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 June 30, 2021

OR

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

For the transition period from _____ to _____

Commission File Number: 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**

The number of shares outstanding of the registrant's common stock as of August 4, 2021: 102,249,517 shares.

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 ☒

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 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 and for 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 transition announced in August 2021; 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, 2020, 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 June 30, 2021 and 2020 are referred to as the second quarter of 2021 and 2020, 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)

	June 30, 2021	December 31, 2020
ASSETS		
Current assets:		
Cash and cash equivalents	$ 80,164	$ 168,215
Marketable securities	163,842	205,391
Accounts receivable, net	7,119	3,105
Inventory	1,074	10,461
Prepaid expenses and other current assets	20,289	17,921
Total current assets	272,488	405,093
Property and equipment, net	1,872	2,152
Operating lease assets	15,213	17,305
Intangible assets, net	44,926	47,002
Restricted cash and other assets	18,050	2,021
Total assets	$ 352,549	$ 473,573
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 7,295	$ 10,163
Accrued expenses	28,669	28,572
Current portion of operating lease obligation	4,929	4,665
Total current liabilities	40,893	43,400
Operating lease obligation, net of current portion	12,832	15,409
Related party long-term debt, net of debt discount	216,052	215,670
Other long-term liabilities	—	21
Related party liability related to sale of future royalties	15,143	14,176
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; 102,250 shares and 101,627 shares issued and outstanding, respectively	10	10
Additional paid-in capital	1,154,844	1,137,470
Accumulated other comprehensive income (loss)	(2)	3
Accumulated deficit	(1,123,350)	(988,713)
Total stockholders' equity	67,629	184,897
Total liabilities and stockholders' equity	$ 352,549	$ 473,573

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 June 30,		Six Months Ended June 30,	
	2021	2020	2021	2020
Revenue:				
Product revenue, net	$ 7,984	$ 2,234	$ 14,175	$ 3,519
Collaboration and other revenue	5,026	233	6,466	303
Total revenue	13,010	2,467	20,641	3,822
Operating expenses:				
Cost of revenue	2,492	1,022	5,346	1,637
Research and development	34,858	26,352	67,561	51,516
Selling, general and administrative	33,891	32,659	70,303	59,584
Total operating expenses	71,241	60,033	143,210	112,737
Operating loss	(58,231)	(57,566)	(122,569)	(108,915)
Other (expense) income, net:				
Interest (expense) income, net	(5,581)	(569)	(11,057)	187
Other expense, net	(54)	(15)	(44)	(64)
Related party non-cash interest expense related to sale of future royalties	(497)	(301)	(967)	(596)
Other (expense) income, net	(6,132)	(885)	(12,068)	(473)
Net loss	$ (64,363)	$ (58,451)	$ (134,637)	$ (109,388)
Other comprehensive income (loss):				
Unrealized (loss) gain on available-for-sale securities	(8)	535	(5)	441
Comprehensive loss	$ (64,371)	$ (57,916)	$ (134,642)	$ (108,947)
Net loss per share attributable to common stockholders:				
Basic	$ (0.63)	$ (0.58)	$ (1.32)	$ (1.09)
Diluted	$ (0.63)	$ (0.58)	$ (1.32)	$ (1.09)
Weighted-average common shares outstanding used in net loss per share attributable to common stockholders:				
Basic	102,053	101,104	101,922	100,360
Diluted	102,053	101,104	101,922	100,360

See notes to condensed consolidated financial statements.

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

	Six Months Ended June 30,	
	2021	**2020**
CASH FLOWS FROM OPERATING ACTIVITIES:		
Net loss	$ (134,637)	$ (109,388)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	2,595	1,362
Stock-based compensation	13,733	14,802
Amortization of discount (premium) on investments	665	(362)
Amortization of debt discount	382	169
Loss on disposal of property and equipment	—	19
Non-cash interest expense associated with the sale of future royalties	967	596
Changes in operating assets and liabilities:	—	
Accounts receivable	(4,014)	820
Inventory	(6,629)	(9,864)
Prepaid expenses and other current assets	(2,109)	(5,468)
Accounts payable	(2,886)	(4,221)
Accrued expenses	(59)	(499)
Deferred revenue	—	128
Operating lease assets	2,092	1,758
Operating lease liabilities	(2,313)	(595)
Other assets and liabilities	(33)	47
Net cash used in operating activities	(132,246)	(110,696)
CASH FLOWS FROM INVESTING ACTIVITIES:		
Purchases of available-for-sale securities	(170,659)	(94,120)
Maturities of available-for-sale securities	211,539	131,616
Purchase of intangible asset	—	(50,000)
Purchases of property and equipment	(221)	(329)
Net cash (used in) provided by investing activities	40,659	(12,833)
CASH FLOWS FROM FINANCING ACTIVITIES:		
Proceeds from issuance of common stock, net of commissions	1,534	—
Payment of offering costs	(105)	(79)
Proceeds from the issuance of debt	—	45,000
Payment of debt issuance costs	—	(93)
Proceeds from the issuance of common stock in connection with the exercise of the Put Option, net of financing costs	—	49,915
Proceeds from stock options exercised	916	5,810
Issuance of shares under employee stock purchase plan	1,191	646
Net cash provided by financing activities	3,536	101,199
Net (decrease) increase in cash, cash equivalents and restricted cash	(88,051)	(22,330)
Cash, cash equivalents and restricted cash, beginning of period	169,724	140,991
Cash, cash equivalents and restricted cash, end of period	$ 81,673	$ 118,661
SUPPLEMENTAL CASH FLOW INFORMATION:		
Interest paid	$ 10,785	$ 2,182
Unpaid offering costs	$ 154	$ —
Property and equipment included in accounts payable or accruals	$ 18	$ 181

See notes to condensed consolidated financial statements

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

	Common Stock		Preferred Stock		Additional Paid-In	Accumulated	Accumulated Other Comprehensive	Total Stockholders'
	Shares	Amount	Shares	Amount	Capital	Deficit	Income (Loss)	Equity
Balance at December 31, 2019	97,783,476	$ 10	350,000	$ 37,432	$ 1,050,695	$ (757,019)	$ 19	$ 331,137
Issuance of common stock in connection with the exercise of the Put Option (net of financing costs of $85)	2,500,000	—	—	—	49,915	—	—	49,915
Issuance of common stock in connection with the conversion of series A convertible preferred stock	122,000	—	(12,200)	(1,305)	1,305	—	—	—
Exercise of stock options and vesting of restricted stock units	579,919	—	—	—	3,140	—	—	3,140
Stock-based compensation	—	—	—	—	6,475	—	—	6,475
Issuance of shares under employee stock purchase plan	60,576	—	—	—	646	—	—	646
Issuance of shares of common stock in lieu of board fees	1,404	—	—	—	35	—	—	35
Unrealized loss on available for sale securities	—	—	—	—	—	—	(94)	(94)
Net loss	—	—	—	—	—	(50,937)	—	(50,937)
Balance at March 31, 2020	101,047,375	$ 10	337,800	$ 36,127	$ 1,112,211	$ (807,956)	$ (75)	$ 340,317
Exercise of stock options and vesting of restricted stock units	—	—	—	—	$ 2,670	—	—	2,670
Stock-based compensation	414,150	—	—	—	8,257	—	—	8,257
Issuance of shares of common stock in lieu of board fees	—	—	—	—	35	—	—	35
Unrealized gain on available for sale securities	2,229	—	—	—	—	—	535	535
Net loss	—	—	—	—	—	(58,451)	—	(58,451)
Balance at June 30, 2020	101,463,754	$ 10	$ 337,800	$ 36,127	$ 1,123,173	$ (866,407)	$ 460	$ 293,363
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
Issuance of common stock (net of commissions and offering costs of $49)	182,866	—	—	—	1,534	—	—	1,534
Exercise of stock options and vesting of restricted stock units	93,237	—	—	—	717	—	—	717
Stock-based compensation	—	—	—	—	6,679	—	—	6,679
Issuance of shares of common stock in lieu of board fees	4,663	—	—	—	39	—	—	39
Unrealized gain on available for sale securities	—	—	—	—	—	—	(8)	(8)
Net loss	—	—	—	—	—	(64,363)	—	(64,363)
Balance at June 30, 2021	102,249,517	$ 10	$ 337,800	$ 36,127	$ 1,154,844	$ (1,123,350)	$ (2)	$ 67,629

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 June 30, 2021, in addition to revenues from product sales, the Company has raised an aggregate of $1,528.9 million to fund its operations. This includes $243.8 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, 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, $841.0 million from the sale of common stock and series A convertible 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 June 30, 2021, the Company had $244.0 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, or ES, and follicular lymphoma, or 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 two FL indications commenced near 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 $1,123.4 million through June 30, 2021 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.

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 of America 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, 2020, 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 June 30, 2021 and 2020 are referred to as the second quarter of 2021 and 2020, 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 and six months ended June 30, 2021 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 and it is not alleviated by the Company's plans or when its 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 as it continues the launch 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 launch of TAZVERIK resulting from the on-going 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, as more fully described in Note 18 to these financial statements.

The analysis of the Company's ability to continue as a going concern for the second quarter of 2021 included consideration of the Company's current cash needs, including its research and development plans, commercialization activities associated with the ongoing launch of TAZVERIK in the ES and FL indications, its existing debt service obligations, anticipated cost savings resulting from the operating expense reductions described in this Quarterly report on Form 10-Q, and an upfront payment of $25.0 million payable to the Company in connection with the license agreement between the Company and Hutchison China MediTech Investment Limited ("HutchMed"), as more fully described in Note 18 to these financial statements. The analysis included forecasted product revenues from sales of TAZVERIK. Such estimates of future sales contain significant judgment as TAZVERIK was recently launched and there is little history with which to base such estimates. Based on this analysis, the Company concluded that its available cash, cash equivalents and marketable securities will be sufficient to fund current planned operations and capital expenditure requirements into the fourth quarter of 2022, which is more than twelve months from the filing date of this Quarterly Report on Form 10-Q with the SEC. 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

Revenue Recognition – Collaboration Revenue

In November 2018, the FASB, issued ASU 2018-18, *Collaborative Arrangements, or ASC 808*, which clarifies that certain transactions between collaborative arrangement participants should be accounted for as revenue when the collaborative arrangement participant is a customer in the context of a unit of account and precludes recognizing as revenue consideration received from a collaborative arrangement participant if the participant is not a customer. The new standard is effective in the first quarter of fiscal 2021.

The Company adopted ASC 808 effective in the first quarter of fiscal 2021 and the Company's adoption of this standard did not have a material effect on the Company's condensed consolidated statements of operations and comprehensive loss or condensed consolidated statements of cash flows.

Income Taxes

In December 2019, the Financial Accounting Standards Board, or the FASB, issued ASU 2019-12, *Income Taxes*, or ASC 740, which simplifies the accounting for income taxes. The new standard is effective in the first quarter of fiscal 2021.

The Company adopted ASC 740 effective in the first quarter of fiscal 2021 and the Company's adoption of this standard did not have a material effect on the Company's condensed consolidated statements of operations and comprehensive loss or condensed consolidated statements of cash flows.

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) and drug product to the Company's licensees or collaborators. The Company recognizes revenue on tazemetostat API and drug product when control has transferred under the terms of each agreement.

Cost of Revenues

The 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 six months ended June 30, 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 June 30, 2021.

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 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.

Prior to receiving its first approval from the U.S. Food and Drug Administration, or FDA, on January 23, 2020 to sell TAZVERIK, the Company expensed all costs incurred related to the manufacture of TAZVERIK as research and development expense because of the inherent risks associated with the development of a product candidate, the uncertainty about the regulatory approval process and the lack of history for the Company of regulatory approval of drug candidates.

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. During the first quarter of 2020 the Company paid a $25.0 million milestone payment under its agreement with Eisai, Co., Ltd., or Eisai, upon regulatory approval of tazemetostat for ES. During the second quarter of 2020 the Company paid a $25.0 million milestone payment under its agreement with Eisai upon regulatory approval of tazemetostat for FL. Both regulatory milestones have been capitalized as intangible assets.

The following table presents intangible assets as of June 30, 2021 (in thousands):

	June 30, 2021	Estimated useful life (years)
In-licensed rights	$ 50,000	12.2
Less: accumulated amortization	(5,074)	
Total intangible asset, net	$ 44,926	

The Company recorded approximately $1.0 million and $2.1 million in amortization expense related to intangible assets, using the straight-line methodology, during the three and six months ended June 30, 2021, respectively. The Company recorded approximately $0.6 million and $0.9 million in amortization expense related to intangible assets, using the straight-line methodology, during the three and six months ended June 30, 2020, respectively. Estimated future amortization expense for intangible assets for the remainder of the year ended December 31, 2021 is $2.1 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 consolidated balance sheet. 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 asset. As a result, the Company performed a recoverability test and determined that the asset was 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 include estimates of significant growth as the product was recently launched and due to the uncertainty of 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 are not achieved, the Company may be required to perform future impairment analyses and record an impairment charge for the intangible asset 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 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 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 consolidated balance sheet. 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 six months ended June 30, 2021:

	Chargebacks, Discounts, and Fees	Government and Other Rebates	Returns	Total
	(In thousands)			
Balance, January 1, 2021	$ 133	$ 428	$ 67	$ 628
Provision	903	1,504	204	2,611
Payments or credits	(682)	(1,347)	—	(2,029)
Balance, June 30, 2021	$ 354	$ 585	$ 271	$ 1,210

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 and six months ended June 30, 2021 and 2020, 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 June 30,		Six Months Ended June 30,	
	2021	2020	2021	2020
Customer 1	31%	51%	36%	54%
Customer 2	8%	19%	11%	14%
Customer 3	46%	12%	37%	12%
Customer 4	14%	11%	16%	14%

As of June 30, 2021 and December 31, 2020, the four individual customers represented as a percentage of accounts receivable as follows:

	June 30, 2021	December 31, 2020
Customer 1	17%	21%
Customer 2	9%	14%
Customer 3	58%	29%
Customer 4	17%	36%

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 condensed consolidated balance sheets that sum to the total of the same such amounts shown in the condensed consolidated statements of cash flows, is as follows:

	As of June 30,	
	2021	2020
	(In thousands)	
Cash and cash equivalents	$ 80,164	$ 117,152
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	$ 81,673	$ 118,661

The $1.5 million in restricted cash as of both June 30, 2021 and June 30, 2020 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 the condensed consolidated balance sheet. 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 June 30, 2021 (in thousands):

Description	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Commercial paper	$ 102,238	$ 6	$ (3)	$ 102,241
Corporate notes	8,367	—	(10)	8,357
U.S. government agency securities and U.S. Treasuries	53,239	5	—	53,244
Total	$ 163,844	$ 11	$ (13)	$ 163,842

The following table summarizes the available-for-sale securities held at December 31, 2020 (in thousands):

Description	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Commercial paper	$ 158,907	$ 14	$ (8)	$ 158,913
Corporate notes	33,437	3	(7)	33,433
U.S. government agency securities and U.S. Treasuries	13,044	1	—	13,045
Total	$ 205,388	$ 18	$ (15)	$ 205,391

Certain short-term debt securities with original maturities of less than 90 days are included in cash and cash equivalents within the 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 June 30, 2021, 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 six months ended June 30, 2021, 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 June 30, 2021 was $38.3 million, which consisted of 7 commercial paper securities and 2 corporate notes securities. The aggregate unrealized loss for those securities in an unrealized loss position for less than twelve months as of June 30, 2021 was less than $0.1 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 determined that there was 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 June 30, 2021. 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 four months at June 30, 2021.

6. Fair Value Measurements

The Company's financial instruments as of June 30, 2021 and December 31, 2020 consisted primarily of cash and cash equivalents, marketable securities and accounts receivable and accounts payable. As of June 30, 2021 and December 31, 2020, the Company's financial assets recognized at fair value consisted of the following:

	Fair Value as of June 30, 2021			
	Total	Level 1	Level 2	Level 3
	(In thousands)			
Cash equivalents	$ 69,985	$ 65,161	$ 4,824	$ —
Marketable securities:				
Commercial paper	102,241	—	102,241	—
Corporate notes	8,357	—	8,357	—
U.S. government agency securities and treasuries	53,244	—	53,244	—
Total	$ 233,827	$ 65,161	$ 168,666	$ —

	Fair Value as of December 31, 2020			
	Total	Level 1	Level 2	Level 3
	(In thousands)			
Cash equivalents	$ 163,264	$ 113,505	$ 49,759	$ —
Marketable securities:				
Commercial paper	158,913	—	158,913	—
Corporate notes	33,433	—	33,433	—
U.S. government agency securities and treasuries	13,045	—	13,045	—
Total	$ 368,655	$ 113,505	$ 255,150	$ —

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 inventories relate to the manufacturing of TAZVERIK. The following table sets forth the Company's inventories as of June 30, 2021 and December 31, 2020:

	June 30, 2021	December 31, 2020
	(In thousands)	
Raw materials	$ 2,060	$ 1,068
Work in process	12,594	8,564
Finished goods	2,436	829
Total	$ 17,090	$ 10,461
Balance sheet classification		
Inventory	$ 1,074	$ 10,461
Restricted cash and other assets	16,016	—
Total	$ 17,090	$ 10,461

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. Due to the revisions to the Company's forecast of future TAZVERIK sales during the three months ended June 30, 2021, the Company classified a portion of its inventory as long-term.

As of June 30, 2021 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:

	June 30, 2021	December 31, 2020
	(In thousands)	
Employee compensation and benefits	$ 8,873	$ 11,921
Research and development expenses	13,867	10,664
Professional services and other	5,929	5,987
Accrued expenses	$ 28,669	$ 28,572

9. Income Taxes

The Company did not record a federal or state income tax provision or benefit for the three months ended June 30, 2021 and 2020 due to the expected and known loss before income taxes to be incurred, or incurred, as applicable, for the years ended December 31, 2021 and 2020, 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 and six months ended June 30, 2021, as compared to those disclosed in Note 9, *Commitments and Contingencies*, included in its Annual Report.

11. Leases

The Company enters into lease arrangements for its facilities as well as certain equipment. A summary of the arrangements are 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, or 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. Under the current terms of the Technology Square Lease, the Company does not have any further right to extend the term beyond November 30, 2022.

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 condensed consolidated balance sheet. In applying the ASU 2016-02, *Leases*, or ASC 842, transition guidance, the Company determined the classification of this lease to be operating and recorded a lease liability and a right-of-use asset on January 1, 2019.

On August 16, 2019, the Company entered into a lease, or the Hampshire Street Lease, with BMR-Hampshire LLC, or 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 consolidated balance sheet. 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 and six months ended June 30, 2021 and 2020:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2021	2020	2021	2020
Lease cost				
Operating lease cost	$ 1,515	$ 1,555	$ 3,031	$ 3,105
Variable lease cost	566	524	1,046	946
Total lease cost	$ 2,081	$ 2,079	$ 4,077	$ 4,051
Other information				
Operating cash flows used for operating leases	$ 1,621	$ 1,000	$ 3,225	$ 1,981
Weighted average remaining lease term	4.6 years	5.1 years	4.6 years	5.1 years
Weighted average discount rate	9.86%	9.68%	9.86%	9.68%

Future minimum lease payments under the Company's non-cancelable operating leases as of June 30, 2021, are as follows:

	(In thousands)
2021	$ 3,211
2022	6,256
2023	2,984
2024	3,053
Thereafter	6,966
Total lease payments	$ 22,470
Less: imputed interest	(4,709)
Total operating lease liabilities at June 30, 2021	$ 17,761

12. Collaborations

GSK

In January 2011, the Company entered into a collaboration and license agreement with Glaxo Group Limited (an affiliate of GlaxoSmithKline plc), or 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. Additionally, as part of the research collaboration, the Company agreed to provide research and development services related to the licensed targets pursuant to agreed upon research plans during a research term that ended January 8, 2015. 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. The two other targets, PRMT5 and PRMT1, continue to be subject to the agreement and were not impacted by the termination with respect to the third target. The Company substantially completed all research obligations under this agreement by the end of the first quarter of 2015 and completed the transfer of the remaining data and materials for these programs to GSK in the second quarter of 2015.

Agreement Structure

Under the agreement, the Company has received and recognized as collaboration revenue totaling $89.0 million, consisting of upfront payments, fixed research funding, research and development services and preclinical and research and development milestone payments. As of June 30, 2021, for the two remaining targets, the Company is eligible to receive up to $50.0 million in clinical development milestone payments, up to $197.0 million in regulatory milestone payments and up to $128.0 million in sales-based milestone payments. As a result of the termination of the agreement as it relates to the third target, the Company will receive no additional payments related to that target. In addition, GSK is required to pay the Company royalties, at percentages from the mid-single digits to the low double-digits, on a licensed product-by-licensed product basis, on worldwide net product sales, subject to reduction in specified circumstances. Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, the Company may not receive any additional milestone payments or royalty payments from GSK. GSK became solely responsible for development and commercialization for each licensed target in the collaboration when the research term ended on January 8, 2015.

Collaboration Revenue

Through June 30, 2021, the Company has earned a total of $89.0 million in total collaboration revenue since inception of the GSK agreement, which the Company recognized as collaboration revenue in the condensed consolidated statements of operations and comprehensive loss. The Company did not recognize any collaboration revenue under the agreement in the three and six months ended June 30, 2021 and 2020, respectively. The Company did not have any deferred revenue related to this agreement as of June 30, 2021 and 2020, respectively. Any future revenues pursuant to this arrangement will relate to any milestone payments and royalties received under the agreement with respect to the two remaining targets. All remaining milestone payments as of June 30, 2021 have been deemed not probable and therefore have not been recognized as revenue.

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.

As of December 31, 2014, the Company had completed its performance obligations under the original agreement.

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.

Under the original collaboration and license agreement, Eisai was solely responsible for funding all research, development and commercialization costs for EZH2 compounds. Under the Eisai License Agreement, the Company is solely responsible for funding global development, manufacturing and commercialization costs for EZH2 compounds outside of Japan, including the remaining development costs due under a companion diagnostics agreement with Roche Molecular Systems, Inc., or Roche Molecular, which was amended to assign all of Roche Molecular's rights and obligations under the companion diagnostics agreement to Roche Sequencing, effective January 1, 2020. Eisai is solely responsible for funding Japan-specific development and commercialization costs for EZH2 compounds.

The Company recorded the reacquisition of worldwide rights, excluding Japan, to the EZH2 program, including tazemetostat, under the Eisai License Agreement, as an acquisition of an in-process research and development asset. As this asset was acquired without corresponding processes or activities that would constitute a business, had not achieved regulatory approval for marketing and, absent obtaining such approval, had no alternative future use, the Company recorded the $40.0 million upfront payment made to Eisai in March 2015 as research and development expense in the consolidated statements of operations and comprehensive loss. The Company also agreed to pay Eisai up to $20.0 million in clinical development milestones, and up to $50.0 million in regulatory milestone payments, and royalties at a percentage in the mid-teens on worldwide net sales of any EZH2 product, excluding net sales in Japan. The Company is eligible to receive from Eisai royalties at a percentage in the mid-teens on net sales of any EZH2 product in Japan.

Pursuant to the Eisai License Agreement, the Company has paid total milestone payments of $70.0 million, $50.0 million of which related to regulatory approval of tazemetostat for ES and FL, which were capitalized as intangible assets on the Company's condensed consolidated balance sheets.

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. 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 as other collaboration revenue during the three months ended June 30, 2021 upon delivery of the Company's waiver to the drug substance manufacturer. During the three and six months ended June 30, 2021, the Company recognized $5.0 million and $6.3 million, respectively, related to the Company's waiver of its exclusive right to supply of tazemetostat drug substance from the Company's drug substance manufacturer and delivery of tazemetostat drug product in collaboration and other revenue.

During the three and six months ended June 30, 2020, Eisai purchased $0.3 and $0.7 million, respectively, 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 June 30, 2021 and December 31, 2020, the Company had accounts receivable of less than $0.1 million for both periods, due from Eisai.

During the three and six months ended June 30, 2021, the Company recorded $1.2 and $2.1 million, respectively, related to the worldwide royalties due under the Eisai License Agreement in cost of revenue based on U.S. sales of TAZVERIK. During the three and six months ended June 30, 2020, the Company recorded $0.3 and $0.5 million, respectively, in cost of revenue related to the worldwide royalties due under the Eisai License Agreement based on U.S. sales of TAZVERIK. As of June 30, 2021 and 2020, $1.2 million and $0.3 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 Roche group, and this assignment became effective as of January 1, 2020. As of June 30, 2021, 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 payment 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 follicular lymphoma 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.

Boehringer Ingelheim

In November 2018, the Company entered into a collaboration and license agreement with Boehringer Ingelheim International GmbH ("Boehringer Ingelheim") to discover, research, develop and commercialize small molecule compounds that are inhibitors of an undisclosed histone acetyltransferase, or HAT, target and an undisclosed helicase target, along with associated predictive biomarkers (the "Target Projects"). Under the terms of the agreement, the Company granted to Boehringer Ingelheim an exclusive, worldwide license to the undisclosed target inhibitors technology. The agreement also included reciprocal licenses to utilize each other's know-how, patents and technologies for activities under the agreement. Further, each party was granted the license to develop, manufacture, commercialize and otherwise exploit any compound or product that successfully achieves start of lead optimization ("SoLO"). The Company was also obligated to provide R&D services through SoLO approval for both Target Projects, and to serve on the Joint Steering Committee ("JSC") throughout the term of the contract. The parties were to jointly research and develop the shared helicase target program and will share commercialization activities within the United States. Boehringer Ingelheim had agreed to assume responsibility for commercialization outside of the United States. On December 21, 2020, the Company received written notice from Boehringer Ingelheim that it has elected to terminate the Collaboration Agreement without cause, and in accordance with the terms of the Collaboration Agreement and the parties' agreement. The termination became effective on January 31, 2021. The Target Project for the helicase target and the reciprocal licenses terminated as of this date. The Company is entitled to pursue the HAT target and helicase target programs in all fields worldwide without further obligation to Boehringer Ingelheim.

Agreement Structure

Under the terms of the agreement, the Company received a $15.0 million upfront payment and $5.0 million in research funding for the costs to be incurred by the Company in connection with its research activities, payable quarterly in four equal installments during 2019. At its discretion, Boehringer Ingelheim had the option to extend the research period by up to one year, subject to the Company's agreement to the specified research activities and additional research funding. During the third quarter of 2019, Boehringer Ingelheim's option to extend the research period expired unexercised, and therefore the research period ended on December 31, 2019. In March 2020, the Company and Boehringer Ingelheim amended the agreement to extend the research period for the shared program targeting enzymes within helicase families with Boehringer Ingelheim providing research funding of $0.4 million. Additionally, in March 2020, the Company received notice of termination for the program targeting enzymes with HAT families, which program termination became effective in June 2020. In September 2020, the Company and Boehringer Ingelheim further amended the

agreement to extend the research period for the shared program targeting enzymes within helicase families with Boehringer Ingelheim to provide research funding of $0.1 million. The additional research activities were completed prior to the end of 2020.

Collaboration Revenue

Through June 30, 2021, the Company has recognized $26.0 million in total collaboration revenue since the inception of this collaboration. During the three and six months ended June 30, 2021, the Company did not recognize collaboration revenue under its agreement with Boehringer Ingelheim. During the three and six months ended June 30, 2020, the Company recognized $0.2 and $0.3 million, respectively, in collaboration revenue under its agreement with Boehringer Ingelheim.

As of June 30, 2021 and December 31, 2020, the Company did not have any deferred revenue or accounts receivable related to this agreement.

13. Sale of Future Royalties

On November 4, 2019, the Company 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. As of June 30, 2021, 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*). Under the Amended and Restated Loan Agreement the Company has the right to request up to an additional $150.0 million in secured term loans, subject to the approval of the Lenders, provided that the Company has not prepaid any outstanding term loans at the time of the Company's request and such request is made before November 18, 2021.

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 has the right to sell, and RPI has 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 June 30, 2021 and December 31, 2020, RPI and its affiliates owned approximately 9.0% and 9.0% 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 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 follicular lymphoma (only when standard treatment is not applicable), which caused the Company to reassess the estimated future royalty payments to RPI. As of June 30, 2021, the Company's assessment of the estimated future royalty payments to RPI resulted in a current effective interest rate of approximately 13.2%.

The following table shows the activity of the Royalty Obligation since the transaction inception through June 30, 2021:

	As of June 30, 2021
	(In thousands)
Proceeds from sale of future royalties	$ 12,601
Non-cash interest expense recognized	2,542
Liability related to the sale of future royalties - ending balance	$ 15,143

During the three and six months ended June 30, 2021 and 2020, no non-cash royalties from net sales of tazemetostat in Japan were recorded and the Company recorded $0.5 million and $0.9 million, respectively, and $0.3 million and $0.6 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 has not prepaid any outstanding term loans at the time of such request and such request is 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.

Under the Amended and Restated Loan Agreement the Company has the right to request from the Lenders, subject to the Lenders' agreement to lend additional amounts to the Company, up to an additional $150.0 million, provided that the Company has not prepaid any outstanding term loans at the time of the Company's request and such request is made before November 18, 2021.

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 June 30, 2021 (in thousands):

	As of June 30, 2021 (In thousands)
2021	$ —
2022	—
2023	—
2024	70,000
2025	75,000
2026	75,000
Total minimum payments	220,000
Less amounts representing interest and discount	(3,948)
Less current portion	—
Long-term debt, net of current portion	$ 216,052

For the three and six months ended June 30, 2021 and 2020, interest expense related to the Company's Amended and Restated Loan Agreement was approximately $5.4 million and $10.8 million, respectively, and $1.3 million and $2.1 million, respectively. The total carrying value of debt is classified as long-term on the condensed consolidated balance sheet as of June 30, 2021 and December 31, 2020.

15. Stockholders' (Deficit) Equity

Common Stock

On March 24, 2020, 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, $0.0001 par value per share, from 125,000,000 to 150,000,000 (the "2020 Charter Amendment"). At the Company's 2020 Annual Meeting of Stockholders, the stockholders of the Company approved the 2020 Charter Amendment, which was filed with the Secretary of State of the State of Delaware on May 29, 2020. 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 these Charter Amendments.

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.

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.

During the three months ended June 30, 2021, the Company sold a total of 182,866 shares of the Company's common stock under the ATM Sale Agreement, at a volume weighted average gross selling price of approximately $8.53 per share for net proceeds of approximately $1.5 million. During the three months ended June 30, 2021, in addition to sales commissions to Jefferies of approximately $48 thousand, which have been accounted for as an offset to additional paid-in capital, the Company incurred approximately $0.3 million of legal, accounting and other costs to establish and activate the ATM program.

RPI Put Option

In February 2020, the Company sold 2,500,000 shares of its common stock in connection with the exercise of its Put Option to sell shares of its common stock for an aggregate of $49.9 million in net proceeds after deducting financing costs of $0.1 million.

Convertible Preferred Stock

The Company has 337,800 shares of Series A Convertible Preferred Stock outstanding as of June 30, 2021 and as of December 31, 2020.

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 were classified as equity and recorded at their relative fair value of $8.4 million to additional paid-in capital on the consolidated balance sheets. The Common Stock Warrant remain outstanding as of June 30, 2021.

16. Stock-Based Compensation

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 $6.7 million and $8.3 million for the three months ended June 30, 2021 and June 30, 2020, respectively, and $13.7 million and $14.8 million for the six months ended June 30, 2021 and June 30, 2020, respectively.

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2021	2020	2021	2020
	(In thousands)		(In thousands)	
Research and development	$ 2,023	$ 2,804	$ 4,253	$ 4,966
General and administrative	4,695	5,488	9,480	9,836
Total	$ 6,718	$ 8,292	$ 13,733	$ 14,802

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 $5.10 and $9.29 per option for those options granted during the three months ended June 30, 2021 and 2020, respectively, and $6.41 and $12.25 for those options granted during the six months ended June 30, 2021 and 2020, respectively.

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2021	2020	2021	2020
Risk-free interest rate	0.8%	0.3%	0.5%	1.1%
Expected life of options	5.71 years	5.91 years	5.94 years	5.96 years
Expected volatility of underlying stock	70.7%	72.0%	70.5%	70.7%
Expected dividend yield	0.0%	0.0%	0.0%	0.0%

The following is a summary of stock option activity for the six months ended June 30, 2021:

	Number of Options (In thousands)	Weighted Average Exercise Price per Share	Weighted Average Remaining Contractual Term (In years)	Aggregate Intrinsic Value (In thousands)
Outstanding at December 31, 2020	10,225	$ 14.77		
Granted	3,149	10.42		
Exercised	(104)	8.83		
Forfeited	(1,212)	14.67		
Outstanding at June 30, 2021	12,058	$ 13.69	7.41	$ 255
Exercisable at June 30, 2021	5,576	$ 14.47	6.18	$ 125

As of June 30, 2021, there was $47.2 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 2.60 years.

Restricted Stock Units

During the six months ended June 30, 2021, 971,845 restricted stock units (“RSUs”) were granted to executives and employees and 72,540 RSUs were granted to non-employee directors. The awards were service-based. Assuming all service conditions are achieved, the executive and employee RSUs will vest as to 25% of the shares of Company common stock underlying the RSUs on an annual basis over a four year period of time from the grant dates, and the non-employee director RSUs will vest as to 100% of the shares of Company common stock underlying the RSUs in full on the earlier of the first anniversary of the grant date and the date of the succeeding annual meeting of stockholders.

	Number of Service Based RSU Shares (in thousands)	Weighted Average Grant Date Fair Value
Outstanding at December 31, 2020	668	$ 17.56
Granted	1,044	10.82
Vested	(177)	17.35
Forfeited	(177)	13.67
Outstanding at June 30, 2021	1,358	$ 12.91

Compensation expense totaling $1.2 million and $2.2 million was recognized for the service-based RSUs for the three and six months ended June 30, 2021, respectively. Compensation expense totaling $0.7 million and $1.2 million was recognized for the service-based RSUs for the three and six months ended June 30, 2020, respectively.

As of June 30, 2021, there was $14.1 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 3.03 years.

During 2019, the Company granted 604,000 RSUs to executives and employees, which contained performance conditions, and 20% of the RSUs vested on June 30, 2019, 25% of the RSUs vested on January 23, 2020, 20% of the RSUs vested on March 24, 2020, and 30% of the RSUs vested on June 25, 2020 in connection with achievement of the final performance milestone. There was no unrecognized compensation cost as of June 30, 2021, related to performance-based RSUs.

Compensation expense totaling $2.1 million and $3.5 million was recognized for the performance-based RSUs for the three and six months ended June 30, 2020, respectively. There was no compensation expense recognized for the performance-based RSUs for the three and six months ended June 30, 2021.

17. Loss Per Share

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2021	2020	2021	2020
	(In thousands except per share data)		(In thousands except per share data)	
Net loss	$ (64,363)	$ (58,451)	$ (134,637)	$ (109,388)
Weighted average shares outstanding	102,053	101,104	101,922	100,360
Basic and diluted loss per share allocable to common stockholders	$ (0.63)	$ (0.58)	$ (1.32)	$ (1.09)

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:

	For the Three and Six Months Ended As of June 30,	
	2021	2020
	(In thousands)	
Stock options	12,058	10,025
Restricted stock units	1,358	679
Shares issuable under employee stock purchase plan	113	33
Series A Preferred Stock (if converted)	3,378	3,378
Warrants	2,500	2,500
	19,407	16,615

18. Subsequent Events

HutchMed License Agreement

On August 7, 2021, the Company entered into a license agreement (the “HutchMed License Agreement”) with 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 epithelioid sarcoma, follicular lymphoma, 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”).

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. During the term of the HutchMed License Agreement, each party and its affiliates is prohibited from developing or commercializing in the Field in the Territory any other compound or product that inhibits, modulates or degrades EZH1, EZH2, or any other member of the polycomb repressive complex 2, including the EED protein, provided that, subject to limitations specified in the HutchMed License Agreement, HutchMed may develop, without the use of know-how or patent rights licensed by Epizyme, its existing preclinical compound that inhibits EZH1 and EZH2.

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. Subject to the execution of a clinical supply agreement or commercial supply agreement, as applicable, and 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 or 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 EZH-302 global studies, however under certain circumstances where the EZH-302 global study is not considered a confirmatory trial for regulatory approval in China, the Company shall be responsible for the costs of the trial in the Territory.

Pursuant to the HutchMed License Agreement, the Company is entitled to receive an upfront payment of $25.0 million. 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 (the "Warrant") to HutchMed, 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. The Company has agreed to file a registration statement registering for resale the shares of the Company's common stock issuable upon exercise of the Warrant.

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.

Operating Cost Reduction

On August 9, 2021, the Company announced a cross-functional reduction of approximately 11% of its current workforce under a cost reduction plan. Affected employees will be offered separation benefits, including severance payments along with temporary healthcare coverage assistance. The Company estimates that the severance and termination-related costs will be approximately $2.0 million and expects to record these charges in the third quarter of 2021. The Company expects that payments of these costs will be made through the end of the first quarter of 2022.

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, 2020 filed with the Securities and Exchange Commission on February 23, 2021 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 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 FDA's approval in June 2020 of TAZVERIK for follicular lymphoma, or FL. Our commercial and medical affairs field teams are continuing to use virtual formats as well as in-person interactions where possible in order to allow us to serve the needs of healthcare providers, patients and other stakeholders. However, the COVID-19 pandemic has continued to negatively impact epithelioid sarcoma, or ES, and FL patient visits to physicians, new patient starts across all lines of treatment, and the ability of our field-based teams to fully access ES and FL prescribers, and these challenges continued through the second quarter of 2021. As a result, commercial demand for TAZVERIK has been negatively impacted. On August 9, 2021, we announced changes to our commercial strategy and organization and adjustments to our operating plans, including operating expense reductions, as we work to optimize the commercialization of TAZVERIK in ES and FL while prioritizing our investment of company resources on what we believe to be our most important value-driving clinical trials and programs, including the generation of additional clinical data for TAZVERIK across treatment lines and in combinations to support increased adoption in the longer term.

Although patient demand for TAZVERIK increased by three percent in the second quarter of 2021 compared to the first quarter of 2021, our net revenue for TAZVERIK was negatively impacted by a higher utilization of our Patient Assistance Program over the same period and did not meet our expectations. However, we continue to see new prescriptions being written for both EZH2 mutation and wild-type patients, in the academic and community settings, and across multiple treatment lines in relapsed or refractory FL patients. In addition, payor coverage for ES and FL continues to be in-line with the TAZVERIK label.

We continue to operate under a remote operating model for all employees other than certain members of our laboratory and facilities staff. As part of this remote operating model, our laboratory staff who engage in research and development activities continue to have restricted access to our laboratories. Accordingly, our laboratory staff are not yet back to their full daily output as existed prior to the onset of the COVID-19 pandemic. We continue to evaluate our remote operating model for our offices based on guidance from federal, state and local government authorities, and we expect that some form of this remote operating model will exist for us through at least the third quarter of 2021.

In addition, although the initiation, enrollment and completion of our ongoing and planned clinical trials are on schedule, 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 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 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. 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 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 commercialization efforts of TAZVERIK and to continue to advance the development of our pipeline, while making the health and safety of our employees and their families, healthcare providers, patients and communities a top priority. 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 or the impact that this pandemic will have in 2021 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, 2020 filed with the Securities and Exchange Commission on February 23, 2021 and in Part II, Item 1A. Risk Factors of this Quarterly Report on Form 10-Q for further discussion of risks related to the COVID-19 pandemic.

Operating Expense Reductions

In response to the challenges we have continued to face since we commenced the launch of TAZVERIK in FL in June 2020, we are implementing changes to our commercial strategy and organization in an effort to accelerate commercial adoption of TAZVERIK in appropriate patients as well as a broader operational cost reduction plan that will reduce our headcount across different areas of the organization and prioritize our investment of company resources in what we believe to be our most important value-driving clinical trials and programs, including our EZH-302, EZH-1401, EZH-1101, and two proposed signal finding basket studies that we plan to initiate in the second half of 2021 and our novel SETD2 inhibitor EZM0414 program. To further accelerate these important programs, we plan to reduce and manage our operating expenses commensurate with our ability to drive top-line revenue growth.

We expect that these actions will allow us to keep the company in a financial position that will enable us to continue to achieve important near-term milestones and execute on our long-term strategy, which remain unchanged. On August 9, 2021, we announced a cross-functional reduction of our 2021 budgeted headcount by approximately 20% which includes approximately 11% of our current workforce under the cost reduction plan. Affected employees will be offered separation benefits, including severance payments along with temporary healthcare coverage assistance. We estimate that the severance and termination-related costs will be approximately $2.0 million and expect to record these charges in the third quarter of 2021. We expect that payments of these costs will be made through the end of the first quarter of 2022.

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.

Our vision is focused on four transformative critical imperatives that we refer to as *The Next EPIsode: Rewriting Oncology Treatment with Epigenetics*. The four pillars of this five-year corporate strategy are:

- Maximize our effectiveness as a commercial organization to achieve adoption of TAZVERIK among as many FL and ES patients as possible, including in earlier treatment lines and in combination regimens with the data to support this expanded use;
- Build on TAZVERIK’s pipeline-in-a-drug potential, demonstrating tazemetostat’s benefit in additional hematological malignancies and solid tumors;
- Expand our pipeline and evolving oncology portfolio, bringing novel oncology therapeutics into clinical development to maintain our position as a leader in epigenetics; and
- Leverage options to expand patient reach and increase shareholder value, including through commercial, clinical, and research collaborations.

We continue to see these four pillars as the core of our five-year corporate strategy to promote growth and value creation, and we believe that our refined commercial strategy, organizational structure, and operational changes will provide the capital flexibility to execute on these pillars.

In January 2020, the U.S. Food and Drug Administration, or 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 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 global, randomized, controlled Phase 1b/3 confirmatory trial (EZH-301) assessing TAZVERIK 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 we expect to commence the Phase 3 efficacy portion of the trial in 2021. We reported safety and preliminary activity data from the patients in the safety run-in portion of the study at the American Society of Clinical Oncology annual meeting in June 2021.

In June 2020, the FDA approved a supplemental New Drug Application, or sNDA, for TAZVERIK for the following FL indications: (1) adult patients with relapsed or refractory 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 (2) 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 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 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) assessing the combination of TAZVERIK with “R2” (Revlimid® plus rituximab), an approved chemotherapy-free treatment regimen, compared with R2 plus placebo for FL patients in the second-line or later treatment setting.

During the second quarter of 2021, we completed enrollment of all Phase 1b safety run-in cohorts of the Phase 1b/3 trial with a total of 36 patients, including patients at the 600mg TAZVERIK twice daily dosing regimen and patients at the 800mg TAZVERIK twice daily dosing regimen per FDA’s requested number of patients. The safety profile observed in the patients in both the 800mg and 600mg dose cohorts has been consistent with that described in the respective reference safety information documents in the label. Most notably, no DLTs have been reported during the first cycle of treatment. Of the 36 patients enrolled, 17 patients are currently considered evaluable for efficacy based on the availability of tumor scans. All 17 patients responded to treatment, with six patients having a complete response, and 11 patients having a partial response. For all response evaluable patients, the duration on therapy is in the range between 2 and 10 months of therapy. The Phase 1b safety run-in portion of the trial is currently ongoing, and we are following patients to obtain more data. As we continue to conduct the Phase 1b safety run-in portion of the trial, we are using the time to activate as many study sites as possible, globally, to ensure we can enroll the Phase 3 portion of the trial quickly once we have obtained approval from the FDA. We plan to present further data from the safety run-in portion of the trial at the American Society of Hematology annual meeting in December 2021.

The Phase 3 portion of the trial will be a global, randomized, adaptive Phase 1b/3 confirmatory trial (EZH-302) assessing the combination of TAZVERIK with “R2” (Revlimid® plus rituximab), an approved chemotherapy-free treatment regimen, compared with R2 plus placebo for FL patients in the second-line or later treatment setting. We expect to conduct this part of the trial in 500 patients globally. The IND that we filed in China for EZH-302 has recently received China’s Center for Drug Evaluation, or CDE, approval in July 2021, following official CDE acceptance of our IND filing in May 2021. The primary endpoint for the trial will be based on progression free survival as determined by investigator. Based on discussions with the FDA, the trial will include two interim analyses, the first of which is for futility only and second of which will be conducted for futility, and once 65% of progression free survival events have occurred, will also include an efficacy evaluation.

Through our planned development efforts, our intention is to eventually make TAZVERIK available in all lines of treatment for patients with FL. We plan to leverage the confirmatory trial and post-marketing commitments to expand TAZVERIK into the second-line treatment setting. In collaboration with The Lymphoma Study Association, or LYSA, and based on clinical activity observed with tazemetostat in combination with R-CHOP as a front-line treatment for patients with high risk diffuse large B-cell lymphoma, or DLBCL, we commenced a Phase 2 clinical trial that is being conducted by LYSA evaluating this combination as a front-line treatment for high-risk patients with FL. We also converted an investigator-sponsored study to evaluate tazemetostat in combination with rituximab with FL in the third-line or later treatment settings to a Company-sponsored study in order to expand the number of participating sites, and this study (EZH-1401) is currently enrolling patients. We expect to share the full dataset for the EZH-1401 study at a medical conference in mid-2022. In addition, we are 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 developing tazemetostat for the treatment of a broad range of 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 advance life-cycle development for tazemetostat to support its potential utility in additional indications and combinations.

In connection with these efforts, we are conducting a global, multi-center, randomized Phase 1b/2 trial (EZH-1101) evaluating tazemetostat in combination with enzalutamide or abiraterone, the standard of care treatments for metastatic castration-resistant prostate cancer, or mCRPC, plus prednisone in chemo-naïve patients with mCRPC. As of February 2021, we had completed enrollment in the Phase 1b safety run-in portion of the EZH-1101 trial with a total of 21 men with mCRPC. In March 2021, we announced preliminary data from the Phase 1b safety run-in portion of the trial.
Among the 21 patients enrolled in the safety run-in portion of the trial, which was conducted using a standard dose escalation design, no DLTs were observed at any dose of tazemetostat up to a maximum dose of 1600mg twice daily for patients receiving tazemetostat plus enzalutamide and 800mg twice daily for patients receiving tazemetostat plus abiraterone. As of mid-February 2021, initial data from the trial also showed:

- Seven out of 21 patients had a PSA response of ≥50%; one additional patient had a PSA response of ≥35%.
- Six of the PSA50 responses were in the tazemetostat + enzalutamide cohort (n=13) and one was in the tazemetostat + abiraterone/prednisone cohort (n=8).
- We also observed a 47% disease control rate to-date and presented an example of radiographic response in a patient achieving a confirmed PR in the trial.
- All responses were in ARV7 negative patients identified using the EPIC platform. Only one ARV7 positive patient was enrolled in the safety run-in portion of the trial.

We anticipate reporting further safety and preliminary activity data from the Phase 1b safety run-in portion of the EZH-1101 trial at the European Society for Medical Oncology (ESMO) Congress in September 2021.

Based on these early safety and activity findings observed in the Phase 1b safety run-in portion of the EZH-1101 trial, in the first quarter of 2021 we initiated enrollment in the Phase 2 efficacy portion of the trial evaluating tazemetostat in combination with enzalutamide compared to enzalutamide alone in 80 men with mCRPC. The primary endpoint for the trial is radiographic progression free survival.

There are four areas where we see the greatest potential for tazemetostat, all of which are based on a strong scientific hypothesis and for diseases that need 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 prostate cancer, small cell lung cancer, and ovarian cancer; and
- Immunotherapy resistant tumor settings (primary or acquired), including small cell lung cancer, prostate cancer, and others.

To efficiently evaluate tazemetostat's potential safety and efficacy across multiple new types of hematological malignancies and solid tumors, we plan to initiate two signal finding basket studies in the second half of 2021, a Phase 1b/2 trial evaluating tazemetostat with multiple combinations in hematological malignancies, and a Phase 2 trial evaluating tazemetostat with multiple combinations across three solid tumor types. In July 2021, we received "study may proceed" from the FDA with respect to our IND for the proposed solid tumor basket study. By using this approach, we will study multiple combinations with standard of care therapies and novel mechanisms of action as we seek to expand the potential of TAZVERIK to patients and the physicians who treat them efficiently and effectively.

We own the global development and commercialization rights to tazemetostat outside of Japan. On August 7, 2021, we granted a license to Hutchison China MediTech Investment Limited, or HutchMed, for the co-exclusive (with us) development and exclusive commercialization of tazemetostat, either as a monotherapy or as a part of combinations with other therapies, including HutchMed proprietary compounds, agreed by us and HutchMed for the treatment of epithelioid sarcoma, follicular lymphoma, diffuse large B-cell lymphoma in humans, and any additional indications agreed by us and HutchMed in mainland China, Taiwan, Hong Kong and Macau. Eisai Co. Ltd, or Eisai, holds the rights to develop and commercialize tazemetostat in Japan.

TAZVERIK is available to eligible patients in the United States via a specialty distribution network. To commercialize TAZVERIK for the ES and FL indications in the United States, we have built a focused field presence and marketing capabilities. In August 2021, we announced changes to our commercial strategy and organization, including realignment of our commercial organization by creating and expanding new field roles intended to better reach thought leaders and large community accounts, while reducing traditional sales roles and overall headcount. Additionally, we will be shifting some of our resources to implement digital approaches to reach both healthcare providers and patients directly. In June 2021, to help provide access to information that we believe will help evolve the treatment of FL, we launched the EZH2Now™ testing program with Quest Diagnostics to provide EZH2 mutation testing for patients with FL. We believe that these changes will allow us to better deliver on our commercial goals.

For 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.

On August 7, 2021 we entered into a license agreement, or the HutchMed License Agreement, with Hutchison China MediTech Investment Limited, or 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, for the treatment of epithelioid sarcoma, follicular lymphoma, diffuse large B-cell lymphoma in humans, and any additional indications agreed by the parties in mainland China, Taiwan, Hong Kong and Macau, or the HutchMed Territory, which is intended to bring TAZVERIK to patients in the HutchMed Territory and to further extend the clinical development of TAZVERIK in new treatment combinations. We are entitled to receive an upfront payment of $25.0 million from HutchMed under the HutchMed License Agreement. We are 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 tazemetostat products in the HutchMed Territory under the HutchMed License Agreement, and up to $175.0 million in the aggregate for achievement of specified sales milestones in the HutchMed Territory with respect to tazemetostat products under the HutchMed License Agreement. We 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 tazemetostat products in the HutchMed Territory. See Note 18, *Subsequent Events*, of the notes to our condensed consolidated financial statements included in this Quarterly Report on Form 10-Q for a description of the HutchMed License Agreement.

In Europe, we are continuing to explore and understand what may be necessary in order for us to submit a marketing authorization application to the European Medicines Agency, or EMA, in an effort to obtain marketing approval of tazemetostat from the EMA in ES and FL. We expect to define a path to regulatory submission in Europe by the end of 2021.

Tazemetostat is covered by claims of U.S. and European composition of matter patents, which are expected to expire in 2032, exclusive of any patent term or other extensions. Tazemetostat has been granted Fast Track designation by the FDA in patients with relapsed or refractory FL, relapsed or refractory DLBCL with EZH2 activating mutations and metastatic or locally advanced ES who have progressed on or following an anthracycline-based treatment regimen. The FDA has also granted orphan drug designation to tazemetostat for the treatment of patients with malignant rhabdoid tumors, or MRT, soft tissue sarcoma, and mesothelioma, and a seven-year orphan drug exclusivity period from the dates of our respective approvals of TAZVERIK for the treatment of patients with ES and for the treatment of patients with FL.

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.

The most advanced of these product candidates is a novel oral inhibitor of SETD2 (EZM0414). SETD2 is an HMT, similar to EZH2, which 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 diffuse large B-cell lymphoma, 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, and we plan to initiate a first-in-human clinical trial by the end of 2021. This planned clinical trial is intended to evaluate the safety and optimize the dose and schedule of EZM0414 in r/r multiple myeloma and DLBCL patients. Once we have optimized the dose, we then expect to further expand to three patient cohorts: t(4;14) multiple myeloma, non t(4;14) multiple myeloma and DLBCL.

To date, we have entered into various strategic collaborations, including with HutchMed, Glaxo Group Limited (an affiliate of GlaxoSmithKline plc), or GSK, Eisai, 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 strategic collaborations to further support and grow our business in and outside of the United States.

Through June 30, 2021, in addition to revenues from product sales, we have raised an aggregate of $1,528.9 million to fund our operations. This includes $243.8 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 an amended and restated loan agreement, or the Amended and Restated 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, $841.0 million from the sale of common stock and series A convertible 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 June 30, 2021, we had $244.0 million in cash, cash equivalents and marketable securities.

We commenced active operations in early 2008, and since inception, have incurred significant operating losses. Our net loss was $64.4 million and $134.6 million for the three and six months ended June 30, 2021, respectively. As of June 30, 2021, our accumulated deficit totaled $1,123.4 million. Notwithstanding our sales of TAZVERIK, we expect to continue to incur significant expenses and operating losses over the next several years. Our expenses and net losses may fluctuate significantly from quarter to quarter and year to year as we continue to fund our most important value-driving clinical trials and programs; implement and execute changes to our commercial strategy; make any royalty payments provided for and achieved under the amended and restated collaboration and license agreement with Eisai; pay interest and principal associated with 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 a purchase agreement with RPI on November 4, 2019, or the RPI Purchase Agreement. 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.

Under the Amended and Restated Loan Agreement, we have the right to request from the Lenders, subject to the Lenders' agreement to lend additional amounts to us, up to an additional $150.0 million, provided that we have not prepaid any outstanding term loans at the time of our request and such request is made before November 18, 2021.

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 condensed 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 and six months ended June 30, 2021 and 2020:

	Three Months Ended June 30,			Six Months Ended June 30,		
	2021	2020	Change	2021	2020	Change
	(In millions)			(In millions)		
Product revenues, net	$ 8.0	$ 2.2	$ 5.8	$ 14.2	$ 3.5	$ 10.7
Collaboration and other revenue	5.0	0.2	$ 4.8	6.5	0.3	6.2
Total revenues	$ 13.0	$ 2.4	$ 10.6	$ 20.7	$ 3.8	$ 16.9

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 June 30, 2021 and 2020, net product revenues were $8.0 million and $2.2 million, respectively. The $5.8 million increase reflects the timing of approval of TAZVERIK for ES in January 2020 and the approval of TAZVERIK for FL in June 2020. During the six months ended June 30, 2021 and 2020, net product revenues were $14.2 million and $3.5 million, respectively. The $10.7 million increase reflects the timing of approval of TAZVERIK for ES in January 2020 and the approval of TAZVERIK for FL in June 2020. Product revenue during the three months ended June 30, 2021 included $3.2 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 or collaborators.

In the three and six months ended June 30, 2021, we recognized $5.0 million and $6.5 million, respectively, in collaboration and other revenue. This collaboration revenue was recognized as part of our supply agreement with Eisai for the Company's waiver of its exclusive right to its manufacturer for the supply of tazemetostat drug substance, the manufacture and supply of tazemetostat and technical support services. In the three and six months ended June 30, 2020, we recognized $0.2 million and $0.3 million in collaboration revenue as part of our Boehringer Ingelheim collaboration. We recognized revenue as our research services were performed. In December 2020, we received written notice from Boehringer Ingelheim to terminate the collaboration agreement, effective January 31, 2021.

Cost of Revenues

The following is a comparison of cost of revenue for the three and six months ended June 30, 2021 and 2020:

	Three Months Ended June 30,			Six Months Ended June 30,		
	2021	2020	Change	2021	2020	Change
	(In millions)			(In millions)		
Cost of product revenue	$ 2.5	$ 1.0	$ 1.5	$ 4.5	$ 1.6	$ 2.9
Cost of other revenue	—	—	—	0.8	—	0.8
Total cost of revenue	$ 2.5	$ 1.0	$ 1.5	$ 5.3	$ 1.6	$ 3.7

The cost of revenues primarily consists of costs related to 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 June 30, 2021 and 2020, the cost of product revenue was $2.5 million and $1.0 million, respectively, and consisted of $0.3 million and $0.1 million, respectively, in costs associated with manufacturing TAZVERIK, $1.0 million and $0.6 million, respectively, in amortization expense related to the two $25.0 million milestone payments under our agreement with Eisai upon regulatory approval of TAZVERIK for epithelioid sarcoma and upon

regulatory approval of TAZVERIK for follicular lymphoma, and $1.2 million and $0.3 million, respectively, in worldwide royalties due under the Eisai License Agreement on net sales of TAZVERIK. We did not have cost of other revenues in the three months ended June 30, 2021.

During the six months ended June 30, 2021 and 2020, the cost of product revenue was $4.5 million and $1.6 million, respectively, and consisted of $0.3 million and $0.2 million, respectively, in costs associated with manufacturing TAZVERIK, $2.1 million and $0.9 million, respectively, in amortization expense related to the $25.0 million milestone payment under our agreement with Eisai upon regulatory approval of tazemetostat for epithelioid sarcoma, and $2.1 million and $0.5 million, respectively, in worldwide royalties due under the Eisai License Agreement on net sales of TAZVERIK. Cost of other revenue during the six months ended June 30, 2021 consisted of $0.8 million of costs related to sales of tazemetostat drug product to Eisai. All product costs incurred prior to FDA approval of TAZVERIK in January 2020 were expensed as research and development expenses. We expect our cost of product revenues to continue to be positively impacted during 2021 and in future periods, as we sell through certain inventory that was expensed prior to FDA approval of TAZVERIK in January 2020.

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 and six months ended June 30, 2021 and 2020:

	Three Months Ended June 30,			Six Months Ended June 30,		
	2021	2020	Change	2021	2020	Change
	(In millions)			(In millions)		
Research and development	$ 34.9	$ 26.4	$ 8.5	$ 67.6	$ 51.5	$ 16.1

During the three and six months ended June 30, 2021, total research and development expenses increased by $8.5 million and $16.1 million, respectively, compared to the three and six months ended June 30, 2020. The increase in both the three and six months ended June 30, 2021 relates to increases in clinical trial expenses and discovery research activities related to tazemetostat in other indications, which were offset by decreases in costs associated with the build-out of our regulatory and late-stage development groups.

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

Product Program	Three Months Ended June 30,			Six Months Ended June 30,		
	2021	2020	Change	2021	2020	Change
	(In millions)			(In millions)		
External research and development expenses:						
Tazemetostat and related EZH2 programs	$ 15.3	$ 10.1	$ 5.2	$ 27.0	$ 18.7	$ 8.3
Discovery and preclinical stage product programs, collectively	5.9	3.1	2.8	11.7	6.8	4.9
Unallocated personnel and other expenses	13.7	13.2	0.5	28.9	26.0	2.9
Total research and development expenses	$ 34.9	$ 26.4	$ 8.5	$ 67.6	$ 51.5	$ 16.1

External research and development costs 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 program and expenses associated with our companion diagnostic program.

External research and development expenses for tazemetostat and related EZH2 programs increased $5.2 million and $8.3 million, respectively, for the three and six months ended June 30, 2021 compared to the three and six months ended June 30, 2020. The increase for the three and six months ended June 30, 2021 relates to increases in clinical trial expenses and discovery research activities related to tazemetostat in other indications, which were offset by decreases in costs associated with the build-out of our regulatory and late-stage development groups.

External research and development expenses for discovery and preclinical stage product programs increased $2.9 million and $4.9 million, respectively, for the three and six months ended June 30, 2021 compared to the three and six months ended June 30, 2020, primarily related to increased spending for discovery research activities and development activities related to our preclinical programs.

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 and six months ended June 30, 2021 increased $0.5 million and $2.8 million, respectively, compared to the three and six months ended June 30, 2020. The increase is a result of increases in facilities and equipment related expenses and in unallocated personnel costs, offset by an increase in the allocation of expenses to projects.

We expect that research and development expenses will decrease in the second half of 2021, as we implement our operating expense reductions and prioritize our investment of company resources in what we believe to be our most important value-driving clinical trials and programs, including our EZH-302, EZH-1401, EZH-1101, and two proposed basket studies and our EZM0414 program.

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 and six months ended June 30, 2021 and 2020:

	Three Months Ended June 30,			Six Months Ended June 30,		
	2021	2020	Change	2021	2020	Change
	(In millions)			(In millions)		
Selling, general and administrative	$ 33.9	$ 32.7	$ 1.2	$ 70.3	$ 59.6	$ 10.7

For the three and six months ended June 30, 2021, our selling, general and administrative expenses increased $1.2 million and $10.7 million, respectively, compared to the three and six months ended June 30, 2020. The increase for the three and six months ended June 30, 2021 compared to the three and six months ended June 30, 2020 is due to increased commercialization activities, including the build-out of our sales force and commercial infrastructure to support the commercial launch of TAZVERIK in the approved ES and FL indications in 2020, and increased personnel related expenses.

We expect that selling, general and administrative expenses will decrease in the second half of 2021, 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 and six months ended June 30, 2021 and 2020:

	Three Months Ended June 30,			Six Months Ended June 30,		
	2021	2020	Change	2021	2020	Change
	(In millions)			(In millions)		
Other (expense) income, net						
Interest income	$ 0.0	$ 0.8	$ (0.8)	$ 0.1	$ 2.3	$ (2.2)
Interest expense	(5.6)	(1.3)	(4.3)	(11.1)	(2.1)	(9.0)
Other income (expense), net	(0.0)	(0.0)	(0.0)	(0.1)	(0.1)	0.0
Non-cash interest expense related to sale of future royalties	(0.5)	(0.3)	(0.2)	(1.0)	(0.6)	(0.4)
Other (expense) income, net	$ (6.1)	$ (0.8)	$ (5.3)	$ (12.1)	$ (0.5)	$ (11.6)

Other (expense) income, net consists of interest income earned on our cash equivalents and marketable securities. The increase in other expense for the three months ended June 30, 2021 is principally due to an increase in interest expense of $4.3 million incurred in connection with our long-term debt obligations under our Amended and Restated Loan Agreement and an increase in non-cash interest expense related to the sale of future royalties of $0.2 million. The increase in other expense for the six months ended June 30, 2021 is principally due to an increase in interest expense of $9.0 million incurred in connection with our long-term debt obligations under our Amended and Restated Loan Agreement, and an increase in non-cash interest expense related to the sale of future royalties of $0.4 million.

Income Tax Expense

We did not record a federal or state income tax provision or benefit for the three and six months ended June 30, 2021 and 2020 due to the expected and known loss before income taxes to be incurred, or incurred, as applicable, for the years ended December 31, 2021 and 2020, 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 June 30, 2021, in addition to revenues from product sales, we have raised an aggregate of $1,528.9 million to fund our operations. This includes $243.8 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), $841.0 million from the sale of common stock and series A convertible 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 June 30, 2021, we had $244.0 million in cash, cash equivalents and marketable securities.

On May 6, 2021, we entered into an Open Market Sale Agreement℠, or ATM Sale Agreement, with Jefferies LLC, or 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, which we refer to as 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. Through June 30, 2021, we have sold 182,866 shares of our common stock under the ATM Offering resulting in net proceeds of approximately $1.5 million.

In November 2019, we raised approximately $123.1 million in net proceeds from the sale to RPI of 6,666,667 shares of our common stock, the Warrant and the Japan Royalty for, as well as from proceeds of the Tranche A Loan borrowings under the Loan Agreement. 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 March 27, 2020, we received proceeds of the Tranche B Loan borrowings of $25.0 million under the Loan Agreement. On June 30, 2020, we received proceeds of the Tranche C Loan borrowings of $20.0 million under the Loan Agreement. On November 18, 2020 we received proceeds of the Tranche D Loan borrowings of $150.0 million under the Amended and Restated Loan Agreement.

In addition to our existing cash, cash equivalents and marketable securities, we are eligible to earn a significant amount of milestone payments under our collaboration agreement with GSK. 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 indications that we are exploring or that we may plan to explore. Because 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 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 which includes the anticipated savings resulting from the cost reduction plan we announced in August 2021, we expect that our existing cash, cash equivalents and marketable securities as of June 30, 2021, together with the cash we expect to generate from product sales, and the $25 million upfront payment to be received under our license agreement with HutchMed, 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 fourth quarter of 2022, without giving effect to any potential future milestone payments we may receive under our collaboration agreements with HutchMed or GSK. 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, and 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 six months ended June 30, 2021 and 2020:

	Six Months Ended June 30,		
	2021	2020	Change
	(In millions)		
Net cash (used in) operating activities	$ (132.2)	$ (110.7)	$ (21.5)
Net cash (used in) provided by investing activities	40.7	(12.8)	53.5
Net cash provided by financing activities	3.5	101.2	(97.7)

Net Cash Used in Operating Activities

Net cash used in operating activities was $132.2 million during the six months ended June 30, 2021 compared to $110.7 million during the six months ended June 30, 2020. The increase in net cash used in operating activities primarily relates to our net loss of $134.6 million and changes in working capital of $16.0 million, partially offset by net depreciation and amortization of $3.6 million, non-cash stock-based compensation of $13.7 million, and non-cash interest expense associated with the sale of future royalties of $0.9 million.

Net cash used in operating activities during the six months ended June 30, 2020 primarily relates to our net loss of $109.4 million and changes in working capital of $17.9 million, partially offset by net depreciation and amortization of $1.2 million, non-cash stock-based compensation of $14.8 million, and non-cash interest expense associated with the sale of future royalties of $0.6 million.

Net Cash (Used in) Provided by Investing Activities

Net cash used in investing activities during the six months ended June 30, 2021 reflects maturities of available-for-sale securities of $211.5 million, offset by $170.7 million of purchases of available-for-sale securities, and $0.2 million of purchases of property and equipment.

Net cash provided by investing activities during the six months ended June 30, 2020 reflects maturities of available-for-sale securities of $131.6 million, offset by $94.1 million of purchases of available-for-sale securities, a $25.0 million milestone payment under the Eisai collaboration agreement upon regulatory approval of tazemetostat for ES, a $25.0 million milestone payment under the Eisai collaboration agreement upon regulatory approval of tazemetostat for FL, and $0.3 million of purchases of property and equipment.

Net Cash Provided by Financing Activities

Net cash provided by financing activities of $3.5 million during the six months ended June 30, 2021 primarily reflects net proceeds from the sale of common stock under the ATM Sale Agreement of $1.5 million, the purchases of shares under our employee stock purchase plan of $1.2 million and stock option exercises of $0.9 million.

Net cash provided by financing activities of $101.2 million during the six months ended June 30, 2020 primarily reflects cash received from the sale of common stock of $50.0 million in connection with our exercise of our Put Option to sell shares of our common stock to RPI, net cash received during the period from Tranche B Loan borrowings of $25.0 million under the Loan Agreement, net cash received during the period from Tranche C Loan borrowings of $20.0 million under the Loan Agreement, stock option exercises of $5.8 million, and the purchases of shares under our employee stock purchase plan of $0.6 million, partially offset by payments of debt issuance costs of $0.1 million and offering costs of $0.1 million.

Contractual Obligations

There were no material changes to our contractual obligations and commitments described under “Management’s Discussion and Analysis and Results of Operations” in our Annual Report on Form 10-K for the fiscal year ended December 31, 2020.

Critical Accounting Policies and Use of Estimates

Our management’s discussion and analysis of financial condition and results of operations is based upon our condensed consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States of America. The preparation of these condensed 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, inventories 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 condensed 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, inventories, stock-based compensation and research and development expenses, including our accounting for clinical trial expenses and accruals. As our clinical development plan for tazemetostat progresses, we expect research and development expenses and, in particular, our accounting for clinical trial accruals to be an increasingly important critical accounting policy.

Except as described below with respect to intangible assets, net, during the six months ended June 30, 2021, there have been no material changes with respect to our critical accounting policies disclosed in our Annual Report on Form 10-K for our fiscal year ended December 31, 2020.

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 we 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 our consolidated balance sheets net of accumulated amortization and impairments, if applicable. The amortization expense is recognized as cost of product revenue in our consolidated statement of operations.

We assess our 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 our 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, we perform a recoverability test by comparing the sum of the estimated undiscounted cash flows of each intangible asset to its carrying value on the consolidated balance sheet. If the undiscounted cash flows used in the recoverability test are less than the carrying value, we 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.

Our assessment of the recoverability of our intangible assets requires the use of estimates, in particular the estimated future revenues to be generated from the intangible asset, as well as the direct costs associated with the revenues. Due to our 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 are not achieved, we may be required to perform future impairment analyses and record an impairment charge for the intangible asset in future periods.

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 June 30, 2021, we had cash and cash equivalents and marketable securities of $244.0 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 June 30, 2021 by $0.1 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 Chief Executive Officer) and the principal financial officer (our Executive Vice President, Chief Strategy and Business 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 Chief Executive Officer and Executive Vice President, Chief Strategy and Business Officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of June 30, 2021.

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 June 30, 2021 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, 2020, or the 2020 10-K and in Part II, Item 1A. "Risk Factors" in our Quarterly Report on Form 10-Q for the quarter ended March 31, 2021, or the Q1 2021 10-Q. Any of the risk factors contained in this Quarterly Report on Form 10-Q, the Q1 2021 10-Q and the 2020 10-K 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 Q1 2021 10 A and the 2020 10-K, and the risk factor disclosure in the Q1 2021 10 A and the 2020 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.

Our recent changes to our commercial strategy and organization, adjustments to our operating plans, including operating expense reductions, and leadership transition that were announced in August 2021 may not be successful, may not result in accelerated commercial adoption of TAZVERIK and greater product revenues or anticipated savings, could result in total costs and expenses that are greater than expected and could disrupt our business.

On August 9, 2021, we announced changes to our leadership team with the resignation of our President and Chief Executive Officer, Robert Bazemore, and the appointment of Grant Bogle, a member of our board of directors since September 2019, as President and Chief Executive Officer, each effective as of August 9, 2021. Mr. Bazemore will move into a consultancy role, serving as an advisor to the Company, and in particular to Mr. Bogle, for 12 months to assist with the transition.

In addition, on August 9, 2021, we announced changes to our commercial strategy and organization in an effort to accelerate commercial adoption of TAZVERIK as well as a broader operational cost reduction plan. As part of our cost reduction plan, we are implementing a cross-functional reduction of approximately 11% of our current workforce.

We may not realize, in full or in part, the anticipated benefits, savings and improvements from these changes. For instance, the changes to our commercial strategy and organization may not result in accelerated commercial adoption of TAZVERIK or greater product revenues. We believe that the commercial launch has been adversely affected by the COVID-19 pandemic and may continue to be adversely affected by the pandemic. In addition, market acceptance of TAZVERIK and product revenues have been adversely impacted by other factors, including competitive therapies and the use of our patient assistance program, which our changes may not address. The reduction in the size of our field organization and the planned transition of our Chief Commercial Officer may also limit the success of our refined strategy.

Our organizational changes, operating plan adjustments and operating expense reductions also may not be successful. If we are unable to realize the expected operational efficiencies and cost savings from these recent changes, our operating results and financial condition would be adversely affected. We also cannot ensure that we will not have to undertake additional workforce reductions or other cost-cutting measures in the future. Furthermore, these recent changes as well as the leadership transition may be disruptive to our operations. For example, our workforce reductions and leadership changes could yield unanticipated consequences, such as attrition beyond planned staff reductions and negative impact on employee morale or could make it more difficult to fulfill our day-to-day operations. Our workforce reductions and leadership changes could also harm our ability to attract and retain qualified management, scientific, clinical, manufacturing and sales and marketing personnel who are critical to our business. Year to date, our annualized turnover rate is higher than in prior years and these changes could further that trend. Any failure to attract or retain qualified personnel could prevent us from successfully commercializing TAZVERIK and discovering and developing any other future products or product candidates in the future.

We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.

The development and commercialization of new drug products is highly competitive. We face competition with respect to tazemetostat, and will likely face competition with respect to any product candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of many of the indications for which we are selling TAZVERIK and for which we are developing tazemetostat. Some of these competitive products and therapies are based on scientific approaches that are the same as or

similar to our approach, and others are based on entirely different approaches. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization of pharmaceutical products that may compete with our products or product candidates. Tazemetostat and any future product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

In the relapsed and refractory FL patient setting, both current and near-term competition exists. The most common current treatments for FL are chemotherapies, usually combined with the CD-20 antibodies Rituxan or Gazyva. Multiple PI3K therapies, such as idelalisib (ZYDELIG), copanlisib (ALIQOPA), duvelisib (COPIKTRA), and umbralisib (UKONIQ) are approved for patients with relapsed/refractory FL. These therapies are utilized predominantly in the third line or later treatment. While CD20 and PI3K therapies are approved in FL, there are no therapies that are approved specifically for the treatment of tumors associated with EZH2 activating mutations. There are a number of companies currently evaluating investigational agents in the relapsed and refractory follicular lymphoma patient setting including the development of CAR-T therapies and bispecific monoclonal antibodies. In the first quarter of 2021, Kite Pharma, a subsidiary of Gilead Sciences, received FDA approval for its CAR-T therapy, YESCARTA, for the treatment of relapsed or refractory FL patients.

In the ES patient setting, there are no therapies approved specifically for epithelioid sarcoma, other than TAZVERIK. Most of the approved therapies utilized in ES are more broadly approved for soft tissue sarcoma in general. Furthermore, the only therapies in late stage clinical trials are being developed broadly for the treatment of soft tissue sarcoma as well.

There are a large number of companies developing or marketing treatments for cancer, including many major pharmaceutical and biotechnology companies. Companies that are developing new epigenetic treatments for cancer that target histone methyltransferases, or HMTs, and protein arginine methyltransferases, or PRMTs, include GSK, Johnson & Johnson, Pfizer, Inc., Daiichi Sankyo Company Limited, and Constellation Pharmaceuticals. Further, companies which are known to have EZH2 inhibitor programs or related programs include: Constellation Pharmaceuticals, developing an EZH2 inhibitor (CPI-0209, Phase 1/2 for advanced tumors (solid tumors and diffuse large B-cell lymphoma, or DLBCL)); Novartis AG, developing an EED inhibitor which indirectly blocks EZH2 (MAK683, Phase 1/2 for advanced malignancies (DLBCL)); Daiichi Sankyo, developing a EZH1/EZH2 dual inhibitor (valemetostat, DS-3201, Phase 1 for relapsed or refractory non-Hodgkin lymphomas, as well as Phase 2 for small cell lung cancer and relapsed or refractory adult T-cell leukemia/lymphoma); Pfizer, developing an EZH2 inhibitor (PF-06821497, Phase 1 for relapsed or refractory small cell lung cancer, castration-resistant prostate cancer, FL and diffuse large B-cell lymphoma); and Jiangsu Hengrui Pharmaceutical, developing an EZH2 inhibitor (SHR2554, Phase 2 for B-cell malignancies) in China. In addition, many companies are developing cancer therapeutics that work by targeting epigenetic mechanisms other than HMTs, including Celgene Corporation (now part of Bristol-Myers Squibb), or Celgene, Merck & Co., Inc., Secura Bio, Spectrum Pharmaceuticals, and Otsuka Pharmaceuticals Co., Ltd., which are marketing cancer treatments that work by targeting epigenetic mechanisms other than HMTs.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than tazemetostat for ES, FL or any indication for which we may develop tazemetostat or any other products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for tazemetostat for any future indication for which we may develop tazemetostat or any other product we may develop, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic products. Generic products are currently on the market for many of the indications that we are pursuing, and additional products are expected to become available on a generic basis over the coming years. We expect that tazemetostat will continue to be priced at a significant premium over competitive generic products.

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do.

Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

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
3.1	Certificate of Amendment of Restated Certificate of Incorporation of the Company, as amended. (1)
31.1	Certification of Principal Executive 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)
31.2	Certification of 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 Robert B. Bazemore, President and Chief Executive Officer of the Company, and Matthew Ros, Executive Vice President 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: August 9, 2021

EPIZYME, INC.

By: /s/ Matthew Ros
Matthew Ros
Executive Vice President, Chief Strategy and Business Officer
(Principal Financial Officer)

Exhibit 3.1

RESTATED CERTIFICATE OF INCORPORATION

OF

EPIZYME, INC.

Epizyme, Inc. (the "Corporation"), a corporation organized and existing under the General Corporation Law of the State of Delaware (the "DGCL"), does hereby certify that:

That the name of the Corporation is Epizyme, Inc. The original Certificate of Incorporation of the Corporation was filed with the Secretary of State of the State of Delaware on November 1, 2007, was amended on November 7, 2007, was further amended on November 16, 2007, was amended and restated on February 28, 2008, was further amended and restated on September 17, 2009, was further amended and restated on December 4, 2009, was further amended and restated on April 2, 2012 and was further amended on May 13, 2013.

A resolution was duly adopted by the Board of Directors of the Corporation pursuant to Sections 242 and 245 of the DGCL proposing this Restated Certificate of Incorporation and declaring the advisability of this Restated Certificate of Incorporation. The stockholders of the Corporation duly approved and adopted this Restated Certificate of Incorporation by written consent in accordance with Sections 228, 242 and 245 of the DGCL.

Accordingly, the Certificate of Incorporation of this Corporation, as previously amended and restated, is hereby further amended and restated in its entirety to read as follows.

FIRST: The name of the Corporation is Epizyme, Inc.

SECOND: The address of the Corporation's registered office in the State of Delaware is Corporation Trust Center, 1209 Orange Street, in the City of Wilmington, County of New Castle, 19801. The name of its registered agent at that address is The Corporation Trust Company.

THIRD: The nature of the business or purposes to be conducted or promoted by the Corporation is to engage in any lawful act or activity for which corporations may be organized under the General Corporation Law of the State of Delaware.

FOURTH: The total number of shares of all classes of stock which the Corporation shall have authority to issue is 130,000,000 shares, consisting of (i) 125,000,000 shares of Common Stock, $.0001 par value per share ("Common Stock"), and (ii) 5,000,000 shares of Preferred Stock, $.0001 par value per share ("Preferred Stock").

The following is a statement of the designations and the powers, privileges and rights, and the qualifications, limitations or restrictions thereof in respect of each class of capital stock of the Corporation.

A COMMON STOCK.

1. General. The voting, dividend and liquidation rights of the holders of the Common Stock are subject to and qualified by the rights of the holders of the Preferred Stock of any series as may be designated by the Board of Directors of the Corporation (the "Board of Directors") upon any issuance of the Preferred Stock of any series.

2. Voting. The holders of the Common Stock shall have voting rights at all meetings of stockholders, each such holder being entitled to one vote for each share thereof held by such holder; provided, however, that, except as otherwise required by law, holders of Common Stock shall not be entitled to vote on any amendment to this Certificate of Incorporation (which, as used herein, shall mean the certificate of incorporation of the Corporation, as amended from time to time, including the terms of any certificate of designations of any series of Preferred Stock) that relates solely to the terms of one or more outstanding series of Preferred Stock if the holders of such affected series are entitled, either separately or together as a class with the holders of one or more other such series, to vote thereon pursuant to this Certificate of Incorporation. There shall be no cumulative voting.

The number of authorized shares of Common Stock may be increased or decreased (but not below the number of shares thereof then outstanding) by the affirmative vote of the holders of a majority of the stock of the

Corporation entitled to vote, irrespective of the provisions of Section 242(b)(2) of the General Corporation Law of the State of Delaware.

3. Dividends. Dividends may be declared and paid on the Common Stock from funds lawfully available therefor as and when determined by the Board of Directors and subject to any preferential dividend or other rights of any then outstanding Preferred Stock.

4. Liquidation. Upon the dissolution or liquidation of the Corporation, whether voluntary or involuntary, holders of Common Stock will be entitled to receive all assets of the Corporation available for distribution to its stockholders, subject to any preferential or other rights of any then outstanding Preferred Stock.

B PREFERRED STOCK.

Preferred Stock may be issued from time to time in one or more series, each of such series to have such terms as stated or expressed herein and in the resolution or resolutions providing for the issue of such series adopted by the Board of Directors as hereinafter provided. Any shares of Preferred Stock which may be redeemed, purchased or acquired by the Corporation may be reissued except as otherwise provided by law.

Authority is hereby expressly granted to the Board of Directors from time to time to issue the Preferred Stock in one or more series, and in connection with the creation of any such series, by adopting a resolution or resolutions providing for the issuance of the shares thereof and by filing a certificate of designations relating thereto in accordance with the General Corporation Law of the State of Delaware, to determine and fix the number of shares of such series and such voting powers, full or limited, or no voting powers, and such designations, preferences and relative participating, optional or other special rights, and qualifications, limitations or restrictions thereof, including without limitation thereof, dividend rights, conversion rights, redemption privileges and liquidation preferences, as shall be stated and expressed in such resolutions, all to the full extent now or hereafter permitted by the General Corporation Law of the State of Delaware. Without limiting the generality of the foregoing, the resolutions providing for issuance of any series of Preferred Stock may provide that such series shall be superior or rank equally or be junior to any other series of Preferred Stock to the extent permitted by law.

The number of authorized shares of Preferred Stock may be increased or decreased (but not below the number of shares then outstanding) by the affirmative vote of the holders of a majority of the voting power of the capital stock of the Corporation entitled to vote thereon, voting as a single class, irrespective of the provisions of Section 242(b)(2) of the General Corporation Law of the State of Delaware.

FIFTH: Except as otherwise provided herein, the Corporation reserves the right to amend, alter, change or repeal any provision contained in this Certificate of Incorporation, in the manner now or hereafter prescribed by statute and this Certificate of Incorporation, and all rights conferred upon stockholders herein are granted subject to this reservation.

SIXTH: In furtherance and not in limitation of the powers conferred upon it by the General Corporation Law of the State of Delaware, and subject to the terms of any series of Preferred Stock, the Board of Directors shall have the power to adopt, amend, alter or repeal the By-laws of the Corporation by the affirmative vote of a majority of the directors present at any regular or special meeting of the Board of Directors at which a quorum is present. The stockholders may not adopt, amend, alter or repeal the By-laws of the Corporation, or adopt any provision inconsistent therewith, unless such action is approved, in addition to any other vote required by this Certificate of Incorporation, by the affirmative vote of the holders of at least seventy-five percent (75%) of the votes that all the stockholders would be entitled to cast in any annual election of directors or class of directors. Notwithstanding any other provisions of law, this Certificate of Incorporation or the By-laws of the Corporation, and notwithstanding the fact that a lesser percentage may be specified by law, the affirmative vote of the holders of at least seventy-five percent (75%) of the votes which all the stockholders would be entitled to cast in any annual election of directors or class of directors shall be required to amend or repeal, or to adopt any provision inconsistent with, this Article SIXTH.

SEVENTH: Except to the extent that the General Corporation Law of the State of Delaware prohibits the elimination or limitation of liability of directors for breaches of fiduciary duty, no director of the Corporation shall be personally liable to the Corporation or its stockholders for monetary damages for any breach of fiduciary duty as a director, notwithstanding any provision of law imposing such liability. No amendment to or repeal of this

provision shall apply to or have any effect on the liability or alleged liability of any director of the Corporation for or with respect to any acts or omissions of such director occurring prior to such amendment or repeal. If the General Corporation Law of the State of Delaware is amended to permit further elimination or limitation of the personal liability of directors, then the liability of a director of the Corporation shall be eliminated or limited to the fullest extent permitted by the General Corporation Law of the State of Delaware as so amended.

EIGHTH: The Corporation shall provide indemnification as follows:

1. Actions, Suits and Proceedings Other than by or in the Right of the Corporation. The Corporation shall indemnify each person who was or is a party or threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of the Corporation) by reason of the fact that he or she is or was, or has agreed to become, a director or officer of the Corporation, or is or was serving, or has agreed to serve, at the request of the Corporation, as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise (including any employee benefit plan) (all such persons being referred to hereafter as an "Indemnitee"), or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys' fees), liabilities, losses, judgments, fines (including excise taxes and penalties arising under the Employee Retirement Income Security Act of 1974), and amounts paid in settlement actually and reasonably incurred by or on behalf of Indemnitee in connection with such action, suit or proceeding and any appeal therefrom, if Indemnitee acted in good faith and in a manner which Indemnitee reasonably believed to be in, or not opposed to, the best interests of the Corporation, and, with respect to any criminal action or proceeding, had no reasonable cause to believe his or her conduct was unlawful. The termination of any action, suit or proceeding by judgment, order, settlement, conviction or upon a plea of nolo contendere or its equivalent, shall not, of itself, create a presumption that Indemnitee did not act in good faith and in a manner which Indemnitee reasonably believed to be in, or not opposed to, the best interests of the Corporation, and, with respect to any criminal action or proceeding, had reasonable cause to believe that his or her conduct was unlawful.

2. Actions or Suits by or in the Right of the Corporation. The Corporation shall indemnify any Indemnitee who was or is a party to or threatened to be made a party to any threatened, pending or completed action or suit by or in the right of the Corporation to procure a judgment in its favor by reason of the fact that Indemnitee is or was, or has agreed to become, a director or officer of the Corporation, or is or was serving, or has agreed to serve, at the request of the Corporation, as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise (including any employee benefit plan), or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys' fees) and, to the extent permitted by law, amounts paid in settlement actually and reasonably incurred by or on behalf of Indemnitee in connection with such action, suit or proceeding and any appeal therefrom, if Indemnitee acted in good faith and in a manner which Indemnitee reasonably believed to be in, or not opposed to, the best interests of the Corporation, except that no indemnification shall be made under this Section 2 in respect of any claim, issue or matter as to which Indemnitee shall have been adjudged to be liable to the Corporation, unless, and only to the extent, that the Court of Chancery of Delaware or the court in which such action or suit was brought shall determine upon application that, despite the adjudication of such liability but in view of all the circumstances of the case, Indemnitee is fairly and reasonably entitled to indemnity for such expenses (including attorneys' fees) which the Court of Chancery of Delaware or such other court shall deem proper.

3. Indemnification for Expenses of Successful Party. Notwithstanding any other provisions of this Article EIGHTH, to the extent that an Indemnitee has been successful, on the merits or otherwise, in defense of any action, suit or proceeding referred to in Sections 1 and 2 of this Article EIGHTH, or in defense of any claim, issue or matter therein, or on appeal from any such action, suit or proceeding, Indemnitee shall be indemnified against all expenses (including attorneys' fees) actually and reasonably incurred by or on behalf of Indemnitee in connection therewith. Without limiting the foregoing, if any action, suit or proceeding is disposed of, on the merits or otherwise (including a disposition without prejudice), without (i) the disposition being adverse to Indemnitee, (ii) an adjudication that Indemnitee was liable to the Corporation, (iii) a plea of guilty or nolo contendere by Indemnitee, (iv) an adjudication that Indemnitee did not act in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of the Corporation, and (v) with respect to any criminal proceeding, an adjudication that Indemnitee had reasonable cause to believe his or her conduct was unlawful, Indemnitee shall be considered for the purposes hereof to have been wholly successful with respect thereto.

4. Notification and Defense of Claim. As a condition precedent to an Indemnitee's right to be indemnified, such Indemnitee must notify the Corporation in writing as soon as practicable of any action, suit, proceeding or investigation involving such Indemnitee for which indemnity will or could be sought. With respect to any action, suit, proceeding or investigation of which the Corporation is so notified, the Corporation will be entitled to participate therein at its own expense and/or to assume the defense thereof at its own expense, with legal counsel reasonably acceptable to Indemnitee. After notice from the Corporation to Indemnitee of its election so to assume such defense, the Corporation shall not be liable to Indemnitee for any legal or other expenses subsequently incurred by Indemnitee in connection with such action, suit, proceeding or investigation, other than as provided below in this Section 4. Indemnitee shall have the right to employ his or her own counsel in connection with such action, suit, proceeding or investigation, but the fees and expenses of such counsel incurred after notice from the Corporation of its assumption of the defense thereof shall be at the expense of Indemnitee unless (i) the employment of counsel by Indemnitee has been authorized by the Corporation, (ii) counsel to Indemnitee shall have reasonably concluded that there may be a conflict of interest or position on any significant issue between the Corporation and Indemnitee in the conduct of the defense of such action, suit, proceeding or investigation or (iii) the Corporation shall not in fact have employed counsel to assume the defense of such action, suit, proceeding or investigation, in each of which cases the fees and expenses of counsel for Indemnitee shall be at the expense of the Corporation, except as otherwise expressly provided by this Article EIGHTH. The Corporation shall not be entitled, without the consent of Indemnitee, to assume the defense of any claim brought by or in the right of the Corporation or as to which counsel for Indemnitee shall have reasonably made the conclusion provided for in clause (ii) above. The Corporation shall not be required to indemnify Indemnitee under this Article EIGHTH for any amounts paid in settlement of any action, suit, proceeding or investigation effected without its written consent. The Corporation shall not settle any action, suit, proceeding or investigation in any manner which would impose any penalty or limitation on Indemnitee without Indemnitee's written consent. Neither the Corporation nor Indemnitee will unreasonably withhold or delay its consent to any proposed settlement.

5. Advance of Expenses. Subject to the provisions of Section 6 of this Article EIGHTH, in the event of any threatened or pending action, suit, proceeding or investigation of which the Corporation receives notice under this Article EIGHTH, any expenses (including attorneys' fees) incurred by or on behalf of an Indemnitee in defending an action, suit, proceeding or investigation or any appeal therefrom shall be paid by the Corporation in advance of the final disposition of such matter; provided, however, that the payment of such expenses incurred by or on behalf of Indemnitee in advance of the final disposition of such matter shall be made only upon receipt of an undertaking by or on behalf of Indemnitee to repay all amounts so advanced in the event that it shall ultimately be determined by final judicial decision from which there is no further right to appeal that Indemnitee is not entitled to be indemnified by the Corporation as authorized in this Article EIGHTH; and provided further that no such advancement of expenses shall be made under this Article EIGHTH if it is determined (in the manner described in Section 6) that (i) Indemnitee did not act in good faith and in a manner he or she reasonably believed to be in, or not opposed to, the best interests of the Corporation, or (ii) with respect to any criminal action or proceeding, Indemnitee had reasonable cause to believe his or her conduct was unlawful. Such undertaking shall be accepted without reference to the financial ability of Indemnitee to make such repayment.

6. Procedure for Indemnification and Advancement of Expenses. In order to obtain indemnification or advancement of expenses pursuant to Section 1, 2, 3 or 5 of this Article EIGHTH, an Indemnitee shall submit to the Corporation a written request. Any such advancement of expenses shall be made promptly, and in any event within 60 days after receipt by the Corporation of the written request of Indemnitee, unless (i) the Corporation has assumed the defense pursuant to Section 4 of this Article EIGHTH (and none of the circumstances described in Section 4 of this Article EIGHTH that would nonetheless entitle the Indemnitee to indemnification for the fees and expenses of separate counsel have occurred) or (ii) the Corporation determines within such 60-day period that Indemnitee did not meet the applicable standard of conduct set forth in Section 1, 2 or 5 of this Article EIGHTH, as the case may be. Any such indemnification, unless ordered by a court, shall be made with respect to requests under Section 1 or 2 only as authorized in the specific case upon a determination by the Corporation that the indemnification of Indemnitee is proper because Indemnitee has met the applicable standard of conduct set forth in Section 1 or 2, as the case may be. Such determination shall be made in each instance (a) by a majority vote of the directors of the Corporation consisting of persons who are not at that time parties to the action, suit or proceeding in question ("disinterested directors"), whether or not a quorum, (b) by a committee of disinterested directors designated by majority vote of disinterested directors, whether or not a quorum, (c) if there are no disinterested directors, or if the

disinterested directors so direct, by independent legal counsel (who may, to the extent permitted by law, be regular legal counsel to the Corporation) in a written opinion, or (d) by the stockholders of the Corporation.

7. Remedies. The right to indemnification or advancement of expenses as granted by this Article EIGHTH shall be enforceable by Indemnitee in any court of competent jurisdiction. Neither the failure of the Corporation to have made a determination prior to the commencement of such action that indemnification is proper in the circumstances because Indemnitee has met the applicable standard of conduct, nor an actual determination by the Corporation pursuant to Section 6 of this Article EIGHTH that Indemnitee has not met such applicable standard of conduct, shall be a defense to the action or create a presumption that Indemnitee has not met the applicable standard of conduct. In any suit brought by Indemnitee to enforce a right to indemnification, or brought by the Corporation to recover an advancement of expenses pursuant to the terms of an undertaking, the Corporation shall have the burden of proving that Indemnitee is not entitled to be indemnified, or to such advancement of expenses, under this Article EIGHTH. Indemnitee's expenses (including attorneys' fees) reasonably incurred in connection with successfully establishing Indemnitee's right to indemnification, in whole or in part, in any such proceeding shall also be indemnified by the Corporation. Notwithstanding the foregoing, in any suit brought by Indemnitee to enforce a right to indemnification hereunder it shall be a defense that the Indemnitee has not met any applicable standard for indemnification set forth in the General Corporation Law of the State of Delaware.

8. Limitations. Notwithstanding anything to the contrary in this Article EIGHTH, except as set forth in Section 7 of this Article EIGHTH, the Corporation shall not indemnify an Indemnitee pursuant to this Article EIGHTH in connection with a proceeding (or part thereof) initiated by such Indemnitee unless the initiation thereof was approved by the Board of Directors. Notwithstanding anything to the contrary in this Article EIGHTH, the Corporation shall not indemnify an Indemnitee to the extent such Indemnitee is reimbursed from the proceeds of insurance, and in the event the Corporation makes any indemnification payments to an Indemnitee and such Indemnitee is subsequently reimbursed from the proceeds of insurance, such Indemnitee shall promptly refund indemnification payments to the Corporation to the extent of such insurance reimbursement.

9. Subsequent Amendment. No amendment, termination or repeal of this Article EIGHTH or of the relevant provisions of the General Corporation Law of the State of Delaware or any other applicable laws shall adversely affect or diminish in any way the rights of any Indemnitee to indemnification under the provisions hereof with respect to any action, suit, proceeding or investigation arising out of or relating to any actions, transactions or facts occurring prior to the final adoption of such amendment, termination or repeal.

10. Other Rights. The indemnification and advancement of expenses provided by this Article EIGHTH shall not be deemed exclusive of any other rights to which an Indemnitee seeking indemnification or advancement of expenses may be entitled under any law (common or statutory), agreement or vote of stockholders or disinterested directors or otherwise, both as to action in Indemnitee's official capacity and as to action in any other capacity while holding office for the Corporation, and shall continue as to an Indemnitee who has ceased to be a director or officer, and shall inure to the benefit of the estate, heirs, executors and administrators of Indemnitee. Nothing contained in this Article EIGHTH shall be deemed to prohibit, and the Corporation is specifically authorized to enter into, agreements with officers and directors providing indemnification rights and procedures different from those set forth in this Article EIGHTH. In addition, the Corporation may, to the extent authorized from time to time by its Board of Directors, grant indemnification rights to other employees or agents of the Corporation or other persons serving the Corporation and such rights may be equivalent to, or greater or less than, those set forth in this Article EIGHTH.

11. Partial Indemnification. If an Indemnitee is entitled under any provision of this Article EIGHTH to indemnification by the Corporation for some or a portion of the expenses (including attorneys' fees), liabilities, losses, judgments, fines (including excise taxes and penalties arising under the Employee Retirement Income Security Act of 1974) or amounts paid in settlement actually and reasonably incurred by or on behalf of Indemnitee in connection with any action, suit, proceeding or investigation and any appeal therefrom but not, however, for the total amount thereof, the Corporation shall nevertheless indemnify Indemnitee for the portion of such expenses (including attorneys' fees), liabilities, losses, judgments, fines (including excise taxes and penalties arising under the Employee Retirement Income Security Act of 1974) or amounts paid in settlement to which Indemnitee is entitled.

12. Insurance. The Corporation may purchase and maintain insurance, at its expense, to protect itself and any director, officer, employee or agent of the Corporation or another corporation, partnership, joint venture, trust or other enterprise (including any employee benefit plan) against any expense, liability or loss incurred by him or her in

any such capacity, or arising out of his or her status as such, whether or not the Corporation would have the power to indemnify such person against such expense, liability or loss under the General Corporation Law of the State of Delaware.

13. Savings Clause. If this Article EIGHTH or any portion hereof shall be invalidated on any ground by any court of competent jurisdiction, then the Corporation shall nevertheless indemnify each Indemnitee as to any expenses (including attorneys' fees), liabilities, losses, judgments, fines (including excise taxes and penalties arising under the Employee Retirement Income Security Act of 1974) and amounts paid in settlement in connection with any action, suit, proceeding or investigation, whether civil, criminal or administrative, including an action by or in the right of the Corporation, to the fullest extent permitted by any applicable portion of this Article EIGHTH that shall not have been invalidated and to the fullest extent permitted by applicable law.

14. Definitions. Terms used herein and defined in Section 145(h) and Section 145(i) of the General Corporation Law of the State of Delaware shall have the respective meanings assigned to such terms in such Section 145(h) and Section 145(i).

NINTH: This Article NINTH is inserted for the management of the business and for the conduct of the affairs of the Corporation.

1. General Powers. The business and affairs of the Corporation shall be managed by or under the direction of the Board of Directors.

2. Number of Directors; Election of Directors. Subject to the rights of holders of any series of Preferred Stock to elect directors, the number of directors of the Corporation shall be established by the Board of Directors. Election of directors need not be by written ballot, except as and to the extent provided in the By-laws of the Corporation.

3. Classes of Directors. Subject to the rights of holders of any series of Preferred Stock to elect directors, the Board of Directors shall be and is divided into three classes, designated Class I, Class II and Class III. Each class shall consist, as nearly as may be possible, of one-third of the total number of directors constituting the entire Board of Directors. The Board of Directors is authorized to assign members of the Board of Directors already in office to Class I, Class II or Class III at the time such classification becomes effective.

4. Terms of Office. Subject to the rights of holders of any series of Preferred Stock to elect directors, each director shall serve for a term ending on the date of the third annual meeting of stockholders following the annual meeting of stockholders at which such director was elected; provided that each director initially assigned to Class I shall serve for a term expiring at the Corporation's first annual meeting of stockholders held after the effectiveness of this Restated Certificate of Incorporation; each director initially assigned to Class II shall serve for a term expiring at the Corporation's second annual meeting of stockholders held after the effectiveness of this Restated Certificate of Incorporation; and each director initially assigned to Class III shall serve for a term expiring at the Corporation's third annual meeting of stockholders held after the effectiveness of this Restated Certificate of Incorporation; provided further, that the term of each director shall continue until the election and qualification of his or her successor and be subject to his or her earlier death, resignation or removal.

5. Quorum. The greater of (a) a majority of the directors at any time in office and (b) one-third of the number of directors fixed pursuant to Section 2 of this Article NINTH shall constitute a quorum of the Board of Directors. If at any meeting of the Board of Directors there shall be less than such a quorum, a majority of the directors present may adjourn the meeting from time to time without further notice other than announcement at the meeting, until a quorum shall be present.

6. Action at Meeting. Every act or decision done or made by a majority of the directors present at a meeting duly held at which a quorum is present shall be regarded as the act of the Board of Directors unless a greater number is required by law or by this Certificate of Incorporation.

7. Removal. Subject to the rights of holders of any series of Preferred Stock, directors of the Corporation may be removed only for cause and only by the affirmative vote of the holders of at least seventy-five percent (75%) of the votes which all the stockholders would be entitled to cast in any annual election of directors or class of directors.

8. Vacancies. Subject to the rights of holders of any series of Preferred Stock, any vacancy or newly created directorship in the Board of Directors, however occurring, shall be filled only by vote of a majority of the directors then in office, although less than a quorum, or by a sole remaining director and shall not be filled by the stockholders. A director elected to fill a vacancy shall hold office until the next election of the class for which such director shall have been chosen, subject to the election and qualification of a successor and to such director's earlier death, resignation or removal.

9. Stockholder Nominations and Introduction of Business, Etc. Advance notice of stockholder nominations for election of directors and other business to be brought by stockholders before a meeting of stockholders shall be given in the manner provided by the By-laws of the Corporation.

10. Amendments to Article. Notwithstanding any other provisions of law, this Certificate of Incorporation or the By-laws of the Corporation, and notwithstanding the fact that a lesser percentage may be specified by law, the affirmative vote of the holders of at least seventy-five percent (75%) of the votes which all the stockholders would be entitled to cast in any annual election of directors or class of directors shall be required to amend or repeal, or to adopt any provision inconsistent with, this Article NINTH.

TENTH: Stockholders of the Corporation may not take any action by written consent in lieu of a meeting. Notwithstanding any other provisions of law, this Certificate of Incorporation or the By-laws of the Corporation, and notwithstanding the fact that a lesser percentage may be specified by law, the affirmative vote of the holders of at least seventy-five percent (75%) of the votes which all the stockholders would be entitled to cast in any annual election of directors or class of directors shall be required to amend or repeal, or to adopt any provision inconsistent with, this Article TENTH.

ELEVENTH: Special meetings of stockholders for any purpose or purposes may be called at any time by only the Board of Directors, the Chairman of the Board of Directors or the Chief Executive Officer of the Corporation, and may not be called by any other person or persons. Business transacted at any special meeting of stockholders shall be limited to matters relating to the purpose or purposes stated in the notice of meeting. Notwithstanding any other provisions of law, this Certificate of Incorporation or the By-laws of the Corporation, and notwithstanding the fact that a lesser percentage may be specified by law, the affirmative vote of the holders of at least seventy-five percent (75%) of the votes which all the stockholders would be entitled to cast in any annual election of directors or class of directors shall be required to amend or repeal, or to adopt any provision inconsistent with, this Article ELEVENTH.

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IN WITNESS WHEREOF, this Restated Certificate of Incorporation, which restates, integrates and amends the certificate of incorporation of the Corporation, and which has been duly adopted in accordance with Sections 228, 242 and 245 of the General Corporation Law of the State of Delaware, has been executed by its duly authorized officer this fifth day of June, 2013.

EPIZYME, INC.

By: /s/ Robert J. Gould
Robert J. Gould
President and Chief Executive Officer

CERTIFICATE OF AMENDMENT OF

RESTATED CERTIFICATE OF INCORPORATION

OF

EPIZYME, INC.

(Pursuant to Section 242 of the
General Corporation Law of the State of Delaware)

Epizyme, Inc. (the "Corporation"), a corporation organized and existing under and by virtue of the provisions of the General Corporation Law of the State of Delaware, does hereby certify as follows:

A resolution was duly adopted by the Board of Directors of the Corporation pursuant to Section 242 of the General Corporation Law of the State of Delaware setting forth a proposed amendment to the Restated Certificate of Incorporation of the Corporation and declaring said amendment to be advisable. The stockholders of the Corporation duly approved said proposed amendment in accordance with Section 242 of the General Corporation Law of the State of Delaware. The resolution setting forth the amendment is as follows:

RESOLVED: That the first sentence of Article FOURTH of the Restated Certificate of Incorporation of the Corporation be and hereby is deleted in its entirety and the following is inserted in lieu thereof:

"FOURTH: The total number of shares of all classes of stock which the Corporation shall have the authority to issue is 155,000,000 shares, consisting of (i) 150,000,000 shares of Common Stock, $0.0001 par value per share ("Common Stock"), and (ii) 5,000,000 shares of Preferred Stock, $0.0001 par value per share ("Preferred Stock")."

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IN WITNESS WHEREOF, this Certificate of Amendment has been executed by a duly authorized officer of the Corporation on this 29th day of May, 2020.

EPIZYME, INC.

By: /s/ Robert B. Bazemore
Name: Robert B. Bazemore
Title: Chief Executive Officer

CERTIFICATE OF AMENDMENT OF

RESTATED CERTIFICATE OF INCORPORATION

OF

EPIZYME, INC.

(Pursuant to Section 242 of the
General Corporation Law of the State of Delaware)

Epizyme, Inc. (the "Corporation"), a corporation organized and existing under and by virtue of the provisions of the General Corporation Law of the State of Delaware, does hereby certify as follows:

A resolution was duly adopted by the Board of Directors of the Corporation pursuant to Section 242 of the General Corporation Law of the State of Delaware setting forth a proposed Amendment to the Restated Certificate of Incorporation of the Corporation and declaring said amendment to be advisable. The stockholders of the Corporation duly approved said proposed amendment in accordance with Section 242 of the General Corporation Law of the State of Delaware. The resolution setting forth the amendment is as follows:

RESOLVED: That the first sentence of Article FOURTH of the Restated Certificate of Incorporation of the Corporation be and hereby is deleted in its entirety and the following is inserted in lieu thereof:

"FOURTH: The total number of shares of all classes of stock which the Corporation shall have the authority to issue is 230,000,000 shares, consisting of (i) 225,000,000 shares of Common Stock, $0.0001 par value per share ("Common Stock"), and (ii) 5,000,000 shares of Preferred Stock, $0.0001 par value per share ("Preferred Stock")."

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IN WITNESS WHEREOF, this Certificate of Amendment has been executed by a duly authorized officer of the Corporation on this 11th day of June, 2021.

EPIZYME, INC.

By: /s/ Robert B. Bazemore
Name: Robert B. Bazemore
Title: Chief Executive Officer

Exhibit 31.1

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

I, Robert B. Bazemore, 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 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 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: August 9, 2021

/s/ Robert B. Bazemore
Robert B. Bazemore
President and Chief Executive Officer

Exhibit 31.2

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

I, Matthew Ros, 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 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 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: August 9, 2021

/s/ Matthew Ros
Matthew Ros

Executive Vice President, Chief Strategy and Business Officer
(Principal Financial Officer)

Exhibit 32.1

**CERTIFICATIONS OF CEO 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 June 30, 2021, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), each of the undersigned, Robert B. Bazemore, President and Chief Executive Officer of the Company, and Matthew Ros, Executive Vice President, Chief Strategy and Business Officer (*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: August 9, 2021

/s/ Robert B. Bazemore

Robert B. Bazemore
President and Chief Executive Officer
(Principal Executive Officer)

/s/ Matthew Ros

Matthew Ros
Executive Vice President, Chief Strategy and Business Officer
(Principal Financial Officer)