supply agreement as contemplated by the HutchMed License Agreement. For a further discussion of these agreements see Note 12, *Collaborations and License Agreements*.

Conversion of Preferred Stock

In May 2022, the holders of 337,800 shares of Series A Preferred Stock elected to convert such shares into 3,378,000 shares of the Company's common stock. As a result of the conversion, no shares of Series A Preferred Stock remain outstanding.

Equity Inducement Awards

On April 1, 2022, the Company granted options to purchase an aggregate of 800,000 shares of the Company's common stock to a new employee as equity inducement awards outside of the Company's 2013 Stock Incentive Plan and material to the employee’s acceptance of employment with the Company. These options have an exercise price of $1.14 per share, which is equal to the closing price of the Company's common stock on April 1, 2022, the grant date of these options. These equity awards were approved in accordance with Nasdaq Listing Rule 5635(c)(4), and these equity awards remain outstanding as of the date of the filing of this Quarterly Report on Form 10-Q.

Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations

Our management's discussion and analysis of our financial condition and results of operations are based upon our condensed consolidated financial statements included in this Quarterly Report on Form 10-Q, which have been prepared by us in accordance with accounting principles generally accepted in the United States, or GAAP, and with Regulation S-X promulgated under the Securities Exchange Act of 1934, as amended. This discussion and analysis should be read in conjunction with these condensed consolidated financial statements and the notes thereto included elsewhere in this Quarterly Report on Form 10-Q. Some of the information contained in this discussion and analysis or set forth elsewhere in this Quarterly Report on Form 10-Q, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in Part I, Item 1A. Risk Factors of our Annual Report on Form 10-K for the year ended December 31, 2021 filed with the Securities and Exchange Commission on March 1, 2022 and in Part II, Item 1A. Risk Factors of this Quarterly Report on Form 10-Q, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Note on the COVID-19 Pandemic

The ongoing COVID-19 pandemic continues to have widespread, evolving, and unpredictable impacts on global economies, supply chains, financial markets, business practices and societies. The complex challenges created by the COVID-19 pandemic have had an adverse impact on our business, operations, and financial performance, and as such we continue to take steps to respond to these challenges and adjust our commercial strategy and operating plans accordingly.

We believe that the COVID-19 pandemic has had an adverse impact on sales of TAZVERIK since the June 2020 FDA approval of TAZVERIK for FL. Our commercial and medical affairs field teams continue to use virtual formats as well as in-person interactions, where possible, to allow us to serve the needs of healthcare providers, patients and other stakeholders. However, access to prescribers remains restrictive, and we expect these challenges to continue.

In response, we have taken steps to adjust our commercial strategy and continue to further refine our commercial strategy, recognizing that some of the changes brought about by the COVID-19 pandemic, such as ongoing restrictions to access prescribers by traditional sales personnel, will likely persist after the resolution of the pandemic. We are evolving our commercial strategies and deployment of resources to address these changes in market dynamics as we seek to increase awareness of TAZVERIK in ES and FL.

Although the initiation, enrollment and completion of our ongoing and planned clinical trials have not been materially disrupted, we have experienced some delays in clinical trial startup activities due to what we believe to be mostly COVID-19 related capacity constraints and resulting delays in the packaging and labeling of clinical drug supply at a third-party manufacturer. We are aware of the impact that COVID-19 continues to have on other clinical trials in our industry and there is a risk of material impact on the conduct of our clinical trials as well. We are continuing to work with our clinical trial sites as we seek to ensure study continuity, enable medical monitoring, facilitate study procedures and maintain clinical data and records, including the use of local laboratories for testing, home delivery of study drug and remote data and records monitoring.

To date, the COVID-19 pandemic has not had a material impact on our commercial supply chain, and we currently have a consistent supply of tazemetostat and TAZVERIK that we believe will cover our ongoing clinical development as well as the ongoing commercialization for ES and FL. From time to time, however, we have experienced some occasional delays in connection with our clinical supply, including delays related to packaging and labeling. As a proactive measure, we have taken certain steps to try to reduce the risk to our supply chain, such as advancing orders for long-lead items in anticipation of potential future delays or shortages. Because the ongoing COVID-19 pandemic could materially adversely impact our suppliers and result in delays or disruptions in our current or future supply chain, we are continuing to monitor and manage our supply chain accordingly.

We are implementing a multi-stage return to office plan. In October 2021 we opened our facilities to all employees who expressed interest in participating in a return-to-office pilot program, and starting in April 2022 we encouraged all Cambridge-based employees to return to the office in a hybrid model. In leveraging feedback from our pilot program, we have embraced a hybrid virtual/in-office model that will balance health, safety, and flexibility with the benefits of in-office work and collaboration as we safely welcome our team back to the office. Our hybrid approach will continue to be based primarily on guidance from federal, state and local government authorities, and we expect that some form of a hybrid model will continue to exist for us in the future.

We are closely monitoring the impact of the COVID-19 pandemic and related developments on our business, operations and financial performance. We plan to continue to assess the potential duration, scope and severity of the COVID-19 pandemic and its impacts on our business, operations and financial performance, and to continue to work closely with our third-party vendors, collaborators and other parties in order to seek to continue to advance our efforts with respect to the commercialization of TAZVERIK and to continue

to advance the development of EZM0414 and our pipeline, while making the health and safety of our employees and their families, healthcare providers, patients and communities a top priority. Additionally, we continue to monitor the impact of conditions globally, including for example the impact of lockdowns in China, on drug supply and research activities. Due to the evolving and uncertain global impacts of the COVID-19 pandemic, however, we cannot precisely determine or quantify the impact that this pandemic has had on our business, operations and financial performance to date or the impact that this pandemic will have in 2022 and beyond.

Please refer to our risk factors set forth in Part I, Item 1A. Risk Factors of our Annual Report on Form 10-K for the year ended December 31, 2021 for further discussion of risks related to the COVID-19 pandemic.

Operating Expense Reductions

In addition to organizational changes and cross-functional headcount reduction that we implemented in August 2021, in March 2022, we implemented further reductions of our expenses, including a cross-functional workforce reduction of approximately 12% of our then-current employees, as well as a pipeline reprioritization. Given the breadth of our then-current tazemetostat clinical development program, we discontinued enrollment in our Phase 2 study of tazemetostat in combination with rituximab with FL in the third-line or later treatment settings (SYMPHONY-2, EZH-1401), as well as in our Phase 1/1b basket study evaluating tazemetostat combinations in patients with solid tumors (EZH-1301). We have enrolled five patients in the EZH-1401 study and one patient in the EZH-1301 study and plan to continue to follow the patients currently enrolled in each of these two studies. The decision to discontinue these studies was based on evolving market dynamics and a continued focus on optimizing our investments and eliminating potentially overlapping studies. We continue to study tazemetostat in combination with other therapies for both hematologic and solid tumor malignancies, both in ongoing Company-sponsored studies as well as investigator-initiated studies.

As part of those headcount reductions and our pipeline reprioritization, we have implemented changes to our commercial strategy, to our medical affairs and clinical development teams and to our broader organization. We remain focused on accelerating commercial adoption of TAZVERIK in appropriate patients and optimizing our investment of company resources in important clinical trials and programs, including our SYMPHONY-1 (EZH-302), CELLO-1 (EZH-1101), ARIA (EZH-1501) and SET-101 trials.

The severance and termination-related costs associated with the March 2022 workforce reduction were approximately $2.5 million. We recorded these costs in the first quarter of 2022 and expect that payments of these costs will be made through the end of the fourth quarter of 2022.

We plan to continue to implement our broader operational expense reduction effort, and to monitor and seek opportunities to further reduce our operating expenses.

Overview

We are a commercial-stage biopharmaceutical company that is committed to rewriting treatment for people with cancer through the discovery, development, and commercialization of novel epigenetic medicines. We aspire to change the standard of care for patients and physicians by developing targeted medicines with fundamentally new mechanisms of action directed at specific causes of hematological malignancies and solid tumors.

We have one approved product, TAZVERIK (tazemetostat), which was granted accelerated approval by the FDA in January 2020 for ES and in June 2020 for FL. Our focus is on maximizing our effectiveness as a commercial organization to achieve adoption of TAZVERIK among as many appropriate patients as possible, including in earlier treatment lines and in combination regimens with the data to support this expanded use; building on TAZVERIK's pipeline-in-a-drug potential; and expanding our pipeline and evolving oncology portfolio, including with SET-101, our first-in-human Phase 1/1b trial of EZM0414, our novel, first-in-class, oral SETD2 inhibitor. We are leveraging our drug discovery platform and expertise as a leader in epigenetics, as well as our team's deep experience across clinical development and commercialization to execute on our strategy.

In January 2020, the FDA granted accelerated approval of TAZVERIK (tazemetostat), an oral, first in class, selective small molecule inhibitor of the EZH2 histone methyltransferase, or HMT, for the treatment of adult and pediatric patients aged 16 years and older with metastatic or locally advanced ES not eligible for complete resection. This approval was based on overall response rate and duration of response data shown in the ES cohort of our Phase 2 trial in patients with INI1-negative tumors. We continue to make TAZVERIK available to eligible patients and their physicians in the United States.

As part of the accelerated approval for ES, continued approval for this indication is contingent upon verification and description of clinical benefit in a confirmatory trial. To provide this confirmatory evidence to support a full approval of TAZVERIK for this indication, we are conducting a single, randomized, controlled Phase 1b/3 confirmatory trial in the United States (EZH-301) assessing tazemetostat in combination with doxorubicin compared with doxorubicin plus placebo as a front-line treatment for ES. The trial is

expected to enroll approximately 152 patients. We have completed the planned enrollment in the Phase 1b safety run-in portion of the trial and the Phase 3 efficacy portion of the trial is open for accrual. We reported safety and preliminary activity data from the patients in the safety run-in portion of the EZH-301 trial at the American Society of Clinical Oncology (ASCO) Annual Meeting in June 2021.

In June 2020, the FDA approved a supplemental New Drug Application, or sNDA, for TAZVERIK for adult patients with relapsed or refractory (R/R) FL whose tumors are positive for an EZH2 mutation as detected by an FDA-approved test and who have received at least two prior systemic therapies, and adult patients with relapsed or refractory FL who have no satisfactory alternative treatment options. These indications were approved under accelerated approval with a priority review, based on overall response rate and duration of response data shown in the FL cohorts of our Phase 2 clinical trial in patients with EZH2 mutations and wild-type EZH2. We continue to make TAZVERIK available to eligible patients and their physicians in the United States.

As part of the accelerated approval for FL, continued approval for these R/R FL indications is contingent upon verification and description of clinical benefit in a confirmatory trial. To provide this confirmatory evidence to support a full approval of TAZVERIK for these indications, we are conducting a single global, randomized, adaptive Phase 1b/3 confirmatory trial (EZH-302, SYMPHONY-1) assessing the combination of tazemetostat with "R2" (lenalidomide and rituximab), an approved chemotherapy-free treatment regimen, compared with R2 plus placebo for R/R FL patients in the second-line or later treatment setting. We plan to leverage the confirmatory trial and also conduct post-marketing commitments to expand the TAZVERIK label into the second-line treatment setting.

In December 2021 we presented updated safety and activity data from the Phase 1b safety run-in portion of this confirmatory trial at the 2021 American Society of Hematology (ASH) Annual Meeting. We continue to follow the 40 patients in the Phase 1b safety run-in portion of the trial, and recently, SYMPHONY-1 was accepted for a poster presentation, which will be shared at the upcoming ASCO Annual Meeting in Chicago in June 2022 and will include updated data from the Phase 1b cohort of SYMPHONY-1. We also plan to present additional updated data from the safety run-in portion of the trial later in 2022.

We expect that the Phase 3 portion of the SYMPHONY-1 trial will be a global, randomized and adaptive confirmatory trial in 500 patients. Based on the Phase 1b safety run-in results, in December 2021 we submitted a protocol amendment to the FDA with 800 mg twice-daily as the recommended tazemetostat dose (RP3D) for the Phase 3 portion of the trial and have completed the 30-day voluntary waiting period following submission of the protocol amendment for 800 mg RP3D without any objection from the FDA. In March 2022, we dosed the first patient in the randomized Phase 3 portion of the SYMPHONY-1 trial. The SYMPHONY-1 trial is open globally and is actively screening and enrolling patients. The primary endpoint for the Phase 3 portion of the trial will be based on progression free survival as determined by investigator. Based on discussions with the FDA, this portion of the trial will include two interim analyses, the first of which is for futility only and the second of which will be conducted for futility, and if 65% of progression free survival events have occurred, the trial will also include an efficacy evaluation. In July 2021 China's Center for Drug Evaluation, or CDE, approved the Investigational New Drug Application, or IND, we filed in China for SYMPHONY-1.

Through our planned development efforts, our intention is to eventually make TAZVERIK available in all lines of treatment for patients with FL. In collaboration with The Lymphoma Study Association, or LYSA, and based on clinical activity observed with tazemetostat in combination with R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone) as a front-line treatment for patients with high risk diffuse large B-cell lymphoma, or DLBCL, LYSA is conducting a Phase 1b/2 clinical trial to evaluate this combination as a front-line treatment for high-risk patients with FL and DLBCL. The Phase 1b portion of the trial has completed, and patient enrollment in the Phase 2 portion of this trial is nearly complete, with enrollment in the FL arm complete. In collaboration with LYSA, we expect that top-line results from the Phase 2 portion of this trial will be presented at a medical conference in the second half of 2022. We are also finalizing plans for investigator-sponsored studies to evaluate tazemetostat in combination with venetoclax or BTK inhibitors for the treatment of patients with FL in the third-line or later treatment settings.

We are also developing tazemetostat for the treatment of a broad range of other cancer types in multiple treatment settings. Tazemetostat has shown meaningful clinical activity as an investigational monotherapy in multiple cancer indications and has been generally well-tolerated across clinical trials to date. We believe tazemetostat is a "pipeline in a product" opportunity and plan to explore its potential utility in additional indications and combinations.

There are four areas where we see the greatest potential for tazemetostat, all of which are based on a strong scientific hypothesis and are for patients suffering from diseases that would benefit from a new effective and safe treatment option, including:

- Lymphomas and B-cell malignancies, such as DLBCL, mantle cell lymphoma, or MCL, multiple myeloma and others;
- Molecularly defined solid tumors, such as chordoma, melanoma, mesothelioma, and tumors harboring an EZH2 or SWI/SNF alteration;

- PARPi-resistant tumors, such as castration-resistant prostate cancer, small cell lung cancer, and others; and
- Immuno-oncology sensitive tumors, such as small cell lung cancer, prostate cancer and others.

As part of these broader tazemetostat development efforts, we are conducting a global, multi-center, open-label randomized Phase 1b/2 trial (EZH-1101, CELLO-1). The Phase 2 efficacy portion of the CELLO-1 trial, which is evaluating tazemetostat plus enzalutamide compared to enzalutamide monotherapy in patients with metastatic castration-resistant prostate cancer, or mCRPC, is 85% enrolled toward a target of 80 patients and we expect to complete enrollment in the randomized Phase 2 portion of the trial in 2022. We plan to present updated data from the safety run-in portion of the trial as well as interim data from the Phase 2 portion of the trial in the second half of 2022.

To efficiently evaluate tazemetostat's potential safety and efficacy across multiple types of hematological malignancies, we initiated a signal-finding Phase 1b/2 basket study (ARIA, EZH-1501) evaluating tazemetostat with multiple combinations in hematological malignancies in December 2021. We continue to screen patients for enrollment in this study, and we plan to provide updates in the second half of 2022.

We own the global development and commercialization rights to tazemetostat outside of Japan and greater China. Eisai Co. Ltd, or Eisai, holds the rights to develop and commercialize tazemetostat in Japan, and Hutchmed Limited (formerly known as Hutchison China MediTech Investment Limited), or HutchMed, holds certain rights to develop and commercialize tazemetostat in greater China.

TAZVERIK is available to eligible patients in the United States via a specialty distribution network. Through this specialty distribution network, we sell TAZVERIK principally to a limited number of specialty pharmacies, which dispense the product directly to patients, and specialty distributors, which in turn sell the product to hospital pharmacies and community practice pharmacies for the treatment of patients. To commercialize TAZVERIK for the approved ES and FL indications in the United States, we have built a focused field presence and marketing capabilities.

On August 7, 2021, we entered into a strategic collaboration pursuant to a license agreement with HutchMed through which we granted a license to HutchMed for the co-exclusive (with us) development and exclusive commercialization of tazemetostat, either as monotherapy or as a part of combinations with other therapies, including HutchMed proprietary compounds, agreed by us and HutchMed for the treatment of ES, FL and DLBCL in humans, and any additional indications agreed to by us and HutchMed in mainland China, Taiwan, Hong Kong and Macau, or the HutchMed Territory. On May 6, 2022, we agreed with HutchMed to amend the terms of the HutchMed license agreement to clarify certain development and regulatory responsibilities of the parties in the HutchMed Territory, among other things.

For other geographies outside the United States, we are evaluating the most efficient path to obtain marketing approval, commercialize and distribute TAZVERIK to reach patients, including pursuing potential strategic collaborations. Based on comparators and the regulatory landscape, we have decided not to pursue marketing approval of tazemetostat as monotherapy from the European Medicines Agency, or EMA at this time.

Beyond tazemetostat, we are utilizing our drug discovery platform to progress preclinical efforts and discover and identify additional product candidates to expand our pipeline of inhibitors against several classes of chromatin modifying proteins, or CMPs, including HMTs, histone acetyltransferases, or HATs, and helicases.

Our most advanced product candidate, EZM0414, is a novel first-in-class oral inhibitor of the SETD2 HMT.

SETD2 is an HMT that plays multiple important roles in oncogenesis. Based on the potential of SETD2 inhibition demonstrated in multiple preclinical settings, including multiple myeloma, and in particular high risk t(4;14) multiple myeloma and in other B-cell malignancies such as DLBCL, as well as in combination with existing and emerging therapies including tazemetostat, we submitted an IND for EZM0414 to the FDA in July 2021. We received "study may proceed" from the FDA with respect to our IND for EZM0414 in July 2021. In October 2021, EZM0414 was granted Fast Track designation by the FDA in adult patients with relapsed or refractory DLBCL and in January 2022 we received orphan drug designation from the FDA for EZM0414 for the treatment of multiple myeloma. In the fourth quarter of 2021, we initiated a Phase 1/1b trial (SET-101) intended to evaluate the safety and optimize the dose and schedule of EZM0414 in R/R multiple myeloma and DLBCL patients. The Phase 1 portion of our SET-101 trial is a Bayesian optimal interval dose escalation design and includes six planned dose levels ranging from 100 mg to 900 mg once daily. Once we have optimized the dose, we then expect to expand the trial to two patient cohorts in multiple myeloma: t(4;14) multiple myeloma and non t(4;14) multiple myeloma. Based on dose optimization data from the trial, we may add a third patient cohort in DLBCL. We continue to screen patients for enrollment for the Phase 1 dose escalation portion of the SET-101 trial, which we expect will enroll between 30-36 patients. We plan to provide updates on the trial in the second half of 2022.

To date we have entered into various strategic collaborations, including with Eisai, HutchMed, Roche and other third parties. As one of several key aspects of our strategy, we plan to continue to leverage our existing collaborations and to seek to identify new potential strategic collaborations to further support and grow our business in and outside of the United States.

Through March 31, 2022, in addition to revenues from product sales, we have raised an aggregate of $1,650.2 million to fund our operations. This includes $268.8 million of non-equity funding through our collaboration agreements, $368.1 million of funding, consisting of $150.0 million in equity funding received through agreements with RPI Finance Trust, or RPI, and $218.1 million in debt financing received through a loan agreement with BioPharma Credit Investments V (Master) LP and BPCR Limited Partnership (as transferee of BioPharma Credit Investments V (Master) LP's interest as a lender), or the Lenders, $937.3 million from the sale of common stock and Series A Preferred Stock in our public and at-the-market offerings and $76.0 million from the sale of redeemable convertible preferred stock in private financings prior to our initial public offering in May 2013.

As of March 31, 2022, we had $199.7 million in cash, cash equivalents and marketable securities. In January 2022, the Company raised approximately $79.5 million in net proceeds (after deducting underwriting discounts and commissions and estimated offering costs) from the sale of 56,666,667 shares of its common stock in a public offering at a price of $1.50 per share.

We commenced active operations in early 2008, and since inception, have incurred significant operating losses. Our net loss was $55.5 million for the three months ended March 31, 2022. As of March 31, 2022, our accumulated deficit totaled $1,295.3 million. Notwithstanding our sales of TAZVERIK, we expect to continue to incur significant expenses and operating losses over the next several years. Our net losses may fluctuate significantly from quarter to quarter and year to year. We expect our expenses to increase in connection with our ongoing activities, particularly as we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. In addition, we expect our expenses to increase as we fund our tazemetostat development program; make any milestone and royalty payments provided for and achieved under the amended and restated collaboration and license agreement with Eisai; pay interest and principal associated with our amended and restated loan agreement with BioPharma Credit Investments V (Master) LP, BPCR Limited Partnership and BioPharma Credit PLC, or the Amended and Restated Loan Agreement; and continue research and development and initiate clinical trials of, and seek regulatory approval for, any future product candidates.

Funding Agreements with BioPharma Credit Investments V (Master) LP, BPCR Limited Partnership, BioPharma Credit PLC and RPI Finance Trust

We executed the RPI Purchase Agreement on November 4, 2019. Pursuant to the RPI Purchase Agreement, we sold to RPI 6,666,667 shares of our common stock and a warrant to purchase up to 2,500,000 shares of our common stock at an exercise price of $20.00 per share, or the Common Stock Warrant. We also sold our rights to receive royalties from Eisai with respect to net sales by Eisai of tazemetostat products in Japan, or the Japan Royalty, pursuant to the amended and restated collaboration and license agreement between us and Eisai, dated as of March 12, 2015, or the Eisai License Agreement. In consideration for the sale of shares of our common stock, the Common Stock Warrant and the Japan Royalty, RPI paid us $100.0 million upon the closing of the RPI Purchase Agreement in November 2019. In addition, RPI agreed, in connection with RPI's acquisition from Eisai of the right to receive royalties from us under the Eisai License Agreement, to reduce our royalty obligation by low single digits upon the achievement of specified annual net sales levels. We also had the option to sell to RPI $50.0 million of shares of common stock for an 18-month period beginning November 4, 2019, or the Put Option. On February 11, 2020, we sold 2,500,000 shares of common stock to RPI for an aggregate of $50.0 million in proceeds at a sale price of $20.00 per share of common stock pursuant to the Put Option.

On November 4, 2019, we also entered into a Loan Agreement with BioPharma Credit PLC, or the Collateral Agent, and the Lenders, providing for up to $70.0 million in secured term loans to be advanced in up to three tranches, or the Loan Agreement. We borrowed $70.0 million in the aggregate under the three tranches pursuant to the Loan Agreement.

On November 3, 2020, we, the Collateral Agent and the Lenders amended and restated the Loan Agreement, or, as amended and restated, the Amended and Restated Loan Agreement. The Amended and Restated Loan Agreement provides for, among other things, an additional secured term loan facility of $150.0 million, or the Tranche D Loan. On November 18, 2020, we borrowed the Tranche D Loan.

The obligations under the Amended and Restated Loan Agreement remain secured by a first priority security interest that was granted at the time of the Loan Agreement in and a lien on substantially all of our assets, subject to certain exceptions.

The Amended and Restated Loan Agreement contains certain customary representations and warranties, affirmative and negative covenants and events of default applicable to us and our subsidiaries. If an event of default occurs and is continuing, the Collateral Agent under the Amended and Restated Loan Agreement may, among other things, accelerate the loans and foreclose on the

collateral. See Note 14, *Long-Term Debt*, of the notes to our consolidated financial statements included in this Quarterly Report on Form 10-Q for a description of the key terms of the Amended and Restated Loan Agreement.

Results of Operations

Revenues

The following is a comparison of total revenues for the three months ended March 31, 2022 and 2021:

	Three Months Ended March 31,		
	2022	2021	Change
	(In millions)		
Product revenues, net	$ 8.7	$ 6.2	$ 2.5
Collaboration and other revenue	0.0	1.4	$ (1.4)
Total revenues	$ 8.7	$ 7.6	$ 1.1

Product Revenues, net

Net product revenues represent U.S. sales from our sole commercial product, TAZVERIK, which was first approved by the FDA on January 23, 2020, less allowances and accruals. During the three months ended March 31, 2022 and 2021, net product revenues were $8.7 million and $6.2 million, respectively. The $2.5 million increase reflects the increase in TAZVERIK product sales following its approval TAZVERIK for ES in January 2020 and the approval of TAZVERIK for FL in June 2020. The increase includes product revenue during the 2022 period of $0.5 million related to the sale of commercial product by one of our customers to a third-party pharmaceutical company for use in its clinical trials. Sales allowances and accruals consisted of patient financial assistance, distribution fees, discounts, and chargebacks.

Collaboration and Other Revenue

Our collaboration and other revenue during the periods included amounts recognized from deferred revenue related to upfront payments for licenses or options to obtain licenses in the future, research and development services revenue earned, milestone payments earned under collaboration and license agreements with our collaboration partners and revenue from the sale of tazemetostat active pharmaceutical ingredient (API) and drug product to our licensees and collaborators.

In the three months ended March 31, 2022 and 2021, we recognized $0.0 and $1.4 million, respectively, in collaboration and other revenue. The collaboration and other revenue in the three months ended March 31, 2022 consists of less than $0.1 million of non-cash royalties from net sales of tazemetostat in Japan. The collaboration and other revenue of $1.4 million in the three months ended March 31, 2021 was recognized as part of our supply agreement with Eisai for the manufacture and supply of tazemetostat and technical support services.

Cost of Revenue

The following is a comparison of cost of revenue for the three months ended March 31, 2022 and 2021:

	Three Months Ended March 31,		
	2022	2021	Change
	(In millions)		
Cost of product revenue	$ 2.6	$ 2.1	$ 0.5
Cost of other revenue	—	0.8	(0.8)
Total cost of revenue	$ 2.6	$ 2.9	$ (0.3)

The cost of revenue primarily consists of costs related to our product revenue for the sales of TAZVERIK and sales of tazemetostat API and finished goods to our collaborators or licensors. These costs include materials, labor, manufacturing overhead, amortization of milestone payments, and royalties payable on net sales of TAZVERIK. During the three months ended March 31, 2022 and 2021, the cost of product revenue was $2.6 million and $2.1 million, respectively, and consisted of $0.3 million and $0.1 million, respectively, in costs associated with manufacturing TAZVERIK, $1.0 million and $1.0 million, respectively, in amortization expense related to the two $25.0 million milestone payments we paid under our agreement with Eisai upon regulatory approval of TAZVERIK

for ES and upon regulatory approval of TAZVERIK for FL, and $1.3 million and $0.9 million, respectively, in worldwide royalties due under the Eisai License Agreement on net sales of TAZVERIK. Cost of other revenue during the three months ended March 31, 2021 consisted of $0.8 million of costs related to sales of tazemetostat drug product to Eisai. We did not have cost of other revenues in the three months ended March 31, 2022.

Research and Development

Research and development expenses consist of expenses incurred in performing research and development activities, including clinical trials and related clinical manufacturing expenses, fees paid to external providers of research and development services, third-party clinical research organizations, or CROs, compensation and benefits for full-time research and development employees, facilities expenses, overhead expenses, and other outside expenses. Most of our research and development costs are external costs, which we track on a program-by-program basis. Our internal research and development costs are primarily compensation expenses for our full-time research and development employees, including stock-based compensation expense.

The following is a comparison of research and development expenses for the three months ended March 31, 2022 and 2021:

	Three Months Ended March 31,		
	2022	2021	Change
	(In millions)		
Research and development	$ 29.8	$ 32.7	$ (2.9)

During the three months ended March 31, 2022, total research and development expenses decreased by $2.9 compared to the three months ended March 31, 2021. The decrease relates to increases in clinical trial expenses and discovery research activities related to tazemetostat in other indications as well as EZM0414, our SETD2 inhibitor program, which were offset by decreases in our discovery and preclinical stage product programs. Additionally, severance and termination-related costs totaling $0.8 million were recorded in the three months ended March 31, 2022 related to the March 2022 expense reductions.

The following table illustrates the components of our research and development expenses:

	Three Months Ended March 31,		
Product Program	2022	2021	Change
	(In millions)		
External research and development expenses:			
Tazemetostat and related EZH2 programs	$ 12.1	$ 11.7	$ 0.4
SETD2 inhibitor EZM0414 program	1.2	-	1.2
Discovery and preclinical stage product programs, collectively	1.7	5.9	(4.2)
Unallocated personnel and other expenses	14.8	15.1	(0.3)
Total research and development expenses	$ 29.8	$ 32.7	$ (2.9)

External research and development expenses include external manufacturing costs related to the acquisition of active pharmaceutical ingredient and manufacturing of clinical drug supply, ongoing clinical trial costs, discovery and preclinical research in support of the tazemetostat, EZM0414 program, and other pipeline preclinical programs and expenses associated with our companion diagnostic program.

External research and development expenses for tazemetostat and related EZH2 programs increased $0.4 million for the three months ended March 31, 2022 compared to the three months ended March 31, 2021. The increase for the three months ended March 31, 2022 relates to increases in clinical trial expenses related to tazemetostat in other indications.

External research and development expenses for EZM0414 increased $1.2 million for the three months ended March 31, 2022 compared to the three months ended March 31, 2021. We designated the program as a clinical development program in the third quarter of 2021. Prior to the designation of the program as a clinical development program, we allocated costs related to EZM0414 to external research and development expenses for discovery and preclinical stage product programs.

External research and development expenses for discovery and preclinical stage product programs decreased by $4.2 million for the three months ended March 31, 2022 compared to the three months ended March 31, 2021. The decrease in the three months ended March 31, 2022 is primarily related to a decrease in spending for discovery research activities combined with reduced preclinical costs in connection with EZM0414 as a result of the designation of EZM0414 as a clinical development program in the third quarter of 2021.

Unallocated personnel and other expenses are comprised of compensation expenses for our full-time research and development employees and other general research and development expenses. Unallocated personnel and other expenses during the three months ended March 31, 2022 decreased $0.3 million compared to the three months ended March 31, 2021. The decrease was a result of decreases in facilities and equipment related expenses and in unallocated personnel costs and an increase in the allocation of expenses to projects.

We expect that research and development expenses will decrease through 2022, as we continue to implement our operating expense reductions and re-prioritize our investment of company resources in important clinical trials and programs, including our SYMPHONY-1 (EZH-302), CELLO-1 (EZH-1101), ARIA (EZH-1501) and SET-101 trials.

Selling, General and Administrative

Selling, general and administrative expenses consist primarily of salaries and related benefits, including stock-based compensation, related to our executive, finance, intellectual property, business development and support functions. Other selling, general and administrative expenses include allocated facility-related costs not otherwise included in research and development expenses, travel expenses and professional fees for auditing, tax and legal services, including intellectual property and general legal services.

The following is a comparison of selling, general and administrative expenses for the three months ended March 31, 2022 and 2021:

	Three Months Ended March 31,		
	2022	2021	Change
	(In millions)		
Selling, general and administrative	$ 27.2	$ 36.4	$ (9.2)

For the three months ended March 31, 2022, our selling, general and administrative expenses decreased $9.2 million, compared to the three months ended March 31, 2021. The decrease for the three months ended March 31, 2022 compared to the three months ended March 31, 2021 is due to the cross-functional expense reductions starting in August of 2021 and the related decrease in external expenses and personnel related expenses across our selling, general and administrative departments. The decrease was partially offset by severance and termination-related costs totaling $1.7 million which were recorded in the three months ended March 31, 2022 related to the March 2022 cost reduction plan.

We expect that selling, general and administrative expenses will decrease through 2022, as we implement changes to our commercial strategy and organization in an effort to accelerate commercial adoption of TAZVERIK in appropriate patients as well as an operational cost reduction across general and administrative functions as part of our prioritization of our investment of company resources in what we believe to be our most important value-driving clinical trials and programs.

Other (Expense) Income, Net

The following is a comparison of other (expense) income, net for the three months ended March 31, 2022 and 2021:

	Three Months Ended March 31,		
	2022	2021	Change
	(In millions)		
Other (expense) income, net			
Interest income	$ 0.1	$ 0.1	$ —
Interest expense	(5.6)	(5.5)	(0.1)
Other expense, net	(0.1)	—	(0.1)
Change in fair value of warrants to purchase common stock	1.4	—	1.4
Non-cash interest expense related to sale of future royalties	(0.4)	(0.5)	0.1
Other (expense) income, net	$ (4.6)	$ (5.9)	$ 1.3

Other (expense) income, net consists of interest income earned on our cash equivalents and marketable securities, interest expense related to our long-term debt obligations, non-cash changes in the fair value of warrant liabilities and non-cash interest expense related to the sale of future royalties. There was a $1.3 million decrease in other expense for the three months ended March 31, 2022 compared to the three months ended March 31, 2021, principally due to income recognized for the $1.4 million decrease in fair value of warrant liability. This decrease in other expense was partially offset by a $0.1 million increase in interest expense during the three months ended March 31, 2022 compared to the three months ended March 31, 2021.

Income Tax Expense

We recorded a federal and state income tax provision for the three months ended March 31, 2022 of less than $0.1 million due to the expected and known loss before income taxes to be incurred, or incurred, as applicable, for the year ended December 31, 2022, as well as our continued maintenance of a full valuation allowance against our net deferred tax assets, with the exception of the deferred tax asset related to alternative minimum tax credit. We did not record a federal or state income tax provision or benefit for the three months ended March 31, 2021 due to the expected and known loss before income taxes to be incurred, or incurred, as applicable, for the year ended December 31, 2021, as well as our continued maintenance of a full valuation allowance against our net deferred tax assets, with the exception of the deferred tax asset related to alternative minimum tax credit.

Liquidity and Capital Resources

Through March 31, 2022, in addition to revenues from product sales, we have raised an aggregate of $1,650.2 million to fund our operations. This includes $268.8 million of non-equity funding through our collaboration agreements, including the $25.0 million upfront payment received from HutchMed in September 2021, $368.1 million of funding, consisting of $150.0 million in equity funding received through agreements with RPI and $218.1 million in debt financing received through a loan agreement with BioPharma Credit Investments V (Master) LP and BPCR Limited Partnership (as transferee of BioPharma Credit Investments V (Master) LP's interest as a lender), $937.3 million from the sale of common stock and Series A Preferred Stock in our public offerings and at-the-market offerings and $76.0 million from the sale of redeemable convertible preferred stock in private financings prior to our initial public offering in May 2013. As of March 31, 2022, we had $199.7 million in cash, cash equivalents and marketable securities.

In January 2022, we raised approximately $79.5 million in net proceeds (after deducting underwriting discounts and commissions and estimated offering costs, but excluding any expenses and other costs reimbursed by the underwriters) from the sale of 56,666,667 shares of our common stock in a public offering at a price of $1.50 per share.

On May 6, 2021, we entered into the ATM Sale Agreement with Jefferies to sell, from time to time, shares of our common stock having an aggregate offering price of up to $200,000,000 through an "at the market offering" as defined in Rule 415 under the Securities Act of 1933, as amended, under which Jefferies would act as sales agent. The shares that may be sold under the ATM Sale Agreement, if any, are issued and sold pursuant to our shelf registration statement on Form S-3 that was declared effective by the SEC on May 13, 2021. From the initiation of the ATM Offering through March 31, 2022, we have issued and sold 5,314,135 shares under the ATM Offering, resulting in aggregate net proceeds of $18.3 million after deducting issuance costs of $0.6 million.

In addition to our existing cash, cash equivalents and marketable securities, we are eligible to earn milestone payments under our collaboration agreement with HutchMed. Our ability to earn these payments and the timing of earning these payments is dependent upon the outcome of our research and development activities and is uncertain at this time.

Funding Requirements

Our primary uses of capital are clinical trial costs, third-party research and development services, expenses related to commercialization, debt service obligations, compensation and related expenses, laboratory and related supplies, legal and other regulatory expenses and general overhead costs.

Because the continued approval of TAZVERIK in the approved indications is contingent upon verification and description of clinical benefit in confirmatory trials, and because we are developing tazemetostat for other indications, we cannot estimate the actual amounts necessary to successfully complete the development and commercialization of TAZVERIK for the approved indications or the indications that we are exploring or that we may plan to explore. Because EZM0414 is an early clinical product candidate and any future product candidates are in various stages of preclinical development with uncertain outcomes, we also cannot estimate the actual amounts necessary to successfully complete the development and commercialization of EZM0414 or future product candidates. Because of these uncertainties, we also cannot estimate whether, or when, we may achieve profitability. Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity or debt financings and collaboration arrangements. Except for any obligations of our collaborators to make license, milestone or royalty payments under our agreements with them, we do not have any committed external sources of liquidity. To the extent that we raise additional capital through the future sale of equity or debt, the ownership interest of our stockholders may be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our existing common stockholders. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through collaboration arrangements in the future, we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise any additional funds that may be needed through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Outlook

Based on our current operating plan, we expect that our existing cash, cash equivalents and marketable securities as of March 31, 2022, will be sufficient to fund our planned operating expenses and capital expenditure requirements and pay our debt service obligations as they become due into the third quarter of 2023, without giving effect to any potential milestone payments we may receive under our collaboration agreements. We have based this estimate on assumptions that may prove to be wrong, such as the revenue that we expect to generate from the sale of our products, or as to our clinical development costs, particularly as the process of testing drug candidates in clinical trials is costly and the timing of progress in these trials is uncertain. As a result, we could use our capital resources sooner than we expect.

Cash Flows

The following is a summary of cash flows for the three months ended March 31, 2022 and 2021:

	Three Months Ended March 31,		
	2022	2021	Change
	(In millions)		
Net cash (used in) operating activities	$ (59.2)	$ (75.6)	$ 16.4
Net cash provided by investing activities	(44.2)	(20.3)	(23.9)
Net cash provided by financing activities	82.5	1.4	81.1

Net Cash Used in Operating Activities

Net cash used in operating activities was $59.2 million during the three months ended March 31, 2022 compared to $75.6 million during the three months ended March 31, 2021. The decrease in net cash used in operating activities primarily relates to our net loss of $55.5 million, changes in working capital of $9.6 million, and the $1.4 million change in fair value of warrants, partially offset by net depreciation and amortization of $1.6 million, non-cash stock-based compensation of $5.3 million, and non-cash interest expense associated with the sale of future royalties of $0.4 million.

Net cash used in operating activities during the three months ended March 31, 2021 primarily relates to our net loss of $70.3 million, changes in working capital of $14.6 million, partially offset by net depreciation and amortization of $1.8 million, non-cash stock-based compensation of $7.0 million, and non-cash interest expense associated with the sale of future royalties of $0.5 million.

Net Cash Provided by Investing Activities

Net cash used in investing activities during the three months ended March 31, 2022 reflects maturities of available-for-sale securities of $47.8 million, offset by $92.0 million of purchases of available-for-sale securities, and less than $0.1 million of purchases of property and equipment.

Net cash provided by investing activities during the three months ended March 31, 2021 reflects maturities of available-for-sale securities of $100.4 million, offset by $120.6 million of purchases of available-for-sale securities, and $0.1 million of purchases of property and equipment.

Net Cash Provided by Financing Activities

Net cash provided by financing activities of $82.5 million during the three months ended March 31, 2022 primarily reflects net proceeds from the sale of common stock through a public offering and under the ATM Sale Agreement of $82.3 million, and the purchases of shares under our employee stock purchase plan of $0.4 million, partially offset by the payment of offering costs of $0.2 million related to the public offering.

Net cash provided by financing activities of $1.4 million during the three months ended March 31, 2021 reflects cash received from the purchases of shares under our employee stock purchase plan of $1.3 million and stock option exercises of $0.2 million.

Critical Accounting Estimates

Our management's discussion and analysis of financial condition and results of operations is based upon our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States of America. The preparation of these consolidated financial statements requires us to make estimates, judgments and assumptions that affect the reported amounts of assets and liabilities and disclosures of contingent assets and liabilities as of the date of the balance sheets and the reported amounts of collaboration revenue, inventory and expenses during the reporting periods. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances at the time such estimates are made. Actual results and outcomes may differ materially from our estimates, judgments and assumptions. We periodically review our estimates in light of changes in circumstances, facts and experience. The effects of material revisions in estimates are reflected in the consolidated financial statements prospectively from the date of the change in estimate.

We define our critical accounting policies as those accounting principles generally accepted in the United States of America that require us to make subjective estimates and judgments about matters that are uncertain and are likely to have a material impact on our financial condition and results of operations as well as the specific manner in which we apply those principles. Management has determined that our most critical accounting policies are those relating to revenue recognition, research and development expenses, including our accounting for clinical trial expense and accruals, inventory and going concern. As our clinical development plan for tazemetostat and EZM0414 progresses, we expect research and development expenses and, in particular, our accounting for clinical trial accruals to be an increasingly important critical accounting policy.

During the three months ended March 31, 2022, there have been no material changes with respect to our critical accounting estimates disclosed in our Annual Report on Form 10-K for our fiscal year ended December 31, 2021.

Recently Adopted Accounting Pronouncements

For detailed information regarding recently issued accounting pronouncements and the expected impact on our condensed consolidated financial statements, see Note 2, *Summary of Significant Accounting Policies—Recently Adopted Accounting Pronouncements*, in the accompanying Notes to Condensed Consolidated Financial Statements included in Item 1 of this Quarterly Report on Form 10-Q.

Item 3. Quantitative and Qualitative Disclosures About Market Risk

The market risk inherent in our financial instruments and in our financial position represents the potential loss arising from adverse changes in interest rates. As of March 31, 2022, we had cash, cash equivalents and marketable securities of $199.7 million, consisting of money market funds, corporate bonds, commercial paper and government-related obligations. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. We estimate that a hypothetical 100-basis point change in market interest rates would impact the fair value of our investment portfolio as of March 31, 2022 by $0.4 million.

We contract with contract research organizations and manufacturers globally. Transactions with these providers are predominantly settled in U.S. dollars and, therefore, we believe that we have only minimal exposure to foreign currency exchange risks. We do not hedge against foreign currency risks.

Item 4. Controls and Procedures

Disclosure Controls and Procedures

We have established disclosure controls and procedures designed to ensure that information required to be disclosed in the reports that we file or submit under the Securities Exchange Act of 1934, as amended, or the Exchange Act, is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms and is accumulated and communicated to management, including the principal executive officer and the principal financial officer, to allow timely decisions regarding required disclosure.

Our management, under the supervision and with the participation of the principal executive officer (our President and Chief Executive Officer) and the principal financial officer (our President and Chief Executive Officer), has evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) as of the end of the period covered by this Quarterly Report on Form 10-Q. Management recognizes that any disclosure controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives. Our disclosure controls and procedures have been designed to provide reasonable assurance of achieving their objectives. Based on such evaluation, our President and Chief Executive Officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of March 31, 2022.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during the quarter ended March 31, 2022 that materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

PART II — OTHER INFORMATION

Item 1A. Risk Factors

The following information updates, and should be read in conjunction with, the risk factors discussed in Part I, Item 1A, "Risk Factors" in our Annual Report on Form 10-K for the year ended December 31, 2021, or the 2021 10-K. Any of the risk factors contained in the 2021 10-K and in this Quarterly Report on Form 10-Q could materially affect our business, financial condition or future results, and such risk factors may not be the only risks we face. The COVID-19 pandemic has heightened, and in some cases manifested, certain of the risks we normally face in operating our business, including those disclosed in the 2021 10-K, and the risk factor disclosure in the 2021 10-K is qualified by the information relating to COVID-19 that is described in this Quarterly Report on Form 10-Q. Additional risks and uncertainties not currently known to us or that we currently deem to be immaterial also may materially adversely affect our business, financial condition or future results.

If we fail to comply with the continued listing requirements on the Nasdaq Global Select Market ("Nasdaq"), our common stock could be delisted from Nasdaq, which would adversely affect the liquidity of our common stock and our ability to raise additional capital or enter into strategic transactions.

We must satisfy Nasdaq's continued listing requirements, including, among other things, a minimum closing bid price of $1.00 per share (the "Minimum Bid Price"), or risk delisting, which would have a material adverse effect on our business. From April 7, 2022 through the date of this Quarterly Report on Form 10-Q, the bid price of our common stock has closed below the Minimum Bid Price for continued listing on Nasdaq. If the bid price of our common stock continues to close below the Minimum Bid Price for 30 consecutive business days, we may receive a deficiency letter from the Listing Qualifications Department of the Nasdaq Stock Market notifying us that, for the last 30 consecutive business days, the bid price for our common stock had closed below the Minimum Bid Price for continued inclusion on Nasdaq (the "Minimum Bid Price Rule"). In accordance with Nasdaq Listing Rules, we would have an initial period of 180 calendar days (the "Initial Cure Period") after receipt of such deficiency letter to regain compliance with the Minimum Bid Price Rule. If at any time before the end of the Initial Cure Period the bid price for our common stock closes at $1.00 or more per share for a minimum of 10 consecutive business days, the Nasdaq Listing Qualifications Department staff will provide written notification to us that we are in compliance with the Minimum Bid Price Rule, unless the staff exercises its discretion to extend this 10-day period pursuant to the Nasdaq Listing Rules.

If we receive a deficiency letter and then do not regain compliance with the Minimum Bid Price Rule by the end of the Initial Cure Period, we may be eligible for an additional 180 calendar day compliance period. To qualify, we would need to transfer the listing of our common stock to the Nasdaq Capital Market, provided that we meet the continued listing requirement for the market value of publicly held shares and all other initial listing standards, with the exception of the Minimum Bid Price Rule. To effect such a transfer, we would also need to pay an application fee to Nasdaq and would need to provide written notice to the Nasdaq Listing Qualifications Department staff of our intention to cure the deficiency during the additional compliance period.

If we do not regain compliance with the Minimum Bid Price Rule by the required date and we are not eligible for any additional compliance period at that time, the Nasdaq Listing Qualifications Department staff will provide us written notification that our common stock may be delisted. At that time, we may appeal the staff's delisting determination to a Nasdaq Listing Qualifications Panel. We expect that our common stock would remain listed pending the panel's decision. However, there can be no assurance that, even if we appeal the staff's delisting determination to the Nasdaq Listing Qualifications Panel, such appeal would be successful.

We intend to monitor the closing bid price of our common stock and may, if appropriate, consider available options to maintain or regain, as applicable, compliance with the Minimum Bid Price Rule, which could include seeking to effect a reverse stock split. However, there can be no assurance that we will be able to maintain or regain, as applicable, compliance with the Minimum Bid Price Rule.

There are many factors that may adversely affect our minimum bid price, including those described in Part I, Item 1A. Risk Factors of our Annual Report on Form 10-K for the year ended December 31, 2021 filed with the Securities and Exchange Commission on March 1, 2022. Many of these factors are outside of our control. As a result, we may not be able to sustain compliance with the Minimum Bid Price Rule in the long term. Any potential delisting of our common stock from Nasdaq would likely result in decreased liquidity and increased volatility for our common stock and would adversely affect our ability to raise additional capital or to enter into strategic transactions. Any potential delisting of our common stock from the Nasdaq would also make it more difficult for our stockholders to sell our common stock in the public market.

Item 5. Other Information

Amendment to HutchMed License Agreement

On May 6, 2022, the Company and Hutchmed entered into an amendment to the HutchMed License Agreement (the "HutchMed Amendment"). Under the HutchMed Amendment, HutchMed has responsibility for the SYMPHONY-1 trial in the Territory at HutchMed's expense, except the Company is responsible for regulatory interactions and filings in mainland China and for the conduct of the SYMPHONY-1 trial in Taiwan, in each case subject to HutchMed's reimbursement of the Company's expenses commencing as of the HutchMed Effective Date, and Epizyme has oversight of the conduct of the SYMPHONY-1 trial to ensure consistency with the conduct of the trial globally. In addition, as part of the HutchMed Amendment, the parties agreed to remove the provision from the HutchMed License Agreement regarding the potential for assumption by the Company of the costs for the SYMPHONY-1 trial in mainland China, which would have been triggered if the authorities determined that the SYMPHONY-1 trial could not be used as a confirmatory trial for regulatory approval of Licensed Product as a monotherapy in mainland China. Concurrent with the execution of the HutchMed Amendment on May 6, 2022, the Company, HutchMed, and Hutchmed (Hong Kong) Limited entered into a manufacturing technology transfer and supply agreement; and the Company, Hutchmed Limited (formerly known as Hutchison MediPharma Limited) and a contract research organization (the "CRO") entered into an agreement pursuant to which the CRO shall provide management and oversight services in mainland China for the SYMPHONY-1 trial, at Hutchmed Limited's expense. The foregoing description of the HutchMed Amendment does not purport to be complete and is qualified in its entirety by reference to the HutchMed Amendment, a copy of which will be filed with the SEC as an exhibit to the Company's Quarterly Report on Form 10-Q for the fiscal quarter ending June 30, 2022.

Item 6. Exhibits

The exhibits filed as part of this Quarterly Report on Form 10-Q are as follows:

Exhibit Number	Description of the Exhibit
10.1	Employment Offer Letter dated March 11, 2022 between the Registrant and Jerald Korn (1)
10.2	Executive Severance and Change in Control Plan, as amended (1)
31.1	Certification of Principal Executive Officer and Principal Financial Officer pursuant to Rules 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002. (1)
32.1	Certifications pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of The Sarbanes-Oxley Act of 2002, by Grant Bogle, President, Chief Executive Officer, Principal Executive Officer and Principal Financial Officer of the Company. (2)
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.
101.SCH	Inline XBRL Schema Document.
101.CAL	Inline XBRL Calculation Linkbase Document.
101.LAB	Inline XBRL Labels Linkbase Document.
101.PRE	Inline XBRL Presentation Linkbase Document.
101.DEF	Inline XBRL Definition Linkbase Document.
104	Cover Page Interactive Data (embedded within the Inline XBRL document).

(1) Filed with this Form 10-Q.

(2) This certification is being furnished solely to accompany this Quarterly Report on Form 10-Q pursuant to 18 U.S.C. Section 1350, and is not being filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to the liability of that section, nor shall it be deemed incorporated by reference into any filing of the registrant under the Securities Act of 1933, as amended, or Securities Exchange Act of 1934, as amended, whether made before or after the date hereof, regardless of any general incorporation language in such filing.

SIGNATURES

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

Dated: May 10, 2022

EPIZYME, INC.

By: /s/ Grant Bogle
Grant Bogle
President and Chief Executive Officer
(Principal Executive Officer and Principal Financial Officer)

Exhibit 10.1

400 Technology Square, 4th Floor
Cambridge, MA 02139

February 28, 2022

Mr. Jerald Korn

Delivered via email

Dear Jerald,

I am pleased to offer you the position of Chief Operating Officer with Epizyme, Inc. reporting to Grant Bogle CEO.

Salary
You will receive a semi-monthly salary of $19,791.67, which is equivalent to $475,000 annually. It is understood and agreed that, as an integral part of the services you will render to the Company, you will not engage in any other employment, consulting, or other business activities (whether full-time or part-time), except as expressly authorized in writing by the Company's Board of Directors (the "Board").

Bonus
You will also be eligible to receive, for each fiscal year of the Company an annual target bonus equal to up to 40% of your base salary. Although you will be employed by the Company for a partial year in 2022, you shall be eligible for the full year target bonus of $190,000. The target bonus or actual percentage attained thereof shall be awarded upon the attainment, as determined by good faith and reasonable assessment of the Board or the Compensation Committee, of Individual and Company goals at the beginning of each fiscal year. You must be employed on the date that the bonus is paid in order to be eligible to receive such bonus.

Sign-On Bonus
You will also receive a one-time payment of $100,000 on the first payroll after your start date, as set forth in and subject to the Cash Sign-On Bonus Agreement which contains the terms and conditions of the sign-on bonus.

Equity
Subject to Compensation Committee approval, you will be awarded the following new-hire inducement grants pursuant to Nasdaq Listing Rule 5635(c)(4) (the " Inducement Awards"), which are intended to be a material inducement to your employment by the Company:

(i) a stock option grant for the purchase of 800,000 shares of common stock of the Company at a price per share equal to the closing price of the Company's common stock on the Nasdaq Global Market on the grant date. The stock option grant shall be subject to all terms, vesting schedules and other provisions set forth in the corresponding stock option agreement.

You may also be eligible for other grants of stock options, restricted stock units, or other equity awards as determined by and in the sole discretion of the Board. Nothing in this section shall affect your status as an employee at will, as set forth herein.

Benefits
You will also be eligible to participate in the company's Medical, Dental, and Vision Insurance Programs as well as the Life, AD&D, Short- and Long-Term Disability Plans. You will accrue three weeks (15 days) paid vacation each year and receive 12 paid holidays annually in accordance with the company holiday schedule. In addition, you will be eligible to participate in the Savings and Investment Plan and the Flexible Spending Program for daycare and medical care expenses. Epizyme also provides transportation benefits.

The offer of employment is contingent upon satisfactory reference checks, your signing of the I-9 Employment Verification Form, and your signing of the Employee Invention, Non-Disclosure, Non-Competition and Non-Solicitation Agreement with the Company (attached with this letter). You acknowledge that your receipt of the option grant described above in this offer letter is contingent upon your agreement to the non-competition provisions set forth in the Employee Invention, Non-Disclosure, Non-Competition and Non-Solicitation Agreement, and you further acknowledge that such consideration was mutually agreed upon by you and the Company and is fair and reasonable in exchange for your compliance with such non-competition obligations. You will be required to submit documentation that establishes identity and employment eligibility in accordance with the US Immigration and Naturalization requirements. If there are any other agreements of any type that you are aware of which may impact or limit your ability to perform your job at Epizyme, please let us know as soon as possible.

It is important for you to understand that Massachusetts is an "at will" employment state. This means that you will have the right to terminate your employment relationship with Epizyme at any time for any reason. Similarly, Epizyme will have the right to terminate its employment relationship with you at any time for any reason.

We look forward to your employment with us! We are confident that you will make many significant contributions to the Company's growth.

Sincerely,

Grant Bogle
President and Chief Executive Officer

Signed and agreed to:

/s/ Jerald Korn_____ 3/11/22_____
Jerald Korn Date

Prior Attachment(s): Sign-on Bonus Agreement; Employee Invention and Non-Disclosure Agreement

Exhibit 10.2

EPIZYME, INC.
Severance and Change in Control Plan
(as amended through March 4, 2022)

Section I: Establishment and Purpose of Plan

Epizyme, Inc. (the "Company") hereby establishes an unfunded Severance and Change in Control Plan (the "Plan"), which is intended to be a welfare benefit plan within the meaning of Section 3(1) of the Employee Retirement Income Security Act of 1974, as amended ("ERISA"). The Plan is in effect for all employees (the "Participants" as defined below). This document is intended to serve as the plan document and the summary plan description of the Plan.

Section II: Definitions

For purposes of this Plan:

"Participant" means:

(a) the Chief Executive Officer of the Company; (b) all C-level executives and Executive Vice Presidents of the Company (each, a "Senior Executive"); (c) all Senior Vice Presidents of the Company; (d) all Vice Presidents of the Company (e) such other employees who are designated by the Board or an authorized committee thereof to be Participants for purposes of this Plan and (f) solely for purposes of Section III(b)(iv), all employees of the Company. Any individual who is a Participant immediately prior to a Change in Control shall remain a Participant for the twelve (12) month period immediately following the Change in Control, notwithstanding (without limitation) any subsequent changes to such individual's position.

"Cause" means any of the following:

(a) with respect to a termination prior to or more than twelve (12) months following a Change in Control, (I) a Participant's conviction of, or plea of guilty or nolo contendere to, any crime involving dishonesty or moral turpitude or any felony; or (II) a good faith finding by the Company that the Participant has (i) engaged in dishonesty, willful misconduct or gross negligence, (ii) breached or threatened to breach the terms of any restrictive covenants or confidentiality agreement or any similar agreement with the Company, (iii) violated Company policies or procedures, and/or (iv) failed to perform his or her assigned duties to the Company's satisfaction, following notice of such failure by the Company and a period of 15 days to cure; or

(b) with respect to a termination upon or during the twelve (12) month period following a Change in Control (i) the Participant's conviction of, or plea of guilty or nolo contendere to, any felony; (ii) the willful and continued failure by the

Participant (other than any such failure resulting from the Participant's incapacity due to physical or mental illness) to perform substantially the duties and responsibilities of the Participant's position after a written demand for substantial performance (providing a period of 15 days to cure) is delivered to the Participant by the Company; (iii) the material breach by the Participant of the terms of any restrictive covenants or confidentiality agreement with the Company; or (iv) the willful engaging by the Participant in fraud or dishonesty which is demonstrably and materially injurious to the Company or its reputation, monetarily or otherwise. No act, or failure to act, on the Participant's part shall be deemed "willful" unless committed or omitted by the Participant in bad faith and without reasonable belief that the Participant's act or failure to act was in, or not opposed to, the best interest of the Company.

"Change in Control" means any of the following:

(i) the acquisition by an individual, entity or group (within the meaning of Section 13(d)(3) or 14(d)(2) of the Securities Exchange Act of 1934 (the "Exchange Act")) (a "Person") of beneficial ownership of any capital stock of the Company if, after such acquisition, such Person beneficially owns (within the meaning of Rule 13d-3 under the Exchange Act) more than 50% of either (x) the then-outstanding shares of common stock of the Company (the "Outstanding Company Common Stock") or (y) the combined voting power of the then-outstanding securities of the Company entitled to vote generally in the election of directors (the "Outstanding Company Voting Securities"); provided, however, that for purposes of this subsection any acquisition directly from the Company will not be a Change in Control, nor will any acquisition by any individual, entity, or group pursuant to a Business Combination (as defined below) that complies with the Exception to clause (ii) of this definition;

(ii) the consummation of (a) a merger, consolidation, reorganization, recapitalization or share exchange involving the Company or a subsidiary of the Company or (b) a sale or other disposition of all or substantially all of the assets of the Company (a "Business Combination"), unless, in the case of a clause (a) Business Combination, immediately following such Business Combination, all or substantially all of the individuals and entities who were the beneficial owners of the Outstanding Company Common Stock and Outstanding Company Voting Securities immediately prior to such Business Combination beneficially own, directly or indirectly, more than 50% of the then-outstanding shares of common stock and the combined voting power of the then-outstanding securities entitled to vote generally in the election of directors, respectively, of the resulting or acquiring corporation in such Business Combination (which shall include a corporation that as a result of such transaction owns the Company or substantially all of the Company's assets either directly or through one or more subsidiaries) in substantially the same proportions as their ownership of the Outstanding Company Common Stock and Outstanding Company Voting Securities, respectively, immediately prior to such Business Combination (the "Exception"); or

(iii) the liquidation or dissolution of the Company;

provided that, where required to avoid additional taxation under Section 409A, the event that occurs must also be a "change in the ownership or effective control of a corporation, or a change in the ownership of a substantial portion of the assets of a corporation" as defined in Treasury Reg. § 1.409A-3(i)(5).

"Good Reason" means the occurrence, without the Participant's prior written consent, of any of the following events:

(i) a material reduction in the Participant's authority, duties, or responsibilities; (ii) the relocation of the principal place at which the Participant provides services to the Company by at least 30 miles and to a location such that his or her daily commuting distance is increased; or (iii) a material reduction of the Participant's base salary.

No resignation will be treated as a resignation for Good Reason unless (x) the Participant has given written notice to the Company of his or her intention to terminate his or her employment for Good Reason, describing the grounds for such action, no later than 90 days after the first occurrence of such circumstances, (y) the Participant has provided the Company with at least 30 days in which to cure the circumstances, and (z) if the Company is not successful in curing the circumstances, the Participant ends his or her employment within 30 days following the cure period in (y).

Section III: Severance Benefits

(a) **Severance Benefits Not Contingent on a Change in Control**. If, prior to or more than twelve (12) months following a Change in Control, the Company terminates the Participant's employment without Cause or, if the Participant is the Chief Executive Officer of the Company, the Participant terminates his or her employment for Good Reason, and provided the Participant abides by the conditions set forth in Section IV below, the Participant shall be eligible to receive the following severance benefits:

(i) the Company will pay to the Participant as severance pay an aggregate amount equivalent to (a) in the case of the Chief Executive Officer, twelve months of his or her then current base salary, (b) in the case of a Senior Executive level Participant, nine months of his or her then current base salary, (c) in the case of a Senior Vice President level Participant, six months of his or her then current base salary, or (d) in the case of a Vice President level Participant, three months of his or her then current base salary, in each case, less all applicable taxes and withholdings. The foregoing severance pay will be paid ratably in installments in accordance with the Company's normal payroll practices, but in no event shall payment begin earlier than the eighth day after the Participant's execution

and timely return of the "Severance Agreement" (as defined in Section IV below); and

(ii) should the Participant timely elect and be eligible to continue receiving group medical coverage pursuant to the "COBRA" law, and so long as the Company can provide such benefit without violating the nondiscrimination requirements of applicable law, the Company will (a) in the case of the Chief Executive Officer, for a period of twelve months following his or her termination, (b) in the case of a Senior Executive level Participant, for a period of nine months following his or her termination, (c) in the case of a Senior Vice President level Participant, for a period of six months following his or her termination, or (d) in the case of a Vice President level Participant, for a period of three months following his or her termination continue to pay the share of the premium for such coverage that is paid by the Company for active and similarly-situated employees who receive the same type of coverage. The remaining balance of any premium costs shall timely be paid by the Participant on a monthly basis for as long as, and to the extent that, such Participant remains eligible for COBRA continuation.

(b) **Severance Benefits Contingent on a Change in Control**. If, upon or within twelve (12) months following a Change in Control, a Participant's employment is terminated by the Company without Cause or by the Participant for Good Reason, and provided the Participant abides by the conditions set forth in Section IV below, the Participant shall be eligible to receive the following severance benefits:

(i) the Company will pay to the Participant as severance pay an aggregate amount equivalent to (a) in the case of the Chief Executive Officer, eighteen months of his or her then current base salary, (b) in the case of a Senior Executive level Participant, twelve months of his or her then current base salary, (c) in the case of a Senior Vice President level Participant, twelve months of his or her then current base salary, (d) in the case of a Vice President level Participant, nine months of his or her then current base salary, (e) in the case of a Director level Participant, six months of his or her then current base salary, (f) in the case of a Manager level Participant, four months of his or her then current base salary, or (g) in the case of a Participant below the Manager level, three months of his or her then current base salary, in each case, less all applicable taxes and withholdings. The foregoing severance pay will be paid ratably in installments in accordance with the Company's normal payroll practices, but in no event shall payment begin earlier than the eighth day after the Participant's execution and timely return of the Severance Agreement;

(ii) the Company will pay to the Participant as a severance bonus an amount equivalent to (a) in the case of the Chief Executive Officer, 150% of his or her target bonus for the year in which his or her employment is terminated, (b) in the case of a Senior Executive level Participant, 100% of his or her

target bonus for the year in which his or her employment is terminated, (c) in the case of a Senior Vice President level Participant, 100% of his or her target bonus for the year in which his or her employment is terminated, (d) in the case of a Vice President level Participant, 75% of his or her target bonus for the year in which his or her employment is terminated, (e) in the case of a Director level Participant, 50% his or her target bonus for the year in which his or her employment is terminated, (f) in the case of a Manager level Participant, 33% his or her target bonus for the year in which his or her employment is terminated, or (g) in the case of a Participant below the Manager level, 25% of his or her target bonus for the year in which his or her employment is terminated, in each case, less all applicable taxes and withholdings. The foregoing severance bonus will be paid in lieu of any other bonus the Participant may have been eligible to receive with respect to the year in which his or her termination occurs, and shall be paid in one lump sum at such time as the first installment of the severance pay is made; provided, however, that to the extent necessary to comply with Section 409A for a Participant who had an alternate severance arrangement in place prior to March 22, 2013, the foregoing severance bonus shall be paid to the Participant at such time as is required by the provisions of Section 409A;

(iii) should the Participant timely elect and be eligible to continue receiving group medical coverage pursuant to the "COBRA" law, and so long as the Company can provide such benefit without violating the nondiscrimination requirements of applicable law, the Company will (a) in the case of the Chief Executive Officer, for a period of eighteen months following his or her termination, (b) in the case of a Senior Executive level Participant, for a period of twelve months following his or her termination, (c) in the case of a Senior Vice President level Participant, for a period of twelve months following his or her termination, or (d) in the case of a Vice President level Participant, for a period of nine months following his or her termination, (e) in the case of a Director level Participant, for a period of six months following his or her termination, (f) in the case of a Manager level Participant, for a period of four months following his or her termination, (g) in the case of a Participant below the Manager level, for a period of three months following his or her termination continue to pay the share of the premium for such coverage that is paid by the Company for active and similarly-situated employees who receive the same type of coverage. The remaining balance of any premium costs shall timely be paid by the Participant on a monthly basis for as long as, and to the extent that, such Participant remains eligible for COBRA continuation; and

(iv) in the case of any Participant, any unvested stock options or restricted stock unit awards (or, in the case of restricted stock awards, any such awards that remain subject to repurchase by the Company) the Participant may have as of his or her termination date will not terminate upon such termination of employment and shall immediately vest (or become free

from repurchase) and, if applicable, become exercisable in full upon the effectiveness of the Severance Agreement.

For purposes of calculating amounts due under this Section III(b), the Participant's base salary and target bonus will be the higher of (i) the base salary and target bonus in effect immediately prior to the Change in Control and (ii) the base salary and target bonus in effect immediately prior to the Participant's termination of employment.

Section IV: Severance Agreement and Release

As a condition of the Participant's receipt of the severance benefits set forth in Section III, the Participant must timely execute and return to the Company a severance and release of claims agreement provided by and satisfactory to the Company (the "Severance Agreement"), and such Severance Agreement must become binding and enforceable within 60 calendar days after the Participant's termination of employment (or such shorter period as the Company may direct). Severance pay will begin, and any applicable severance bonus will be made, in the first pay period beginning after the Severance Agreement becomes binding, provided that if the foregoing 60-day period would end in a calendar year subsequent to the year in which the Participant's employment ends, payment will not begin or be made before the first payroll period of the subsequent year.

Section V: Miscellaneous Provisions

1. No Employment Rights. Nothing in this Plan shall be construed to provide any Participant with a guarantee of employment or shall supersede the Company's policy of employment at will.

2. Governing Law. The Plan and the rights of all persons under the Plan shall be construed in accordance with and under applicable provisions of ERISA, and the regulations thereunder, and the laws of the Commonwealth of Massachusetts (without regard to conflict of laws provisions) to the extent not preempted by federal law.

3. No Limitation upon Rights of Company. The Plan shall not affect in any way the right or power of the Company to make adjustments, reclassifications or changes of its capital or business structure; to merge or consolidate; to dissolve or liquidate; or to sell or transfer all or any part of its business or assets.

4. Indemnification. To the extent permitted by law, the Plan Administrator (as defined in Appendix A) and all employees, officers, directors, agents and representatives of the Plan Administrator will be indemnified by the Company and held harmless against any claims and the expenses of defending against such claims, resulting from any action or conduct relating to the administration of the Plan except to the extent that such claims arise from gross negligence, willful neglect, or willful misconduct.

5. Plan Name and Type. The name of the Plan is the Epizyme, Inc. Severance and Change in Control Plan. The Plan is intended to constitute an "Employee Welfare Benefits Plan" under

Department of Labor Regulation 2510.3-2(b) and other applicable regulations and statutes. The Plan must be construed and interpreted in a manner consistent with the foregoing intent.

6. Funding. The Plan is unfunded and all payments under the Plan will be made from the Company's general assets.

7. Name and Address of Employer. The Plan is sponsored by:

   Epizyme, Inc.
   400 Technology Square 4th Floor
   Cambridge, MA 02139

8. Employer and Plan Identification Number. The Internal Revenue Service has assigned the Company the following employer identification number: 26-1349956. The ERISA plan number assigned to this program is 502.

9. Agent for Service of Legal Process. Legal process with respect to claims under the Plan may be served on the Plan Administrator.

10. ERISA. The provisions set forth in Appendix A are incorporated herein and made a part of this Plan.

11. Fiscal Year of the Plan. The Plan and its records are kept on a calendar-year basis. The first plan year will be a short plan year beginning on March 22, 2013 and ending on December 31, 2013. Subsequent plan years are the 12-month period beginning January 1 and ending December 31.

12. Entire Agreement. This Plan supersedes any and all severance or equity acceleration plans, policies, and provisions applying to the Participants, including, without limitation, any provision in any Participant's offer letter, employment agreement, or equity agreement providing the Participant with any pay, benefits, or equity acceleration following a change in control of the Company and/or termination of his or her employment for any reason (including termination due to death or disability). To the extent any such plan, policy, or provision contradicts the Plan, the terms of the Plan shall govern.

13. Successor and Assigns. The Company shall require any successor (whether direct or indirect, by purchase, merger, consolidation or otherwise) to all or substantially all of the business and/or assets of the Company to expressly assume and agree to perform the Company's obligations under the Plan in the same manner and to the same extent that the Company would be required to perform such obligations it if no such succession had taken place.

14. Severability. In case any one or more of the provisions of this Plan (or part thereof) shall be held to be invalid, illegal or unenforceable in any respect, such invalidity, illegality or unenforceability shall not affect the other provisions hereof, and this Plan shall be construed as if such invalid, illegal or unenforceable provisions (or part thereof) never had been contained herein.

15. Non-Assignability. No right or interest of any Participant shall be assignable or transferable in whole or in part either directly or by operation of law or otherwise, including, but not limited to, execution, levy, garnishment, attachment, pledge or bankruptcy; provided, however, that this provision shall not be applicable in the case of the obligations of the Company.

16. Duration; Amendment or Termination. The Plan is effective March 22, 2013 and will continue in force until the Company terminates the Plan. The Company reserves the right to modify, amend or terminate the Plan in whole or in part at any time. Such amendment, modification or termination shall be effected by a written instrument executed by an authorized officer of the Company. However, in no event shall such modification, amendment or termination reduce or diminish any equity acceleration or severance benefits owing or other rights under the Plan prior to the date of such modification, amendment or termination without the consent of the Participant to whom the benefits are owed. Notwithstanding the foregoing or anything to the contrary in the Plan, no amendment to the Plan following a Change in Control shall be effective until the date that is twelve (12) months following the Change in Control.

17. Integration with Other Pay or Benefits Requirements. The severance benefits provided for in the Plan are the maximum benefits that the Company will pay to covered Participants. To the extent that the Company owes any amounts in the nature of severance benefits under any other program, policy, or plan of the Company, or to the extent that any federal, state, or local law, including so called "plant closing" laws, requires the Company to give advance notice or make a payment of any kind to an employee because of that employee's involuntary termination due to a layoff, reduction in force, plant or facility closing, sale of business, or similar event, the benefits provided under this Plan or the other arrangement will either be reduced or eliminated to avoid any duplication of payment. The Company intends for the benefits provided under this Plan to partially or fully satisfy any and all statutory obligations that may arise out of an employee's involuntary termination for the foregoing reasons and the Plan Administrator must so construe and implement the terms of the Plan.

Section VI: Section 409A

It is expected that payments under this Plan will be exempt from the application of Section 409A of the Internal Revenue Code of 1986, as amended, and the guidance issued thereunder ("Section 409A") either because of the application of the short-term deferral rule or because of the Two Times Exception (as described below). The following rules shall apply with respect to distribution of the payments to be provided under this Plan to Participants. Each installment of the payments provided under this policy will be treated as a separate "payment" for purposes of Section 409A. Neither the Company nor any Participant will have the right to accelerate or defer the delivery of any such payments or benefits except to the extent specifically permitted or required by Section 409A.

If, as of the date of the "separation from service" of the Participant from the Company, the Participant is not a "specified employee" (each within the meaning of Section 409A), then each installment of the payments and benefits will be made on the dates and terms set forth in this

Plan. If, as of the date of the separation from service of the Participant from the Company, the Participant is a specified employee, then:

(A) Each installment of the payments and benefits due under this Plan that will be paid within the Short-Term Deferral Period (as hereinafter defined) will be treated as a short-term deferral within the meaning of Section 409A to the maximum extent permissible under Section 409A. For purposes of this Plan, the "Short-Term Deferral Period" means the period ending on the later of the 15th day of the third month following the end of the Participant's tax year in which the Participant's separation from service occurs and the 15th day of the third month following the end of the Company's tax year in which the Participant's separation from service occurs; and

(B) Each installment of the payments and benefits due under this Plan that is not paid within the Short-Term Deferral Period and that would, absent this subsection, be paid within the six-month period following the separation from service of the Participant will not be paid until the date that is six months and one day after such separation from service (or, if earlier, the death of the Participant) (as applicable, the "New Payment Date"), with any such installments that are required to be delayed being accumulated during the six-month period and paid in a lump sum in the payroll period next following the New Payment Date and any subsequent installments, if any, being paid in accordance with the dates and terms set forth herein; provided, however, that the preceding provisions of this sentence shall not apply to any installment of payments and benefits if and to the maximum extent that that such installment is deemed to be paid under a separation pay plan that does not provide for a deferral of compensation by reason of the application of Treasury Regulation 1.409A-1(b)(9)(iii) (relating to separation pay upon an involuntary separation from service, the "Two Times Exception"), including the dollar limit in the Two Times Exception. Any installments that qualify for the Two Times Exception must be paid no later than the last day of the second taxable year of the Participant following the taxable year of the Participant in which the separation from service occurs.

In any event, the Company makes no representations or warranty and will have no liability to any Participant or any other person if any provisions of or payments under this Plan are determined to constitute deferred compensation subject to Section 409A of the Code but not to satisfy the conditions of that section.

Section VII: Section 280G/4099

(a) Anything in this document to the contrary notwithstanding, if it is determined that any payment by the Company to a Participant or for his or her benefit (whether paid or payable or distributed or distributable pursuant to the terms of this Plan or otherwise) (the "Payments") would be subject to the excise tax imposed by Section 4999 (or any successor provisions) of the Code, or any interest or penalty would be incurred by the Participant with respect to such excise tax (such excise tax, together with any such interest and penalties, is hereinafter collectively

referred to as the "Excise Tax"), then the Payments shall be reduced (but not below zero) if and to the extent that such reduction would result in the Participant's retaining a larger amount, on an after-tax basis (taking into account federal, state and local income taxes and the imposition of the Excise Tax), than if he or she received all of the Payments. To that end, the Payments will be reduced or eliminated as follows, as determined by mutual agreement of the Participant and the Company.

(b) All determinations required to be made under this Section, including whether and when an adjustment to any Payment is required and, if applicable, which Payments are to be so adjusted, shall be made by an independent accounting firm or any nationally recognized financial planning and benefits consulting company (the "Accounting Firm") selected by the Company, which shall provide detailed supporting calculations both to the Company and to the Participant within fifteen (15) business days of the receipt of notice by the Company. All fees and expenses of the Accounting Firm shall be borne solely by the Company. Any determination by the Accounting Firm shall be binding upon the Company and the Participant.

Adopted by Epizyme, Inc. on March 22, 2013

Amended by Epizyme, Inc. on February 25, 2016

Amended by Epizyme, Inc. on January 24, 2019

Amended by Epizyme, Inc. on March 4, 2022

By: /s/ Grant Bogle
Name: Grant Bogle

Title: President and Chief Executive Officer

APPENDIX A

Plan Administration

The Company's Head of Human Resources is the Plan Administrator. The general administration of the Plan and the responsibility for carrying out its provisions are vested in the Plan Administrator. The Plan Administrator will be the "administrator" within the meaning of Section 3(16) of ERISA and will have all the responsibilities and duties contained therein.

The Plan Administrator can be contacted at the following address: Epizyme, Inc., 400 Technology Square, 4th Floor, Cambridge, MA 02139; or through the Human Resources Department at 617-500-0721. The Plan Administrator will operate, interpret and implement the Plan. The Plan Administrator's decisions and determinations (including determinations of the meaning and reference of terms used in the Plan) will be conclusive upon all persons. The Plan Administrator will be the Named Fiduciary for purposes of ERISA.

The Plan Administrator will have the full power and discretionary authority to administer the Plan in all its details and such powers and discretion as are necessary to discharge its duties, including interpretation and construction of the Plan, the determination of all questions of eligibility, participation and benefits and all other related or incidental matters, and such duties and powers of plan administration that are not assumed from time to time by any other appropriate entity, individual, or institution. The Plan Administrator will decide all such questions in accordance with the terms of the controlling legal documents and applicable law, and its good faith decision will be binding on the Participant, the Participant's spouse or other dependent or beneficiary and all other interested parties.

The Plan Administrator may adopt rules and regulations of uniform applicability in its interpretation and implementation of the Plan.

The Plan Administrator may require each Participant to submit, in such form as it considers reasonable and acceptable, proof of any information that the Plan Administrator finds necessary or desirable for the proper administration of the Plan.

The Plan Administrator must maintain such records as are necessary to carry out the provisions of the Plan. The Plan Administrator must also make all disclosures that are required by ERISA.

If there has been a mistake in the amount of a Participant's benefits paid under the Plan, the Plan Administrator may correct the mistake when the mistake is discovered. The mistake may be corrected in any reasonable manner authorized by the Plan Administrator (e.g., by offset against payments remaining to be paid or by payments between the Participant and the Company). In appropriate circumstances (e.g., where a mistake is not timely discovered), the Plan Administrator may waive the making of any correction.

The Company will pay all costs and expenses incurred in administering this Plan, including expenses of the Plan Administrator and its designee(s).

Statement of ERISA Rights

The following statement is required by federal law and regulations. ERISA provides that all Plan Participants are entitled to:

- Examine, without charge at the Plan Administrator's office and at other specified locations, such as work sites, all Plan documents, and copies of all documents filed by the Plan with the U.S. Department of Labor, such as detailed annual reports and Plan descriptions.
- Obtain copies of all Plan documents and the Plan information upon written request to the Plan Administrator. The Plan Administrator may make a reasonable charge for copies.
- Receive a copy of a summary of the Plan's annual financial report. The Plan Administrator is required by law to furnish each Participant with a copy of this Summary Annual Report.
- Obtain a statement advising the Participant whether he or she has a right to receive benefits under the Plan and what benefits he or she may receive. This statement must be requested in writing and is not required to be given more than once a year. The Plan Administrator must provide the statement free of charge.

In addition to creating rights for Participants, ERISA imposes duties upon the people who are responsible for the operation of the employee benefit plan. The people who operate the Plan, called "fiduciaries" of the Plan, have a duty to do so prudently and in the interest of Plan Participants and beneficiaries. Neither employers nor any other person may fire an employee or otherwise discriminate against an employee in any way to prevent an employee from obtaining a benefit under the Plan or exercising the employee's rights under ERISA.

If an employee's claim for a benefit is denied in whole or in part, the employee must receive a written explanation of the reason for the denial. The employee has the right to have the Plan Administrator review and reconsider the employee's claim. Under ERISA, there are steps an employee can take to enforce the above rights. For instance, if the employee requests materials from the Plan Administrator and does not receive them within 30 days, the employee may file suit in a federal court. In such a case, the court may require the Plan Administrator to provide the materials and pay the employee up to $110 per day until the employee receives the materials, unless the materials were not sent because of reasons beyond the control of the Plan Administrator.

If an employee's claim for benefits is denied or ignored, in whole or in part, the employee may file suit in a state or federal court. If the Plan fiduciaries misuse the Plan's funds, or if an employee is discriminated against for asserting his or her rights, the employee may seek assistance from the U.S. Department of Labor or may file suit in a federal court. The court will decide who should pay court costs and legal fees.

If an employee is successful, the court may order the person sued to pay costs and fees. If the employee loses, the court may order the employee to pay these fees (for example, if the claim is frivolous). Employees should contact the Plan Administrator concerning questions about the Plan. Employees who have any questions about this statement or rights under ERISA should

contact the nearest area office of the Employee Benefits Security Administration, U.S. Department of Labor listed in the telephone directory or the Division of Technical Assistance and Inquiries, Employee Benefits Security Administration, U.S. Department of Labor, 200 Constitution Avenue, N.W., Washington, DC 20210.

Claims Procedure

Ordinarily, benefits will be provided to eligible employees without their having to file a claim or take any action other than signing a Severance Agreement and, where applicable, not revoking such agreement during the applicable revocation period. Any Participant who believes he or she is entitled to benefits under the Plan that are not being provided may submit a written claim to the Plan Administrator. Any claim for benefits shall be in writing, addressed to the Plan Administrator and must be sufficient to notify the Plan Administrator of the benefit claimed. If the claim of a Participant is denied, the Plan Administrator shall, within a reasonable period of time, provide a written notice of denial to the Participant. The notice will include the specific reasons for denial, the provisions of the Plan on which the denial is based, and the procedure for a review of the denied claim. Where appropriate, it will also include a description of any additional material or information necessary to complete or perfect the claim and an explanation of why that material or information is necessary. The Participant may request in writing a review of a claim denied by the Plan Administrator and may review pertinent documents and submit issues and comments in writing to the Plan Administrator. The Plan Administrator shall provide to the Participant a written decision upon such request for review of a denied claim. The decision of the Plan Administrator upon such review shall be final.

Exhibit 31.1

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER AND PRINCIPAL FINANCIAL OFFICER PURSUANT TO RULE 13a-14(a) / RULE 15d-14(a) OF THE SECURITIES EXCHANGE ACT OF 1934, AS AMENDED

I, Grant Bogle, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Epizyme, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: May 10, 2022

/s/ Grant Bogle
Grant Bogle
President and Chief Executive Officer
(Principal Executive Officer and Principal Financial Officer)

Exhibit 32.1

CERTIFICATIONS OF PRINCIPAL EXECUTIVE OFFICER AND PRINCIPAL FINANCIAL OFFICER PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with this Quarterly Report on Form 10-Q of Epizyme, Inc. (the "Company") for the period ended March 31, 2022, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Grant Bogle, President and Chief Executive Officer of the Company (*Principal Executive Officer and Principal Financial Officer*), hereby certifies, pursuant to 18 U.S.C. (section) 1350, as adopted pursuant to (section) 906 of the Sarbanes-Oxley Act of 2002, that to the best of his knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: May 10, 2022

/s/ Grant Bogle

Grant Bogle
President and Chief Executive Officer
(Principal Executive Officer and Principal Financial Officer)