ANNUAL REPORT

REWRITING TREATMENT

for cancer through novel epigenetic medicines

2020

Epizyme®

DEAR FELLOW STAKEHOLDERS,

2020 was an unpredictable yet pivotal year for Epizyme which encompassed remarkable progress toward our mission of re-writing treatment for cancer through novel epigenetic medicines.

We reached a critical milestone with the TAZVERIK® (tazemetostat) accelerated approvals in epithelioid sarcoma (ES), a solid tumor cancer, and follicular lymphoma (FL), a common hematological malignancy. These approvals made TAZVERIK the first and only treatment specifically indicated for ES patients and the first and only FDA-approved EZH2 inhibitor currently on the market and transformed Epizyme into a fully-integrated biopharmaceutical company.

We achieved these back-to-back FDA approvals within five months, launched TAZVERIK into ES and FL, continued to enroll additional clinical trials and advanced our preclinical pipeline while working almost entirely remotely and navigating through the chaos that characterized 2020.

I am proud of and grateful for all of my colleagues here at Epizyme, whose actions over the last year reflect a level of dedication that signals to people living with cancer, to the physicians treating them and to our shareholders, that our mission at Epizyme is something we take very seriously. It is because of their efforts that we were able to execute across our 2020 initiatives.

In the face of the ongoing COVID-19 pandemic, the launch of TAZVERIK has been anything but conventional. The challenges of launching any drug in a virtual environment with little to no direct access to customers is hard to overstate. This, combined with the unique impact the pandemic has had on the frequency with which physicians have been able to have in-office visits with their FL patients, has increased the time needed to build physician adoption of a new treatment option. Despite these challenges, we have demonstrated our ability to execute on numerous metrics, including generating high physician awareness of TAZVERIK among both academic and community oncologists, achieving a high promotional presence among target accounts, increasing the number of physicians prescribing TAZVERIK month over month, and ensuring broad payer coverage of TAZVERIK consistent with our label.

While we do not expect these challenges caused by the pandemic to reverse themselves immediately, these dynamics will not last forever.

As we look to the remainder of 2021 and beyond, we have high hopes and expectations for TAZVERIK commercial performance, clinical expansion and pipeline diversification. We recently held a "Vision Call" on March 2, 2021 where we outlined our strategy for the next five years. As part of the call, we provided an update for ongoing and planned clinical trials, including encouraging preliminary results from the safety run-in portion of our confirmatory EZH-302 study evaluating TAZVERIK plus R2 in relapsed / refractory FL patients and the Phase 1b safety run-in portion of our EZH-1101 study of TAZVERIK plus enzalutamide or abiraterone in patients with metastatic castration-resistant prostate cancer. We also shared insights on our next clinical candidate, an inhibitor of SETD2 which has potential application across multiple settings, including high risk t(4;14) multiple myeloma and in other B-cell malignancies such as large-cell lymphoma, as well as in combination with existing and emerging therapies including tazemetostat.

Ultimately, our vision is to continue to build a well-established, sustainable, oncology-focused biotechnology company. This vision is focused on four 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:

1. **Maximize our effectiveness** as a commercial organization to achieve adoption of TAZVERIK among as many eligible FL and ES patients as possible, including in earlier treatment lines and in combination regimens with the data to support this expanded use;

2. **Build on TAZVERIK's pipeline-in-a-drug potential**, demonstrating tazemetostat's benefit in additional hematological malignancies and solid tumors;

3. **Expand our pipeline and evolving oncology portfolio**, bringing novel oncology therapeutics into clinical development to maintain our position as a leader in epigenetics; and

4. **Leverage options to expand patient reach and increase shareholder value**, including through commercial, clinical and research collaborations.

To maximize global commercial adoption of TAZVERIK in FL and ES patients, we believe that we must continue to evolve our commercial model to be successful expanding adoption even during COVID-19 and to drive post-pandemic launch acceleration.

Supported by physician feedback, we believe TAZVERIK has the potential to become a backbone of therapy across all lines of treatment for patients suffering from FL. Due to its novel mechanism, durable responses, generally well-tolerated safety profile and oral administration, we believe TAZVERIK can be uniquely positioned as both monotherapy and a combination agent that patients can take over an extended period. Our ongoing FL trials evaluating TAZVERIK in combinations and in earlier lines of therapy are expected to read out a steady flow of data over the next five years.

As part of the effort to bring TAZVERIK to patients in need worldwide, we plan to pursue strategic partnerships and collaborations to support our international efforts.

Beyond FL and ES, we believe TAZVERIK has the potential to benefit patients with other solid tumors and B-cell lymphomas as EZH2 has emerged as a key mechanism to target across multiple tumor types. Because of tazemetostat's generally well-tolerated profile as an oral agent, our hope is that it can be safely combined with a number of both standard-of-care and novel oncology agents.

We have established a broad tazemetostat development strategy to maximize our ability to generate important data quickly, which includes two basket trials evaluating combinations in solid tumors and hematological malignancies. We expect these studies to begin in the second half of 2021 and are leveraging innovative clinical trial designs that are intended to efficiently identify signals or support paths to registration.

While most of our attention has been focused on TAZVERIK launches and development, we've been building a pipeline of innovative epigenetic programs at Epizyme. 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 heme and solid tumor cancers. Our ambition is to deliver five of these programs to the clinic in the next five years and we are not afraid to tackle difficult challenges. Some of the programs we are advancing involve targets that have never been successfully drugged. We believe we can solve for important medical needs in people with cancer.

Finally, I want to express our utmost appreciation for the patients, their families and caregivers, along with their physicians and others who have advocated for TAZVERIK and who continue to be supportive of Epizyme.

We are excited for this next chapter here at Epizyme and we hope that you share our enthusiasm. We look forward to providing periodic updates as our clinical programs advance and we have news to share.

Robert Bazemore
President and Chief Executive Officer

EPIZYME OVER THE NEXT 5 YEARS

THE NEXT EPIsode

MAXIMIZE COMMERCIAL EFFECTIVENESS

- TAZVERIK adopted as a backbone therapy for FL
- TAZVERIK utilized in multiple combination regimens

BUILD ON TAZVERIK'S PIPELINE-IN-A-DRUG POTENTIAL

- TAZVERIK approved in additional heme and solid tumor indications
- Robust flow of data read-outs

EXPAND PIPELINE & PORTFOLIO TO OVERCOME UNDRUGGABLE TARGETS

- Five new clinical-stage programs
- Evolving oncology portfolio company

COLLABORATE TO EXPAND PATIENT REACH & BUILD VALUE

- TAZVERIK partnered to reach ex-US markets
- Multiple clinical and scientific collaborations

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

FORM 10-K

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

For the fiscal year ended December 31, 2020

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**

Securities registered pursuant to Section 12(g) of the Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. ☒ Yes ☐ No

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Exchange Act. ☐ Yes ☒ No

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. ☒ Yes ☐ No

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). ☒ Yes ☐ No

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See definitions of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act.

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

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

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes Oxley-Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report ☒

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

The aggregate market value of the registrant's common stock, par value $0.0001 per share, held by non-affiliates of the registrant on June 30, 2020, the last business day of the registrant's most recently completed second fiscal quarter, was approximately $794.6 million based on the closing price of the registrant's common stock on the Nasdaq Global Select Market on that date.

The number of outstanding shares of the registrant's common stock, par value $0.0001 per share, as of February 18, 2021 was 101,785,162.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement that the registrant intends to file with the Securities and Exchange Commission pursuant to Regulation 14A in connection with the registrant's 2021 Annual Meeting of Stockholders are incorporated by reference into Part III of this Annual Report on Form 10-K to the extent stated herein.

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Epizyme, Inc.

Annual Report on Form 10-K for the Fiscal Year Ended December 31, 2020

Table of Contents

Item No.		Page
	PART I	
Item 1.	Business	4
Item 1A.	Risk Factors	41
Item 1B.	Unresolved Staff Comments	80
Item 2.	Properties	81
Item 3.	Legal Proceedings	81
Item 4.	Mine Safety Disclosures	81
	PART II	
Item 5.	Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities	82
Item 6.	Selected Financial Data	83
Item 7.	Management's Discussion and Analysis of Financial Condition and Results of Operations	84
Item 7A.	Quantitative and Qualitative Disclosures about Market Risk	104
Item 8.	Financial Statements and Supplementary Data	104
Item 9.	Changes in and Disagreements with Accountants on Accounting and Financial Disclosure	106
Item 9A.	Controls and Procedures	106
Item 9B.	Other Information	108
	PART III	
Item 10.	Directors, Executive Officers and Corporate Governance	109
Item 11.	Executive Compensation	109
Item 12.	Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters	109
Item 13.	Certain Relationships and Related Transactions, and Director Independence	109
Item 14.	Principal Accounting Fees and Services	109
	PART IV	
Item 15.	Exhibits, Financial Statement Schedules	110
Item 16.	Form 10-K Summary	115
	Signatures	116

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Forward-looking Information

This Annual Report on Form 10-K 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 and other serious diseases;
- 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; 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 Annual Report on Form 10-K 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 Annual Report on Form 10-K 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 Annual Report on Form 10-K, 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 Annual Report on Form 10-K which modify or impact any of the forward-looking statements contained in this Annual Report on Form 10-K will be deemed to modify or supersede such statements in this Annual Report on Form 10-K.

Note regarding certain references in this Annual Report on Form 10-K

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 Annual Report on Form 10-K to "TAZVERIK (tazemetostat)," "TAZVERIK" 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.

Risk Factors Summary

Our business is subject to a number of risks of which you should be aware in evaluating our company and our business. These risks are discussed more fully below in the "Risk Factors" section of this Annual Report on Form 10-K for the year ended December 31, 2020. These risks include the following:

- We are dependent on the successful development and commercialization of tazemetostat. If we do not successfully commercialize TAZVERIK for the indications for which TAZVERIK is approved or are unable to develop, obtain marketing approval of, and commercialize tazemetostat for additional indications, either alone or through collaborations, or if we experience significant delays in doing so, our business could be harmed.
- In connection with the accelerated approval of our epithelioid sarcoma, or ES, new drug application, or NDA, and our follicular lymphoma, or FL, supplemental NDA, or sNDA, continued approval of TAZVERIK for these approved indications is contingent upon verification and description of clinical benefit in a confirmatory program in each indication. We are conducting Phase 1b/3 trials to confirm the clinical benefit of TAZVERIK in each indication. These trials are expensive and time-consuming and may not confirm such benefit. If a confirmatory program does not verify clinical benefit for an indication, we may have to withdraw our accelerated approval for that indication, which could significantly harm our business.
- The marketing approval process is expensive, time-consuming and uncertain and we may be unable to obtain approvals for the commercialization of tazemetostat in the United States for any additional indication or in any foreign jurisdiction, or of any other future product candidates we may develop. If we are not able to obtain, or if there are delays in obtaining, required marketing approvals of tazemetostat in the United States for any additional indication or in any foreign jurisdiction, or of any other future product candidates we may develop, we will not be able to commercialize tazemetostat for such indications or in such foreign jurisdiction or such other future product candidates, and our ability to generate revenue will be materially impaired.
- The COVID-19 pandemic has impacted our commercial launch efforts for TAZVERIK in FL and ES, may affect our ability to initiate and complete preclinical studies and our ongoing and planned clinical trials, disrupt regulatory activities, further disrupt commercialization of TAZVERIK, or have other adverse effects on our business and operations.
- Tazemetostat or any other future product candidate that we commercialize may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success. If tazemetostat or any other future product candidate does not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable.
- If we are unable to maintain effective sales, marketing and distribution capabilities, we may not be successful in commercializing tazemetostat or any other future product candidates that we commercialize.
- We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do. 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 other

indication for which we may develop tazemetostat or any other future product candidates that we may commercialize.

- Tazemetostat and any other future product candidate that we commercialize may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, which could adversely impact the product revenues we may generate from tazemetostat or such other future product candidate and harm our business.
- Our research and development is focused on the creation of novel epigenetic therapies for patients with cancer and other diseases, which is a rapidly evolving area of science, and the approach we are taking to discover and develop drugs is novel.
- Clinical drug development is a lengthy and expensive process, with an uncertain outcome. We are conducting multiple clinical trials of tazemetostat in different potential indications as a monotherapy and in combination with other products. A failure of one or more of these clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, the outcome of a clinical trial for an indication may not be predictive of the success of clinical trials for other indications, and interim results of a clinical trial do not necessarily predict final results. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products.
- If we are required by the U.S. Food and Drug Administration, or FDA, to obtain approval of a companion or complementary diagnostic in connection with approval of a therapeutic product, and there are delays in obtaining such FDA approval of a diagnostic device, we will not be able to commercialize the product candidate and our ability to generate revenue will be materially impaired.
- We may not be successful in our efforts to use and expand our proprietary drug discovery platform to build or advance a pipeline of future product candidates.
- Our existing therapeutic collaborations are important to our business and provide us with resources and capabilities we may not otherwise have. If we are unable to enter into additional therapeutic collaborations on acceptable terms or at all or maintain any of these collaborations, or if these collaborations are not successful, our business could be adversely affected.
- We contract with third parties for the manufacture of tazemetostat for commercialization and clinical testing, and expect to contract with third parties for the manufacture of any other future product candidates that we develop for preclinical and clinical testing and commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of tazemetostat or other future product candidates or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.
- Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary technology and products. If we are unable to obtain and maintain patent protection for our technology and products or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully commercialize our technology and products may be impaired.
- We have incurred significant losses since our inception. We expect to incur significant expenses and operating losses over the next several years and may never achieve or maintain profitability.
- We will need substantial additional funding to maintain and grow our operations. If we are unable to raise capital when needed or on acceptable terms, we could be forced to delay, reduce or eliminate our research and development programs or our commercialization efforts.
- We have incurred secured indebtedness of $220.0 million under our amended and restated loan agreement with BioPharma Credit Investments V (Master) LP, BPCR Limited Partnership and BioPharma Credit PLC. Our debt service obligations could limit cash flow available for our operations and expose us to risks that could adversely affect our business, financial condition and results of operations. In the event of a default of our obligations under the loan agreement, we may not have sufficient funds or the ability to raise capital to repay our indebtedness.

PART I

Item 1. Business

Note on the COVID-19 Pandemic

While the COVID-19 pandemic has had an impact on our business, operations, and financial performance, we have taken and plan to continue to take steps to evaluate, monitor, manage, and respond to the challenges that have arisen from the COVID-19 pandemic and to new challenges that may arise. 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 first half 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 epithelioid sarcoma, or ES, and follicular lymphoma, or 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.

For our ongoing commercialization activities for TAZVERIK, our commercial and medical affairs field teams are continuing to use virtual formats where possible in order to allow us to serve the needs of healthcare providers, patients and other stakeholders during this critical time. During the third and fourth quarters of 2020, the COVID-19 pandemic continued to negatively impact ES and FL patient visits to physicians, new patient starts across all lines of treatment as well as the ability of our field-based teams to fully access ES and FL prescribers, and these challenges continued in the first quarter of 2021. Notwithstanding these challenges, new prescriptions for TAZVERIK in FL have increased month over month and are 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 adapt our commercial strategy to the COVID-19 pandemic to support increased adoption of TAZVERIK in appropriate patients.

We 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 we 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, as quickly as possible, 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 in Part I, Item 1A. of this Annual Report on Form 10-K for further discussion of risks related to the COVID-19 pandemic.

Overview

We are a commercial-stage biopharmaceutical company that is committed to rewriting treatment for people with cancer and other serious diseases through the discovery, development, and commercialization of novel epigenetic medicines. By focusing on the genetic drivers of disease, our science seeks to match targeted medicines with the patients who need them.

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 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. The safety run-in portion of the trial is fully enrolled and we expect to commence the efficacy portion of the trial in 2021. We anticipate reporting safety and preliminary activity data from the safety run-in portion of the study at a medical meeting in 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 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. The trial is expected to enroll approximately 500 FL patients, stratified based on their EZH2 mutation status. The safety run-in portion of the trial is fully enrolled and we expect to commence the efficacy portion of the trial in 2021. We anticipate reporting safety and preliminary activity data from the safety run-in portion of the study at a medical meeting in 2021. In addition, we plan to conduct post-marketing commitments, including expanding our ongoing Phase 2 clinical trial with a cohort of FL patients with wild-type EZH2 to evaluate tazemetostat as a monotherapy in patients who have been treated with at least one prior systemic treatment, in order to inform the label and potentially expand it in the approved indications in the relapsed and refractory setting in the future.

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 are also supporting an investigator-sponsored study to evaluate tazemetostat in combination with rituximab with FL in the third-line or later treatment settings, which is currently enrolling. We intend to have this investigator-sponsored study transferred to a Company sponsored study in 2021. 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 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. The safety run-in portion of the trial is fully enrolled and we expect to commence the efficacy portion of the trial in 2021. We anticipate reporting safety and preliminary activity data from the safety run-in portion of the study at a medical meeting in 2021.

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, chronic lymphocytic leukemia, or CLL, chronic myeloid leukaemia, or CML, and others;
- Molecularly defined solid tumors, such as chordoma, melanoma, mesothelioma, and tumors harboring an EZH2 or SWI/SNF alteration;
- Chemotherapy or treatment-resistant tumors, such as triple-negative breast cancer, small cell lung cancer, ovarian cancer, and as described above, mCRPC; and
- Immuno-oncology-sensitive tumors, such as colorectal cancer, bladder cancer, soft tissue sarcomas and non-small cell lung cancer.

We own the global development and commercialization rights to tazemetostat outside of Japan. 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. This includes an efficiently sized field-based organization of approximately 76 individuals.

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 through potential strategic collaborations.

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.

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, or STS, and mesothelioma, and a seven-year orphan drug exclusivity period 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.

To date, we have entered into various strategic collaborations, including therapeutic collaborations and other collaborations, including with 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.

Our Corporate Strategy

We are a commercial-stage biopharmaceutical company developing and commercializing novel epigenetic therapies for people with cancer and other serious diseases. With the launch of TAZVERIK in the United States in 2020, we have transitioned to a fully integrated biopharmaceutical company commercializing our first product.

The key elements of our corporate strategy are to:

- successfully commercialize TAZVERIK in the United States for the treatment of ES and FL patients in the United States;
- advance life-cycle development for tazemetostat to support its potential utility in additional indications and combinations;
- leverage existing and enter into new strategic collaborations that can contribute to our ability to rapidly develop and commercialize TAZVERIK and any product candidates we may identify and develop, including developing and commercializing TAZVERIK and any product candidates we may identify and develop outside of the United States; and
- utilize our drug discovery platform to progress preclinical efforts and pursue additional product candidates to expand our pipeline of inhibitors against several classes of CMPs, including HMTs, HATs, and helicases.

TAZVERIK (tazemetostat) for Epithelioid Sarcoma

In January 2020, the FDA granted accelerated approval of TAZVERIK (tazemetostat) for the treatment of adults 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 an open-label, single-arm cohort of a multi-cohort, global Phase 2 trial of tazemetostat in adults with INI1-negative tumors. The cohort was conducted in 62 patients with histologically confirmed, metastatic or locally advanced ES. Patients were required to have INI1 loss, detected using local tests, and an Eastern Cooperative Oncology Group performance status, or ECOG PS, of 0-2. Patients in the cohort received TAZVERIK 800 mg orally twice daily until disease progression or unacceptable toxicity. Tumor response assessments were performed every eight weeks. The major efficacy outcome measures were confirmed overall response rate, or ORR, according to Response Evaluation Criteria in Solid Tumors, or RECIST, v1.1, as assessed by blinded independent central review and duration of response. Median duration of follow-up was 14 months (range 0.4 to 31).

Among the 62 patients who received TAZVERIK, the median age was 34 years (range 16 to 79); 63% were male, 76% were White, 11% were Asian, 44% had proximal disease, 92% had an Eastern Cooperative Oncology Group performance status (ECOG PS) of 0 or 1, and 8% had an ECOG PS of 2. Prior surgery occurred in 77% of patients; 61% received prior systemic chemotherapy.

In the total 62 patients treated, the overall response rate (95% confidence interval) was 15% (7%, 26%), with 1.6% of patients achieving a complete response and 13% achieving a partial response. Among responders in the trial, 67% had a duration of response of six months or longer as of the data cutoff date of September 17, 2018.

Serious adverse reactions occurred in 37% of patients receiving TAZVERIK. The serious adverse reactions in ≥3% of patients who received TAZVERIK were hemorrhage, pleural effusion, skin infection, dyspnea, pain, and respiratory distress.

One patient (2%) permanently discontinued TAZVERIK due to an adverse reaction of altered mood.

Dosage interruptions due to an adverse reaction occurred in 34% of patients who received TAZVERIK. The most frequent adverse reactions requiring dosage interruptions in ≥3% of patients were hemorrhage, increased alanine aminotransferase (ALT), and increased aspartate aminotransferase (AST). Dose reduction due to an adverse reaction occurred in one (2%) patient who received TAZVERIK due to decreased appetite.

The most common adverse reactions (≥20%, any grade) were pain, fatigue, nausea, decreased appetite, vomiting, and constipation.

The label for TAZVERIK includes warning and precautions for the increase in risk of developing secondary malignancies following treatment with TAZVERIK and the risk of embryo fetal toxicity when administered to pregnant women.

Additionally, *The Lancet Oncology* published results of our Phase 2 trial evaluating TAZVERIK for the treatment of ES in October 2020.

We continue to make TAZVERIK available to eligible patients and their physicians in the United States.

TAZVERIK for Epithelioid Sarcoma Post-Marketing Requirements

As part of the accelerated approval for epithelioid sarcoma, 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 tazemetostat for this indication, we are conducting a global 1:1 randomized, controlled Phase 1b/3 clinical trial in the front-line treatment setting comparing TAZVERIK in combination with doxorubicin, a commonly used systemic treatment in this setting, versus placebo plus doxorubicin. The trial is expected to enroll approximately 152 ES patients. The primary efficacy endpoint is progression-free survival, and secondary efficacy endpoints include overall survival, disease control rate, overall response rate, duration of response and health-related quality of life. The safety run-in portion of the trial is fully enrolled and we expect to commence the efficacy portion of the trial in 2021. We anticipate reporting safety and preliminary activity data from the safety run-in portion of the study at a medical meeting in 2021.

We have several additional post-marketing activities underway, intended to address aspects of the label in the future. These include clinical pharmacology evaluations to assess the effect of TAZVERIK on liver function and the effect of CYP3A inhibitors and inducers on TAZVERIK for patients with ES. We have also expanded enrollment in a cohort of our Phase 2 study in adults with INI1-negative tumors, to enroll a total of at least 60 epithelioid sarcoma patients. The cohort is a paired biopsy cohort designed to assess potential immune biomarkers, and the expansion is intended to provide more experience in patients with ES.

Background on ES: Epithelioid sarcoma is an ultra-rare and aggressive type of soft tissue sarcoma, comprising less than 1 percent of all soft tissue sarcoma cases, and is characterized by a loss of the INI1 protein. It is most commonly diagnosed in young adults (20-40 years old) and is often fatal. There is no established standard-of-care for treating these patients, who are typically resistant to chemotherapy. Patients diagnosed with metastatic disease typically have a 5-year overall survival rate of 0 percent and there are no approved treatment options specifically indicated for epithelioid sarcoma other than TAZVERIK. Typically, once patients have been deemed appropriate for systemic therapy, most are treated with chemotherapy. There are an estimated 800 patients in the United States living with epithelioid sarcoma with approximately 300 patients with metastatic or locally advanced disease that are eligible for systemic therapy.

TAZVERIK for Follicular Lymphoma

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.

TAZVERIK was evaluated in an open-label, single-arm, multi-center Phase 2 clinical trial in patients with histologically confirmed FL whose disease had progressed following at least two prior systemic treatment regimens. Patients were enrolled into two cohorts: one cohort enrolled 45 patients with EZH2 activating mutations and a second cohort enrolled 54 patients with wild-type EZH2. All patients were treated with 800 mg of tazemetostat, administered orally twice a day. The major efficacy outcome measures were overall response rate (ORR) and duration of response (DOR) according to the International Working Group Non-Hodgkin Lymphoma (IWG-NHL) criteria (Cheson 2007) as assessed by Independent Review Committee. Median duration of follow-up was 22 months for patients with EZH2 activating mutations and 36 months for patients with wild-type EZH2.

Among the 45 FL patients with an EZH2 activating mutation who received TAZVERIK, the median age was 62 years (range 38 to 80); 42% were male; 42% had early progression following front-line therapy (POD24); and all had an ECOG performance status (PS) of 0 or 1. The median number of lines of prior systemic therapy was 2.0 (range 1 to 11); 49% were refractory to rituximab and 49% were refractory to their last therapy. In the 42 patients treated with at least 2 prior systemic therapies, the ORR (95% confidence interval) was 69% (53%, 82%), with 12% of patients achieving a complete response and 57% achieving a partial response. The median DOR was 10.9 months and ongoing.

Among the 54 FL patients with wild-type EZH2 who received TAZVERIK, the median age was 61 years (range 36 to 87); 63% were male; 59% had POD24; and 91% had an ECOG PS of 0 or 1. The median number of lines of prior systemic therapy was 3.0 (range 1 to 8); 59% were refractory to rituximab and 41% were refractory to their last therapy. In the 53 patients treated with at least 2 prior systemic therapies, the ORR (95% confidence interval) was 34% (22%, 48%), with 4% of patients achieving a complete response and 30% achieving a partial response. The median DOR was 13.0 months.

Serious adverse reactions, irrespective of attribution, occurred in 30% of patients receiving TAZVERIK. Serious adverse reactions in ≥2% of patients who received TAZVERIK were general physical health deterioration, abdominal pain, pneumonia, sepsis, and anemia. The most common (≥20%) adverse reactions are fatigue, upper respiratory tract infection, musculoskeletal pain, nausea and abdominal pain.

Eight patients (8%) discontinued due to adverse reaction during the trial. There were no reported deaths on study, and no black box warnings or contraindications.

Additionally, *The Lancet Oncology* published results of our Phase 2 trial evaluating TAZVERIK for the treatment of FL in October 2020.

We continue to make TAZVERIK available to eligible patients and their physicians in the United States.

Background on FL: Follicular lymphoma is the most common indolent lymphoma and the second most common non-Hodgkin lymphoma – accounting for about 10-20% of all lymphomas in Western countries. FL is considered to be incurable with existing treatments and is characterized by cycles of relapse that become increasingly difficult to treat with each disease progression. We estimate that approximately 14,000 patients are diagnosed with follicular lymphoma in the United States annually, of whom the majority have advanced disease at diagnosis. We estimate that there are approximately 10,000 patients with relapsed and/or refractory disease in the United States. Based on literature and an extensive natural history study that we conducted, we believe that approximately 20% of FL tumors carry an EZH2 activating mutation. Common treatments for FL include multi-agent chemotherapy, usually combined with rituximab (RITUXAN), including R-CHOP and R-Bendamustine. Upon clinical progression, treatment regimens are typically other combinations of rituximab, and other chemotherapy regimens, utilization of off-label agents, clinical trials or one of the four approved PI3k inhibitors: duvelisib, idealisib, copanlisib or umbralisib.

TAZVERIK for Follicular Lymphoma Post-Marketing Requirements

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 to evaluate the combination of TAZVERIK with "R2" (Revlimid plus rituximab) compared with R2 plus placebo for FL patients in the second-line or later treatment setting. The trial is expected to enroll approximately 500 FL patients, stratified based on their EZH2 mutation status. The safety run-in portion of the trial is fully enrolled and we expect to commence the efficacy portion of the trial in 2021. We anticipate reporting safety and preliminary activity data from the safety run-in portion of the study at a medical meeting in 2021.

In addition, we plan to conduct post-marketing commitments, including expanding our ongoing Phase 2 relapsed or refractory non-Hodgkin's lymphoma, or NHL, clinical trial with a cohort of FL patients with wild-type EZH2 to evaluate tazemetostat as a monotherapy in patients who have been treated with at least one prior systemic treatment, in order to inform the label and potentially expand in the relapsed and refractory setting in the future.

FL Development Expansion: Through our planned development efforts, our intention is to make TAZVERIK available in all lines of treatment for patients with FL. We plan to leverage the confirmatory trial to expand TAZVERIK into the second-line treatment setting.

In collaboration with The Lymphoma Study Association, or LYSA, a premier cooperative group in France dedicated to clinical and translational research for lymphoma, and based on clinical activity observed with tazemetostat in a combination Phase 1b/2 study with R-CHOP as a front-line treatment for patients with high risk diffuse large B-cell lymphoma, or DLBCL, a Phase 2 clinical expansion trial was commenced that is being conducted by LYSA evaluating this combination as a front-line treatment for high-risk patients with FL. The Phase 1b part of the study has completed, and we are currently enrolling for high-risk patients with both FL and DLBCL in the Phase 2 trial.

We are also supporting an investigator-sponsored study to evaluate tazemetostat in combination with rituximab with FL in the third-line or later treatment settings, which is currently enrolling. We intend to have this investigator-sponsored study transferred to a Company-sponsored study in 2021. 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.

Tazemetostat Life-Cycle Development

Tazemetostat has shown meaningful clinical activity as an investigational monotherapy in multiple cancer indications and has been generally well-tolerated across clinical trials to date. We believe tazemetostat is a "pipeline in a product" opportunity and plan to explore its utility in additional indications and combinations through both company and investigator sponsored studies. 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.

Lymphomas and B-Cell Malignancies

We are developing tazemetostat for lymphomas and B-cell malignancies, including DLBCL, MCL, CLL, and CML, because of the role EZH2 plays in B-cell biology. When oncogenic mutations occur, they can "lock" B-cells in the germinal center state, leading to a variety of hematologic cancers. Regardless of the oncogenic mutation, these cancer cells are governed by EZH2 expression, which enables their growth and proliferation. By inhibiting EZH2, we believe we can inhibit tumor proliferation, leading to anti-tumor activity, as seen in FL patients with wild-type EZH2.

DLBCL Combination with R-CHOP. In collaboration with LYSA, we are conducting a multi-center Phase 1b/2 trial of tazemetostat in combination with R-CHOP in front-line, elderly high-risk patients with DLBCL. The trial is expected to enroll up to 133 patients. Primary endpoints in the trial include complete response rate, safety and tolerability of the combination. Secondary endpoints include ORR and progression-free survival, or PFS. The trial was initiated in the fourth quarter of 2016. At ASH 2018, LYSA reported interim data from 17 patients in the trial as

of March 2018 showing that the combination of the two agents had been generally well-tolerated and confirming the recommended tazemetostat dose for the combination to be 800 mg twice-daily. Clinical activity was observed, with 87 percent of patients experiencing a metabolic complete response. We agreed in 2020 to expand the trial to also include an expansion cohort for the front-line treatment of high-risk patients with FL. The Phase 1b part of the study has completed, and we commenced a Phase 2 clinical expansion trial in front-line treatment and are enrolling for high-risk patients with both FL and DLBCL.

Molecularly Defined Solid Tumors

We are exploring the use of tazemetostat to treat multiple molecularly defined solid tumors, such as chordoma, melanoma, mesothelioma and tumors with a SWI/SNF alteration or other mutations. In these tumors, a loss of certain proteins or the presence of a certain mutation can result in abnormal EZH2 activity or exaggerated dependence on EZH2, which leads to cancer cell growth. By inhibiting EZH2 with tazemetostat, we believe we can inhibit that abnormal function, thereby indirectly restoring cells to their natural state, which could result in a therapeutic benefit.

Adults with INI1-Negative Tumors: We are assessing tazemetostat for the treatment of adults with chordoma in a cohort of our ongoing global Phase 2 trial in adults with INI1-negative tumors. Patients in the cohort are dosed at 800 mg twice daily with tablets taken orally. The primary endpoint for the trial is overall response rate. The cohort is open for enrollment.

Pediatrics with INI1-Negative Tumors: We are conducting a global Phase 1 clinical trial of tazemetostat in approximately 110 children with INI1-negative solid tumors. In the trial, we are using an oral suspension formula of tazemetostat. The primary endpoint of the trial is safety, with the objective of establishing the recommended Phase 2 dose in pediatric patients. Secondary endpoints include pharmacokinetics, objective response rate, duration of response, PFS and overall survival. We have completed the dose-escalation portion of the trial and have advanced to the dose-expansion stage of this trial.

Chemotherapeutic/Treatment-Resistant Tumors

We are assessing the use of tazemetostat for solid tumors that are resistant to chemotherapy or other treatments, such as triple negative breast, small cell lung and ovarian cancers, and castration-resistant prostate cancer. When chemotherapy is given, DNA becomes damaged, resulting in abnormal or overactive EZH2 activity. This prevents transcription of certain genetic markers, which leads to cancer cell growth. By adding an EZH2 inhibitor, like tazemetostat, we believe we can turn that disease-targeting genetic marker back on, resulting in a re-sensitization of the tumor to chemotherapy or other treatments. In addition, EZH2 plays a role in the resistance to poly adenosine diphosphate ribose polymerase, or PARP, inhibitors. When PARP inhibitors are given, DNA is damaged, which leads to increased EZH2 activity and limits the responsiveness to the PARP inhibitor. By blocking EZH2 with tazemetostat, we believe we can also re-sensitize tumors to PARP inhibition treatment.

Castration-Resistant Prostate Cancer: Prostate cancer is the most frequently diagnosed and second most frequent cause of cancer deaths among men in the United States. We believe, based on published literature, that EZH2 protein expression has been correlated with progression of metastatic castration-resistant prostate cancer, or mCRPC; moderate to high EZH2 expression has been associated with worse survival; and, treatment with an EZH2 inhibitor after resistance to the standards-of-care may result in recovery of sensitivity to these agents. We are conducting a global, multi-center, randomized Phase 1b/2 trial evaluating tazemetostat in combination with enzalutamide or abiraterone, the standard of care treatments for this disease, plus prednisone in chemo-naïve patients with metastatic castration resistant prostate cancer. The safety run-in portion of the trial is fully enrolled and we expect to commence the efficacy portion of the trial in 2021. We anticipate reporting safety and preliminary activity data from the safety run-in portion of the study at a medical meeting in 2021.

Platinum-Resistant Solid Tumors: We are planning to investigate the therapeutic potential of tazemetostat as a combination therapy with a PARP inhibitor for the treatment of platinum-resistant tumors, such as small-cell lung cancer, triple-negative breast cancer and ovarian cancer. In platinum-resistant cancers, PARP inhibitors have shown modest monotherapy activity, and we believe tazemetostat may have the potential to enhance the clinical response to PARP inhibitors. We have completed the preclinical development to determine the potential design of a clinical trial, which includes selecting the PARP inhibitor to administer in combination with tazemetostat. We are evaluating the preclinical data and plan to begin this trial in 2021.

Immuno-oncology-sensitive Tumors

We are assessing the use of tazemetostat for immuno-oncology-sensitive tumors, such as colorectal cancer, bladder cancer, soft tissue sarcomas and non-small cell lung cancer. We believe tazemetostat may enhance the antitumor immune response by interfering with multiple EZH2 functions in the cell. EZH2 inhibition results in tumor-intrinsic and tumor-extrinsic effects that reshape the tumor microenvironment to favor antitumor immunity, including increasing antigen presentation, increasing effector T cell trafficking, modulating the adaptive anti-tumor response, impairing regulatory T cells, inducing the expression of tumor antigens and endogenous retroviruses, and increasing NK cell maturation and killing. By inhibiting EZH2, we believe we can influence biologic activity in the tumor microenvironment, which could enable tumors to be more sensitive or re-sensitized to immune-oncology therapies.

Tazemetostat CRADA with NCI

In October 2016, we announced a Cooperative Research and Development Agreement, or CRADA, with the National Cancer Institute, or NCI, to evaluate tazemetostat in clinical trials in a variety of hematologic malignancies and solid tumors. Under this CRADA, we are evaluating tazemetostat in a Phase 2 clinical trial in adult patients with ovarian cancer and in a Phase 2 trial in pediatric patients with solid tumors and lymphoma. As part of the CRADA, we may undertake additional clinical trials. NCI will predominantly fund the studies and manage trial operations.

The NCI's Pediatric MATCH trial includes a Phase 2 evaluation of tazemetostat as one of its treatment cohorts. Conducted under our CRADA executed with NCI in 2016, this multi-institutional trial is evaluating tazemetostat as a monotherapy for pediatric patients with advanced solid tumors, including CNS tumors, NHL or histiocytic disorders that harbor EZH2 activating mutations, or loss of function mutations in the SWI/SNF complex subunits SMARCB1 or SMARCA4. The Pediatric MATCH trial, conducted by the Children's Oncology Group, aims to match targeted agents, such as tazemetostat, with specific molecular changes identified through genomic sequencing of refractory or recurrent tumors from children and adolescents with cancer is now enrolling patients.

Research Pipeline

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 CMPs, including HMTs, HATs, and helicases. These programs are directed against both hematological malignancies and solid tumors and include biomarker approaches to patient stratification.

Under our collaboration with GSK, GSK is developing two small molecule inhibitors against novel HMT targets, that were discovered by us using our proprietary drug discovery platform. In September 2016, GSK advanced the first of these programs into clinical testing. This drug candidate, GSK3326595, a PRMT5 inhibitor, is currently being tested in a Phase 2 clinical trial in patients with solid tumors and NHL. In 2018, GSK initiated patient dosing in a Phase 1 clinical trial of GSK3368715, a PRMT1 inhibitor.

In November 2018, we entered into a global collaboration with Boehringer Ingelheim International GmbH, or Boehringer Ingelheim, focused on the research, development and commercialization of novel small molecules, directed toward two previously undisclosed epigenetic targets as potential therapies for people with cancer. Specifically, these targets are enzymes within the helicase and HAT families that when dysregulated have been linked to the development of cancers that currently lack therapeutic options. Boehringer Ingelheim terminated the collaboration without cause by notice to us in December 2020, and as agreed, the termination became effective on January 31, 2021. As a result of the termination, we are entitled to pursue the HAT target and helicase target programs in all fields worldwide without further obligation to Boehringer Ingelheim.

In April 2012, we entered into a collaboration and license agreement with Celgene Corporation, or Celgene. Under our collaboration with Celgene, we developed small molecule inhibitors directed to three HMT targets, in addition to pinometostat. Under the collaboration, we were responsible for all preclinical discovery work as well as Phase 1 clinical development for all three targets. Celgene had the option to acquire worldwide rights to inhibitors directed at two of the three targets, and the option to acquire ex-U.S. rights to inhibitors directed to the third target. On November 3, 2020, Celgene terminated the collaboration and license agreement without cause, effective January 2, 2021.

Pinometostat for DOT1L Cancers

DOT1L is an HMT that can become oncogenic and cause certain subtypes of acute leukemia, such as MLL-r. We discovered pinometostat using our proprietary drug discovery product platform. Following the termination of our collaboration agreement with Celgene, we have worldwide rights to pinometostat.

Pinometostat has been granted orphan drug designation by the FDA and the European Commission for the treatment of acute myeloid leukemia, or AML, and acute lymphoblastic leukemia, or ALL.

Under the CRADA that we entered with the NCI in October 2016 for pinometostat, the NCI has agreed to evaluate the safety and efficacy of pinometostat in patients with acute leukemias. Initial studies will evaluate the combination of pinometostat with standard-of-care therapies or targeted agents in acute leukemia. As part of the agreement, additional clinical trials will be considered. NCI will predominantly fund the studies and manage trial operations.

Our Epigenetic Approach

Epigenetics refers to a broad regulatory system that controls gene expression without altering the sequence of the genes themselves. Genes are composed of DNA, and in nature, this DNA is wrapped around a core of proteins known as histones. Together, the DNA and histone proteins form a complex known as chromatin that is the basic structural component of chromosomes.

Gene regulation is determined by chromatin structure. The dynamics of chromatin structure are regulated through multiple mechanisms by CMPs. Some CMPs place chemical groups onto specific sites on histones or DNA, some remove these marks in site-specific ways, others recognize the uniquely marked sites on histones and bind to these marked sites, and still other CMPs drive topological changes to histone-DNA interactions within chromatin. Where, when and how such chromatin structure changes occur, determines which genes in a cell are turned “on” or “off” at any particular time. When the function of these CMPs is altered, the program of gene expression is changed in ways that can lead to disease.

To further support our leadership position in epigenetics, we are discovering and developing inhibitors of CMPs as novel therapeutics for patients with cancer and other diseases. Our focus is on the discovery, development and commercialization of small molecule inhibitors of CMPs for applications in diseases that are uniquely dependent on the enzyme activity of a specific CMP. Among the CMP target classes, we have had a particular emphasis on the HMTs, which have been shown to play pathogenic roles in a number of human diseases. Today, we have programs in HMTs as well as additional target classes, including HATs, and helicases. Targeting pathogenic CMPs affords us multiple opportunities to create, develop and commercialize novel therapeutics.

Our Collaborations

We have entered into several key strategic collaborations, including therapeutic collaborations and other collaborations. The therapeutic collaborations have provided us with $243.8 million in non-equity funding through December 31, 2020. Key terms of our ongoing collaborations are summarized below.

GSK

Overview. In January 2011, we entered into a collaboration and license agreement with GSK, to discover, develop and commercialize novel small molecule HMT inhibitors directed to available targets from our product platform. Under the terms of the agreement, we granted GSK exclusive worldwide license rights to HMT inhibitors directed to three targets. Additionally, as part of the research collaboration, we 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, we and GSK amended certain terms of this agreement, including revising the definition of licensed compounds and amending the corresponding financial terms, including reallocating milestone payments and increasing royalty rates, for one target. Subsequent to a GSK strategic portfolio prioritization, we 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 us. 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. We

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 material for these programs to GSK in the second quarter of 2015. GSK is responsible for all future development and commercialization.

Under the agreement, we have received and recognized collaboration revenue totaling $89.0 million, consisting of upfront payments, fixed research funding, research and development services and preclinical and research milestone payments. As of December 31, 2020, for the two remaining targets, we are eligible to earn 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, we will receive no additional payments related to that target. In addition, GSK is required to pay us 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.

Exclusivity Provisions. Subject to exceptions specified in the agreement, during the term of the agreement, neither we nor GSK may research, develop or commercialize HMT inhibitors directed to the two targets selected by GSK, other than pursuant to the agreement.

Term and Termination. The agreement will expire in its entirety upon the expiration of all applicable royalty terms for all licensed products in all countries. The royalty term for each licensed product in each country is the period commencing with first commercial sale of the applicable licensed product in the applicable country and ending on the later of expiration of specified patent coverage or ten years following the first commercial sale. GSK has the right to terminate the agreement at any time with respect to one or more selected targets or in its entirety, upon 90 days' prior written notice to us. The agreement may also be terminated with respect to one or more selected targets or in its entirety by either GSK or us in the event of a material breach by the other party. The agreement may be terminated with respect to selected targets by us in the event GSK participates or actively assists in a legal challenge to one of the patents exclusively licensed to GSK under the agreement with respect to the applicable selected target.

Eisai

Overview. In March 2015, we entered into an amended and restated collaboration and license agreement with Eisai, under which we reacquired worldwide rights, excluding Japan, to our EZH2 program, including tazemetostat. Under the amended and restated collaboration and license agreement, we will be 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, including the 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, we had granted Eisai an exclusive worldwide license to our small molecule HMT inhibitors directed to EZH2, including 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.

Upon the execution of the amended and restated collaboration agreement in March 2015, we agreed to pay Eisai a $40.0 million upfront payment. We also agreed to pay Eisai up to $20.0 million in clinical development milestone payments, including a $10.0 million milestone payment upon the earlier of initiation of a first phase 3 clinical trial of any EZH2 product or the first submission of an NDA or Market Authorization Application, or MAA, and a $10.0 million milestone upon the earlier of initiation of a first phase 3 clinical trial of any EZH2 product or the first submission of an NDA or MAA for a second indication, and up to $50.0 million in regulatory milestone payments, including a $25.0 million milestone payment upon regulatory approval of the first NDA or MAA, and a $25.0 million milestone payment upon regulatory approval of the NDA or MAA for the second indication. We are obligated to pay royalties at a percentage in the mid-teens on worldwide net sales of any EZH2 product, excluding net sales in Japan. In 2019, Eisai sold its rights to these royalties to RPI Finance Trust, which has agreed to certain reductions in these royalties in the event certain net sales thresholds are achieved. We are eligible to receive from Eisai royalties at a percentage in the mid-teens on net sales of any EZH2 product in Japan. In November 2019, we sold our rights to these royalties to RPI Finance Trust. In 2019, we triggered the payment of the two $10.0 million milestone payments upon the submission of the NDAs for accelerated approval of tazemetostat for epithelioid

sarcoma and follicular lymphoma. In January 2020, we triggered the payment of the $25.0 million milestone payment upon regulatory approval in the United States of tazemetostat for epithelioid sarcoma and in June 2020 we triggered the payment of an additional $25.0 million milestone payment upon regulatory approval in the United States of tazemetostat for follicular lymphoma.

Under the original agreement, Eisai was solely responsible for funding all research, development and commercialization costs for licensed compounds. Under the amended and restated agreement, we are solely responsible for funding global development, manufacturing and commercialization costs for EZH2 compounds outside of Japan, and Eisai is solely responsible for funding Japan-specific development and commercialization costs for EZH2 compounds. In connection with the amended and restated agreement, we and Eisai agreed to the transition to us of ongoing development and manufacturing activities that were being conducted by or on behalf of Eisai. In January 2017, as part of Eisai's obligations under the amended and restated collaboration agreement, Eisai enrolled and dosed the first patient in a Phase 1 study of tazemetostat in patients with relapsed or refractory B-cell NHL in Japan.

In the event that we are awarded a priority review voucher from the FDA with respect to an EZH2 product, Eisai is entitled to specified compensation if we use the voucher on a non-EZH2 program or sell the voucher to a third party.

Governance. Under the amended and restated collaboration and license agreement, development will be guided by a joint steering committee, with our company retaining final decision-making authority with respect to global development other than with respect to Japan-specific development and commercialization.

Exclusivity Restrictions. Subject to exceptions specified in the agreement, for an exclusivity period extending until eight years after the first commercial sale of a product covered by the agreement, neither we nor Eisai may research, develop or commercialize HMT inhibitors directed to EZH2, other than pursuant to the agreement.

Term and Termination. Our agreement with Eisai will remain in effect until the expiration of all payment obligations under the agreement with respect to all licensed products. The royalty term for each licensed product in each country commences on the first commercial sale of the applicable licensed product in the applicable country and ends on the latest of expiration of specified patent coverage, expiration of specified regulatory exclusivity or ten years following the first commercial sale. We or Eisai may terminate the agreement for convenience as to our respective territories, upon 90 days' prior written notice. The agreement will also terminate as to our territory if we cease all development and commercialization activities for the United States and specified major countries in Europe and as to Eisai's territory if Eisai ceases all development and commercialization activities for Japan. The agreement may also be terminated by either party in the event of an uncured material breach by the other party or by us in the event Eisai, or an affiliate or sublicensee, participates or actively assists in an action or proceeding challenging or denying the validity of one of our patents. If we terminate the agreement for our convenience, the agreement terminates as a result of our cessation of development and commercialization activities or Eisai terminates the agreement for our uncured material breach, Eisai may elect to have worldwide development and commercialization rights revert to Eisai, and if Eisai so elects, Eisai will be required to pay us specified royalties on net sales of the licensed products and reimburse certain development expenses incurred by us. If Eisai terminates the agreement for its convenience, the agreement terminates as a result of Eisai's cessation of development and commercialization activities or we terminate the agreement for Eisai's uncured material breach or Eisai's, or its affiliate's or sublicensee's, participation in, or assistance with, an action or proceeding challenging or denying the validity of one of our patents, Japanese development and commercialization rights to the licensed products revert to us, and we will be required to pay Eisai specified royalties on net sales of licensed products in Japan.

LYSARC

In May 2016, we entered into a collaboration agreement with the Lymphoma Academic Research Organization, or LYSARC, to conduct a combination trial of tazemetostat. LYSARC is the operational arm of the Lymphoma Study Association, or LYSA, a premier cooperative group in France dedicated to clinical and translational research for lymphoma. This Phase 1b/2 study is evaluating tazemetostat in combination with R-CHOP, as a front-line treatment for patients with high risk diffuse large B-cell lymphoma, or DLBCL, and is being sponsored by LYSARC. We agreed in 2020 to expand the trial to also include an expansion cohort for the front-line treatment of high-risk patients with FL. The Phase 1b part of the study has completed, and we commenced a Phase 2 clinical expansion

trial in front-line treatment for high-risk patients with both FL and DLBCL. LYSA is managing the study operations for the trial, and we are recognizing our share of the related expenses as those costs are incurred over the duration of the trial. Primary endpoints in the trial include complete response rate, safety and tolerability of the combination. Secondary endpoints include ORR and PFS.

Boehringer Ingelheim

In November 2018, we entered into a collaboration and license agreement with Boehringer Ingelheim International GmbH, or Boehringer Ingelheim. As previously disclosed, Boehringer Ingelheim terminated the collaboration without cause, effective January 31, 2021.

Celgene

In April 2012, we entered into a collaboration and license agreement between the Company and Celgene International Sàrl and Celgene Corporation, or Celgene, which was subsequently amended by the amended and restated collaboration and license agreement between the Company and Celgene Corporation and Celgene RIVOT Ltd. in July 2015, or the Celgene Collaboration Agreement. As previously disclosed, the Celgene Collaboration Agreement was terminated by Celgene without cause, effective January 2, 2021.

Genentech

In June 2016, we entered into a collaboration agreement with Genentech, a member of the Roche Group, to conduct a Phase 1b clinical trial to investigate the anti-cancer effects of our EZH2 inhibitor, tazemetostat, and Genentech's anti-PD-L1 cancer immunotherapy, atezolizumab, when used in combination for the treatment of patients with relapsed or refractory DLBCL. The trial has been completed and in November 2020 we received the final study report from Genentech. As a result, the collaboration agreement expired by its terms. There are no further payments due by either party to the other.

Companion Diagnostics

Roche

In December 2012, Eisai and we entered into a companion diagnostics agreement with Roche Molecular under which Eisai and we 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 we assumed responsibility for the remaining development costs due under the agreement. In December 2015, we 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, we were responsible for remaining development costs of $10.4 million due under the agreement as of March 2018 and Eisai agreed to reimburse us $0.9 million of this amount related to a regulatory milestone for Japan. In July 2019, we entered into a fourth amendment to the companion diagnostics agreement. Under the amended agreement, we 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 us as part of the signed amendment, and the remaining $0.5 million was paid by us 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 Solutions, or RSS, effective as of January 1, 2020. As of December 31, 2020, we are responsible for the remaining development costs of $1.0 million due under the agreement. The $0.9 million that Eisai has agreed to reimburse us related to a regulatory milestone for Japan was achieved as of June 30, 2020 with 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 RSS, RSS is obligated to use commercially reasonable efforts to develop and to make commercially available the companion diagnostic kit. RSS has exclusive rights to commercialize the companion diagnostic kit developed pursuant to this agreement. On June 18, 2020 the FDA approved the companion diagnostic kit that is intended to identify FL patients with an EZH2 mutation for treatment with tazemetostat.

The agreement with RSS will expire when we and Eisai are no longer developing or commercializing tazemetostat. We and Eisai may terminate the agreement by giving RSS 90 days' written notice if we and Eisai discontinue development and commercialization of tazemetostat or determine, in conjunction with RSS, 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 other 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, RSS may become entitled to specified termination fees.

Intellectual Property

We strive to protect the proprietary compounds and technologies that we believe are important to our business, including seeking and maintaining patent protection intended to cover the composition of matter of our product candidates, their methods of use, related technologies, diagnostics and other inventions. Our patent portfolio is currently composed of over 300 issued patents and allowed patent applications and over 550 pending patent applications in the major pharmaceutical markets, that we own as well as license from other parties. In addition to patent protection, we also rely on trade secrets and careful monitoring of our proprietary information to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

Our success will depend significantly on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business, defend and enforce our patents, maintain our licenses to use intellectual property owned by third parties, preserve the confidentiality of our trade secrets and operate without infringing the valid and enforceable patents and other proprietary rights of third parties. We also rely on know-how, continuing technological innovation and in-licensing opportunities to develop, strengthen, and maintain our proprietary position in the field of HMTs, as well as to develop a proprietary position for new target classes, such as HATs and helicases.

We plan to continue to expand our intellectual property estate by filing patent applications directed to dosage forms, methods of treatment and additional CMP and HMT inhibitor compounds and their derivatives, and to other new target classes. Specifically, we seek patent protection in the United States and internationally for novel compositions of matter covering the compounds, the chemistries and processes for manufacturing these compounds and the use of these compounds in a variety of therapies.

The patent portfolios for our most advanced programs are summarized below.

EZH2. Our EZH2 patent portfolio includes U.S. Patent No. 8,410,088 covering the composition of matter of tazemetostat. This patent issued on April 2, 2013 and is expected to expire in 2032, not including extensions. Our EZH2 portfolio also includes 50 additional U.S. patents and more than 250 foreign patents, expected to expire between 2031 and 2036, not including extensions. The claims of these patents cover the composition of matter of EZH2 inhibitor compounds and various methods of their making and use. Patent applications in the same families as these patents are pending in a variety of worldwide jurisdictions, including the United States. The EZH2 program portfolio encompasses more than 40 patent families with pending patent applications relating to compositions of matter and methods of making and use of EZH2 inhibitors. The patent families in this portfolio are in various stages of prosecution and include patent applications filed in a variety of worldwide jurisdictions, including the United States; Patent Cooperation Treaty, or PCT, applications that are eligible for filing in most worldwide jurisdictions, including the United States, and at least one U.S. provisional application that may be used as the basis for non-provisional U.S. applications, PCT applications and other national filings worldwide. Our patent applications in the EZH2 portfolio, if issued, would be expected to expire between 2031 and 2041, not including extensions.

DOT1L. Our DOT1L patent portfolio includes U.S. Patent No. 8,580,762 covering the composition of matter of pinometostat. The patent issued on November 12, 2013 and is expected to expire in 2032, not including extensions. Our DOT1L portfolio also includes 16 additional U.S. patents and more than 45 foreign patents, expected to expire between 2031 and 2034, not including extensions. The DOT1L program portfolio encompasses more than fifteen

patent families relating to compositions of matter of DOT1L inhibitor compounds and methods of their making and use. The patent families in this portfolio are in various stages of prosecution and include patent families with applications filed in a variety of worldwide jurisdictions including the United States. These patents and patent applications are wholly owned by us. Our patent applications in the DOT1L portfolio, if issued, would be expected to expire between 2031 and 2035, not including extensions.

EHMT2. Our EHMT2 patent portfolio includes more than eight patent families directed to various product candidates and methods of use, with applications filed in the United States and internationally. Patents, if issued from currently pending applications in the EHMT2 portfolio, are expected to expire between 2037 and 2038, not including extensions.

Other Targets. We also have patent portfolios directed to targets other than EZH2, DOT1L, and EHMT2, including the HMT targets PRMT1, PRMT3, CARM1 (also known as PRMT4), PRMT5, PRMT6, PRMT8, SMYD2 and SMYD3. These patent portfolios have more than 35 patent families directed to various product candidates with applications filed in the United States, PCT applications that are eligible for filing in most worldwide jurisdictions, including the United States, and U.S. provisional applications that may be used to establish non-provisional U.S. applications, PCT applications and other national filings worldwide. Patents, if issued in these portfolios are expected to expire between 2033 and 2041. We have more than 20 granted U.S. patents that cover PRMT5 inhibitors and their methods of use. These patents are expected to expire in 2033, not including extensions.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing a non-provisional patent application.

In the United States, the patent term of a patent that covers an FDA-approved drug may also be eligible for patent term extension, which permits patent term restoration as compensation for the patent term lost during the FDA regulatory review process. The Hatch-Waxman Act permits a patent term extension of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug is under regulatory review. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved drug may be extended. Similar provisions are available in Europe and other non-United States jurisdictions to extend the term of a patent that covers an approved drug. We have applied for patent term extension on a patent that covers the TAZVERIK drug substance (tazemetostat) based on the regulatory review of TAZVERIK for the treatment of adult and pediatric patients aged 16 years and older with metastatic or locally advanced ES not eligible for complete resection. In the future, if and when any additional pharmaceutical products receive FDA approval, we expect to apply for patent term extensions on patents covering those products. We intend to seek patent term extensions to any of our issued patents in any jurisdiction where these are available, however there is no guarantee that the applicable authorities, including the FDA in the United States, will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions.

We also rely on trade secret protection for our confidential and proprietary information. Although we take steps to protect our proprietary information and trade secrets, including through contractual means with our employees and consultants, third parties may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose our technology. Thus, we may not be able to meaningfully protect our trade secrets. It is our policy to require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information concerning our business or financial affairs developed or made known to the individual during the course of the individual's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. In the case of employees, the agreements also provide that all inventions conceived by the individual, and which are related to our current or planned business or research and development or made during normal working hours, on our premises or using our equipment or proprietary information, are our exclusive property.

Manufacturing

We do not have any manufacturing facilities and currently rely, and expect to continue to rely, on third parties for the manufacture of our development-stage product candidates as well as our commercial products. We have entered into clinical and commercial supply agreements with contract manufacturers for the clinical development and commercialization of tazemetostat.

Tazemetostat is a small molecule and is manufactured in third-party facilities that are equipped, staffed, and experienced in the manufacture of such pharmaceutical products. All such facilities have successful track-records manufacturing products for the United States, European Union, and rest of world markets, meeting regulatory and compliance requirements as appropriate.

We expect that any product candidates that we may develop will be small molecules that may be produced cost-effectively at contract manufacturing facilities.

We rely on third parties for the manufacture of any diagnostics we may need or if required and may continue to enter into similar agreements for the manufacture of other diagnostics. We are currently collaborating with RSS for a diagnostic for its use with tazemetostat. As described above, under the agreement with RSS, RSS is obligated to use commercially reasonable efforts to develop and to make commercially available the companion diagnostic. In June 2020 the FDA approved the companion diagnostic that is intended to identify follicular lymphoma patients with an EZH2 mutation for treatment with tazemetostat.

Commercialization

TAZVERIK is available to eligible patients in the United States via a specialty distribution network. Through this specialty distribution network, we sell TAZVERIK principally to a limited number of specialty pharmacies, which dispense the product directly to patients, and specialty distributors, which in turn sell the product to hospital pharmacies and community practice pharmacies for the treatment of patients. To commercialize TAZVERIK for the ES and FL indications in the United States, we have built a focused field presence and marketing capabilities. This includes an efficiently sized field-based organization of approximately 76 individuals.

We are pursuing three strategic imperatives that we believe are integral to early success for TAZVERIK in the United States:

- ensure eligible ES and FL patients have access to TAZVERIK by educating healthcare providers, patients and payers on the TAZVERIK data in approved indications,
- ensure that TAZVERIK becomes widely adopted by physicians as an essential treatment option for each labeled indication, and
- ensure our company sponsored programs for patients and providers (EpizymeNOW) offer a positive experience when TAZVERIK is prescribed. EpizymeNOW has been facilitating patient access to new TAZVERIK prescriptions.

Subject to receiving marketing approvals for additional indications or products, we expect to use our existing sales organization in the United States or to seek to expand our sales organization in the United States to sell our products. We believe that such an organization will be able to address the hematologists and oncologists who are the key specialists in treating the patient populations for which tazemetostat is being developed and for which any future product candidates may be developed. Outside the United States, we may choose to enter into distribution and other marketing arrangements with third parties for any of our product candidates that obtain marketing approval, or may choose to commercialize our products in certain markets, depending upon many factors, including the target market size, availability of reimbursement, and our financial resources at the time.

We own the global development and commercialization rights to tazemetostat outside of Japan. Eisai holds the rights to develop and commercialize tazemetostat in Japan. For geographies outside the United States, we are evaluating the most efficient path to reaching patients, including through leveraging existing and identifying new strategic collaborations that can contribute to our ability to rapidly develop and commercialize tazemetostat outside of the United States.

We expect that our collaborators for any companion or complementary diagnostics we may develop in the future for use with our therapeutic products will hold the commercial rights to these diagnostic products, as is the case for our collaboration with RSS. We expect to coordinate closely with any diagnostic collaborators in connection with the marketing and sale of any related therapeutic products.

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our technology, knowledge, experience and scientific resources provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions. Any 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. Current competition includes CD20 combinations, multiple PI3K inhibitors, and CAR T therapies, which are starting to be used. Near-term competition includes new PI3K inhibitors, CAR T therapies and bi-specific monoclonal antibodies, which are investigational agents with varying mechanisms of action, some of which have recently been granted special designations from the FDA. In the ES patient setting, competition includes several clinical trials run by competitors that recruit patients with soft tissue sarcoma, which is inclusive of ES.

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, advanced tumors (solid tumors and DLBCL), Novartis AG, developing an EED inhibitor which indirectly blocks EZH2 (MAK683, Phase 1/2, advanced malignancies), Daiichi Sankyo, developing a EZH1/EZH2 dual inhibitor (valemetostat, DS-3201, Phase 1, relapsed or refractory non-Hodgkin lymphomas, AML, ALL as well as Phase 2 for small cell lung cancer and relapsed or refractory adult T-cell leukemia/lymphoma), and Pfizer, developing EZH2 inhibitor PF-06821497, Phase 1, relapsed or refractory SCLC, castration-resistant prostate cancer, FL and diffuse large B-cell lymphoma. In addition, many companies are developing cancer therapeutics that work by targeting epigenetic mechanisms other than HMTs, and some including Celgene (now part of Bristol-Myers Squibb), Merck & Co., Inc., Secura Bio, Spectrum Pharmaceuticals, and Otsuka, are now marketing cancer treatments that work by targeting epigenetic mechanisms other than HMTs.

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

The key competitive factors affecting the success of all of our therapeutic product candidates, if approved, are likely to be their efficacy, safety, convenience, price, the effectiveness of companion diagnostics in guiding the use of related therapeutics, the level of generic competition and the availability of reimbursement from government and other third-party payors.

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 any 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 ours, 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 that broadly address these indications are currently on the market for the indications that we are pursuing, and additional products are expected to become available on a generic basis over the coming years. If our product candidates achieve marketing approval, we expect that they will be priced at a significant premium over competitive generic products.

The most common methods of treating patients with cancer are surgery, radiation and drug therapy. There are a number of products in late stage clinical development to treat cancer. These products in development may provide efficacy, safety, convenience and other benefits that are not provided by currently marketed therapies. As a result, they may provide significant competition for any of our product candidates for which we obtain marketing approval.

Tazemetostat. The most common treatments for FL are chemotherapies, usually combined with the monoclonal antibody Rituxan, or Gazyva, which is an antibody that acts against the same target as Rituxan, CD20. While Rituxan and a number of other widely used anti-cancer agents are labeled broadly for follicular lymphoma, no therapies 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.

In the relapsed and refractory follicular lymphoma patient setting, both current and near term competition exists. Current competition includes CD20 combinations along with multiple PI3K inhibitors. Near term competition includes companies currently evaluating investigational agents with varying mechanisms of action.

Other than TAZVERIK, there are no therapies which have been approved specifically for the treatment of epithelioid sarcoma. Epithelioid sarcoma, an INI1-negative tumor, is typically treated with surgical resection when it presents as localized disease. When epithelioid sarcoma recurs or metastasizes, it may be treated with systemic chemotherapy or investigational agents because, other than TAZVERIK, there are no approved systemic therapies specifically indicated for this disease. To the best of our knowledge there are no competitive products in development specifically for epithelioid sarcoma. However, we are aware of several clinical trials run by competitors that recruit patients with soft tissue sarcoma, which is inclusive of epithelioid sarcoma.

Government Regulation and Product Approval

Government authorities in the United States, at the federal, state and local level, and in other countries and foreign jurisdictions, including the European Union, extensively regulate, among other things, the research, development, testing, manufacture, quality control, packaging, storage, record-keeping, labeling, advertising, promotion, distribution, marketing, pricing, reimbursement, import and export of pharmaceutical products such as those we are developing. The processes for obtaining regulatory approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations, require the expenditure of substantial time and financial resources.

United States Government Regulation

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations. It is the responsibility of the company seeking to market a drug to test it and submit evidence that the drug is safe and effective. The failure to comply with the applicable United States regulatory requirements at any time during the product development process, approval process or after approval, may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve pending NDAs, withdrawal of an approval, imposition of a clinical hold, issuance of warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties.

The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests and animal studies in compliance with the FDA's good laboratory practice regulations;
- submission to the FDA of an IND which must become effective before human clinical trials may begin;
- manufacture of drug substance and drug product to support clinical trials in compliance with FDA's cGMP regulations;
- approval by an independent institutional review board, or IRB, at each clinical site before each trial may be initiated;

- performance of human clinical trials, including adequate and well-controlled clinical trials, in accordance with good clinical practices, or GCP, to establish the safety and efficacy of the proposed drug product for each indication;
- submission to the FDA of an NDA or sNDA;
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current good manufacturing practices, or cGMP, and to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity, as well as satisfactory completion of an FDA inspection of selected clinical sites and/or clinical CROs to determine GCP compliance;
- satisfactory completion of an FDA inspection of the NDA sponsor to assess compliance with GxPs;
- payment of user fees per published Prescription Drug User Fee Act, or PDUFA, guidelines for that year, if applicable;
- FDA review and approval of the NDA or sNDA; and
- commitment to comply with any post-approval requirements, including the potential requirements, to implement a Risk Evaluation and Mitigation Strategy, or REMS, and the potential requirement to conduct post-approval studies.

Preclinical Studies and an IND. Before an applicant begins testing a compound with potential therapeutic value in humans, the product candidate enters the preclinical testing stage. Preclinical studies include laboratory evaluation of product chemistry, toxicity and formulation, as well as animal studies to assess its potential safety and effectiveness. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data and any available clinical data or literature, among other things, to the FDA as part of an IND. An IND is an exemption from the FDCA that allows an unapproved product candidate to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer such investigational product to humans. Such authorization must be secured prior to interstate shipment and administration of any product candidate that is not the subject of an approved NDA. An IND automatically becomes effective 30 days after submission and receipt by the FDA, unless before that time the FDA either provides a "safe to proceed" letter, or raises concerns or questions related to one or more proposed clinical trials and places the clinical trial on a clinical hold or partial hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing a clinical trial to commence.

Clinical Trials. Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the trial, the parameters to be used in monitoring safety and the efficacy criteria to be evaluated, if appropriate. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, an IRB at each institution participating in the clinical trial must review and approve the protocol for any clinical trial before it commences at that institution, and the IRB must continue to oversee the clinical trial while it is being conducted. Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, often known as a data safety monitoring board or committee, or DSMB.

Human clinical trials are typically conducted in four sequential phases, which may overlap or be combined. In Phase 1, the candidate drug is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an initial indication of its effectiveness. In Phase 2, the investigational drug typically is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage. In Phase 3, the candidate drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the

product for approval, to establish the overall risk-benefit profile of the product and to provide adequate information for the labeling of the product. In Phase 4, post-approval studies may be conducted to gain additional experience from the treatment of patients in the intended therapeutic indication.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. Clinical trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients.

In general, the FDA accepts foreign safety and efficacy studies that were not conducted under an IND provided that they are well designed, well conducted, performed by qualified investigators, and conducted in accordance with ethical principles acceptable to the international community. The conduct of these studies must meet at least minimum standards for assuring human subject protection. Therefore, for studies submitted in support of an NDA that were conducted outside the United States and not under an IND, the agency requires demonstration that such studies were conducted in accordance with GCP.

Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on the ClinicalTrials.gov website.

Expanded Access to an Investigational Drug for Treatment Use.

Expanded access, sometimes called "compassionate use," is the use of investigational new drug products outside of clinical trials to treat patients with serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory alternative treatment options. The rules and regulations related to expanded access are intended to improve access to investigational drugs for patients who may benefit from investigational therapies who do not otherwise qualify for an ongoing clinical trial. FDA regulations allow access to investigational drugs under an IND by the company or the treating physician for treatment purposes on a case-by-case basis for: individual patients (single-patient IND applications for treatment in emergency settings and non-emergency settings); intermediate-size patient populations; and larger populations for use of the drug under a treatment protocol or Treatment IND Application.

When considering an IND application for expanded access to an investigational product with the purpose of treating a patient or a group of patients, the sponsor and treating physicians or investigators will determine suitability when all of the following criteria apply: patient(s) have a serious or immediately life-threatening disease or condition, and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition; the potential patient benefit justifies the potential risks of the treatment and the potential risks are not unreasonable in the context or condition to be treated; and the expanded use of the investigational drug for the requested treatment will not interfere initiation, conduct, or completion of clinical investigations that could support marketing approval of the product or otherwise compromise the potential development of the product. Sponsors are required to make their expanded access policies publicly available upon the earlier of initiation of a Phase 2 or Phase 3 study; or 15 days after the drug or biologic receives designation as a breakthrough therapy, fast track product, or regenerative medicine advanced therapy.

In addition to and separate from expanded access, on May 30, 2018, the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the expanded access program. There is no obligation for a drug manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act, but the manufacturer must develop an internal policy and respond to patient requests according to that policy.

Marketing Approval. Assuming successful completion of the required clinical testing, the results of the preclinical and clinical studies, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. Under federal law, the submission of most NDAs is subject to an application user fee, which for federal fiscal year 2021 is $2,875,842 for an application requiring clinical data. The sponsor of an approved NDA is also subject to an annual program fee, which for fiscal year 2021 is $336,432. Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for products with orphan drug designation and a waiver for certain small businesses.

In addition, under the Pediatric Research Equity Act, or PREA, an NDA or supplement to an NDA must contain data that are adequate to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. The FDA maintains a list of diseases that are exempt from PREA requirements due to low prevalence of disease in the pediatric population. Congress amended the FDA Reauthorization Act of 2017, or FDARA. Previously, drugs that had been granted orphan drug designation were exempt from the requirements of the Pediatric Research Equity Act. Under the amended section 505B, beginning on August 18, 2020, the submission of a pediatric assessment, waiver or deferral will be required for certain molecularly targeted cancer indications with the submission of an NDA application or supplement to an NDA application. FL qualifies for an automatic full pediatric waiver by the FDA because it rarely or never occurs in pediatric patients.

The FDA requires that a sponsor who is planning to submit a marketing application for a drug or biological product that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration submit an initial Pediatric Study Plan, or PSP, within sixty days of an end-of-phase 2 meeting or as may be agreed between the sponsor and FDA. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. FDA and the sponsor must reach agreement on the PSP. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from nonclinical studies, early phase clinical trials, or other clinical development programs.

The FDA also may require submission of a REMS plan to mitigate any identified or suspected serious risks. The REMS plan could include medication guides, physician communication plans, assessment plans, and elements to assure safe use, such as restricted distribution methods, patient registries or other risk minimization tools.

Under PDUFA guidelines that are currently in effect, the FDA has agreed to certain performance goals regarding the timing of its review and disposition of an application. The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA reviews an NDA to determine, among other things, whether the drug is safe and effective and whether the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, quality and purity.

The FDA has the option to refer questions regarding their review of a marketing application for a New Molecular Entity, or NME, to an external advisory committee. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA uses approximately 50 advisory committees and panels to obtain independent expert advice on scientific, technical, and policy matters. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and are adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical trial sites to assure compliance with GCPs, may inspect the clinical CRO(s) to assure compliance with GCPs, and may perform a sponsor inspection.

The product development testing and approval process for an NDA requires substantial time, effort and financial resources, and each may take several years to complete. Data obtained from preclinical and clinical testing are not always conclusive and may be susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. As a result, the FDA may not grant approval of an NDA on a timely basis, or at all.

After evaluating the NDA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue an approval letter, or, in some cases, a complete response letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A complete response letter generally contains a statement of specific conditions that must be met in order to secure final approval of the NDA and may require additional clinical or preclinical testing in order for FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA will typically issue an approval letter.

Even if the FDA approves a product, it may limit the approved indications for use of the product, require that contraindications, warnings or precautions be included in the product labeling, including a boxed warning, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess a drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms under a REMS which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes, and additional labeling claims, are subject to further testing requirements and FDA review and approval.

***Orphan Drug Designation*.** Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug (including a biologic) intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for this type of disease or condition will be recovered from sales in the United States for that drug. Orphan drug designation must be requested before submitting an NDA or biologics license application, or BLA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA.

Orphan drug designation qualifies the sponsor of the drug for various development incentives. For example, a marketing application for a prescription drug product that has received orphan drug designation is not subject to a prescription drug user fee unless the application includes an indication other than for the rare disease or condition for which the drug was designated. Also, orphan drug designation extends the marketing exclusivity period for new drugs for the approved orphan indication from 5 years to 7 years from the date of approval. Furthermore, federal law establishes certain tax credits designed to encourage the development of orphan drugs. With passage of the Tax Cuts and Jobs Act of 2017, that tax credit was halved from 50% to 25%. The granting of an orphan drug designation request does not alter the standard regulatory requirements and process for obtaining marketing approval. Safety and effectiveness of a drug must be established through adequate and well-controlled studies.

Special FDA Expedited Review and Approval Programs. The FDA has various programs, including Fast Track Designation, Accelerated Approval, Priority Review and Breakthrough Therapy Designation, that are intended to expedite or simplify the process for the development and FDA review of drugs that are intended for the treatment of serious or life threatening diseases or conditions and demonstrate the potential to address unmet medical needs. The purpose of these programs is to provide important new drugs to patients earlier than under standard FDA review procedures.

Breakthrough Therapy Designation. Under the provisions of the Food and Drug Administration Safety and Innovation Act, or FDASIA, enacted in 2012, a sponsor can request designation of a product candidate as a "breakthrough therapy." The FDA may grant breakthrough therapy designation to a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA must take certain actions, such as holding timely meetings and providing advice, intended to expedite the development and review of an application for approval of a breakthrough therapy. For drugs and biologics that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Drugs designated as breakthrough therapies by the FDA are also eligible for accelerated approval.

Fast Track Designation. To be eligible for a Fast Track Designation, the FDA must determine, based on the request of a sponsor, that a product is intended to treat a serious or life-threatening disease or condition and demonstrates the potential to address an unmet medical need. The FDA will determine that a product will fill an unmet medical need if it will provide a therapy where none exists or provide a therapy that may be potentially superior to existing therapy based on efficacy or safety factors. For Fast Track products, sponsors may have greater interactions with the FDA regarding drug development and may submit sections of a Fast Track product's NDA on a rolling basis before the entire application is complete.

Priority Review. The FDA may give a priority review designation to drugs that offer major advances in treatment, or provide a treatment where no adequate therapy exists. A priority review means that the goal for the FDA to review an application is six months, rather than the standard review of ten months under current PDUFA guidelines. These six- and ten-month review periods are measured from the "filing" date rather than the receipt date for NDAs for new molecular entities, which typically adds approximately two months to the timeline for review and decision from the date of submission. Most products that are eligible for Fast Track designation are also likely to be considered appropriate to receive a priority review.

Accelerated Approval. In addition, products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval and may be approved on the basis of well-conducted clinical trials establishing that the drug product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. As a condition of accelerated approval, the FDA may require a sponsor to perform post-marketing confirmatory study(ies) to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical endpoints, and the drug may be subject to accelerated withdrawal procedures. Although a drug may be designated as "breakthrough" or "fast track", the determination of accelerated approval is based on the clinical endpoint and not on the expeditious manner in which it is being developed.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

FDA Regulation of Companion Diagnostics. Safe and effective use of a drug may rely upon an in vitro companion diagnostic for use in selecting the patients that will be more likely to respond to the treatment. FDA officials have issued guidance that addresses issues critical to developing in vitro companion diagnostics, such as when the FDA will require that the diagnostic and the drug be approved simultaneously. The guidance issued in August 2014 states that if safe and effective use of a therapeutic product depends on an in vitro diagnostic, then the FDA generally will require approval or clearance of the diagnostic at the same time that the FDA approves the therapeutic product.

The FDA generally requires that devices, or in vitro companion diagnostics, intended to select the patients who will respond to the cancer treatment to obtain Pre-Market Approval, or PMA, simultaneously with approval of the drug. Based on the guidance, and the FDA's past treatment of companion diagnostics, the FDA will typically require PMA approval of one or more in vitro companion diagnostics to identify patient populations suitable for these cancer therapies.

The PMA process, including the gathering of clinical and preclinical data and the submission to and review by the FDA involves a rigorous premarket review during which the applicant must prepare and provide the FDA with reasonable assurance of the device's safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing and labeling. PMA applications are subject to an application fee. For federal fiscal year 2021, the standard fee is $365,657 and the small business fee is $91,414.

After a device is placed on the market, it remains subject to significant regulatory requirements. Medical devices may be marketed only for the uses and indications for which they are cleared or approved. Device manufacturers must also establish registration and device listings with the FDA. A medical device manufacturer's manufacturing processes and those of its suppliers are required to comply with the applicable portions of the Quality System Regulation, or QSR, which cover the methods and documentation of the design, testing, production, processes, controls, quality assurance, labeling, packaging and shipping of medical devices. Domestic facility records and manufacturing processes are subject to periodic unscheduled inspections by the FDA. The FDA also may inspect foreign facilities that export products to the U.S.

Post-Approval Commitments and Requirements. Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA. For example, the FDA may require post-marketing testing, including Phase 4 clinical trials and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market.

Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in mandatory revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off label uses, and a company that is found to have improperly promoted off label uses may be subject to significant liability. If a company is found to have promoted off label uses, it may become subject to adverse public relations and administrative and judicial enforcement by the FDA, the Department of Justice, or the Office of the Inspector General of the Department of Health and Human Services, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes drug products.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, and its implementing regulations, as well as the Drug Supply Chain Security Act, or DSCA, which regulate the distribution and tracing of prescription drugs and prescription drug samples at the federal level, and set minimum standards for the regulation of drug distributors by the states. The PDMA, its implementing regulations and state laws limit the distribution of prescription pharmaceutical product samples, and the DSCA imposes requirements to ensure accountability in distribution and to identify and remove counterfeit and other illegitimate products from the market.

Federal and State Fraud and Abuse and Data Privacy and Security Laws and Regulations. In addition to FDA restrictions on marketing of pharmaceutical products, federal and state fraud and abuse laws restrict business practices in the biopharmaceutical industry. These laws include anti-kickback and false claims laws and regulations as well as data privacy and security laws and regulations.

The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce or in return for purchasing, leasing, ordering, or arranging for or recommending the purchase, lease, or order of any item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. The term "remuneration" has been broadly interpreted to include anything of value. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers, and formulary managers on the other. Although there are a number of statutory exemptions and regulatory safe harbors protecting some common activities from prosecution, the exemptions and safe harbors are drawn narrowly. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases, or recommendations may be subject to scrutiny if they do not qualify for an exemption or safe harbor. Several courts have interpreted the statute's intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare covered business, the statute has been violated.

The reach of the Anti-Kickback Statute was also broadened by the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively PPACA, which, among other things, amended the intent requirement of the federal Anti-Kickback Statute such that a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, PPACA provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act or the civil monetary penalties statute, which imposes penalties against any person who is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent. PPACA also created new federal requirements for reporting, by applicable manufacturers of covered drugs, payments and other transfers of value to physicians and teaching hospitals.

The federal False Claims Act prohibits any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government or knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. A claim includes "any request or demand" for money or property presented to the U.S. government. Several pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of products for unapproved, and thus non-reimbursable, uses. The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA,

created new federal criminal statutes that prohibit knowingly and willfully executing a scheme to defraud any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Also, many states have similar fraud and abuse statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

We may also be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology and Clinical Health Act, or HITECH, and its implementing regulations, imposes specified requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to "business associates," defined as independent contractors or agents of covered entities that receive or obtain protected health information in connection with providing a service on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

In addition, federal transparency requirements known as the federal Physician Payments Sunshine Act, under the Patient Protection and Affordable Care Act, as amended by the Health Care Education Reconciliation Act, or the Affordable Care Act, require certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, within the United States Department of Health and Human Services, information related to payments and other transfers of value made by that entity to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments and other transfers of value to physicians and other health care providers, and restrict marketing practices or require disclosure of marketing expenditures.

To the extent that any of our products are sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws, and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals.

Coverage and Reimbursement. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish corresponding reimbursement levels. In particular, in the United States, private health insurers and other third-party payors often provide reimbursement for products and services based on the level at which the government (through the Medicare or Medicaid programs) provides reimbursement for such treatments. In the United States, the European Union and other potentially significant markets for our product candidates, government authorities and third-party payors are increasingly attempting to limit or regulate the price of medical products and services, particularly for new and innovative products and therapies, which often has resulted in average selling prices lower than they would otherwise be. Further, the increased emphasis on managed healthcare in the United States and on country and regional pricing and reimbursement controls in the European Union will put additional pressure on product pricing, reimbursement and usage, which may adversely affect our future product sales and results of operations. These pressures can arise from rules and practices of managed care groups, judicial decisions and governmental laws and regulations related to Medicare, Medicaid and healthcare reform, pharmaceutical reimbursement policies and pricing in general.

Third-party payors are increasingly imposing additional requirements and restrictions on coverage and limiting reimbursement levels for medical products. For example, federal and state governments reimburse covered prescription drugs at varying rates generally below average wholesale price. These restrictions and limitations influence the purchase of healthcare services and products. Legislative proposals to reform healthcare or reduce

costs under government insurance programs may result in lower reimbursement for our products and product candidates or exclusion of our products and product candidates from coverage. The cost containment measures that healthcare payors and providers are instituting and any healthcare reform could significantly reduce our revenues from the sale of any approved product candidates. We cannot provide any assurances that we will be able to obtain and maintain third-party coverage or adequate reimbursement for our product candidates in whole or in part.

Impact of Healthcare Reform on Coverage, Reimbursement, and Pricing. The Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, imposed new requirements for the distribution and pricing of prescription drugs for Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities that provide coverage of outpatient prescription drugs. Part D plans include both standalone prescription drug benefit plans and prescription drug coverage as a supplement to Medicare Advantage plans. Unlike Medicare Part A and B, Part D coverage is not standardized. Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for any products for which we receive marketing approval. However, any negotiated prices for our future products covered by a Part D prescription drug plan will likely be lower than the prices we might otherwise obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from Medicare Part D may result in a similar reduction in payments from non-governmental payors.

The American Recovery and Reinvestment Act of 2009 provides funding for the federal government to compare the effectiveness of different treatments for the same illness. A plan for the research will be developed by the Department of Health and Human Services, the Agency for Healthcare Research and Quality and the National Institutes for Health, and periodic reports on the status of the research and related expenditures will be made to Congress. Although the results of the comparative effectiveness studies are not intended to mandate coverage policies for public or private payors, it is not clear what effect, if any, the research will have on the sales of any product, if any such product or the condition that it is intended to treat is the subject of a study. It is also possible that comparative effectiveness research demonstrating benefits in a competitor's product could adversely affect the sales of our product candidates. If third-party payors do not consider our product candidates to be cost-effective compared to other available therapies, they may not cover our product candidates, once approved, as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis.

The United States and some foreign jurisdictions are considering enacting or have enacted a number of additional legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell our products profitably. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives, including, most recently, PPACA, which became law in March 2010 and substantially changed the way healthcare is financed by both governmental and private insurers. Among the provisions of the Affordable Care Act of importance to potential product candidates are:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, although this fee would not apply to sales of certain products approved exclusively for orphan indications;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;

- expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price," or AMP, for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices and extending rebate liability to prescriptions for individuals enrolled in Medicare Advantage plans;
- addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- expanded the types of entities eligible for the 340B drug discount program;
- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide a 50% point-of-sale-discount off the negotiated price of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- the Independent Payment Advisory Board, or IPAB, which has authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription drugs. However, the IPAB implementation has been not been clearly defined. PPACA provided that under certain circumstances, IPAB recommendations will become law unless Congress enacts legislation that will achieve the same or greater Medicare cost savings; and
- established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending. Funding has been allocated to support the mission of the Center for Medicare and Medicaid Innovation from 2011 to 2019.

Other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. For example, in August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2012 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2030, pursuant to the CARES Act. In January 2013, the American Taxpayer Relief Act of 2012 became law, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

These healthcare reforms, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price for any approved product and/or the level of reimbursement physicians receive for administering any approved product. Reductions in reimbursement levels may negatively impact the prices or the frequency with which products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. Since enactment of the PPACA, there have been numerous legal challenges and Congressional actions to repeal and replace provisions of the law.

Since enactment of the PPACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by President Trump on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. Additionally, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the PPACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminates the health insurer tax. Further, the Bipartisan Budget Act of 2018, among other things, amended the PPACA, effective January 1, 2019, to increase from 50 percent to 70 percent

the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." The Congress may consider other legislation to replace elements of the PPACA during the next Congressional session.

The Trump Administration also took executive actions to undermine or delay implementation of the PPACA. During his term, President Trump signed two Executive Orders designed to delay the implementation of certain provisions of the PPACA or otherwise circumvent some of the requirements for health insurance mandated by the PPACA. One Executive Order directs federal agencies with authorities and responsibilities under the PPACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the PPACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. The second Executive Order terminates the cost-sharing subsidies that reimburse insurers under the PPACA. On January 28, 2021, however, President Biden issued a new Executive Order which directs federal agencies to reconsider rules and other policies that limit Americans' access to healthcare, and consider actions that will protect and strengthen that access. Under this Order, federal agencies are directed to re-examine: policies that undermine protections for people with pre-existing conditions, including complications related to COVID-19; demonstrations and waivers under Medicaid and the PPACA that may reduce coverage or undermine the programs, including work requirements; policies that undermine the Health Insurance Marketplace or other markets for health insurance; policies that make it more difficult to enroll in Medicaid and the PPACA; and policies that reduce affordability of coverage or financial assistance, including for dependents. Further, on December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the PPACA is an essential and inseverable feature of the PPACA, and therefore because the mandate was repealed as part of the Tax Cuts and Jobs Act, the remaining provisions of the PPACA are invalid as well. On December 18, 2019, the Court of Appeals for the Fifth Circuit affirmed the lower court's ruling that the individual mandate portion of the PPACA is unconstitutional and it remanded the case to the district court for reconsideration of the severability question and additional analysis of the provisions of the PPACA. Thereafter, the U.S. Supreme Court agreed to hear this case. Oral argument in the case took place on November 10, 2020, and a ruling by the Court is expected sometime this year. Litigation and legislation over the PPACA are likely to continue, with unpredictable and uncertain results.

The costs of prescription pharmaceuticals have also been the subject of considerable discussion in the United States To date, there have been several recent U.S. congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. To those ends, President Trump issued five executive orders intended to lower the costs of prescription drug products but it is unclear whether, and to what extent, these orders will remain in force under the Biden Administration. Further, on September 24, 2020, the Trump Administration finalized a rulemaking allowing states or certain other non-federal government entities to submit importation program proposals to the FDA for review and approval. Applicants are required to demonstrate that their importation plans pose no additional risk to public health and safety and will result in significant cost savings for consumers. The FDA has issued draft guidance that would allow manufacturers to import their own FDA-approved drugs that are authorized for sale in other countries (multi-market approved products).

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Exclusivity and Approval of Competing Products

Patent Term Restoration and Extension. A patent claiming a new drug product may be eligible for a limited patent term extension under the Hatch-Waxman Act, which permits a patent restoration of up to five years for patent term lost during product development and the FDA regulatory review. The restoration period granted is typically one-half the time between the effective date of an IND and the submission date of an NDA, plus the time between the submission date of an NDA and the ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved drug product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple drugs for which approval is sought can only be extended in connection with one of the approvals. The United States Patent and Trademark Office, or USPTO, reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

Hatch-Waxman Patent Exclusivity. In seeking approval for a drug through an NDA, applicants are required to list with the FDA each patent with claims that cover the applicant's product or a method of using the product. Upon approval of a drug, each of the patents listed in the application for the drug is then published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. Drugs listed in the Orange Book can, in turn, be cited by potential competitors in support of approval of an abbreviated new drug application, or ANDA, or 505(b)(2) NDA.

Generally, an ANDA provides for marketing of a drug product that has the same active ingredients in the same strengths, dosage form and route of administration as the listed drug and has been shown to be bioequivalent through *in vitro* or *in vivo* testing or otherwise to the listed drug. ANDA applicants are not required to conduct or submit results of preclinical or clinical tests to prove the safety or effectiveness of their drug product, other than the requirement for bioequivalence testing. Drugs approved in this way are commonly referred to as "generic equivalents" to the listed drug, and can often be substituted by pharmacists under prescriptions written for the original listed drug.

A 505(b)(2) application applies to a drug for which the investigations made to show whether or not the drug is safe for use and effective in use and relied upon by the applicant for approval of the application "were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted." As with an ANDA, Section 505(b)(2) authorizes the FDA to approve an NDA based on safety and effectiveness data that were not developed by the applicant. 505(b)(2) NDAs generally are submitted for changes to a previously approved drug product, such as a new dosage form or indication.

The ANDA or 505(b)(2) NDA applicant is required to certify to the FDA concerning any patents listed for the approved product in the FDA's Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval. Specifically, the applicant must certify with respect to each patent that:

- the required patent information has not been filed;
- the listed patent has expired;
- the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or
- the listed patent is invalid, unenforceable, or will not be infringed by the new product.

Generally, the ANDA or 505(b)(2) NDA cannot be approved until all listed patents have expired, except when the ANDA or 505(b)(2) NDA applicant challenges a listed drug. A certification that the proposed product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the applicant does not challenge the listed patents or indicate that it is not seeking approval of a patented method of use, the ANDA or 505(b)(2) NDA application will not be approved until all the listed patents claiming the referenced product have expired.

If the ANDA or 505(b)(2) NDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the application has been accepted for filing by the FDA. The NDA and patent holders may then initiate patent infringement litigation in

response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of notice of the Paragraph IV certification automatically prevents the FDA from approving the ANDA or 505(b)(2) NDA until the earlier of 30 months, expiration of the patent, settlement of the lawsuit or a decision in the infringement case that is favorable to the ANDA applicant.

Hatch—Waxman Non-Patent Exclusivity. Market and data exclusivity provisions under the FDCA also can delay the submission or the approval of ANDAs and 505(b)(2) NDAs for competing products. The FDCA provides a five-year period of non-patent data exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the activity of the drug substance. During the exclusivity period, the FDA may not accept for review an ANDA or a 505(b)(2) NDA submitted by another company that contains the previously approved active moiety. However, an ANDA or 505(b)(2) NDA may be submitted after four years if it contains a certification of patent invalidity or non-infringement.

The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA, or supplement to an existing NDA or 505(b)(2) NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant, are deemed by the FDA to be essential to the approval of the application or supplement. Three-year exclusivity may be awarded for changes to a previously approved drug product, such as new indications, dosages, strengths or dosage forms of an existing drug. This three-year exclusivity covers only the conditions of use associated with the new clinical investigations and, as a general matter, does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for generic versions of the original, unmodified drug product. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA; however, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

The FDA must establish a priority review track for certain generic drugs, requiring the FDA to review a drug application within eight months for a drug that has three or fewer approved drugs listed in the Orange Book and is no longer protected by any patent or regulatory exclusivities, or is on the FDA's drug shortage list. The new legislation also authorizes FDA to expedite review of ''competitor generic therapies'' or drugs with inadequate generic competition, including holding meetings with or providing advice to the drug sponsor prior to submission of the application.

Orphan Drug Exclusivity. Under the Orphan Drug Act, a drug that is approved for the orphan drug designated indication is granted seven years of orphan drug exclusivity. Orphan drug exclusivity means that the FDA may not approve another sponsor's marketing application for the same drug for the same indication for seven years, except in certain limited circumstances. Orphan exclusivity does not block the approval of a different product for the same rare disease or condition, nor does it block the approval of the same product for different indications. If a drug or biologic designated as an orphan drug ultimately receives marketing approval for an indication broader than what was designated in its orphan drug application, it may not be entitled to exclusivity.

Orphan drug exclusivity will also not bar approval of another product under certain circumstances, including if a subsequent product with the same drug or biologic for the same indication is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care, or if the company with orphan drug exclusivity is not able to meet market demand. This is the case despite an earlier court opinion holding that the Orphan Drug Act unambiguously required the FDA to recognize orphan exclusivity regardless of a showing of clinical superiority.

Pediatric Exclusivity. Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent and orphan drug exclusivity periods described above, and any listed patent. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or Orange Book listed patent

protection cover the drug are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve an ANDA or 505(b)(2) application owing to regulatory exclusivity or listed patents. When any of our products is approved, we anticipate seeking pediatric exclusivity when it is appropriate.

European Union Drug Approval Process

In order to market any product outside of the United States, we would need to comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we would need to obtain the necessary approvals by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of the product in those countries. The approval process varies from country to country and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may negatively impact the regulatory process in others.

Clinical Trial Approval in the EU. Pursuant to the currently applicable Clinical Trials Directives, an applicant must obtain approval from the competent national authority of the EU Member State in which the clinical trial is to be conducted. If the clinical trial is conducted in different EU Member States, the competent authorities in each of these EU Member States must provide their approval for the conduct of the clinical trial. Furthermore, the applicant may only start a clinical trial at a specific study site after the competent ethics committee has issued a favorable opinion. In April 2014, the EU adopted a new Clinical Trials Regulation, which is set to replace the current Clinical Trials Directive. The new Clinical Trials Regulation will be directly applicable to and binding in all 27 EU Member States without the need for any national implementing legislation. Under the new coordinated procedure for the approval of clinical trials, the sponsor of a clinical trial will be required to submit a single application for approval of a clinical trial to a reporting EU Reference Member State (RMS) through an EU Portal. The submission procedure will be the same irrespective of whether the clinical trial is to be conducted in a single EU Member State or in more than one EU Member State. The Clinical Trials Regulation also aims to streamline and simplify the rules on safety reporting for clinical trials.

In January 2020, the website of the European Commission reported that the implementation of the Clinical Trials Regulation was dependent on the development of a fully functional clinical trials portal and database, which would be confirmed by an independent audit which was conducted in December 2020, and that the new legislation would come into effect six months after the European Commission publishes a notice of this confirmation. The Regulation becomes applicable six months after the European Commission publishes notice of this confirmation and has published an expected system “go live” in December 2021. When the Regulation becomes applicable, the existing EU Clinical Trial Directive and national legislation put in place to implement the Directive will be repealed. Following implementation of the EU Clinical Trials Regulation, a transitional period will be in effect for one year where new clinical trial applications can be submitted either under the existing EU Clinical Trials Directive or under the new Clinical Trials Regulation. It will also apply to trials authorized under the previous legislation if they are still ongoing three years after the Regulation has come into operation.

As in the United States, information about certain clinical trials must be submitted within specific timeframes to the European Union (EudraCT) website: https://eudract.ema.europa.eu/ and other countries.

Marketing Authorization. To obtain marketing approval of a drug under European Union regulatory systems, we may submit marketing authorization applications, or MAAs, either under a centralized or decentralized procedure. The centralized procedure provides for the grant of a single marketing authorization that is valid for all EU member states. The centralized procedure is compulsory for medicines produced by specified biotechnological processes, products designated as orphan medicinal products, and products with a new active substance indicated for the treatment of specified diseases, and optional for those products that are highly innovative or for which a centralized process is in the interest of patients. Under the centralized procedure in the European Union, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the Scientific Advice Working Party

of the Committee of Medicinal Products for Human Use, or the CHMP. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest, defined by three cumulative criteria: the seriousness of the disease, such as heavy disabling or life-threatening diseases, to be treated; the absence or insufficiency of an appropriate alternative therapeutic approach; and anticipation of high therapeutic benefit. In this circumstance, the European Medicines Agency, or EMA, ensures that the opinion of the CHMP is given within 150 days.

The decentralized procedure provides for approval by one or more other, or concerned, member states of an assessment of an application performed by one-member state, known as the reference member state. Under this procedure, an applicant submits an application, or dossier, and related materials, including a draft summary of product characteristics, and draft labeling and package leaflet, to the reference member state and concerned member states. The reference member state prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. Within 90 days of receiving the reference member state's assessment report, each concerned member state must decide whether to approve the assessment report and related materials. If a member state cannot approve the assessment report and related materials on the grounds of potential serious risk to public health, the disputed points may eventually be referred to the European Commission, whose decision is binding on all member states. For the EMA, an agreed Pediatric Investigation Plan, which could include a request for waiver or deferral, is required prior to submitting an MAA for use for drugs in pediatric populations.

Data and Market Exclusivity. In the European Union, new chemical entities qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. This data exclusivity, if granted, prevents regulatory authorities in the European Union from assessing a generic (abbreviated) application for eight years, after which generic marketing authorization can be submitted but not approved for two years. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity and the sponsor is able to gain the prescribed period of data exclusivity, another company nevertheless could also market another version of the drug if such company can complete a full MAA with a complete human clinical trial database and obtain marketing approval of its product.

General Data Protection Regulation. The collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the EU, including personal health data, is subject to the EU General Data Protection Regulation, or GDPR, which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EU, including the United States and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR will be a rigorous and time-intensive process that may increase the cost of doing business or require companies to change their business practices to ensure full compliance.

Orphan Drug Exclusivity. The EMA grants orphan drug designation to promote the development of products that may offer therapeutic benefits for life-threatening or chronically debilitating conditions affecting not more than five in 10,000 people in the European Union. In addition, orphan drug designation can be granted if the drug is intended for a life threatening, seriously debilitating or serious and chronic condition in the European Union and without incentives it is unlikely that sales of the drug in the European Union would be sufficient to justify developing the drug. Orphan drug designation is only available if there is no other satisfactory method approved in the European Union of diagnosing, preventing or treating the condition, or if such a method exists, the proposed orphan drug will be of significant benefit to patients. Orphan drug designation provides opportunities for free protocol assistance, fee reductions for access to the centralized regulatory procedures before and during the first year after marketing authorization and 10 years of market exclusivity of the designated indication following drug approval. Fee

reductions are not limited to the first year after authorization for small and medium enterprises. The exclusivity period may be reduced to six years if the designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity.

Priority Medicines, or PRIME, Drug Designation. EMA may grant PRIME drug designation to medicine developers to treat an unmet medical need upon selection. Medicines eligible for PRIME must address an unmet medical need, have data available showing the potential to address this need and bring a major therapeutic advantage to patients. PRIME designation provides early and enhanced support from EMA to optimize the development of eligible medicines, speeds up their evaluation, and contributes to timely patients' access. Once a candidate is selected for PRIME designation, the EMA will provide scientific advice at key development milestones and confirm potential for accelerated assessment at the time of an application for marketing authorization. These medicines are considered priority medicines by EMA.

Brexit and the Regulatory Framework in the United Kingdom.

On June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the EU, commonly referred to as Brexit. Following protracted negotiations, the United Kingdom left the EU on January 31, 2020. Under the withdrawal agreement, there is a transitional period until December 31, 2020 (extendable by up to two years). On December 24, 2020, the United Kingdom and the European Union entered into a Trade and Cooperation Agreement. The agreement sets out certain procedures for approval and recognition of medical products in each jurisdiction. Since the regulatory framework for pharmaceutical products in the United Kingdom covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from EU directives and regulations, Brexit could materially impact the future regulatory regime that applies to products and the approval of product candidates in the United Kingdom.

Furthermore, while the Data Protection Act of 2018 in the United Kingdom that "implements" and complements the European Union's General Data Protection Regulation, or GDPR, has achieved Royal Assent on May 23, 2018 and is now effective in the United Kingdom, it is still unclear whether transfer of data from the European Economic Area, or EEA, to the United Kingdom will remain lawful under GDPR. The Trade and Cooperation Agreement provides for a transitional period during which the United Kingdom will be treated like an European Union member state in relation to processing and transfers of personal data for four months from January 1, 2021. This may be extended by two further months. After such period, the United Kingdom will be a "third country" under the GDPR unless the European Commission adopts an adequacy decision in respect of transfers of personal data to the United Kingdom. The United Kingdom has already determined that it considers all of the EU 27 and EEA member states to be adequate for the purposes of data protection, ensuring that data flows from the United Kingdom to the EU/EEA remain unaffected.

Employees and Human Capital Resources

As of February 15, 2021, we had 304 full-time employees, 94 of whom were primarily engaged in research and development activities.

Our human capital is integral in helping us achieve our mission to rewrite treatment for cancer and other serious diseases through novel epigenetic medicines. We have built a culture of community, along with our EpiExcellence cultural attributes, and many of these qualities are foundational. Our EpiExcellence cultural attributes include:

- *Camaraderie*: connectedness, humor, liking each other, fun, in it together, mutual respect
- *Collaboration*: integrated decision-making, teamwork, internal/external partnerships, interdependent, "right people, right time, right involvement"
- *Disciplined*: execution, prioritization, focus, accountability, consistency, quality
- *Innovative*: risk-tolerant, creativity, evidence-based, curiosity, continuous learning

- *Openness*: honesty, constructive dissent, transparency, courageous conversations, assumption of good intent, trust
- *Patient-focused*: shared purpose, inspired, passionate, motivated, sense of urgency
- *Resilient*: nimble, optimistic, embracing change, evolutionary, adaptable

This work has been intentional to ensure we are creating a culture and company that offers a vibrant community to our employees and ensures that we can fully be ourselves at work. We strive to ensure that Epizyme is a place where all people experience equality, where we value diversity in all its forms, and that we are modeling these behaviors in the world outside Epizyme as corporate citizens.

Information about our Executive Officers

The following table sets forth the name, age and position of each of our executive officers as of February 23, 2021.

Name	Age	Position
Robert B. Bazemore	53	President, Chief Executive Officer and Director
Paolo Tombesi	57	Chief Financial Officer
Shefali Agarwal	47	Executive Vice President, Chief Medical and Development Officer
Matthew E. Ros	54	Executive Vice President, Chief Strategy and Business Officer
Jeffery L. Kutok	54	Chief Scientific Officer
Victoria M. Vakiener	57	Chief Commercial Officer

Robert B. Bazemore has served as a director and our President and Chief Executive Officer since September 2015. Prior to joining us, from September 2014 to June 2015, Mr. Bazemore served as the Chief Operating Officer of Synageva BioPharma Corp., a biopharmaceutical company developing therapeutic products for rare disorders. Prior to joining Synageva, Mr. Bazemore served in increasing levels of responsibility at Johnson & Johnson, a healthcare company, including Vice President, Centocor Ortho Biotech Sales & Marketing from 2008 to 2010, President of Janssen Biotech from January 2010 to October 2013 and Vice President of Global Surgery at Ethicon from October 2013 to September 2014. Prior to Johnson & Johnson, Mr. Bazemore worked at Merck & Co., Inc., for eleven years, where he served in a variety of roles in medical affairs, sales and marketing. Mr. Bazemore is a director of Ardelyx, Inc., a biopharmaceutical company, and Nuvation Bio, a biopharmaceutical company. Mr. Bazemore served as a director of Neon Therapeutics, Inc. (acquired by BioNTech in May 2020) from November 2018 to May 2020. He received a B.S. in biochemistry from the University of Georgia.

Paolo Tombesi has served as our Chief Financial Officer since joining us in August 2019. Prior to joining us, from June 2017 to June 2019 Mr. Tombesi served as the Chief Financial Officer for Insmed Incorporated, or Insmed, a global biopharmaceutical company. Prior to joining Insmed, Mr. Tombesi was Chief Financial and Administrative Officer of Novartis Pharmaceuticals Corporation, a U.S. subsidiary of multinational pharmaceutical company Novartis AG, or Novartis, a position he held from December 2014 through May 2017. Mr. Tombesi was Managing Director and Chief Financial Officer of Novartis Pharma K.K., a Japanese subsidiary of Novartis, from April 2009 to November 2014 and held various finance roles at Novartis from September 2006 to March 2009. Mr. Tombesi held several finance director positions at Bristol-Myers Squibb, a multinational biopharmaceutical company, from August 1996 to September 2006. From January 1988 to July 1996, Mr. Tombesi held various positions in consumer goods at Unilever NV and Johnson & Johnson. Mr. Tombesi holds a B.Ed. in Business and Managerial Economics from Sapienza Università di Roma and a B.A. in Accounting from Duca degli Abruzzi Roma.

Dr. Shefali Agarwal has served as our Executive Vice President, Chief Medical and Development Officer since February 2021 and served as our Chief Medical Officer from June 2018 to February 2021. Prior to joining us, Dr. Agarwal held leadership positions across medical research, clinical development, clinical operations and medical affairs. She most recently served as chief medical officer at SQZ Biotech, a biotechnology company developing cell therapies for patients with a wide range of diseases, from July 2017 to May 2018 and as a non-executive advisor from May 2018 to July 2018, where she built and led the clinical development organization, which included clinical research operations and the regulatory function. Before SQZ Biotech, Dr. Agarwal also held leadership positions at

Curis, Inc. a biotechnology company developing therapeutics for the treatment of cancer, from July 2016 to July 2017 and Tesaro, Inc., an oncology-focused biopharmaceutical company, from July 2013 to July 2017. At Curis, Inc., she oversaw the Phase 2 study for its dual HDAC/PI3K inhibitor in diffuse large B-cell lymphoma, and the Phase 1 study in solid tumors for its oral checkpoint inhibitor. At Tesaro, Inc., she led the NDA and EMA submissions for ZEJULA® (niraparib) in ovarian cancer. Dr. Agarwal also held positions of increasing responsibility at Covidien, a medical devices and health care products company, from April 2010 to December 2011, AVEO Pharmaceuticals, Inc., a biopharmaceutical company advancing targeted oncology medicines, from December 2011 to July 2013 and Pfizer Inc., a pharmaceutical company with a wide range of treatments, from June 2005 to April 2010. Dr. Agarwal received her MBBS medical degree from Karnataka University's Mahadevappa Rampure Medical School in India, Master's Degree in Public Health from Johns Hopkins University, where she led clinical research in the Department of Anesthesiology and Critical Care Medicine, and a Master of Science degree in Business from the University of Baltimore's Merrick School of Business.

Matthew E. Ros has served as our Executive Vice President, Chief Strategy and Business Officer since September 2020, served as our Chief Strategy and Business Officer from September 2018 to September 2020 and served as our Chief Operating Officer from May 2016 to September 2018. Prior to joining us, from September 2010 to May 2016, Mr. Ros served in increasing levels of responsibility at Sanofi, a multinational pharmaceutical company, most recently as Chief Operating Officer/Global Head of the Oncology Business unit from December 2014 to May 2016. From October 2007 to June 2010, Mr. Ros served at ARIAD Pharmaceuticals, Inc., a global oncology company, most recently as Senior Vice President, Commercial Operations. He started his pharmaceutical career in Bristol-Myers Squibb's Oncology Division, serving in roles with increasing responsibility from 1990 to 2007. Mr. Ros is a director of Cogent Biosciences, Inc., a biotechnology company. He received a B.S. from the State University of New York, College at Plattsburgh and completed the Executive Education Program in Finance and Accounting for the Non-Financial Manager at Wharton School of the University of Pennsylvania.

Jeffery L. Kutok, M.D., Ph.D., has served as our Chief Scientific Officer since joining us in April 2020. Dr. Kutok previously served as Chief Scientific Officer of Infinity Pharmaceuticals, Inc., or Infinity, a biotechnology company that develops cancer medication, from February 2017 to March 2020. Dr. Kutok previously served as Infinity's Vice President of Biology and Translational Science from August 2013 to February 2017, and in other roles with increasing responsibility from January 2011 to August 2013. Prior to joining Infinity, Dr. Kutok was an associate professor of pathology at Harvard Medical School and Brigham and Women's Hospital. Dr. Kutok's laboratory focused on translational medicine research and biomarker identification in cancer, and he is an author on over 200 journal articles, reviews and book chapters. Dr. Kutok is board certified in Anatomic Pathology and Hematology and had clinical duties in Hematopathology and Molecular Diagnostics at Brigham and Women's Hospital. Dr. Kutok received his B.S. in biology and his M.D., Ph.D. in medicine and molecular pathology from the State University of New York at Stony Brook. He was also a post-doctoral fellow at Harvard University in the laboratory of Dr. Gary Gilliland, M.D., Ph.D.

Victoria M. Vakiener has served as our Chief Commercial Officer since September 2020 and served as our Senior Vice President, Commercial from December 2018 to September 2020. During her more than 20 years of experience in oncology, Ms. Vakiener has held positions of leadership with increasing responsibility across Johnson & Johnson's pharmaceuticals and diagnostics businesses. Most recently, she was the Vice President and Oncology Global Commercial Leader for Prostate Cancer at Janssen from January 2018 to September 2020 and led a cross-functional team to develop and execute the global commercial strategy for its portfolio of late stage and early pipeline compounds. She also previously served as the Vice President of Oncology Marketing at Janssen Oncology U.S. from November 2014 to December 2018 and during her tenure in this position, Ms. Vakiener was able to launch multiple oncology therapeutics for Janssen, including DARZALEX, ZYTIGA, and IMBRUVICA. Prior to Johnson & Johnson, Ms. Vakiener began her pharmaceutical career at Schering-Plough and spent nine years there in both scientific roles and commercial positions. She received a B.S. in Biochemistry from Albright College, Reading, PA.

Our Corporate Information

We were incorporated under the laws of the state of Delaware on November 1, 2007 under the name Epizyme, Inc. Our principal executive offices are located at 400 Technology Square, 4th Floor, Cambridge, Massachusetts 02139. Our telephone number is (617) 229-5872, and our website is located at www.epizyme.com. References to our

website are inactive textual references only and the content of our website should not be deemed incorporated by reference into this Annual Report on Form 10-K.

Available Information

Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and any amendments to these reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, are available free of charge on our website located at www.epizyme.com as soon as reasonably practicable after they are electronically filed with or furnished to the SEC. These reports are also available at the SEC's Internet website at www.sec.gov.

A copy of our Corporate Governance Guidelines, Code of Business Conduct and Ethics and the charters of the Audit Committee, Compensation Committee and Nominating and Corporate Governance Committee are posted on our website, www.epizyme.com, under "Investor Center" and are available in print to any person who requests copies by contacting Epizyme by calling (617) 229-5872 or by writing to Epizyme, Inc., 400 Technology Square, 4th Floor, Cambridge, Massachusetts 02139.

Item 1A. Risk Factors

Risk Factors

Careful consideration should be given to the following risk factors, in addition to the other information set forth in this Annual Report on Form 10-K and in other documents that we file with the SEC, in evaluating our company and our business. Investing in our common stock involves a high degree of risk. If any of the following risks and uncertainties actually occurs, our business, prospects, financial condition and results of operations could be materially and adversely affected. The risks described below are not intended to be exhaustive and are not the only risks facing our company. New risk factors can emerge from time to time, and it is not possible to predict the impact that any factor or combination of factors may have on our business, prospects, financial condition and results of operations.

In addition, the COVID-19 pandemic has impacted and in the future may exacerbate or further impact risks discussed in this Annual Report on Form 10-K, any of which could have a material effect on us. This situation is changing rapidly and additional impacts may arise.

Risks Related to Product Development and Commercialization

We are dependent on the successful development and commercialization of tazemetostat. If we do not successfully commercialize TAZVERIK for the indications for which TAZVERIK is approved or are unable to develop, obtain marketing approval of, and commercialize tazemetostat for additional indications, either alone or through a collaboration, or if we experience significant delays in doing so, our business could be harmed.

Our EZH2 inhibitor, TAZVERIK, is approved in the United States for the treatment of epithelioid sarcoma, or ES, and for follicular lymphoma, or FL. We have no other products approved for sale. We are investing a significant portion of our efforts and financial resources to fund the development and commercialization of tazemetostat. In January 2020, the U.S. Food and Drug Administration, or FDA, granted accelerated approval of TAZVERIK for the treatment of adults and pediatric patients aged 16 years and older with metastatic or locally advanced ES not eligible for complete resection.

In June 2020, the FDA granted accelerated approval of 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.

In connection with the accelerated approval of our ES new drug application, or NDA and our FL supplemental NDA, or sNDA, continued approval is contingent upon verification and description of clinical benefit in a confirmatory program in each indication. We are conducting Phase 1b/3 trials to assess TAZVERIK in combination with doxorubicin compared with doxorubicin plus placebo as a front-line treatment for ES and to evaluate the combination of TAZVERIK with “R2” (Revlimid plus rituximab), an approved chemotherapy-free treatment regimen, for FL patients in the second-line or later treatment setting. These trials are expensive and time-consuming and may not confirm such benefit and subject the NDAs to withdrawal. If a confirmatory program does not verify clinical benefit for an indication, we may have to withdraw our accelerated approval for that indication. If any of these outcomes occurs, either to TAZVERIK or to any future product candidate for which we may seek marketing approval, we may be forced to abandon our development efforts for tazemetostat or such future product candidates, which could significantly harm our business.

We and our collaborators are conducting clinical trials of tazemetostat in other indications and in combination with other products. All of our other future product candidates are still in preclinical development. As a result, our prospects are substantially dependent on our ability, or the ability of any future collaborator, to successfully commercialize tazemetostat for ES and FL in the approved indications and to develop, obtain marketing approval for and successfully commercialize tazemetostat in one or more additional disease indications.

The success of tazemetostat will depend on several factors, including the following:

- success of the ongoing commercialization of TAZVERIK for ES and FL in the approved indications, whether alone or in combination with other products;
- successful confirmatory trials of TAZVERIK in the approved indications that are satisfactory to the FDA and maintenance of the continued acceptable safety profiles of the products following approval;
- continued implementation and maintenance of effective sales, marketing and distribution capabilities and strategies for commercialization of TAZVERIK;
- acceptance of TAZVERIK for ES, FL, and any other indication for which it may be approved by physicians, patients, third-party payors and others in the medical community;
- timely submission of a marketing authorization application to and timely receipt of marketing approval from the European Medicines Agency, or EMA, for ES, FL or any future indications;
- the extent of any required post-marketing approval commitments to applicable regulatory authorities;
- successful enrollment in and completion of clinical trials for the treatment of additional indications;
- safety, tolerability and efficacy profiles that are satisfactory to the FDA, the EMA, or any comparable foreign regulatory authority for marketing approval for additional indications and maintenance of continued acceptable safety profile following approval;
- effectively competing with other therapies;
- obtaining and maintaining healthcare insurance coverage and adequate reimbursement;
- making arrangements with third-party manufacturers for, or establishing, clinical and commercial manufacturing capabilities;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our products and product candidates;
- protecting our rights in our intellectual property portfolio; and
- effectively and successfully navigating the commercial and operational challenges and impacts resulting from the COVID-19 pandemic.

Many of these factors are beyond our control, including clinical development, the regulatory review process, potential threats to our intellectual property rights and the manufacturing, marketing and sales efforts of any collaborator. If any of these factors adversely affects the development or commercialization of tazemetostat, we may not be able to successfully develop or commercialize tazemetostat on a timely basis or at all, which would materially harm our business.

The COVID-19 pandemic has impacted our commercial launch of TAZVERIK in FL and ES, may affect our ability to initiate and complete preclinical studies and our ongoing and planned clinical trials, disrupt regulatory activities, further disrupt commercialization of TAZVERIK, or have other adverse effects on our business and operations. In addition, the COVID-19 pandemic has caused substantial disruption in the financial markets and may adversely impact economies worldwide, both of which could result in adverse effects on our business and operations.

The COVID-19 pandemic, which began in late 2019 and has spread worldwide, is causing many governments to implement measures to slow the spread of the outbreak through quarantines, travel restrictions, heightened border scrutiny, and other measures. The outbreak and government measures taken in response have also had a significant impact, both direct and indirect, on businesses and commerce, as worker shortages have occurred; supply chains have been disrupted; facilities and production have been suspended; unemployment has increased; and demand for certain goods and services, such as medical services and supplies, has spiked, while demand for other goods and services, such as travel, has fallen. The future progression of the outbreak and its effects on our business and operations are uncertain.

We and our contract manufacturing organizations, or CMOs, and contract research organizations, or CROs, may face disruptions that may affect our ability to initiate and conduct preclinical studies and our planned and ongoing clinical trials, including disruptions in procuring items that are essential for our research and development activities, such as access to raw materials used in the manufacture of tazemetostat and/or our other future product candidates, laboratory supplies used in our preclinical studies and ongoing clinical trials, or animals that are used for preclinical testing for which there are shortages because of ongoing efforts to address the outbreak. We and our CROs and CMOs, as well as clinical trial sites, may face disruptions related to our ongoing clinical trials, planned clinical trials or future clinical trials arising from manufacturing disruptions, staffing disruptions and limitations on our activities and the activities of our CROs and CMOs, and delays in the ability to obtain necessary institutional review board or other necessary site approvals or delays in site initiations or site monitoring visits, as well as other delays at clinical trial sites. We may also face limitations on enrollment and patients withdrawing from our clinical trials or not complying with the protocol procedures, which could delay completion of our clinical trials or adversely affect the data generated by our clinical trials. The response to the COVID-19 pandemic may redirect resources with respect to regulatory and intellectual property matters in a way that could adversely impact our ability to progress regulatory approvals and protect our intellectual property. In addition, we may face impediments to regulatory meetings and approvals due to measures intended to limit in-person interactions.

We commenced commercial sales of TAZVERIK in January 2020, and the pandemic and related government measures have limited our ability to access accounts and healthcare professionals, in person or at all, to provide medical information to promote TAZVERIK. For example, during the third and fourth quarters of 2020, the COVID-19 pandemic continued to negatively impact ES and FL patient visits to physicians, new patient starts across all lines of treatment as well as the ability of our field-based teams to fully access ES and FL prescribers, and these challenges continued in the first quarter of 2021. The pandemic has significantly impacted economies worldwide, which could result in adverse effects on our business and operations. Moreover, the pandemic has also caused substantial disruption in the financial markets and may adversely impact economies worldwide, both of which could result in adverse effects on our business and operations as well as the volatility of our stock price and trading in our stock.

We continue to operate under a remote operating model for all employees other than certain members of our laboratory and facilities staff, and we continue to evaluate this policy for our offices based on guidance from federal, state and local government authorities. Our increased reliance on personnel working from home may negatively impact productivity, or disrupt, delay, or otherwise adversely impact our business. In addition, this could increase our cyber security risk, create data accessibility concerns, and make us more susceptible to communication disruptions, any of which could adversely impact our business operations or delay necessary interactions with local and federal regulators, ethics committees, manufacturing sites, research or clinical trial sites and other important agencies and contractors, including our CROs and CMOs.

For instance, as part of our remote operating model, our laboratory staff engaged in research and development activities continue to have restricted access to laboratories. Accordingly, our laboratory staff are not yet back to their full daily output as existed prior to the onset of the ongoing COVID-19 pandemic. As a result, this could delay timely completion of preclinical activities and initiation of additional clinical trials for other of our development programs.

Due to the evolving and uncertain global impacts of the COVID-19 pandemic, we cannot precisely determine or quantify the impact that the COVID-19 pandemic has had or will have on our business, financial condition, results of operations, and prospects for the fiscal year ending December 31, 2021 and beyond.

Tazemetostat or any other product candidate that we develop may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.

Tazemetostat or any other product candidates that we develop may fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. If tazemetostat or any other such product candidate that we develop does not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of tazemetostat or any other product candidates that we develop will depend on a number of factors, including:

- the efficacy and potential advantages compared to alternative treatments;
- our ability to offer our products for sale at competitive prices;
- the convenience and ease of administration compared to alternative treatments;
- the willingness of the patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support;
- the availability of third-party coverage and adequate reimbursement;
- the prevalence and severity of any side effects;
- any safety events that may have occurred in connection with the development of the product candidate; and
- any restrictions on the use of our products together with other medications.

In addition, the potential market opportunity for tazemetostat is difficult to precisely estimate. Our estimates of the potential market opportunity for tazemetostat include several key assumptions based on our industry knowledge, industry publications, third-party research reports and other surveys. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions. If any of these assumptions proves to be inaccurate, then the actual market for tazemetostat could be smaller than our estimates of our potential market opportunity. If the actual market for tazemetostat is smaller than we expect, our product revenue may be limited and it may be more difficult for us to achieve or maintain profitability.

If we are unable to maintain effective sales, marketing and distribution capabilities, we may not be successful in commercializing tazemetostat or any other product candidates that we may develop if and when such product candidate is approved.

To achieve commercial success for any product for which we obtain marketing approval, we will need to maintain an effective sales and marketing organization.

We have recently established, and plan to continue to build, the infrastructure that we believe is necessary and appropriate to support the ongoing commercialization and marketing of TAZVERIK for the approved indications in the United States and the successful commercial launch and marketing of tazemetostat for other indications and in other jurisdictions and of other future product candidates that may receive marketing approval. There are risks involved with maintaining our own sales, marketing and distribution capabilities. For example, recruiting, training and retaining a sales force is expensive and time consuming and any failure to do so successfully could negatively affect sales or any commercial launch of a product. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. These efforts may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to successfully commercialize our products on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any current or future products;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we are unable to effectively maintain our own sales, marketing and distribution capabilities and as a result we determine to enter into arrangements with third parties to perform these services, our product revenues and our profitability, if any, could be lower than if we were to market, sell and distribute any products that we develop ourselves. In addition, we may determine to seek to enter into arrangements with third parties to perform these services in certain geographies outside the United States or for additional indications. However, we may not be successful in entering into arrangements with third parties to sell, market and distribute TAZVERIK or any future product candidates or may be unable to do so on terms that are acceptable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell, market or distribute our products effectively. If we do not establish and maximize sales, marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing TAZVERIK or any future product candidates.

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 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 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, 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, advanced malignancies); Daiichi Sankyo, developing a EZH1/EZH2 dual inhibitor (valemetostat, DS-3201, Phase 1, relapsed or refractory non-Hodgkin lymphomas, AML, ALL as well as Phase 2 for small cell lung cancer and relapsed or refractory adult T-cell leukemia/lymphoma); and Pfizer, developing EZH2 inhibitor PF-06821497, Phase 1, relapsed or refractory SCLC, castration-resistant prostate cancer, FL and diffuse large B-cell lymphoma. 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, 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.

Tazemetostat and any other future product candidate that we commercialize may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, which could harm our business.

The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drug products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch and market acceptance of the product, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval.

Our ability to successfully commercialize tazemetostat or any other future product candidates that we develop successfully also will depend in part on the extent to which insurance coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and third-party payors, such as private health

insurers and health maintenance organizations, decide which medications they will pay for and establish corresponding reimbursement levels. A significant trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors continue to attempt to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. Coverage and reimbursement may not be available for any product that we commercialize and, even if these are available, the level of reimbursement may not be satisfactory to recoup our investment. Reimbursement may affect the demand for, or the price of, any product candidate for which we obtain marketing approval. Obtaining and maintaining adequate reimbursement for our products may be difficult. We may be required to conduct expensive pharmacoeconomic studies to justify coverage and reimbursement or the level of reimbursement relative to other therapies. If coverage and adequate reimbursement are not available or reimbursement is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

There may be significant delays in obtaining reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or similar regulatory authorities outside of the United States. Moreover, eligibility for reimbursement does not imply that a drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the intended use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

Clinical drug development is a lengthy and expensive process, with an uncertain outcome. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of tazemetostat and any future product candidates.

We are conducting multiple clinical trials of tazemetostat. In addition, under our collaboration with Glaxo Group Limited (an affiliate of GlaxoSmithKline plc), or GSK, GSK has initiated a Phase 2 expansion clinical trial for GSK3326595, a PRMT5 inhibitor, and has initiated patient dosing in a Phase 1 clinical trial of GSK3368715, a PRMT1 inhibitor. The risk of failure is high. It is impossible to predict when or if any product candidates that we may develop will prove effective or safe in humans or will receive regulatory approval. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development, manufacture, and then conduct extensive clinical trials to demonstrate the safety and efficacy of any product candidates in humans.

Product candidates are subject to preclinical safety studies, which may be conducted prior to or concurrently with clinical testing, as well as continued clinical safety assessment throughout clinical testing. The outcomes of these safety studies or assessments may delay the launch of or patient enrollment in clinical studies. For example, in the course of our preclinical safety studies of tazemetostat, we observed the development of lymphoma in Sprague-Dawley rats. As a result of these findings, coupled with our limited clinical experience in FL, at the time of the Investigational New Drug Application submission in December 2015, we were unable to conduct our Phase 2 trial of tazemetostat in FL patients in the United States until the beginning of 2017. In addition, in the second quarter of 2018, following a safety report of a pediatric patient who developed a secondary T-cell lymphoma in our ongoing Phase 1 clinical trial of tazemetostat in pediatric patients, the FDA, the French National Agency for Medicines and Health Products Safety and Germany's Federal Institute for Drugs and Medical Devices each placed a partial clinical hold on new patient enrollment in our ongoing clinical trials of tazemetostat. That partial clinical hold was lifted in September 2018 by the FDA, in November 2018 by Germany's Federal Institute for Drugs and Medical Devices, and in January 2019 by the French National Agency for Medicines and Health Products Safety. In pharmaceutical development, many compounds that initially show promise in early-stage testing for treating cancer

are later found to cause side effects that prevent further development of the compound. If we or our collaborators are unable to fully and adequately address matters such as these when they arise, we may be unable to conduct clinical trials of tazemetostat or any future product candidates, our trials may be limited to certain patient populations or our ability to conduct other trials in the United States or in other countries may be delayed.

Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize tazemetostat or any future product candidates, including:

- regulators or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may experience delays in reaching, or fail to reach, agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- preclinical testing may produce results based on which we may decide, or regulators may require us, to conduct additional preclinical studies before we proceed with certain clinical trials, limit the scope of our clinical trials, halt ongoing clinical trials or abandon product development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate, or patients may drop out of these clinical trials at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- we may have to limit the scope of, suspend or terminate clinical trials of our product candidates for various reasons, including a finding that the patients are being exposed to unacceptable health risks;
- regulators or institutional review boards may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the patients are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate; and
- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or institutional review boards to suspend or terminate the trials.

We and our CROs and CMOs, as well as clinical trial sites, may face disruptions related to our ongoing clinical trials, planned clinical trials or future clinical trials arising from manufacturing disruptions, staffing disruptions and limitations on our activities and the activities of our CROs and CMOs, and delays in the ability to obtain necessary institutional review board or other necessary site approvals, as well as other delays at clinical trial sites. We may also face limitations on enrollment and patients withdrawing from our clinical trials or not complying with the protocols, which could delay completion of our clinical trials or adversely affect the data generated by our clinical trials. The impact of these disruptions on our clinical development activities and plans is uncertain and may depend on the length of the disruptions.

If we are required to conduct additional clinical trials or other testing of tazemetostat or any future product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of tazemetostat or any future product candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling or a risk evaluation mitigation strategy that includes significant use or distribution restrictions or safety warnings;
- be subject to additional post-marketing testing requirements; or
- have the product removed from the market after obtaining marketing approval.

Our product development costs may also increase if we experience delays in clinical testing or in obtaining marketing approvals such as the delays caused by the partial clinical holds in the United States, France and Germany. We do not know whether any of our preclinical studies or clinical trials will continue or begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant preclinical or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

We may not be able to initiate or continue clinical trials for tazemetostat or any future product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside of the United States. In particular, if our product candidates are focused on specific patient populations, our ability to enroll eligible patients may be limited or may result in slower enrollment than we anticipate. For instance, our ongoing clinical trials of tazemetostat in adult and pediatric patients with INI1-negative tumors are targeting rare patient populations. In addition, some of our competitors have ongoing clinical trials, and may in the future initiate new clinical trials, for product candidates being developed for the same or similar diseases or indications as tazemetostat or any future product candidates or that may treat the broader patient populations within which tazemetostat or any future product candidates are being or may be developed for the treatment of a subset of identifiable patients with cancer and other diseases, which could adversely affect enrollment in our trials, particularly in trials for rare disease indications, as patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates. As the COVID-19 pandemic continues, patient recruitment and enrollment in our clinical trials may be adversely affected, delayed or interrupted. Patients may choose to withdraw from our studies or we may choose to or be required to pause enrollment and or patient dosing in our ongoing clinical trials in order to preserve health resources and protect trial participants. It is unknown how long these pauses or disruptions could continue.

Patient enrollment may be affected by other factors including:

- the severity of the disease under investigation;
- the rarity of the disease under investigation;
- the eligibility criteria for the trial in question;
- the perceived risks and benefits of the product candidate under trial;
- the efforts to facilitate timely enrollment in clinical trials;
- the patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment;

- the proximity and availability of clinical trial sites for prospective patients;
- the potential costs to be incurred by prospective patients in order to participate, such as travel, missed work, and/or childcare;
- the lack of scientific interest in the study;
- the ability to identify specific patient populations for molecularly defined study cohorts.

Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for tazemetostat or any future product candidates and could delay or prevent our ability to obtain marketing approval, which may cause the value of our company to decline and limit our ability to obtain additional financing.

Our research and development is focused on the creation of novel epigenetic therapies for patients with cancer and other diseases, which is a rapidly evolving area of science, and the approach we are taking to discover and develop drugs is novel.

The discovery of novel epigenetic therapies for patients with cancer and other serious diseases is an emerging field, and the scientific discoveries that form the basis for our efforts to discover and develop tazemetostat and any future product candidates are relatively new. Although epigenetic regulation of gene expression plays an essential role in biological function, few drugs premised on epigenetics have been discovered. Moreover, those drugs based on an epigenetic mechanism that have received marketing approval, other than TAZVERIK, are in different target classes than the chromatin modifying protein, or CMP, inhibitors where our research and development is principally focused. Although preclinical studies suggest that genetic alterations can result in changes to the activity of CMPs making them oncogenic, and although the FDA has granted accelerated approval for TAZVERIK in ES and FL with continued approval contingent upon verification and description of clinical benefit in a confirmatory trial for each of the ES and FL indications, to date no company has translated broad biological observations regarding CMP inhibitors into systematic drug discovery. We believe that our first four inhibitors of HMTs in clinical trials are all the first molecules against these targets to enter clinical development. Therefore, we do not know if our approach of inhibiting HMTs or other CMPs to treat patients with cancer and other serious diseases will be successful.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on tazemetostat and any future product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we focus on research programs and product candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and on tazemetostat and any future product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for tazemetostat or a particular future product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

If we are required to develop a companion or complementary diagnostic and if we or our collaborators are unable to successfully develop diagnostics for tazemetostat or any future therapeutic product candidates when needed, or experience significant delays in doing so, we may not achieve marketing approval or realize the full commercial potential of our therapeutic product candidates.

We may develop, or we may work with collaborators, to develop diagnostics for tazemetostat or any future therapeutic product candidates to identify patients for our clinical trials who have the specific cancers that we are seeking to treat as appropriate and when existing, available technology may not be sufficient to identify those patients. We do not have experience or capabilities in developing or commercializing diagnostics and plan to rely in

large part on third parties to perform these functions. For example, we have entered into an agreement with Roche Sequencing Solutions, or Roche Sequencing, to develop and commercialize a diagnostic for use with tazemetostat for non-Hodgkin lymphoma, or NHL, patients with EZH2 activating mutations. Companion or complementary diagnostics are subject to regulation by the FDA and similar regulatory authorities outside of the United States as medical devices and require separate regulatory approval prior to commercialization. If any third parties that we engage to assist us are unable to successfully develop companion or complementary diagnostics that are needed for our therapeutic product candidates, or experience delays in doing so:

- the development of our therapeutic product candidates may be adversely affected if we are unable to appropriately select patients for enrollment in our clinical trials;
- our therapeutic product candidates may not receive marketing approval if their safe and effective use depends on a companion or complementary diagnostic; and
- we may not realize the full commercial potential of any therapeutic product candidates that receive marketing approval if, among other reasons, we are unable to appropriately identify patients with the specific genetic alterations targeted by our therapeutic product candidates.

If any of these events were to occur, our business would be harmed, possibly materially.

We may not be successful in our efforts to use and expand our proprietary drug discovery platform to build a pipeline of product candidates.

A key element of our strategy is to utilize our drug discovery platform to progress preclinical efforts and pursue additional product candidates to expand our pipeline of inhibitors against chromatin modifying proteins, or CMPs for the treatment of a variety of different types of cancer and other diseases. We may not be able to develop product candidates that are safe and effective CMP inhibitors. Even if we are successful in continuing to build our pipeline, the potential product candidates that we identify may not be suitable for clinical development, including as a result of being shown to have harmful side effects or other characteristics that indicate that they are unlikely to be products that will receive marketing approval and achieve market acceptance. If we do not successfully develop and commercialize product candidates based upon our technological approach, we will not be able to obtain product revenues in future periods, which likely would result in significant harm to our financial position and adversely affect our stock price.

Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop.

We face an inherent risk of product liability exposure related to the testing and utilization of tazemetostat in connection with the clinical testing and commercial use of tazemetostat and with respect to any other product candidates that we develop or commercialize. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates or products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants or patients;
- significant costs to defend any related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue;
- reduced resources of our management to pursue our business strategy; and
- the inability to commercialize any products that we may develop.

We currently hold $30.0 million in product liability insurance coverage in the aggregate, with a per incident limit of $30.0 million, which may not be adequate to cover all liabilities that we may incur. We will need to increase our insurance coverage as we expand our clinical trials and as we continue to commercialize TAZVERIK, or any other product candidate that we develop. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

Enhanced governmental and private scrutiny over, or investigations or litigation involving, pharmaceutical manufacturer donations to patient assistance programs offered by charitable foundations may require us to modify our patient support programs and could negatively impact our business practices, harm our reputation, divert the attention of management and increase our expenses.

To help patients afford tazemetostat, we have implemented a patient assistance program. These types of programs, designed to assist patients in affording pharmaceuticals, have become the subject of scrutiny. In recent years, some pharmaceutical manufacturers were named in class action lawsuits challenging the legality of components of their patient assistance programs and their support of independent charitable foundations in connection with such programs under a variety of federal and state laws. Our patient assistance program could become the target of similar litigation. In addition, certain state and federal enforcement authorities and members of Congress have initiated inquiries about co-pay assistance programs. Some state legislatures have also been considering proposals that would restrict or ban co-pay coupons.

Further, numerous organizations, including pharmaceutical manufacturers, have received subpoenas from the U.S. Department of Justice, or DOJ, and other enforcement authorities seeking information related to their patient assistance programs and support, and certain of these organizations have entered into, or have otherwise agreed to, significant civil settlements with applicable enforcement authorities. In connection with these civil settlements, the U.S. government has and may in the future require the affected companies to enter into complex corporate integrity agreements that impose significant reporting and other requirements on those companies. We cannot ensure that our compliance controls, policies and procedures will be sufficient to protect against acts of our employees, business partners or vendors that may potentially violate the laws or regulations of the jurisdictions in which we operate. Regardless of whether we have complied with the law, a government investigation could negatively impact our business practices, harm our reputation, divert the attention of management and increase our expenses.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant losses since our inception. We expect to incur losses over the next several years and may never achieve or maintain profitability.

Since inception, we have incurred significant operating losses. Our net loss was $231.7 million for the year ended December 31, 2020, $170.3 million for the year ended December 31, 2019, and $123.6 million for the year ended December 31, 2018. As of December 31, 2020, we had an accumulated deficit of $988.7 million. To date, we have generated only limited revenue from sales of TAZVERIK and have not obtained marketing approval of any other product. We have financed our operations primarily through our collaborations, our public offerings, private placements of our common and preferred stock, our loan facility with BioPharma Credit Investments V (Master) LP, BPCR Limited Partnership and BioPharma Credit PLC, and other funding transactions. We have devoted substantially all of our financial resources and efforts to research and development, including clinical and preclinical studies, seeking marketing approval for product candidates and building our commercial organization with respect to TAZVERIK in the indications for which we have received accelerated approval from the FDA. We are continuing to develop tazemetostat for additional indications and to seek to discover and develop other product candidates. We expect to continue to incur significant expenses and operating losses over the next several years. Our net losses may fluctuate significantly from quarter to quarter and year to year.

We anticipate that we will continue to incur significant expenses if and as we:

- continue to establish and maintain our sales, marketing and distribution infrastructure and scale up external manufacturing capabilities to support the ongoing commercial launch of TAZVERIK and the commercial launch of any other product candidate that is approved;
- grow our medical affairs organization to provide medical support for tazemetostat and any other product candidate that is approved;

- conduct our Phase 1b/3 confirmatory trials in ES and FL;
- design and conduct new and ongoing monotherapy and combination trials of tazemetostat in FL;
- conduct clinical trials or support investigator-sponsored trials to evaluate tazemetostat as a monotherapy or in combinations in additional indications;
- pay any milestone payments provided for and achieved under the amended and restated collaboration and license agreement with Eisai Co Ltd, or Eisai;
- pay interest and principal associated with our amended and restated loan agreement with BioPharma Credit Investments V (Master) LP, BPCR Limited Partnership and BioPharma Credit PLC, or the Amended and Restated Loan Agreement;
- continue the research and development of our other product candidates;
- seek to discover and develop additional product candidates or to expand our product candidates into additional lines of treatment;
- prepare NDA submissions as we seek regulatory approvals for any product candidates that successfully complete clinical trials;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, quality control, manufacturing and scientific personnel; and
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts.

To become and remain profitable, we must generate significant revenue. The ability to generate this revenue requires us to successfully commercialize TAZVERIK in ES and FL and in additional indications for which we may develop and obtain approval for tazemetostat, which requires us to be effective in a range of challenging activities. We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to achieve profitability. Because of the numerous risks and uncertainties, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability.

Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our product offerings or even continue our operations. A decline in the value of our company could cause our stockholders to lose all or part of their investment in our company.

We will need substantial additional funding. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

We expect our expenses to increase in connection with our ongoing activities, particularly as we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales, and distribution. In addition, we expect our expenses to increase as we fund our tazemetostat development program; make any milestone and royalty payments provided for and achieved under the amended and restated collaboration and license agreement with Eisai; pay interest and principal associated with 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. Accordingly, we may need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on acceptable terms, we could be forced to delay, reduce or eliminate our research and development programs or our commercialization efforts.

Based on our current operating plan, we expect that our existing cash, cash equivalents and marketable securities as of December 31, 2020, together with the cash we expect to generate from product sales, will be sufficient to fund our planned operating expenses and capital expenditure requirements and pay our debt service obligations as they become due into 2023, without giving effect to any potential milestone payments we may receive under our collaboration agreements. We have based these expectations on assumptions that may prove to be wrong, such as the

revenue that we expect to generate from the sale of our products, and we could use our capital resources sooner than we expect. Our future capital requirements will depend on many factors, including the following, as well as the uncertain impact of the COVID-19 pandemic on these factors:

- the costs of commercialization activities, including product manufacturing, marketing, sales and distribution and patient support programs for tazemetostat or any of our product candidates;
- revenue received from commercial sales of TAZVERIK;
- the progress and results of our ongoing and planned clinical trials of tazemetostat;
- the number and development requirements of additional indications for tazemetostat and other product candidates that we determine to pursue, including the scope, progress, results and costs of discovery research, preclinical development, laboratory testing and clinical trials for such product candidates;
- the costs, timing and outcome of regulatory review of tazemetostat and other product candidates we may pursue;
- royalties payable by us on sales of TAZVERIK under our amended and restated collaboration and license agreement with Eisai;
- milestones, option exercise fees, license fees, and other revenues, if any, we may receive under collaboration agreements;
- the revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights, defending any intellectual property-related claims, and challenging the intellectual property rights of others;
- the extent to which we acquire or in-license other products and technologies; and
- interest and principal payments under the Amended and Restated Loan Agreement.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and even if regulatory approval is obtained, we may never achieve commercial success. Accordingly, we may need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings and license and development agreements with collaboration partners. We do not have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our existing stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Additional 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. Our existing indebtedness and the pledge of our assets as collateral limit our ability to obtain additional debt financing.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Our indebtedness resulting from our Amended and Restated Loan Agreement could adversely affect our financial condition or restrict our future operations.

In November 2019, we entered into the Loan Agreement with BioPharma Credit PLC, or the Collateral Agent, and 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, providing for up to $70.0 million in secured term loans to be advanced in up to three tranches, or the Loan Agreement, of which $25.0 million was drawn by us in November 2019, $25.0 million was drawn by us in March 2020, and $20.0 million was drawn by us in June 2020. The maturity date of the first three tranches is November 18, 2024, unless terminated earlier.

In November 2020, we entered into an Amended and Restated Loan Agreement with the Collateral Agent and the Lenders, amending and restating the Loan Agreement to provide for, among other things, an additional secured term loan facility of $150.0 million, or the Tranche D Loan. In November 2020, we drew the $150.0 million Tranche D Loan. The maturity date of the Tranche D Loan is November 18, 2026, unless terminated earlier. 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.

Subject to customary exceptions and exclusions, all obligations under the Amended and Restated Loan Agreement are secured pursuant to the terms of the Amended and Restated Loan Agreement, a guaranty and security agreement between us, certain of our subsidiaries, and the Collateral Agent, or the Pledge Agreement, and intellectual property and security agreements between us and Collateral Agent, or the IP Security Agreements. Under the Amended and Restated Loan Agreement, the Pledge Agreement, and the IP Security Agreements, we provided to the Lenders a perfected, first-priority security interest in all of our personal property and a perfected, first-priority security interest in substantially all of our intellectual property related to tazemetostat.

A failure to comply with the conditions of the Amended and Restated Loan Agreement could result in an event of default. An event of default under the term loan facility includes, among other things, a failure to pay any amount due under the Amended and Restated Loan Agreement as well as the occurrence of events that could reasonably be expected to result in a material adverse change. In the event of an acceleration of amounts due under the Amended and Restated Loan Agreement as a result of an event of default, we may not have sufficient funds or may be unable to arrange for additional financing to repay the term loans or to make any accelerated payments.

Risks Related to Our Dependence on Third Parties

Our existing therapeutic collaborations are important to our business, and future collaborations may also be important to us. If we are unable to maintain any of these collaborations, or if these collaborations are not successful, our business could be adversely affected.

Our resources for drug development are limited and we continue to build our sales, marketing, medical affairs and supply chain infrastructure. Accordingly, we have entered into therapeutic collaborations with other companies that we believe can contribute to our ability to rapidly develop and commercialize TAZVERIK and any product candidates we may identify and develop, including our collaboration and license agreement with GSK. Our collaborations have provided us with important funding for our development programs and product platform and we expect to receive additional funding under these collaborations in the future. Our existing therapeutic collaborations, and any future collaborations we enter into, may pose a number of risks, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not have the ability or the development capabilities to perform their obligations as expected, including as a result of the impact of the COVID-19 pandemic on our collaborators' operations or business;
- collaborators may not pursue commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that may divert resources or create competing priorities;

- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, not initiate or delay initiation of clinical trials, pause or stop enrollment in a clinical trial, terminate an ongoing clinical trial, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products and product candidates if the collaborators believe that the competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- a collaborator may fail to comply with applicable regulatory requirements regarding the development, manufacture, distribution or marketing of a product candidate or product;
- a collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such product or products;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or terminations of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and
- collaborations may be terminated for the convenience of the collaborator, and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

If our therapeutic collaborations do not result in the successful development and commercialization of products or if one of our collaborators terminates its collaboration with us, we may not receive the funding under the collaboration that we anticipated. If we do not receive the funding we expect under these agreements, our development of our product platform and product candidates could be delayed and we may need additional resources to develop product candidates and our product platform. All of the risks relating to product development, regulatory approval and commercialization described in this Annual Report on Form 10-K also apply to the activities of our therapeutic collaborators.

Our existing therapeutic collaborations contain restrictions on our ability to engage in activities that are the subject of the collaboration with third parties for specified periods of time. These restrictions may have the effect of preventing us from undertaking development and other efforts that may appear to be attractive to us.

Additionally, subject to its contractual obligations to us, if a collaborator of ours is involved in a business combination, the collaborator might deemphasize or terminate the development or commercialization of any product candidate licensed to it by us. If one of our collaborators terminates its agreement with us, we may find it more difficult to attract new collaborators and our perception in the business and financial communities could be adversely affected. In the fourth quarter of 2020, Celgene and Boehringer Ingelheim International GmbH each terminated their collaborations with us without cause.

For some of our product candidates or for some CMP targets, we may in the future collaborate with pharmaceutical and biotechnology companies for development and potential commercialization of therapeutic products. We face significant competition in seeking appropriate collaborators. Our ability to reach a definitive agreement for a

collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms, or at all, we may have to increase our expenditures and undertake development or commercialization activities for the product candidate or program on our own or at our own expense or curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities. If we elect to fund and undertake development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates or bring them to market or continue to develop our product platform and our business may be materially and adversely affected.

Failure of our third-party collaborators to successfully commercialize diagnostics, developed for use with our therapeutic product candidates, if and when needed, could harm our ability to commercialize these product candidates.

We do not plan to develop diagnostics internally and, as a result, if diagnostics are needed, we will be dependent on the efforts of our third-party collaborators to successfully commercialize diagnostics when existing, available technology may not be sufficient to identify patients for treatment with our therapeutic product candidates. For example, Roche Sequencing has developed a companion or complementary diagnostic for detecting activating mutations in EZH2 in the tazemetostat NHL program. Our collaborators:

- may not perform their obligations as expected or have difficulty responding to accelerated approval timelines alongside the therapeutic product development;
- may encounter production difficulties that could constrain the supply of the diagnostics;
- may encounter delays or have difficulty obtaining regulatory approval for the diagnostic in target markets;
- may have difficulties gaining acceptance of the use of the diagnostics in the clinical community;
- may not pursue commercialization of any diagnostics that achieve regulatory approval;
- may elect not to continue or renew commercialization programs based on changes in the collaborators' strategic focus or available funding, or external factors such as an acquisition, that divert resources or create competing priorities;
- may not commit sufficient resources to the marketing and distribution of such product or products; and
- may terminate their relationship with us.

If required diagnostics for use with our therapeutic product candidates fail to gain market acceptance, our ability to derive revenues from sales of our therapeutic product candidates could be harmed. If our collaborators fail to commercialize these diagnostics, we may not be able to enter into arrangements with another diagnostic company to obtain supplies of an alternative diagnostic test for use in connection with our therapeutic product candidates or do so on commercially reasonable terms, which could adversely affect and delay the development or commercialization of our therapeutic product candidates.

We rely, and expect to continue to rely, on third parties to conduct our clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials.

We currently rely on third-party clinical research organizations to conduct our ongoing clinical trials. We do not plan to independently conduct clinical trials of tazemetostat or any future product candidates. We expect to continue to rely on third parties, such as clinical research organizations, research collaborative groups, clinical data management organizations, medical institutions and clinical investigators, to conduct our clinical trials. These agreements might terminate for a variety of reasons, including a failure to perform by the third parties. If we need to enter into alternative arrangements, our product development activities might be delayed.

Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with standards, commonly referred to as good clinical practices, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants or patients are protected. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within specified timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates.

We also expect to continue to rely on other third parties to store and distribute drug supply for our clinical trials and our commercial operations. Any performance failure on the part of any such distributor could delay clinical development or marketing approval of our product candidates or commercialization of our products, producing additional losses and depriving us of potential product revenue.

We contract with third parties for the manufacture of tazemetostat for commercialization and clinical testing, and expect to contract with third parties for the manufacture of any other product candidates that we develop for preclinical and clinical testing and for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

We do not have any manufacturing facilities and rely, and expect to continue to rely, on third parties for the manufacture of our product candidates for preclinical and clinical testing, as well as for commercial manufacture of tazemetostat and any other product candidates we develop that receive marketing approval. This reliance on third parties increases the risk that we will not have sufficient quantities of tazemetostat or any other product candidate or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

We may be unable to establish any agreements with third-party manufacturers or to do so on a timely basis or on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on such third-party manufacturers entails additional risks, including:

- reliance on the third-party for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreement by the third party;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how; and
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

Third-party manufacturers may not be able to comply with current good manufacturing practices, or cGMP, regulations or similar regulatory requirements outside of the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products.

Tazemetostat and any other product candidate that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

Any performance failure on the part of our existing or future manufacturers could delay clinical development, or marketing approval, and could adversely impact our ability to sell our approved products. We have already built additional redundancy in our supply chain and have plans to continue to qualify additional raw material manufacturers in our TAZVERIK supply chain. If our current contract manufacturers cannot perform as agreed, we may be required to replace such manufacturers. We expect that we would incur added costs and delays in identifying and qualifying any such replacement.

Our current and anticipated future dependence upon others for the manufacture of our product candidates or products may adversely affect our future profit margins and our ability to commercialize any products that receive marketing approval on a timely and competitive basis.

Risks Related to Our Intellectual Property

If we are unable to obtain, maintain and enforce patent protection for our technology, products and product candidates or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology, products or product candidates similar or identical to ours, and our ability to successfully develop and commercialize our technology, products or product candidates may be impaired.

Our success depends in large part on our ability to obtain, maintain and enforce patent protection in the United States and foreign jurisdictions with respect to our proprietary technology, products and product candidates. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our novel technology, products and product candidates.

The patent prosecution process is expensive, time-consuming and complex, and we may not be able to file, prosecute or maintain all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we may fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we do not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties. Therefore, these in-licensed patents and applications may not be prepared, filed, prosecuted or maintained in a manner consistent with the best interests of our business.

Although we enter into non-disclosure and confidentiality agreements with parties who may have access to confidential or patentable aspects of our research and development output, such as our employees, collaborators, contract research organizations, contract manufacturers, consultants, advisors and other third parties, any of these parties may breach the agreements and disclose such output before a patent application is filed, thereby potentially jeopardizing our ability to seek patent protection.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. In addition, the scope of our patent protection outside of the United States is uncertain, and laws of foreign jurisdictions may not protect our rights to the same extent as the laws of the United States. For example, European patent law restricts the patentability of methods of treatment of the human body more than United States law does. With respect to our patent rights, we cannot predict whether the patent applications we and/or our licensors are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient protection from competitors. In addition, publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and foreign jurisdictions are typically not published until 18 months after filing, or in some cases at all. Therefore, neither we nor our licensors can know with certainty whether we were the first to make the inventions claimed in the patents or pending patent applications, or that we or our licensors were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued which protect our technology, products or product candidates, in

whole or in part, or which effectively prevent others from developing or commercializing competitive technologies, products and product candidates. Changes in either the patent laws or interpretation of the patent laws in the United States and foreign jurisdictions may diminish the value of our patent rights or narrow the scope of our patent protection.

Moreover, we may be subject to a third-party preissuance submission of prior art to the U.S. Patent and Trademark Office, or USPTO, or become involved in opposition, derivation, reexamination, *inter partes* review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others. For example, we are involved in an opposition proceeding against one of our European patents, the claims of which cover a method for determining whether a cancer patient is a candidate for treatment with an EZH2 inhibitor based on their EZH2 mutation status. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize our technology or products without infringing, misappropriating or otherwise violating third-party patent rights. In addition, if the breadth or strength of protection provided by our owned and/or in-licensed patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize our technology, products or product candidates. Furthermore, such proceedings also may result in substantial cost and divert the time and attention of our management and employees, even if the eventual outcome is favorable to us.

In addition, the coverage claimed in a patent application may be significantly reduced before the patent is issued, and its scope may be reinterpreted after issuance. Even if our owned and/or in-licensed patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and/or in-licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. Such proceedings also may result in substantial cost and divert the time and attention of our management and employees, even if the eventual outcome is favorable to us. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. Furthermore, our competitors may be able to circumvent our owned and/or in-licensed patents by developing similar or alternative technologies or products in a non-infringing manner. As a result, our owned and/or in-licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing technology and/or products similar or identical to any of our technology and products.

Moreover, some of our owned and/or in-licensed patents and patent applications are, and may in the future be, co-owned with third parties. If we are unable to obtain an exclusive license to any such third-party co-owners' interest in such patents or patent applications, such co-owners may be able to license their rights to other third parties, including our competitors, and our competitors could market competing technology and products. In addition, we may need the cooperation of any such co-owner of our patents in order to enforce such patents against third parties, and such cooperation may not be provided to us.

If we do not obtain patent term extension for our products, our business may be materially harmed.

In the United States, depending upon the timing, duration and specifics of any FDA marketing approval of a product candidate, the patent term of a patent that covers an FDA-approved product may be eligible for patent term extension, which permits patent term restoration as compensation for the patent term lost during the FDA regulatory review process. The Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Act, permits a patent term extension of up to five years beyond the expiration of the patent for those claims covering the approved product, a method for using it or a method for manufacturing such product. Similar provisions are available in Europe and other foreign jurisdictions to extend the term of a patent that covers an approved drug. We have applied for patent term extension on a patent that covers the TAZVERIK drug substance based on the regulatory review of TAZVERIK for the treatment of adult and pediatric patients aged 16 years and older with metastatic or locally advanced ES not eligible for complete resection. In the future, if and when any additional product candidates receive FDA approval, we expect to apply for patent term extensions on patents

covering those approved products. Similarly, in foreign jurisdictions where we have obtained regulatory approval, we intend to seek patent term extensions for any applicable issued patent rights if such extensions are available, however there is no guarantee that the applicable authorities will agree with our assessment of whether such extensions should be granted, and even if granted, the length of any such extensions. We may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of the relevant patent(s), or otherwise failing to satisfy applicable requirements. If we are unable to obtain any patent term extension or the term of any such extension is less than we request, our competitors may obtain approval of competing products following the expiration of our patent rights, and our business, financial condition, results of operations and commercial prospects could be materially harmed.

Changes to patent laws in the United States and foreign jurisdictions could significantly diminish the value of patents in general, thereby impairing our ability to protect our technology, products and product candidates.

Changes in either the patent laws or interpretation of patent laws in the United States by the United States Congress, the federal courts, or the USPTO, including patent reform legislation such as the Leahy-Smith America Invents Act, or the Leahy-Smith Act, or similar changes in other jurisdictions whether by governments, courts or regulators, could increase the uncertainties and costs surrounding the prosecution of our owned or in-licensed patent applications and the enforcement or defense of our issued patent rights. For example, the Leahy-Smith Act includes a number of significant changes to United States patent law. These changes include provisions that affect the way patent applications are prosecuted, redefine prior art, provide more efficient and cost-effective avenues for competitors to challenge the validity of patents, and enable third-party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent at USPTO administered post-grant proceedings, including post-grant review, *inter partes* review and derivation proceedings. Assuming that other statutory requirements for patentability are met, prior to March 2013, in the United States, the first to invent the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. After March 2013, under the Leahy-Smith Act, the United States transitioned to a first inventor to file system in which, assuming that the other statutory requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. Accordingly, changes in either the patent laws or interpretation of patent laws in the United States or in foreign jurisdictions and their implementation could increase the uncertainties and costs surrounding the prosecution of our owned and/or in-licensed patent applications and the enforcement or defense of our issued patent rights, which could have a material adverse effect on our business and financial condition.

We may become involved in lawsuits or other legal proceedings to protect or enforce our patent or other intellectual property rights, which could be expensive, time consuming and unsuccessful.

Competitors may infringe, misappropriate or otherwise violate our patent or other intellectual property rights. As a result, we may need to file infringement, misappropriation or other intellectual property claims, which can be expensive and time consuming. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe, misappropriate or otherwise violate their intellectual property rights. Such parties could also counterclaim that the patent rights we have asserted are invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information, or made a misleading statement, during prosecution. Moreover, third parties may institute such claims before administrative bodies in the United States or abroad, and within or outside of the context of litigation. Such mechanisms include re-examination, post-grant review, *inter partes* review, interference proceedings, derivation proceedings and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings).

An adverse result in any such proceeding could put one or more of our patent rights at risk of being invalidated or interpreted narrowly, and could put one or more of our owned and/or in-licensed patent applications at risk of being found unpatentable. Any of the foregoing could limit our ability to limit our competitors' ability to develop and commercialize competing technologies and products and could have a material adverse impact on our business, financial condition, results of operations and prospects.

We may need to license certain intellectual property from third parties, and such licenses may not be available or may not be available on commercially reasonable terms.

A third party may hold intellectual property rights, including patent rights, that are important or necessary to the development of our technology or product candidates or commercialization of our technology or products. It may be necessary for us to use the patented or proprietary technology of third parties to develop our technology or product candidates or commercialize our technology or products, in which case we may be required to obtain a license from these third parties. Such licenses may not be available on commercially reasonable terms, or at all, or may only be available on a non-exclusive basis, any of which could have a material adverse impact on our business, financial condition, results of operations and prospects.

Third parties may initiate legal proceedings alleging that we are infringing, misappropriating or otherwise violating their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability, and the ability of our collaborators, to develop, manufacture, market and sell our current and future products and use our proprietary technology without infringing, misappropriating or otherwise violating the proprietary rights of third parties. There is considerable intellectual property litigation in the biotechnology and pharmaceutical industries. We may become party to, or threatened with, litigation or administrative proceedings regarding intellectual property rights with respect to our technology, products and product candidates, including interference proceedings, post grant review, *inter partes* review and derivation proceedings before the USPTO and similar proceedings in foreign jurisdictions such as oppositions before the European Patent Office.

Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of merit. For example, with respect to tazemetostat, we are aware of a U.S. patent held by a third party, which could be construed to cover the use of tazemetostat in certain clinical indications. We have preemptively requested *inter partes* review at the USPTO challenging the validity of that patent. In the event that an owner of this patent were to bring an infringement action against us, we believe we have defenses that we could assert in such event, and additionally in the USPTO, including the invalidity of the relevant claims of such patents. However, we may not be successful in asserting these defenses, including proving invalidity, and could be found to infringe this third-party patent.

We may not be aware of all intellectual property rights potentially relating to our technology, products and product candidates and their potential uses. Thus, we do not know with certainty that our technology, products and product candidates or our development and commercialization thereof, do not and will not infringe, misappropriate or otherwise violate any third party's intellectual property.

Even if we believe that third party intellectual property claims are without merit, there is no assurance that a court or other judicial or regulatory body would find in our favor on questions of misappropriation, infringement, validity, enforceability or priority. A court of competent jurisdiction or other applicable regulatory body could disregard any claims that we make and hold that third-party patents are valid, enforceable and infringed. In order to successfully challenge the validity of any U.S. patent in federal court, we would need to overcome a presumption of validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such U.S. patent claim, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U.S. patent.

If we are found to infringe a third party's intellectual property rights, we could be required to obtain a license from such third party to continue developing, manufacturing and marketing our technology, products and product candidates. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us and could require us to make substantial licensing and/or royalty payments. We could be forced, including by court order, to cease developing, manufacturing and/or commercializing the infringing technology, product candidates or products. In addition, we could be found liable for significant monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent or other intellectual property right and could be forced to indemnify our customers or collaborators. A finding of infringement could prevent us from commercializing our technology, product candidates or products and/or could force us to cease

some of our business operations, which could materially harm our business. Additionally, we could be forced to redesign our products or product candidates, seek new regulatory approvals or indemnify third parties pursuant to contractual agreements. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business, financial condition, results of operations and prospects.

Obtaining and maintaining patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance, renewal and annuity fees and various other governmental fees on any issued patent and pending patent application must be paid to the USPTO and foreign patent agencies in several stages or annually over the lifetime of our owned and/or in-licensed patents and patent applications. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. In certain circumstances, we rely on our licensing partners to pay these fees to, or comply with the procedural and documentary rules of, the relevant patent agency. With respect to our patent rights, we employ reputable law firms and other professionals to help us comply, and we rely on an annuity service to remind us of the due dates and to make payment after we instruct them to do so. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules, however the ability to cure may not be possible in some cases or may be subject to certain deadlines or other restrictions that may not be practicable to satisfy. While to date we have not experienced any material abandonment, lapse or loss of patent rights that was not able to be cured, there could be situations in which non-compliance could result in material abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. If we or our licensors fail to maintain the patents and patent applications covering our technology, products or product candidates, potential competitors might be able to enter the market with similar or identical technology, products or product candidates, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

If we fail to comply with our obligations in our intellectual property licenses and funding arrangements with third parties, we could lose rights that are important to our business.

We are party to license and research agreements that impose, and we may enter into additional licensing and funding arrangements with third parties that may impose, on us diligence, development and commercialization timelines, milestone payment, royalty, insurance and other obligations. Under our existing licensing and funding agreements, we are obligated to pay royalties on net product sales of products or related technologies to the extent they are covered by the agreements. If we fail to comply with our obligations under current or future license and funding agreements, our counterparties may have the right to terminate these agreements, in which event we might not be able to develop, manufacture or commercialize any product that is covered by these agreements or may face other penalties under the agreements. Such an occurrence could materially adversely affect the value of the products or product candidates being developed under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new or reinstated agreements with less favorable terms, or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

We may be subject to claims by third parties asserting that our employees, consultants, contractors or we have wrongfully used or disclosed alleged trade secrets of their current or former employers or claims asserting that we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Many of our employees, consultants and contractors were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and contractors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these employees, consultants and contractors or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's former employer. Litigation may be necessary to defend against these claims.

In addition, while it is our policy to require our employees, consultants and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops or has developed intellectual property that we regard as our own. Our and their assignment agreements may not be self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property.

If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could have a material adverse effect on our competitive business position and prospects. Such intellectual property rights could be awarded to a third party, and we could be required to obtain a license from such third party to develop and/or commercialize our technology, product candidates, and/or products, which license may not be available on commercially reasonable terms, or at all, or such license may be non-exclusive. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our management and employees.

Intellectual property litigation or other legal proceedings relating to intellectual property could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and may also have an advantage in such proceedings due to their more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent or other intellectual property litigation or other proceedings could compromise our ability to compete in the marketplace.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patents for some of our technology, products and product candidates, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect these trade secrets and other proprietary technology, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract research organizations, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees, consultants and contractors. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside of the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position could be harmed.

Risks Related to Regulatory Approval of Our Product Candidates and Other Legal Compliance Matters

The marketing approval process is expensive, time-consuming and uncertain and may prevent us from obtaining approvals for the commercialization of some or all of our product candidates. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize tazemetostat for other indications or any other of our product candidates that we develop, and our ability to generate revenue will be materially impaired.

Our product and product candidates, including tazemetostat, and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, export and import are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by the EMA and similar regulatory authorities outside of the United States.

Failure to obtain marketing approval for tazemetostat for any potential indication or of any other product candidate will prevent us from commercializing tazemetostat for that indication or the product candidate. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and rely on third-party clinical research organizations to assist us in this process. Securing marketing approval requires the submission of extensive preclinical, clinical and manufacturing data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety, efficacy and quality. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. Our product candidates for which we seek approval may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use. New cancer drugs frequently are indicated only for patient populations that have not responded to an existing therapy or have relapsed.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical or other studies, or additional manufacturing data. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate on an accelerated basis or at all. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

We received accelerated approval of TAZVERIK in patients with ES and in patients with relapsed or refractory FL. In order to obtain accelerated approval for future indications in tazemetostat or any other product candidate, we must demonstrate that our product candidate provides meaningful therapeutic benefit over existing treatments. In addition, as a condition of accelerated approval of TAZVERIK in ES and FL, continued approval for these indications is contingent upon verification and description of clinical benefit in post-marketing confirmatory trials to verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit, and if the studies are unsuccessful for a given indication, TAZVERIK in ES or FL may be subject to withdrawal procedures.

Additionally, the FDA and comparable foreign regulatory agencies may have slower response times or be under-resourced to continue to monitor our future applications for accelerated approval or our ongoing clinical trials due to the COVID-19 pandemic and, as a result, review, inspection, and other timelines may be materially delayed. It is unknown how long these disruptions could continue, were they to occur. Any elongation or de-prioritization of our clinical trials or delay in regulatory review resulting from such disruptions could materially affect the development and study of our product candidates.

We may not be able to obtain, or may be delayed in obtaining, orphan drug exclusivity for our product candidates and, even if we do, that exclusivity may not prevent the FDA or the EMA from approving other competing products.

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States.

We have obtained orphan drug designations in the United States for tazemetostat for the treatment of patients with FL, chordoma, malignant rhabdoid tumors, or MRT, soft tissue sarcoma, or STS, and mesothelioma. The orphan drug designation for the treatment of MRT applies to INI1-negative MRT as well as SMARCA4-negative malignant rhabdoid tumor of ovary, or MRTO. We have also obtained orphan drug designations for tazemetostat for the treatment of patients with FL, DLBCL and malignant mesothelioma in Europe. We may not receive orphan drug designation for tazemetostat for other indications, or for any other future clinical candidates we may develop.

We have also obtained marketing exclusivity designations for tazemetostat for the treatment of patients with ES and FL. Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the EMA or the FDA from approving another marketing application for the same drug for the same indication for that time period. The applicable period is seven years in the United States and ten years in Europe. The exclusivity period in Europe can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

Even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs can be approved for the same condition. In addition, even after an orphan drug is approved, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

On August 18, 2017, Congress passed the FDA Reauthorization Act of 2017, or FDARA. FDARA, among other things, codified the FDA's pre-existing regulatory interpretation, to require that a drug sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease in order to receive orphan drug exclusivity. The new legislation reverses prior precedent holding that the Orphan Drug Act unambiguously requires that the FDA recognize the orphan exclusivity period regardless of a showing of clinical superiority. The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

In addition, FDARA amended section 505B "Research into pediatric uses for drugs and biological products" of the Federal Food, Drug and Cosmetic Act (21 U.S.C. Section 355c). Previously, drugs that had been granted orphan drug designation were exempt from the requirements of the Pediatric Research Equity Act. Under the amended section 505B, beginning on August 18, 2020, the submission of a pediatric assessment, waiver or deferral will be required for certain molecularly targeted cancer indications with the submission of an NDA application or supplement to an NDA application. Under FDARA, products with orphan drug designation that fall under this category will no longer be exempt from the pediatric research requirement. In December 2019, the FDA issued draft guidance interpreting and implementing these provisions. FL qualifies for an automatic full pediatric waiver by the FDA because it rarely or never occurs in pediatric patients. However, our other indications in development or future product candidates may require a pediatric assessment, which could result in delays in obtaining orphan drug exclusivity and increased costs and delays in obtaining regulatory approval.

We may seek certain designations for our product candidates, including Fast Track and Breakthrough Therapy, designations, but we might not receive such designations, and even if we do, such designations may not lead to a faster development or regulatory review or approval process.

We may seek certain designations for one or more of our product candidates that could expedite review and approval by the FDA. For example, if a drug is intended for the treatment of a serious or life-threatening condition and the drug demonstrates the potential to address unmet medical needs for this condition, the drug sponsor may apply for FDA Fast Track designation. Drugs that have received Fast Track designation from the FDA are eligible for expedited development and priority review, and the opportunity for a rolling review, under certain circumstances.

A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs and biologics that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Drugs designated as breakthrough therapies by the FDA are also eligible for accelerated approval.

We have received Fast Track designation from the FDA for tazemetostat for 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. We intend to seek Fast Track designation for tazemetostat for other indications and for our other product candidates as appropriate. Our submissions for marketing approval of tazemetostat in ES and FL received expedited development and priority review. We may also seek breakthrough therapy designation for tazemetostat or any future product candidate we may develop.

The FDA has broad discretion whether or not to grant such designations, so even if we believe a particular product candidate is eligible for the designation, we cannot assure that the FDA would decide to grant it. Moreover, even if we do receive Fast Track or breakthrough therapy designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. We or the FDA may withdraw these designations if either party believes that the designation is no longer supported by data from our clinical development program.

Failure to obtain marketing approval in foreign jurisdictions would prevent our product candidates from being marketed in those jurisdictions.

In order to market and sell TAZVERIK or any other product candidate that we may develop in the European Union, or EU, and many other foreign jurisdictions, we or our third-party collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside of the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside of the United States, a product must be approved for reimbursement before the product can be approved for sale in that country. We or our third-party collaborators may not obtain approvals from regulatory authorities outside of the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside of the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any market.

Additionally, we could face heightened risks with respect to seeking marketing approval in the United Kingdom as a result of the recent withdrawal of the United Kingdom from the European Union, commonly referred to as Brexit. Since the regulatory framework for pharmaceutical products in the United Kingdom covering quality, safety, and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales, and distribution of pharmaceutical products is derived from EU directives and regulations, Brexit could materially impact the future regulatory regime that applies to products and the approval of product candidates in the United Kingdom . Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, may force us to restrict or delay efforts to seek regulatory approval in the United Kingdom or the European Union for our product candidates, which could significantly and materially harm our business.

If we are required by the FDA to obtain approval of a companion or complementary diagnostic in connection with approval of a candidate therapeutic product, and there are delays in obtaining FDA approval of a diagnostic device, we will not be able to commercialize the product candidate and our ability to generate revenue will be materially impaired.

According to FDA guidance, if the FDA determines that a companion diagnostic device is essential to the safe and effective use of a novel therapeutic product or indication, the FDA generally will not approve the therapeutic product or new therapeutic product indication if the companion or complementary diagnostic is not also approved or cleared for that indication. This is not the case for complementary diagnostics, which are not prerequisites for administration of a drug product. Under the Federal Food, Drug, and Cosmetic Act, companion or complementary diagnostics are regulated as medical devices, and the FDA has generally required companion or complementary diagnostics intended to select the patients who will respond to cancer treatment to obtain Premarket Approval, or a PMA, for the diagnostic. The PMA process, including the gathering of clinical, preclinical, and manufacturing data, and the submission to and review by the FDA, involves a rigorous premarket review during which the applicant must prepare and provide the FDA with reasonable assurance of the device's safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing and labeling. A PMA is not guaranteed and may take considerable time, and the FDA may ultimately respond to a PMA submission with a "not approvable" determination based on deficiencies in the application and require additional clinical trial or other data that may be expensive and time-consuming to generate and that can substantially delay approval. As a result, if we are required by the FDA to obtain approval of a companion diagnostic for a candidate therapeutic product, and we do not obtain or there are delays in obtaining FDA approval of a diagnostic device, we may not be able to commercialize the product candidate on a timely basis or at all and our ability to generate revenue will be materially impaired.

Tazemetostat is, and any other product candidate for which we obtain marketing approval could be, subject to post-marketing restrictions or withdrawal from the market and we may be subject to substantial penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, when and if any of them are approved.

Tazemetostat and any other product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. As a condition of accelerated approval, the FDA may require a sponsor to perform post-marketing confirmatory studies to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical endpoint, and the drug may be subject to accelerated withdrawal procedures. The accelerated approval for tazemetostat subjects us to these conditions. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, including the requirement to implement a risk evaluation and mitigation strategy. New cancer drugs frequently are indicated only for patient populations that have not responded to an existing therapy or have relapsed. If tazemetostat or any other product candidate that we may develop receives marketing approval, the accompanying label may limit the approved use of our drug in this way, which could limit sales of the product.

The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product for any approved indication. The FDA and other agencies, including the Department of Justice, or the DOJ, closely regulate and monitor the post-approval marketing and promotion of drugs to ensure they are marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA and DOJ impose stringent restrictions on manufacturers' communications regarding off-label use, and if we do not market our products for their approved indications, we may be subject to enforcement action for off-label marketing. Violations of the Federal Food, Drug, and Cosmetic Act and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription drugs may lead to investigations and enforcement actions alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws.

In addition, later discovery of previously unknown adverse events or other problems with our products, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- restrictions on such products, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- damage to relationships with any potential collaborators;
- unfavorable press coverage and damage to our reputation;
- refusal to permit the import or export of our products;
- product seizure;
- injunctions or the imposition of civil or criminal penalties; or
- litigation involving patients using our products.

We conduct a substantial portion of our clinical trials in the EU. Non-compliance with EU and UK requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties.

Enacted legislation and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we obtain marketing approval. In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for physician-administered drugs. In addition, this legislation provided authority for limiting the number of drugs that will be covered in any therapeutic class. Cost reduction initiatives and other provisions of this legislation could decrease the coverage and price that we receive for any approved products. While the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the MMA may result in a similar reduction in payments from private payors.

In March 2010, the U.S. Congress passed the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively, the PPACA, a sweeping law which included changes to the coverage and reimbursement of drug products under government healthcare programs. Among the provisions of the PPACA of importance to tazemetostat and to our potential product candidates are the following:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents;

- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- expansion of healthcare fraud and abuse laws, including the False Claims Act and the Anti-Kickback Statute, new government investigative powers, and enhanced penalties for noncompliance;
- a Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices;
- extension of manufacturers' Medicaid rebate liability;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- requirements to report financial arrangements with physicians and teaching hospitals;
- a requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

Further, other legislative changes have been proposed and adopted since the PPACA was enacted. These changes include aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, starting in 2013. In January 2013, the American Taxpayer Relief Act of 2012 became law, which, among other things, reduced Medicare payments to several providers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used. The CARES Act, which was signed into law on March 27, 2020 and designed to provide financial support and resources to individuals and businesses affected by the COVID-19 pandemic, suspended the 2% Medicare sequester from May 1, 2020 to December 31, 2020 and extended the sequester by one year, through 2030, in order to offset the added expense of the 2020 cancellation.

Since enactment of the PPACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by President Trump on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. Additionally, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the PPACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminates the health insurer tax. Further, the Bipartisan Budget Act of 2018, among other things, amended the PPACA, effective January 1, 2019, to increase from 50 percent to 70 percent the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." The Congress may consider other legislation to replace elements of the PPACA during future Congressional session.

Further, on December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the PPACA is an essential and inseverable feature of the PPACA, and therefore because the mandate was repealed as part of the Tax Cuts and Jobs Act, the remaining provisions of the PPACA are invalid as well. On December 18, 2019, the Court of Appeals for the Fifth Circuit affirmed the lower court's ruling that the individual mandate portion of the PPACA is unconstitutional and it remanded the case to the district court for reconsideration of the severability question and additional analysis of the provisions of the PPACA. Thereafter, the U.S. Supreme Court agreed to hear this case. Oral argument in the case took place on November 10, 2020, and a ruling by the Court is expected sometime this year. Litigation and legislation over the PPACA are likely to continue, with unpredictable and uncertain results.

The Trump administration also took executive actions to undermine or delay implementation of the PPACA, including directing federal agencies with authorities and responsibilities under the PPACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the PPACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On January 28, 2021, however, President Biden issued a new executive order which directs federal agencies to reconsider rules and other policies that limit Americans' access to health care, and consider actions that will protect and strengthen that access. Under this Order, federal agencies are directed to re-examine: policies that undermine protections for people with pre-existing conditions, including complications related to COVID-19; demonstrations and waivers under Medicaid and the PPACA that may reduce coverage or undermine the programs, including work requirements; policies that undermine the Health Insurance Marketplace or other markets for health insurance; policies that make it more difficult to enroll in Medicaid and the PPACA; and policies that reduce affordability of coverage or financial assistance, including for dependents.

We expect that these healthcare reforms, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product and/or the level of reimbursement physicians receive for administering any approved product we might bring to market. Reductions in reimbursement levels may negatively impact the prices we receive or the frequency with which our products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors, and such actions could have a material impact on our business.

Current and future legislative efforts may limit the prices for our products, if and when they are licensed for marketing, and that could materially impact our ability to generate revenues.

The prices of prescription pharmaceuticals have been the subject of considerable discussion in the United States. To date, there have been several recent U.S. congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for products. To those ends, President Trump issued five executive orders intended to lower the costs of prescription drug products. Several of these orders are reflected in recently promulgated regulations, and one of these regulations is currently subject to a nationwide preliminary injunction. It remains to be seen whether these orders and resulting regulations will remain in force during the Biden Administration. Further, on September 24, 2020, the Trump administration finalized a rulemaking allowing states or certain other non-federal government entities to submit importation program proposals to the FDA for review and approval. Applicants are required to demonstrate that their importation plans pose no additional risk to public health and safety and will result in significant cost savings for consumers. The FDA has issued draft guidance that would allow manufacturers to import their own FDA-approved drugs that are authorized for sale in other countries (multi-market approved products).

At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, group purchasing organizations and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Finally, outside the United States, in some nations, including those of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. In the future, we plan to submit tazemetostat for approval in the EU and, if tazemetostat is approved, it would be subject to these processes. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a

clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our ability to generate revenues and become profitable could be impaired, or our business could be harmed, possibly materially.

Our relationships with healthcare providers and third-party payors are subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which, in the event of a violation, could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers and third-party payors play a primary role in the recommendation and prescription of TAZVERIK and will play a primary role in the recommendation and prescription of any future product candidates for which we obtain marketing approval. Our current and future arrangements with healthcare providers and third-party payors may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any products for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal Anti-Kickback Statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation or arranging of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid. Several courts have interpreted the statute's intent requirement to mean that if any one purpose of arrangement involving remuneration is to induce referrals of a federal healthcare covered business, the statue has been violated. In addition, the PPACA, amended the intent requirement of the federal Anti-Kickback Statute such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it to have committed a violation. The Anti-Kickback Statute is broad and prohibits many arrangements and practices that are lawful in businesses outside of the healthcare industry. Penalties for violations of the federal Anti-Kickback Statute include criminal penalties and civil sanctions such as fines, imprisonment and possible exclusion from Medicare, Medicaid and other federal healthcare programs;
- the federal False Claims Act imposes criminal and civil penalties, including through civil whistleblower or *qui tam* actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, false or fraudulent claims for payment by a federal healthcare program or making a false statement or record material to payment of a false claim or avoiding, decreasing or concealing an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties, currently set at a minimum of $11,665 and a maximum of $23,331 per false claim;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal Physician Payments Sunshine Act requires applicable manufacturers of covered drugs to report payments and other transfers of value to physicians and teaching hospitals; and
- analogous state laws and regulations, such as state anti-kickback and false claims laws and transparency statutes, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and may require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures.

The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the EU. The provision of benefits or advantages to physicians is governed by the national anti-bribery laws of EU Member States, and, in the UK, the U.K. Bribery Act 2010. Infringement of these laws could result in substantial fines and imprisonment.

Payments made to physicians in certain EU Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual EU Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct applicable in the EU Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

In order to comply with these laws, we have implemented a compliance program to actively identify, prevent and mitigate risk through the implementation of compliance policies and systems and by promoting a culture of compliance. Although we take our obligation to maintain our compliance with these various laws and regulations seriously and our compliance program is designed to prevent the violation of these laws and regulations, we cannot guarantee that our compliance program will be sufficient or effective, that we will be able to integrate the operations of acquired businesses into our compliance program on a timely basis, that our employees will comply with our policies and that our employees will notify us of any violation of our policies, that we will have the ability to take appropriate and timely corrective action in response to any such violation, or that we will make decisions and take actions that will necessarily limit or avoid liability for whistleblower claims that individuals, such as employees or former employees, may bring against us or that governmental authorities may prosecute against us based on information provided by individuals. If we are found to be in violation of any of the laws and regulations described above or other applicable federal, state and foreign healthcare laws, we may be subject to penalties, including civil, criminal and administrative penalties, damages, fines, disgorgement, contractual damages, reputational harm, imprisonment, diminished profits and future earnings, exclusion from government healthcare reimbursement programs, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, and/or the curtailment or restructuring of our operations, any of which could have a material adverse effect on our business, results of operations and growth prospects. Any action against us for violation of these laws or regulations, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Moreover, achieving and sustaining compliance with applicable federal, state and foreign healthcare laws is costly and time-consuming for our management.

Compliance with global privacy and data security requirements could result in additional costs and liabilities to us or inhibit our ability to collect and process data globally, and the failure to comply with such requirements could subject us to significant fines and penalties, which may have a material adverse effect on our business, financial condition or results of operations.

The regulatory framework for the collection, use, safeguarding, sharing, transfer and other processing of information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally, virtually every jurisdiction in which we operate has established its own data security and privacy frameworks with which we must comply. For example, the collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the European Union, including personal health data, is subject to the EU General Data Protection Regulation, or the GDPR, which took effect across all member states of the European Economic Area, or EEA, in May 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including strict rules on the transfer of personal data to countries outside the European Union, including the United States.

As a result, there is increased scrutiny on the extent to which clinical trial sites located in the EEA should apply the GPDR to transfers of personal data from such sites to countries that are considered to lack an adequate level of data protection, such as the United States. The GDPR also permits data protection authorities to require destruction of improperly gathered or used personal information and/or impose substantial fines for violations of the GDPR, which can be up to four percent of global revenues or 20 million Euros, whichever is greater, and it also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR provides that European Union member states may make their own further laws and regulations limiting the processing of personal data, including genetic, biometric or health data.

Similar actions are either in place or under way in the United States. There are a broad variety of data protection laws that are applicable to our activities, and a wide range of enforcement agencies at both the state and federal levels that can review companies for privacy and data security concerns based on general consumer protection laws. The Federal Trade Commission and state Attorneys General all are aggressive in reviewing privacy and data security protections for consumers. New laws also are being considered at both the state and federal levels. For example, the California Consumer Privacy Act—which went into effect on January 1, 2020—is creating similar risks and obligations as those created by GDPR, though the Act does exempt certain information collected as part of a clinical trial subject to the Federal Policy for the Protection of Human Subjects (the Common Rule). Many other states are considering similar legislation. A broad range of legislative measures also have been introduced at the federal level. Accordingly, failure to comply with federal and state laws (both those currently in effect and future legislation) regarding privacy and security of personal information could expose us to fines and penalties under such laws. There also is the threat of consumer class actions related to these laws and the overall protection of personal data. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our reputation and our business.

Given the breadth and depth of changes in data protection obligations, preparing for and complying with such requirements is rigorous and time intensive and requires significant resources and a review of our technologies, systems and practices, as well as those of any third-party collaborators, service providers, contractors or consultants that process or transfer personal data collected in the European Union. The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could require us to change our business practices and put in place additional compliance mechanisms, may interrupt or delay our development, regulatory and commercialization activities and increase our cost of doing business, and could lead to government enforcement actions, private litigation and significant fines and penalties against us and could have a material adverse effect on our business, financial condition or results of operations.

We are subject to U.S. and foreign anti-corruption and anti-money laundering laws with respect to our operations and non-compliance with such laws can subject us to criminal and/or civil liability and harm our business.

We are subject to the U.S. Foreign Corrupt Practices Act of 1977, as amended, or the FCPA, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act, and other state and national anti-bribery and anti-money laundering laws in countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, third-party intermediaries, joint venture partners and collaborators from authorizing, promising, offering, or providing, directly or indirectly, improper payments or benefits to recipients in the public or private sector. We may have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. In addition, we may engage third party intermediaries to coordinate our clinical research activities abroad and/or to obtain necessary permits, licenses, and other regulatory approvals. We can be held liable for the corrupt or other illegal activities of these third-party intermediaries, our employees, representatives, contractors, partners, and agents, even if we do not explicitly authorize or have actual knowledge of such activities.

We have adopted a Code of Business Conduct and Ethics that mandates compliance with the FCPA and other anti-corruption laws applicable to our business throughout the world. We cannot ensure, however, that our employees and third party intermediaries will comply with this code or such anti-corruption laws. Noncompliance with anti-

corruption and anti-money laundering laws could subject us to whistleblower complaints, investigations, sanctions, settlements, prosecution, other enforcement actions, disgorgement of profits, significant fines, damages, other civil and criminal penalties or injunctions, suspension and/or debarment from contracting with certain persons, the loss of export privileges, reputational harm, adverse media coverage, and other collateral consequences. If any subpoenas, investigations, or other enforcement actions are launched, or governmental or other sanctions are imposed, or if we do not prevail in any possible civil or criminal litigation, our business, results of operations and financial condition could be materially harmed. In addition, responding to any such action will likely result in a materially significant diversion of management's attention and resources and significant defense and compliance costs and other professional fees. In certain cases, enforcement authorities may even cause us to appoint an independent compliance monitor which can result in added costs and administrative burdens.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Our internal information systems, or those of any collaborators, contractors, consultants, vendors, business partners or other third parties, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

We collect, store and transmit large amounts of confidential information, including personal information and information relating to intellectual property, on internal information systems and through the information systems of our collaborators, contractors, consultants, vendors, business partners or other third parties.

Despite the ongoing implementation of security measures, our internal information systems and those of third parties are vulnerable to damage from computer viruses, malware, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Such systems are also vulnerable to service interruptions or to security breaches from inadvertent or intentional actions by our employees, our collaborators, contractors, consultants, vendors, business partners and other third parties, or from cyberattacks by malicious third parties over the Internet or through other mechanisms. Cyberattacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cyberattacks could include the deployment of harmful malware, ransomware, denial of service attacks, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information. Cyberattacks also could include phishing attempts or e-mail fraud to cause payments or information to be transmitted to an unintended recipient. Our employees and systems have been and likely will continue to be targeted by such cyberattacks.

While we have not experienced any material system failure, accident, cyber-attack or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs, clinical trials and business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions, in addition to possibly requiring substantial expenditures of resources to remedy. In addition, our remediation efforts may not be successful. For example, the loss of clinical trial data from clinical trials could result in delays or termination of our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. In addition, as risks with respect to our information systems continue to evolve, we will incur additional costs to maintain the security of our information systems and comply with evolving laws and regulations pertaining to cybersecurity and related areas. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, including regulatory fines and other losses with respect to privacy claims, enrollment in our clinical trials could be negatively affected, our competitive position and reputation could be harmed and the further development and commercialization of our product candidates could be delayed. While we maintain cybersecurity insurance, our insurance may be insufficient to cover all liabilities incurred by these incidents, and any incidents may result in loss of, or increased costs of, our cybersecurity insurance.

Risks Related to Employee Matters and Managing Growth

Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on the research and development, clinical and business expertise of our executive officers as well as the other principal members of our management, scientific and clinical teams. Although we have entered into employment letter agreements with our executive officers, each of them may terminate their employment with us at any time. For instance, since January 1, 2017, we have had multiple executive officers, including among others our former Executive Vice President and Chief Financial Officer, our former Chief Business Officer, our former President of Research and Chief Scientific Officer, and our former Executive Vice President and Chief Medical Officer terminate their employment with us. We do not maintain "key person" insurance for any of our executives or other employees.

Recruiting and retaining qualified scientific, clinical, manufacturing, regulatory, and sales and marketing personnel will also be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies, universities and research institutions for similar personnel. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

We expect to expand our development, regulatory, sales, marketing and distribution capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We expect to experience continued growth in the number of our employees and the scope of our operations, particularly in the areas of drug development, regulatory affairs and, sales, marketing and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Risks Related to Our Common Stock

Provisions in our corporate charter documents, under Delaware law and in our collaboration agreements could make an acquisition of our company, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

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

- establish a classified board of directors such that only one of three classes of directors is elected each year;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from our board of directors;
- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal specified provisions of our certificate of incorporation or bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

An active trading market for our common stock may not be sustained.

Although our common stock is listed on The Nasdaq Global Select Market, an active trading market for our shares may not be sustained. If an active market for our common stock does not continue, it may be difficult for our stockholders to sell their shares without depressing the market price for the shares or sell their shares at all. Any inactive trading market for our common stock may also impair our ability to raise capital to continue to fund our operations by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

The price of our common stock has been and may in the future be volatile and fluctuate substantially.

Our stock price has been and may in the future be volatile. The stock market in general and the market for smaller biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. From January 1, 2018 until February 18, 2021, the sale price of our common stock as reported on the Nasdaq Global Select Market ranged from a high of $27.82 to a low of $5.14. The market price for our common stock may be influenced by many factors, including:

- the commercial success of TAZVERIK;
- regulatory developments with respect to tazemetostat;
- the success of competitive products or technologies;
- results of clinical trials of our product candidates or those of our competitors;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our products, product candidates or clinical development programs;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates or products;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or the financial results of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions;
- disruptions in the financial markets caused by the COVID-19 pandemic; and
- the other factors described in this Risk Factors section.

We have broad discretion over the use of our cash and cash equivalents and may not use them effectively.

Subject to certain restrictions in our Amended and Restated Loan Agreement documents or in other third-party agreements we may enter into from time to time, our management has broad discretion to use our cash and cash equivalents to fund our operations and could spend these funds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline, delay the development of our product candidates, or adversely impact the success of our commercialization efforts with respect to TAZVERIK. Pending their use to fund operations, we may invest our cash and cash equivalents in a manner that does not produce income or that loses value.

Changes in tax laws or in their implementation or interpretation could adversely affect our business and financial condition.

Recent changes in tax law may adversely affect our business or financial condition. On December 22, 2017, President Trump signed into law the Tax Cuts and Jobs Act of 2017, or the TCJA, which significantly revised the Internal Revenue Code of 1986, as amended, or the Code. The TCJA, among other things, contained significant changes to corporate taxation, including a reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, the limitation of the tax deduction for interest expense to 30% of adjusted taxable income (except

for certain small businesses), the limitation of the deduction for net operating losses arising in taxable years beginning after December 31, 2017 to 80% of current year taxable income and elimination of net operating loss carrybacks for losses arising in taxable years ending after December 31, 2017 (though any such net operating losses may be carried forward indefinitely), the imposition of a one-time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, the elimination of U.S. tax on foreign earnings (subject to certain important exceptions), the allowance of immediate deductions for certain new investments instead of deductions for depreciation expense over time, and the modification or repeal of many business deductions and credits.

As part of Congress' response to the COVID-19 pandemic, the Families First Coronavirus Response Act, or FFCR Act, was enacted on March 18, 2020, and the Coronavirus Aid, Relief, and Economic Security Act, or CARES Act, was enacted on March 27, 2020. Both contain numerous tax provisions. In particular, the CARES Act retroactively and temporarily (for taxable years beginning before January 1, 2021) suspends application of the 80%-of-income limitation on the use of net operating losses, which was enacted as part of the TCJA. It also provides that net operating losses arising in any taxable year beginning after December 31, 2017, and before January 1, 2021 are generally eligible to be carried back up to five years. The CARES Act also temporarily (for taxable years beginning in 2019 or 2020) relaxes the limitation of the tax deductibility for net interest expense by increasing the limitation from 30 to 50% of adjusted taxable income.

Regulatory guidance under the TCJA, the FFCR Act and the CARES Act is and continues to be forthcoming, and such guidance could ultimately increase or lessen impact of these laws on our business and financial condition. It is also likely that Congress will enact additional legislation in connection with the COVID-19 pandemic, some of which could have an impact on our company. In addition, it is uncertain if and to what extent various states will conform to the TCJA, the FFCR Act or the CARES Act.

We incur significant costs as a result of operating as a public company, and our management is required to devote substantial time to compliance initiatives and corporate governance practices.

As a public company, we incur significant legal, accounting and other expenses. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Global Select Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to continue to devote a substantial amount of time to these compliance initiatives.

We cannot predict or estimate the amount of costs we may incur to continue to operate as a public company, nor can we predict the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies which could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we are required to furnish a report by our management on our internal control over financial reporting. We are also required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we are engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we have and will need to continue to dedicate internal resources, engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. If we or our auditors identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be the sole source of gain for our stockholders.

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. The terms of our Amended and Restated Loan Agreement restrict our ability to pay dividends. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be the sole source of gain for our stockholders for the foreseeable future.

If securities or industry analysts do not continue to publish research or publish inaccurate or unfavorable research about our business, our share price and trading volume could decline.

The trading market for our common stock may be impacted, in part, by the research and reports that securities or industry analysts publish about us or our business. There can be no assurance that analysts will cover us, continue to cover us or provide favorable coverage. If one or more analysts downgrade our stock or change their opinion of our stock, our share price may decline. In addition, if one or more analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause our share price or trading volume to decline.

There is no public market for our series A convertible preferred stock.

There is no established public trading market for our series A convertible preferred stock, and we do not expect a market to develop. In addition, we do not intend to apply for listing of the series A convertible preferred stock on any national securities exchange or other nationally recognized trading system. Without an active market, the liquidity of the series A convertible preferred stock will be limited.

General Risk Factors

Our employees, independent contractors, CROs, consultants, commercial partners, vendors and principal investigators may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements.

We are exposed to the risk of fraud or other misconduct by our employees, independent contractors, CROs, consultants, commercial partners, vendors and, pertaining to clinical trials, our principal investigators. Misconduct by these parties could include intentional failures to comply with FDA regulations or the regulations applicable in the European Union and other jurisdictions, provide accurate information to the FDA, the European Commission and other regulatory authorities, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately, or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements.

Such misconduct also could involve the improper use of information obtained in the course of clinical trials or interactions with the FDA or other regulatory authorities, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of conduct applicable to all of our employees, but it is not always possible to identify and deter misconduct, and the precautions we take to detect and prevent such activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from government investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, financial condition, results of operations and prospects, including the imposition of significant fines or other sanctions.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

Our headquarters are located in Cambridge, Massachusetts, where we occupy approximately 43,066 square feet of office and laboratory space. The term of the lease to our Cambridge headquarters expires November 30, 2022. In addition, we occupy an additional 33,525 square feet in Cambridge, Massachusetts. The term of this lease ends on March 31, 2027, but we have an option to extend the term for one additional five-year period.

Item 3. Legal Proceedings

We are not currently a party to any material legal proceedings.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Market Information

Our common stock is traded on the Nasdaq Global Select Market under the symbol "EPZM." Trading of our common stock commenced on May 31, 2013, following the completion of our initial public offering. Prior to that date, there was no public market for our common stock.

Holders

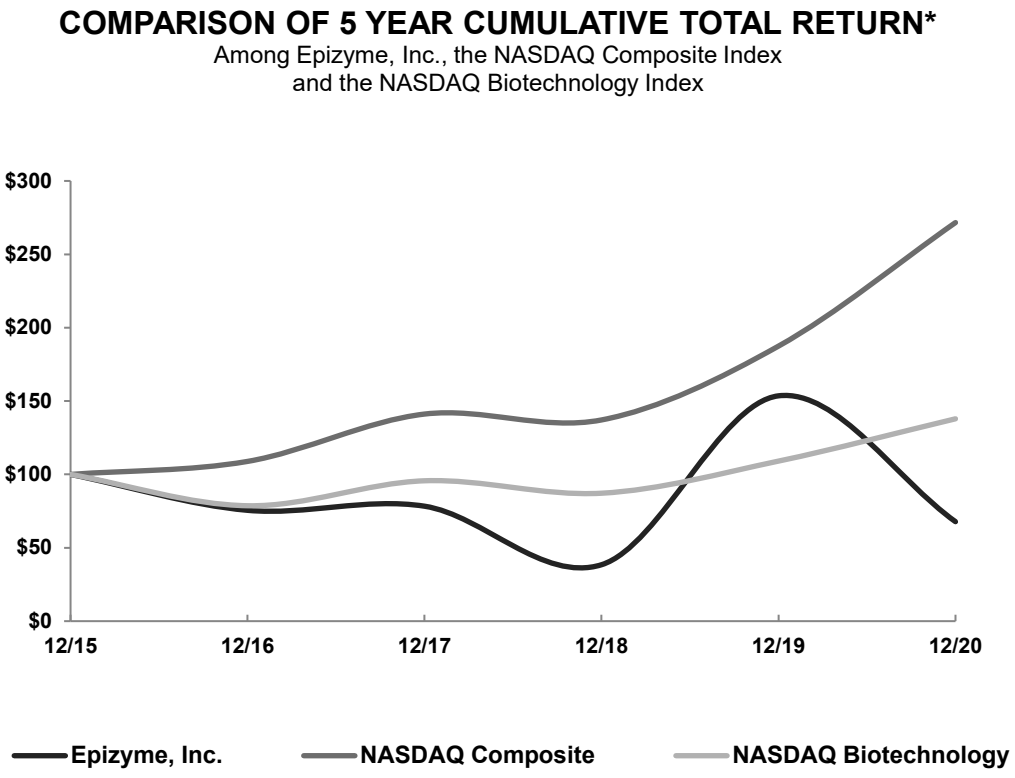
As of February 12, 2021, there were 15 holders of record of our common stock. This number does not include beneficial owners whose shares are held in street name.

Dividends

We have never declared or paid cash dividends on our capital stock. We intend to retain all of our future earnings, if any, to finance the growth and development of our business. The terms of our Amended and Restated Loan Agreement with BPCR Limited Partnership (as transferee of BioPharma Credit Investments V (Master) LP's interest as a lender) and BioPharma Credit PLC, or the Amended and Restated Loan Agreement, restrict our ability to pay dividends. We do not intend to pay cash dividends to our stockholders in the foreseeable future.

Stock Performance Graph

The following graph shows a comparison from December 31, 2015 through December 31, 2020 of the cumulative total return on an assumed investment of $100.00 in cash in our common stock, the Nasdaq Composite Index and the NASDAQ Biotechnology Index. Such returns are based on historical results and are not intended to suggest future performance. Data for the NASDAQ Composite Index and NASDAQ Biotechnology Index assume reinvestment of dividends.



*$100 invested on 12/31/15 in stock or index, including reinvestment of dividends.
Fiscal year ending December 31.

The performance graph in this Item 5 is not deemed to be "soliciting material" or to be "filed" with the SEC for purposes of Section 18 of the Securities and Exchange Act of 1934, as amended, or otherwise subject to the liabilities under that Section, and shall not be deemed incorporated by reference into any of our filings under the Securities Act of 1933 or the Securities Exchange Act of 1934, except to the extent we specifically incorporate it by reference into such a filing.

Item 6. None.

Item 7. 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 consolidated financial statements included in this Annual Report on Form 10-K, 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 consolidated financial statements and the notes thereto included elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, 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 this Annual Report on Form 10-K, 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

While the COVID-19 pandemic has had an impact on our business, operations, and financial performance, we have taken and plan to continue to take steps to evaluate, monitor, manage, and respond to the challenges that have arisen from the COVID-19 pandemic and to new challenges that may arise. 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 first half 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 epithelioid sarcoma, or ES, and follicular lymphoma, or 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.

For our ongoing commercialization activities for TAZVERIK, our commercial and medical affairs field teams are continuing to use virtual formats where possible in order to allow us to serve the needs of healthcare providers, patients and other stakeholders during this critical time. During the third and fourth quarters of 2020, the COVID-19 pandemic continued to negatively impact ES and FL patient visits to physicians, new patient starts across all lines of treatment as well as the ability of our field-based teams to fully access ES and FL prescribers, and these challenges continued in the first quarter of 2021. Notwithstanding these challenges, new prescriptions for TAZVERIK in FL have increased month over month and are 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 adapt our commercial strategy to the COVID-19 pandemic to support increased adoption of TAZVERIK in appropriate patients.

We 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 we 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, as quickly as possible, 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 in Part I, Item 1A. of this Annual Report on Form 10-K for further discussion of risks related to the COVID-19 pandemic.

Overview

We are a commercial-stage biopharmaceutical company that is committed to rewriting treatment for people with cancer and other serious diseases through the discovery, development, and commercialization of novel epigenetic medicines. By focusing on the genetic drivers of disease, our science seeks to match targeted medicines with the patients who need them.

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 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. The safety run-in portion of the trial is fully enrolled and we expect to commence the efficacy portion of the trial in 2021. We anticipate reporting safety and preliminary activity data from the safety run-in portion of the study at a medical meeting in 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 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. The trial is expected to enroll approximately 500 FL patients, stratified based on their EZH2 mutation status. The safety run-in portion of the trial is fully enrolled and we expect to commence the efficacy portion of the trial in 2021. We anticipate reporting safety and preliminary activity data from the safety run-in portion of the study at a medical meeting in 2021. In addition, we plan to conduct post-marketing commitments, including expanding our ongoing Phase 2 clinical trial with a cohort of FL patients with wild-type EZH2 to evaluate tazemetostat as a monotherapy in patients who have been treated with at least one prior systemic treatment, in order to inform the label and potentially expand the approved indications in the relapsed and refractory setting in the future.

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 are also supporting an investigator-sponsored study to evaluate tazemetostat in combination with rituximab with FL in the third-line or later treatment settings, which is currently enrolling. We intend to have this investigator-sponsored study transferred to a Company sponsored study in 2021. 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 explore 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 evaluating tazemetostat in combination with enzalutamide or abiraterone, the standard of care treatments for this disease, plus prednisone in chemo-naïve patients with mCRPC. The safety run-in portion of the trial is fully enrolled and we expect to commence the efficacy portion of the trial in 2021. We anticipate reporting safety and preliminary activity data from the safety run-in portion of the study at a medical meeting in 2021.

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, chronic lymphocytic leukemia, or CLL, chronic myeloid leukaemia, or CML, and others;
- Molecularly defined solid tumors, such as chordoma, melanoma, mesothelioma, and tumors harboring an EZH2 or SWI/SNF alteration;
- Chemotherapy or treatment-resistant tumors, such as triple-negative breast cancer, small cell lung cancer, ovarian cancer, and as described above, mCRPC; and
- Immuno-oncology-sensitive tumors, such as colorectal cancer, bladder cancer, soft tissue sarcomas and non-small cell lung cancer.

We own the global development and commercialization rights to tazemetostat outside of Japan. 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. This includes an efficiently sized field-based organization of approximately 76 individuals.

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 through potential strategic collaborations.

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.

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, or STS, mesothelioma and a seven-year orphan drug exclusivity period for 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.

To date, we have entered into various strategic collaborations, including therapeutic collaborations and other collaborations, including with 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 December 31, 2020, in addition to revenues from product sales, we have raised an aggregate of $1,527.4 million to fund our operations. This includes $243.8 of non-equity funding through our collaboration agreements, $368.1 million of funding, consisting of $150.0 million in equity funding received through agreements with RPI Finance Trust, or RPI, and $218.1 million in debt financing received through a loan agreement with BioPharma Credit Investments V (Master) LP and BPCR Limited Partnership (as transferee of BioPharma Credit Investments V (Master) LP's interest as a lender), or the Lenders, $839.5 million from the sale of common stock and series A convertible preferred stock in our public 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 December 31, 2020, we had $373.6 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 $231.7 million for the year ended December 31, 2020. As of December 31, 2020, our accumulated deficit totaled $988.7 million. Notwithstanding our sales of TAZVERIK, we expect to continue to incur significant expenses and operating losses over the next several years. Our net losses may fluctuate significantly from quarter to quarter and year to year. We expect our expenses to increase in connection with our ongoing activities, particularly as we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. In addition, we expect our expenses to increase as we fund our tazemetostat development program; make any milestone and royalty payments provided for and achieved under the amended and restated collaboration and license agreement with Eisai; pay interest and principal associated with our amended and restated loan agreement with BioPharma Credit Investments V (Master) LP, BPCR Limited Partnership and BioPharma Credit PLC, or the Amended and Restated Loan Agreement; and continue research and development and initiate clinical trials of, and seek regulatory approval for, any future product candidates.

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

We executed 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 13, *Long-Term Debt*, of the notes to our consolidated financial statements included in this Annual Report on Form 10-K for a description of the key terms of the Amended and Restated Loan Agreement.

Collaborations

Refer to Item 1, *Business--Our Collaborations* and Note 11, *Collaborations*, of the notes to our consolidated financial statements in Item 15 of this Annual Report on Form 10-K for a description of the key terms of our arrangements with Glaxo Group Limited (an affiliate of GlaxoSmithKline plc), or GSK, Eisai Co. Ltd, or Eisai, Roche Sequencing Solutions, Inc., or Roche Sequencing, and Boehringer Ingelheim International GmbH, or Boehringer Ingelheim. On November 3, 2020, we received a notice of termination of our collaboration and license agreement with Celgene, effective January 2, 2021. On December 21, 2020 we received written notice from Boehringer Ingelheim that they elected to terminate the collaboration effective January 31, 2021.

Results of Operations for the Years Ended December 31, 2020, 2019 and 2018

Revenues

The following is a comparison of total revenues for the years ended December 31, 2020, 2019, and 2018:

	Year Ended December 31,		
	2020	2019	Change
	(In millions)		
Product revenues, net	$ 11.5	$ —	$ 11.5
Collaboration revenue	4.3	23.8	(19.5)
Total revenues	$ 15.8	$ 23.8	$ (8.0)

	Year Ended December 31,		
	2019	2018	Change
	(In millions)		
Product revenues, net	$ —	$ —	$ —
Collaboration revenue	23.8	21.7	2.1
Total revenues	$ 23.8	$ 21.7	$ 2.1

Product Revenues, net

Net product revenues represent U.S. sales from our sole commercial product, TAZVERIK, which was first approved by the FDA on January 23, 2020, less allowances and accruals. During the year ended December 31, 2020, net product revenues were $11.5 million. Sales allowances and accruals consisted of patient financial assistance, distribution fees, discounts, and chargebacks. We did not have product revenues in 2019 or 2018.

Collaboration Revenue

Our collaboration 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 and milestone payments earned under collaboration and license agreements with our collaboration partners.

The following tables summarize our collaboration revenue, by collaboration partner, for the years ended December 31, 2020, 2019, and 2018:

	Year Ended December 31,			
	2020	2019	Change	%
	(In millions)			
Collaboration Partner				
Celgene	$ 3.8	$ —	$ 3.8	100.0%
BI:	0.5	23.8	(23.3)	(97.9)%
	$ 4.3	$ 23.8	$ (19.5)	-81.9%

	Year Ended December 31,			
	2019	2018	Change	%
	(In millions)			
Collaboration Partner				
GSK:	$ —	$ 20.0	$ (20.0)	(100.0)%
BI:	23.8	1.7	22.1	1300.0%
	$ 23.8	$ 21.7	$ 2.1	9.7%

Collaboration revenue for the year ended December 31, 2020 decreased $19.5 million as compared to the year ended December 31, 2019, primarily as a result of a decrease in revenue related to milestones and services under our agreement with Boehringer Ingelheim, offset by an increase of $3.8 million of revenue under the Celgene collaboration agreement related to the recognition of the remaining deferred revenue related to the agreement, which was recognized as revenue as a result of the termination of the collaboration agreement with Celgene. The revenue recognized under the Boehringer Ingelheim collaboration during the year ended December 31, 2020 was related to amendments to extend the research period under the collaboration agreement under which Boehringer Ingelheim agreed to fund up to $0.5 million of additional research activities. In December 2020, we received written notice from Boehringer Ingelheim to terminate the collaboration agreement, effective January 31, 2021.

Collaboration revenue for the year ended December 31, 2019 increased $2.1 million as compared to the year ended December 31, 2018, primarily as a result of $23.8 million related to milestones and services under our agreement with Boehringer Ingelheim, as compared to the achievement of a $12.0 million milestone and a $8.0 million milestone under our agreement with GSK and $1.7 million related to the commencement of services under our agreement with Boehringer Ingelheim during 2018.

GSK. Under our collaboration agreement with GSK, we have received and recognized collaboration revenue totaling $89.0 million, consisting of upfront payments, fixed research funding, research and development services and preclinical and research milestone payments. In the year ended December 31, 2018, we recognized $20.0 million in

collaboration revenue in connection with achievement of milestones under our collaboration agreement with GSK. As of December 31, 2020, for the two remaining targets, we are 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 in the aggregate. As a result of the termination of the agreement as it relates to the third target, we will receive no additional payments related to that target. In addition, GSK is required to pay us 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, we 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.

Boehringer Ingelheim. Under our collaboration agreement with Boehringer Ingelheim, we have received and recognized collaboration revenue totaling $26.0 million, consisting of upfront payments, fixed research funding, and research and development services. In the years ended December 31, 2020, 2019, and 2018, we recognized $0.5 million, $23.8 million, and $1.7 million, respectively, in collaboration revenue as part of our Boehringer Ingelheim collaboration. The revenue recognized in 2020 was related to amendments to extend the research period under the collaboration agreement under which Boehringer Ingelheim agreed to fund up to $0.5 million of additional research activities. Under the agreement we received $15.0 million in an upfront payment from Boehringer Ingelheim for our license to inhibitor technology of two undisclosed targets and $5.0 million in research funding in 2019. The revenue was recognized as we performed research services through the end of 2019. The research period expired on December 31, 2019, as Boehringer Ingelheim did not elect to extend the research period through December 31, 2020, and subsequently elected to terminate the collaboration agreement without cause, and in accordance with the terms of the collaboration agreement. In 2018, we recognized $1.7 million in collaboration revenue related to the commencement of services under the collaboration agreement.

Cost of Product Revenue

The following is a comparison of cost of product revenue for the years ended December 31, 2020, 2019 and 2018:

	Year Ended December 31,		
	2020	2019	Change
	(In millions)		
Cost of product revenue	$ 5.1	$ —	$ 5.1

	Year Ended December 31,		
	2019	2018	Change
	(In millions)		
Cost of product revenue	$ —	$ —	$ —

The cost of product revenue consists of costs related to the sales of TAZVERIK. These costs include materials, labor, manufacturing overhead, amortization of milestone payments, and royalties payable on net sales of TAZVERIK. During the year ended December 31, 2020, the cost of product revenue was $5.1 million and consisted of $0.4 million in costs associated with manufacturing TAZVERIK, $3.0 million 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 $1.7 million in worldwide royalties owed to Royalty Pharma on net sales of TAZVERIK in the year ended December 31, 2020. 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 (excluding amortization of intangible assets) to continue to be positively impacted during 2021, as we sell through certain inventory that was expensed prior to FDA approval of TAZVERIK in January 2020. We did not have cost of product revenues in 2019 or 2018.

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.

In our early-stage research, we identify and prioritize novel CMPs that are implicated in cancer and other diseases, and seek to develop potent and selective small molecule inhibitors of these targets. During this phase of research, our external costs primarily relate to lead discovery, biology, drug metabolism and pharmacokinetics and chemistry services from a multinational network of third-party providers of research and development services. As our product candidates progress into preclinical and clinical development, external costs are driven by clinical trial costs, manufacturing expenses, and third-party research and development expenses.

In circumstances where our collaboration and license agreements provide for equally co-funded global development under joint risk sharing collaborations, and where we are the study sponsor, amounts received for co-funding are recorded as a reduction to research and development expense.

The following is a comparison of research and development expenses for the years ended December 31, 2020, 2019, and 2018:

	Year Ended December 31,			
	2020	2019	Change	%
	(In millions)			
Research and development	$ 110.9	$ 132.6	$ (21.7)	(16.3)%

	Year Ended December 31,			
	2019	2018	Change	%
	(In millions)			
Research and development	$ 132.6	$ 105.8	$ 26.8	25.3%

During the year ended December 31, 2020, total research and development expenses decreased by $21.7 million compared to the year ended December 31, 2019, primarily due to the payment of $20.0 million in clinical development milestones to Eisai in 2019, and decreases in tazemetostat manufacturing costs as we began to capitalize the cost of manufacturing following the approval of TAZVERIK for the approved ES indication in January 2020 and decreased discovery research activities related to tazemetostat in other indications, which were offset by increases in clinical trial expenses and costs associated with the buildout of our regulatory and late-stage development groups.

During the year ended December 31, 2019 total research and development expenses increased by $26.8 million compared to the year ended December 31, 2018, primarily due to the payment of $20.0 million in clinical development milestones to Eisai, increases in tazemetostat manufacturing costs and the buildout of our regulatory and late-stage development groups, offset by decreases in clinical trial expenses.

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

	Year Ended December 31,			
Product Program	2020	2019	Change	%
	(In millions)			
External research and development expenses:				
Tazemetostat and related EZH2 programs	$ 42.0	$ 67.8	$ (25.8)	(38.1)%
Pinometostat and related DOT1L programs	0.1	0.3	(0.2)	(66.7)
Discovery and preclinical stage product programs, collectively	17.8	18.7	(0.9)	(4.8)
Unallocated personnel and other expenses	51.0	45.8	5.2	11.4
Total research and development expenses	$ 110.9	$ 132.6	$ (21.7)	(16.4)%

Product Program	Year Ended December 31, 2019	2018	Change	%
	(In millions)			
External research and development expenses:				
Tazemetostat and related EZH2 programs	$ 67.8	$ 49.5	$ 18.3	37.0%
Pinometostat and related DOT1L programs	0.3	0.0	0.3	100.0
Discovery and preclinical stage product programs, collectively	18.7	16.0	2.7	16.9
Unallocated personnel and other expenses	45.8	40.3	5.5	13.6
Total research and development expenses	$ 132.6	$ 105.8	$ 26.8	25.3%

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 decreased $25.8 million for the year ended December 31, 2020 compared to the year ended December 31, 2019. The decrease in tazemetostat related research and development expenses in the year ended December 31, 2020 related to a decrease in tazemetostat manufacturing costs, as we began to capitalize the cost of manufacturing following the approval of TAZVERIK for the approved indication in ES in January 2020, and decreased discovery research activities related to tazemetostat in other indications, which was offset by increases in clinical trial expenses and increased costs associated with the buildout of our regulatory and late-stage development groups.

External research and development expenses for tazemetostat and related EZH2 programs increased $18.3 million for the year ended December 31, 2019 compared to the year ended December 31, 2018. The increase in tazemetostat related research and development expenses in the year ended December 31, 2019 related to greater tazemetostat manufacturing costs and the build out of our regulatory and late stage development groups, offset by decreases in clinical trial expenses.

External research and development expenses for pinometostat and related DOT1L programs for the year ended December 31, 2020 decreased $0.2 million compared to the year ended December 31, 2019. The costs incurred in the years ended December 31, 2020 and 2019 were primarily associated with costs attributed to the Cooperative Research and Development Agreement, or CRADA, with the National Cancer Institute, or NCI, to evaluate pinometostat in clinical trials in a variety of hematologic malignancies and solid tumors. There were no costs incurred related to pinometostat in 2018.

External research and development expenses for discovery and preclinical stage product programs decreased $0.9 million for the year ended December 31, 2020 compared to the year ended December 31, 2019, primarily related to reduced spending for discovery research activities and decreased development activities related to our G9a preclinical program. External research and development expenses for discovery and preclinical stage product programs increased $2.7 million for the year ended December 31, 2019 compared to the year ended December 31, 2018, primarily related to decreased spending for discovery research activities, offset by increased development activities related to our G9a preclinical program.

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 for the year ended December 31, 2020 increased $5.2 million compared to the year ended December 31, 2019. 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. Unallocated personnel and other expenses for the year ended December 31, 2019 increased $5.5 million compared to the year ended December 31, 2018. The increase in unallocated personnel and other expenses is a result of the allocation of expenses to projects and increases in facilities and equipment related expenses offset by an increase in unallocated personnel costs.

We expect that research and development expenses will increase in 2021, as we increase our clinical trial activity for tazemetostat and utilize our drug discovery platform to progress preclinical efforts and pursue additional development candidates to expand our pipeline.

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 years ended December 31, 2020, 2019, and 2018:

	Year Ended December 31,			
	2020	2019	Change	%
	(In millions)			
Selling, general and administrative	$ 125.2	$ 68.3	$ 56.9	83.3%

	Year Ended December 31,			
	2019	2018	Change	%
	(In millions)			
Selling, general and administrative	$ 68.3	$ 44.0	$ 24.3	55.3%

For the year ended December 31, 2020, our selling, general and administrative expenses increased $56.9 million compared to the year ended December 31, 2019, primarily 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, and increased personnel related expenses. For the year ended December 31, 2019, our selling, general and administrative expenses increased $24.3 million compared to the year ended December 31, 2018, primarily due to increased pre-commercialization activities, including the build out of our medical affairs and commercial organizations, and increased personnel related expenses.

We expect that selling, general and administrative expenses will increase in 2021, as we continue to increase our commercial activities for tazemetostat.

Other (Expense) Income, Net

The following is a comparison of other (expense) income, net for the years ended December 31, 2020, 2019, and 2018:

	Year Ended December 31,			
	2020	2019	Change	%
	(In millions)			
Other income, net				
Interest income	$ 2.9	$ 7.4	$ (4.5)	(60.8)%
Interest expense	(7.6)	(0.3)	(7.3)	2433.3
Other expense, net	(0.1)	—	(0.1)	100.0
Non-cash interest expense related to sale of future royalties	(1.4)	(0.2)	(1.2)	600.0
Other (expense) income, net	$ (6.2)	$ 6.9	$ (13.1)	(189.9)%

	Year Ended December 31,			
	2019	2018	Change	%
	(In millions)			
Other income, net				
Interest income	$ 7.4	$ 4.6	$ 2.8	60.9%
Interest expense	(0.3)	—	(0.3)	100.0
Other (expense) income, net	—	—	—	0.0
Non-cash interest expense related to sale of future royalties	(0.2)		(0.2)	100.0
Other income, net	$ 6.9	$ 4.6	$ 2.3	50.2%

Other (expense) income, net consists of interest income earned on our cash equivalents and marketable securities, net of imputed interest expense paid under our capital lease obligation. The decrease in other income for the year ended December 31, 2020 is principally due to an increase in interest expense of $7.3 million incurred in connection with our long-term debt obligations under our Amended and Restated Loan Agreement, a decrease in net interest income of $4.5 million, and an increase in non-cash interest expense related to the sale of future royalties of $1.2 million. The increase in other income for the year ended December 31, 2019 as compared to the year ended December 31, 2018 is primarily due to an increase in interest income of $2.8 million as a result of active management of our investment portfolio, an increase in investment yields, and an increased cash balance as a result of the public offering that we conducted in March 2019, the RPI Purchase Agreement and the Loan Agreement. The increase in interest income was offset by non-cash interest expense of $0.2 million related to the sale of future royalties and interest expense of $0.3 million incurred under our Amended and Restated Loan Agreement.

Income Tax Benefit

We evaluated the expected recoverability of our net deferred tax assets as of December 31, 2020 and 2019, and determined that, with the exception of the deferred tax asset related to alternative minimum tax, or AMT, credits, there was insufficient positive evidence to support the recoverability of these net deferred tax assets. The AMT credit becomes refundable no later than 2022 under the Tax Cuts and Jobs Act, and as such, the related deferred tax asset will be able to be realized. The corresponding valuation allowance of $368,000 was reversed as of December 31, 2017 and recognized as a tax benefit. As of December 31, 2018, $184,000 of the deferred tax asset was reclassified to an income tax receivable. Fifty percent of the remaining AMT credit is refundable with the filing of the 2019 tax return. As such, as of December 31, 2019, $92,000 of the deferred tax asset was reclassified to an income tax receivable. There was no tax benefit or provision as a result of the asset reclassification on the balance sheet. Under the Coronavirus Aid, Relief, and Economic Security Act, the AMT Credit became 100% refundable with the filing of the 2019 tax return. The Company re-classed the remaining deferred tax asset to an income tax receivable as part of the 2019 provision to return analysis. At December 31, 2020 there is no deferred tax asset related to AMT credits and the Company has a full valuation allowance against its net deferred tax assets.

Liquidity and Capital Resources

Through December 31, 2020, in addition to revenues from product sales, we have raised an aggregate of $1,527.4 million to fund our operations. This includes $243.8 million was non-equity funding through our collaboration agreements, $368.1 million of funding, consisting of $150.0 million in equity funding received through agreements with RPI Finance Trust, or RPI, and $218.1 million in debt financing received through a loan agreement with BioPharma Credit Investments V (Master) LP and BPCR Limited Partnership (as transferee of BioPharma Credit Investments V (Master) LP's interest as a lender), or the Lenders, $839.5 million from the sale of common stock and series A convertible preferred stock in our public offerings and $76.0 million was from the sale of redeemable convertible preferred stock in private financings prior to our initial public offering in May 2013. As of December 31, 2020, we had $373.6 million in cash, cash equivalents and marketable securities.

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 March 2019, we raised approximately $122.7 million in net proceeds (after deducting underwriting discounts and commissions and estimated offering expenses, but excluding any expenses and other costs reimbursed by the underwriters) from the sale of 11,500,000 shares of our common stock in a public offering at a price of $11.50 per share. We also raised approximately $37.4 million in net proceeds (after deducting underwriting discounts and commissions and estimated offering expenses, but excluding any expenses and other costs reimbursed by the underwriters) from the sale of 350,000 shares of series A convertible preferred stock in a public offering at a price of $115 per share. The series A convertible preferred stock is convertible into 3,500,000 shares of our common stock.

In October 2018, we raised approximately $81.6 million in net proceeds (after deducting underwriting discounts and commissions and offering expenses, but excluding any expenses and other costs reimbursed by the underwriters) from the sale of 9,583,334 shares of our common stock in a public offering at a price of $9.00 per share.

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 agreements. 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, we expect that our existing cash, cash equivalents and marketable securities as of December 31, 2020, together with the cash we expect to generate from product sales, will be sufficient to fund our planned operating expenses and capital expenditure requirements and pay our debt service obligations as they

become due into 2023, without giving effect to any potential milestone payments we may receive under our collaboration agreements. We have based this estimate on assumptions that may prove to be wrong, such as the revenue that we expect to generate from the sale of our products, 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 years ended December 31, 2020, 2019 and 2018:

	Year Ended December 31,			
	2020	2019	Change	%
	(In millions)			
Net cash (used in) operating activities	$ (206.3)	$ (147.2)	$ (59.2)	40.2%
Net cash (used in) investing activities	(14.6)	(85.3)	70.7	(82.9)
Net cash provided by financing activities	249.7	286.3	(36.7)	(12.8)

	Year Ended December 31,			
	2019	2018	Change	%
	(In millions)			
Net cash (used in) operating activities	$ (147.2)	$ (121.6)	$ (25.6)	21.0%
Net cash (used in) investing activities	(85.3)	(102.6)	17.3	(16.8)
Net cash provided by financing activities	286.3	84.2	202.1	240.0

Net Cash Used in Operating Activities

Net cash used in operating activities was $206.3 million during the year ended December 31, 2020 compared to $147.2 million during the year ended December 31, 2019. The increase in net cash used in operating activities primarily relates to our net loss of $231.7 million and changes in working capital of $8.0 million, partially offset by net depreciation and amortization of $4.3 million, non-cash stock-based compensation of $27.6 million, and non-cash interest expense associated with the sale of future royalties of $1.4 million.

Net cash used in operating activities was $147.2 million during the year ended December 31, 2019 compared to $121.6 million during the year ended December 31, 2018. The increase in net cash used in operating activities primarily relates to our net loss of $170.3 million and net depreciation and amortization of $2.3 million, partially offset by changes in working capital of $7.1 million, non-cash stock-based compensation of $18.0 million, and non-cash interest expense associated with the sale of future royalties of $0.2 million.

Net Cash Used in Investing Activities

Net cash used in investing activities during the year ended December 31, 2020 reflects $276.4 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 $0.9 million of purchases of property and equipment, offset by maturities and sales of available for sale securities of $312.7 million.

Net cash used in investing activities during the year ended December 31, 2019 reflects $505.0 million of purchases of available for sale securities and $0.6 million of purchases of property and equipment, offset by maturities/sales of available for sale securities of $420.3 million.

Net cash used in investing activities during the year ended December 31, 2018 reflects $298.7 million of purchases of available-for-sale securities and $0.3 million of purchases of property and equipment, offset by maturities of available-for-sale securities of $196.4 million.

Net Cash Provided by Financing Activities

Net cash provided by financing activities of $249.7 million during the year ended December 31, 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 Royalty Pharma, 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, net cash received during the period from Tranche D Loan borrowings of $150.0 million under the Amended and Restated Loan Agreement, stock option exercises of $6.7 million, and the purchases of shares under our employee stock purchase plan of $1.3 million, partially offset by payments of debt issuance costs of $3.1 million and offering costs of $0.1 million.

Net cash provided by financing activities of $286.3 million during the year ended December 31, 2019 primarily reflects net cash received during the period of $123.1 million in the aggregate received through the RPI Purchase Agreement with RPI and the Loan Agreement with BioPharma Credit Investments V (Master) LP and BioPharma Credit PLC, net cash received from the sale of common stock of $123.0 million and net cash received from the sale of convertible preferred stock of $37.4 million, as well as cash received from stock option exercises.

Net cash provided by financing activities of $84.2 million during the year ended December 31, 2018 primarily reflects net cash received from the sale of common stock in our public offerings in the fourth quarter of 2018 of $81.7 million, cash received from stock option exercises of $1.9 million, and the purchases of shares under our employee stock purchase plan of $0.7 million, partially offset by the payments under our capital lease obligation of $0.1 million.

Contractual Obligations and Contingent Liabilities

The following summarizes our significant contractual obligations as of December 31, 2020:

Contractual Obligations	Total	Less than 1 Year	1 to 3 Years	3 to 5 Years	More than 5 Years
			(In thousands)		
Lease obligations	$ 25,695	$ 6,436	$ 12,293	$ 6,442	$ 524
Long-term debt obligations	220,000	—	70,000	150,000	—
Total obligations	$245,695	$ 6,436	$ 82,293	$ 156,442	$ 524

In addition to commitments under leasing arrangements described in the table above and in Note 10, *Leases* to the financial statements in Item 15 of this Annual Report on Form 10-K, we remain committed to fund $1.0 million of development costs payable to Roche Molecular upon certain development and regulatory milestones, under our amended companion diagnostic agreement. The long-term debt obligations described in the table above were incurred pursuant to our debt financing arrangements with the Lenders and are more fully described in Note 13, *Long-Term Debt* to the financial statements in Item 15 of this Annual Report on Form 10-K.

The contractual obligations table does not include potential future milestones or royalties that we may be required to make under license and collaboration agreements due to the uncertainty of events requiring payment under these agreements.

We enter into contracts in the normal course of business with clinical research organizations for clinical and preclinical research studies, external manufacturers for product for use in our clinical trials, and other research supplies and other services as part of our operations. These contracts generally provide for termination on notice, and therefore are cancelable contracts and not included in contractual commitments.

Critical Accounting Policies and Use of Estimates

Our management's discussion and analysis of financial condition and results of operations is based upon our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States of America. The preparation of these consolidated financial statements requires us to make estimates, judgments and assumptions that affect the reported amounts of assets and liabilities and disclosures of contingent assets and liabilities as of the date of the balance sheets and the reported amounts of collaboration

revenue, inventory and expenses during the reporting periods. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances at the time such estimates are made. Actual results and outcomes may differ materially from our estimates, judgments and assumptions. We periodically review our estimates in light of changes in circumstances, facts and experience. The effects of material revisions in estimates are reflected in the consolidated financial statements prospectively from the date of the change in estimate.

We define our critical accounting policies as those accounting principles generally accepted in the United States of America that require us to make subjective estimates and judgments about matters that are uncertain and are likely to have a material impact on our financial condition and results of operations as well as the specific manner in which we apply those principles. Management has determined that our most critical accounting policies are those relating to revenue recognition, inventory, stock-based compensation and research and development expenses, including our accounting for clinical trial expense 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.

Revenue Recognition – Product Revenue

We recognize revenue when our customer obtains control of promised goods or services, in an amount that reflects the consideration which we expect to receive in exchange for those goods or services. To determine revenue recognition, we perform 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) we satisfy a performance obligation. We only apply the five-step model to contracts when it is probable that we will collect the consideration we are entitled to in exchange for the goods or services we transfer to the customer.

We sell 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 our customers.

Revenue is recognized by us when the customer obtains control of the product, which occurs at a point in time, typically when the product is received by our customers. We provide a right of return to our 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 we are able to monitor inventory levels in the distribution channel, thereby limiting the risk of return.

Reserves for Variable Consideration

Revenues from product sales are recorded 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 us and our customers, health care providers, payors and other indirect customers relating to our 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 our 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 our best estimates of the amount of consideration to which we are entitled based on the terms of the contract. 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 our estimates. If actual results in the future vary from our estimates, we will adjust these estimates, which would affect net product revenue and earnings in the period such variances become known.

Trade Discounts and Allowances: We generally provide customers with discounts that include incentive fees that are explicitly stated in our contracts and are recorded as a reduction of revenue in the period the related product revenue is recognized. In addition, we receive sales order management, data and distribution services from certain customers. To the extent the services received are distinct from our 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, we generally offer customers a limited right of return based on the product's expiration date for product that has been purchased from us, which lapses upon shipment to a patient. We estimate the amount of our product sales that may be returned by our customers and record this estimate as a reduction of revenue in the period the related product revenue is recognized. We currently estimate product return liabilities using available industry data and our own historical sales information, including our visibility into the inventory remaining in the distribution channel.

Provider Chargebacks and Discounts: Chargebacks for fees and discounts to 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 us. Customers charge us 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 we generally issue credits for such amounts within a few weeks of the customer's notification to us of the resale. Reserves for chargebacks consist of credits that we expect to issue for units that remain in the distribution channel inventories at each reporting period end that we expect will be sold to qualified healthcare providers, and chargebacks that customers have claimed but for which we have not yet issued a credit.

Government Rebates: We are subject to discount obligations under state Medicaid programs and Medicare. We estimate our 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 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 consolidated balance sheet. For Medicare, we also estimate the number of patients in the prescription drug coverage gap for whom we will owe an additional liability under the Medicare Part D program. Our 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: We may contract with various private payor organizations, primarily insurance companies and pharmacy benefit managers, for the payment of rebates with respect to utilization of our products. We estimate these rebates and record 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: We also offer 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 we expect to receive associated with product that has been recognized as revenue, but remains in in the distribution channel inventories at period end.

Revenue Recognition – Collaboration Revenue

Effective January 1, 2018, we adopted ASC, Topic 606, *Revenue from Contracts with Customers*, or ASC 606, using the modified retrospective transition method. Under this method, results for reporting periods beginning after January 1, 2018 are presented pursuant to ASC 606, while prior period amounts are not adjusted and continue to be reported in accordance with ASC 605. This standard applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, collaboration arrangements and financial

instruments. Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the entity 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 entity satisfies a performance obligation. We only apply the five-step model to contracts when it is probable that the entity will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, we assess the goods or services promised within each contract and determines those that are performance obligations, and assesses whether each promised good or service is distinct. We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

We have entered into collaboration and license agreements, which are within the scope of ASC 606, to discover, develop, manufacture and commercialize product candidates. The terms of these agreements typically contain multiple promises or obligations, which may include: (i) licenses, or options to obtain licenses, to compounds directed to specific targets (referred to as "exclusive licenses") and (ii) research and development activities to be performed on behalf of the collaboration partner related to the licensed targets. Payments to us under these agreements may include non-refundable license fees, customer option exercise fees, payments for research activities, reimbursement of certain costs, payments based upon the achievement of certain milestones and royalties on any resulting net product sales.

We first evaluate license and/or collaboration arrangements to determine whether the arrangement (or part of the arrangement) represents a collaborative arrangement pursuant to ASC Topic 808, *Collaborative Arrangements,* based on the risks and rewards and activities of the parties pursuant to the contractual arrangement. We account for collaborative arrangements (or elements within the contract that are deemed part of a collaborative arrangement), which represent a collaborative relationship and not a customer relationship, outside the scope of ASC 606. Our collaborations primarily represent revenue arrangements. For the arrangements or arrangement components that are subject to revenue accounting guidance, in determining the appropriate amount of revenue to be recognized as it fulfills its obligations under each of its agreements, we perform the following steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations; and (v) recognition of revenue when (or as) we satisfy each performance obligation. As part of the accounting for these arrangements, we must use significant judgment to determine: a) the number of performance obligations based on the determination under step (ii) above and whether those performance obligations are distinct from other performance obligations in the contract; b) the transaction price under step (iii) above; and c) the stand-alone selling price for each performance obligation identified in the contract for the allocation of transaction price in step (iv) above. We use judgment to determine whether milestones or other variable consideration, except for sales-based royalties, should be included in the transaction price as described further below. The transaction price is allocated to each performance obligation on a relative stand-alone selling price basis, for which we recognize revenue as or when the performance obligations under the contract are satisfied. In determining the stand-alone selling price of a license to our proprietary technology or a material right provided by a customer option, we consider market conditions as well as entity-specific factors, including those factors contemplated in negotiating the agreements as well as internally developed estimates that include assumptions related to the market opportunity, estimated development costs, probability of success and the time needed to commercialize a product candidate pursuant to the license. In validating its estimated stand-alone selling price, we evaluate whether changes in the key assumptions used to determine its estimated stand-alone selling price will have a significant effect on the allocation of arrangement consideration between performance obligations.

Amounts received prior to revenue recognition are recorded as deferred revenue. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified as current portion of deferred revenue in the accompanying consolidated balance sheets. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, net of current portion. Amounts recognized as revenue, but not yet received or invoiced are generally recognized as contract assets.

Exclusive Licenses – If the license to our intellectual property is determined to be distinct from the other promises or performance obligations identified in the arrangement, which generally include research and development services, we recognize revenue from non-refundable, upfront fees allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. In assessing whether a license is distinct from the other promises, we consider relevant facts and circumstances of each arrangement, including the research and development capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. In addition, we consider whether the collaboration partner can benefit from the license for its intended purpose without the receipt of the remaining promises, whether the value of the license is dependent on the unsatisfied promises, whether there are other vendors that could provide the remaining promises, and whether it is separately identifiable from the remaining promises. For licenses that are combined with other promises, we utilize judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. We evaluate the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition. The measure of progress, and thereby periods over which revenue should be recognized, are subject to estimates by management and may change over the course of the research and development and licensing agreement.

Research and Development Services – The promises under our collaboration and license agreements generally include research and development services to be performed by us on behalf of the collaboration partner. For performance obligations that include research and development services, we generally recognize revenue allocated to such performance obligations based on an appropriate measure of progress. We utilize judgment to determine the appropriate method of measuring progress for purposes of recognizing revenue, which is generally an input measure such as costs incurred. We evaluate the measure of progress each reporting period as described under *Exclusive Licenses* above. Reimbursements from the partner that are the result of a collaborative relationship with the partner, instead of a customer relationship, such as co-development activities, are recorded as a reduction to research and development expense.

Customer Options – Our arrangements may provide a collaborator with the right to select a target for licensing either at the inception of the arrangement or within an initial pre-defined selection period, which may, in certain cases, include the right of the collaborator to extend the selection period. Under these agreements, fees may be due to us (i) at the inception of the arrangement as an upfront fee or payment, (ii) upon the exercise of an option to acquire a license or (iii) upon extending the selection period as an extension fee or payment. If an arrangement is determined to contain customer options that allow the customer to acquire additional goods or services, the goods and services underlying the customer options are not considered to be performance obligations at the outset of the arrangement, as they are contingent upon option exercise. We evaluate the customer options for material rights, or options to acquire additional goods or services for free or at a discount. If the customer options are determined to represent a material right, the material right is recognized as a separate performance obligation at the inception of the arrangement. We allocate the transaction price to material rights based on the relative stand-alone selling price, which is determined based on the identified discount and the probability that the customer will exercise the option. Amounts allocated to a material right are not recognized as revenue until, at the earliest, the option is exercised or expires.

Milestone Payments – At the inception of each arrangement that includes development milestone payments, we evaluate whether the milestones are considered probable of being achieved and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within our control or the licensee's control, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. We evaluate factors such as the scientific, clinical, regulatory, commercial, and other risks that must be overcome to achieve the particular milestone in making this assessment. There is considerable judgment involved in determining whether it is probable that a significant revenue reversal would not occur. At the end of each subsequent reporting period, we reevaluate the probability of achievement of all milestones subject to constraint and, if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenues and earnings in the period of adjustment. If a milestone or other variable consideration relates specifically to our efforts to satisfy a single performance obligation or to a specific outcome from satisfying the performance obligation, we generally allocate the milestone amount entirely to that performance obligation once it is probable that a significant revenue reversal would not occur.

Royalties – For arrangements that include sales-based royalties, including milestone payments based on a level of sales, and the license is deemed to be the predominant item to which the royalties relate, we recognize revenue at the later of (i) when the related sales occur or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, we have not recognized any royalty revenue resulting from any of its licensing arrangements.

For a complete discussion of accounting for collaboration revenues, see Note 11, *Collaborations*, in the accompanying Notes to Consolidated Financial Statements included in Item 15. of Part IV of this Annual Report on Form 10-K.

Accrued Research and Development Expenses

As part of the process of preparing our financial statements, we are required to estimate our accrued expenses as of each balance sheet date. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. Examples of estimated accrued research and development expenses include fees paid to:

- contract research organizations in connection with clinical trials;
- investigative sites in connection with clinical trials;
- vendors in connection with non-clinical development activities; and
- vendors related to product manufacturing, development and distribution of clinical supplies.

We generally accrue expenses related to research and development activities based on the services received and efforts expended pursuant to contracts with multiple contract research organizations that conduct and manage clinical trials on our behalf as well as other vendors that provide research and development services. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the expense. Payments under some of these contracts depend on factors such as the successful enrollment of subjects and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we would adjust the accrual or prepaid accordingly.

Although we do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed we may report amounts that are too high or too low in any particular period. To date, there have been no material differences from our estimates to the amount actually incurred.

Inventory

We outsource the manufacturing of TAZVERIK and use contract manufacturers to produce the raw and intermediate materials used in the production of TAZVERIK as well as the finished product. We currently have one supplier qualified for each step in the manufacturing process and are 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. We state inventory at the lower of cost or net realizable value with the cost based on the first-in, first-out method. If we identify excess, obsolete or unsalable items, we write down our 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 us, 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 product revenue.

Prior to receiving our first approval from the U.S. Food and Drug Administration, or FDA, on January 23, 2020 to sell TAZVERIK for the approved FL indications, we 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 us of regulatory approval of drug candidates.

Liability Related to Sale of Future Royalties

We treat the liability related to sale of future royalties as a debt financing, as we have significant continuing involvement in the generation of the cash flows, to be amortized to interest expense using the effective interest rate method over the life of the related royalty stream.

The liability related to sale of future royalties and the related interest expense are based on our current estimates of future royalties expected to be paid over the life of the arrangement. We will periodically assess the expected royalty payments using a combination of internal projections and forecasts from external sources. To the extent our future estimates of royalty payments are greater or less than previous estimates or the estimated timing of such payments is materially different than its previous estimates, we will prospectively recognize related non-cash interest expense.

Going Concern

We continually evaluate our ability to continue as a going concern within one year of the date of issuance of financial statements in both our Quarterly Reports on Form 10-Q and Annual Report on Form 10-K. Our evaluation entails analyzing forward looking budgets and forecasts for expectations of our cash needs, and comparing those needs to our current cash, cash equivalent and marketable security balances.

Based on our current operating plan, we expect that our existing cash, cash equivalents and marketable securities will be sufficient to fund our planned operating expenses and capital expenditure requirements into 2023, without giving effect to any potential milestone payments we may receive under our collaboration agreements.

Recently Adopted Accounting Pronouncements

For detailed information regarding recently issued accounting pronouncements and the expected impact on our consolidated financial statements, see Note 2, *Summary of Significant Accounting Policies—Recently Adopted Accounting Pronouncements*, in the accompanying Notes to Consolidated Financial Statements included in Item 15. of Part IV of this Annual Report on Form 10-K.

Item 7A. 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 December 31, 2020, we had cash equivalents and available for sale securities of $373.6 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 December 31, 2020 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 8. Financial Statements and Supplementary Data

The information required by this item may be found on pages F-2 through F-32 as listed below, including the quarterly information required by this item.

INDEX

	Page
Report of Independent Registered Public Accounting Firm	F-2
Consolidated Balance Sheets	F-4
Consolidated Statements of Operations and Comprehensive Loss	F-5
Consolidated Statements of Cash Flows	F-6
Consolidated Statements of Stockholders' Equity	F-7
Notes to Consolidated Financial Statements	F-8

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None.

Item 9A. Controls and Procedures

Disclosure Controls and Procedures

Our management, with the participation of our principal executive officer and principal financial officer, evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act) as of December 31, 2020. In designing and evaluating our disclosure controls and procedures, management recognized that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives, and our management necessarily applied its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on this evaluation, our principal executive officer and principal financial officer concluded that as of December 31, 2020, our disclosure controls and procedures were (1) designed to ensure that material information relating to us is made known to our management including our principal executive officer and principal financial officer by others, particularly during the period in which this report was prepared and (2) effective, in that they provide reasonable assurance that information required to be disclosed by us in the reports we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms.

Management's Annual Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rules 13a-15(f) and 15d-15(f) promulgated under the Exchange Act as a process designed by, or under the supervision of, our principal executive and principal financial officers and effected by our board of directors, management and other personnel, 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 and includes those policies and procedures that:

- pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of the assets of our company;
- provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of our company are being made only in accordance with authorizations of our management and directors; and
- provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate. Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2020. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission, or COSO, in *Internal Control—Integrated Framework (2013)*. Based on its assessment, management believes that, as of December 31, 2020, our internal control over financial reporting is effective based on those criteria.

Ernst & Young LLP, our independent registered public accounting firm has audited the consolidated financial statements included in this Annual Report on Form 10-K and, as part of the audit, has issued a report on the effectiveness of our internal control over financial reporting as of December 31, 2020, which report is included herein.

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Epizyme, Inc.

Opinion on Internal Control over Financial Reporting

We have audited Epizyme, Inc.'s internal control over financial reporting as of December 31, 2020, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). In our opinion, Epizyme, Inc. (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2020, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of the Company as of December 31, 2020 and 2019, the related consolidated statements of operations and comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2020, and the related notes and our report dated February 23, 2021 expressed an unqualified opinion thereon.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Annual Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects.

Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control Over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ Ernst & Young LLP

Boston, Massachusetts
February 23, 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 December 31, 2020 that materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

Information regarding our directors, including the audit committee and audit committee financial experts, and executive officers and compliance with Section 16(a) of the Exchange Act will be included in our 2021 Proxy Statement and is incorporated herein by reference.

We have adopted a Code of Business Conduct and Ethics for all of our directors, officers and employees as required by NASDAQ governance rules and as defined by applicable SEC rules. Stockholders may locate a copy of our Code of Business Conduct and Ethics on our website at www.epizyme.com or request a copy without charge from:

Epizyme, Inc.
Attention: Investor Relations
400 Technology Square, 4th Floor
Cambridge, MA 02139

We will post to our website any amendments to the Code of Business Conduct and Ethics, and any waivers that are required to be disclosed by the rules of either the SEC or NASDAQ.

Item 11. Executive Compensation

The information required by this item regarding executive compensation will be included in our 2021 Proxy Statement and is incorporated herein by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required by this item regarding security ownership of certain beneficial owners and management and securities authorized for issuance under equity compensation plans will be included in our 2021 Proxy Statement and is incorporated herein by reference.

Item 13. Certain Relationships and Related Transactions, and Director Independence

The information required by this item regarding certain relationships and related transactions and director independence will be included in our 2021 Proxy Statement and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services

The information required by this item regarding principal accounting fees and services will be included in our 2021 Proxy Statement and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules

(a) The following documents are included in this Annual Report on Form 10-K:

1. The following Report and Consolidated Financial Statements of the Company are included in this Annual Report:

   Report of Independent Registered Public Accounting Firm

   Consolidated Balance Sheets

   Consolidated Statements of Operations and Comprehensive Loss

   Consolidated Statements of Cash Flows

   Consolidated Statements of Stockholders' Equity

   Notes to Consolidated Financial Statements

2. All financial schedules have been omitted because the required information is either presented in the consolidated financial statements or the notes thereto or is not applicable or required.

3. Exhibits:

Exhibit Number	Description of Exhibit
3.1	Restated Certificate of Incorporation of the Registrant, as amended (24)
3.2	Amended and Restated Bylaws of the Registrant (2)
4.1	Form of Series A Preferred Stock Certificate (19)
4.2	Amended and Restated Investor Rights Agreement dated as of April 2, 2012 (1)
4.3	Certificate of Designation of Series A Convertible Preferred Stock of the Company (19)
4.4	Description of Securities of the Registrant (22)
10.1+	2008 Stock Incentive Plan (1)
10.2+	Form of Incentive Stock Option Agreement under 2008 Stock Incentive Plan (1)
10.3+	Form of Nonstatutory Stock Option Agreement under 2008 Stock Incentive Plan (1)
10.4+	Form of Restricted Stock Agreement under 2008 Stock Incentive Plan (1)
10.5+	2013 Stock Incentive Plan, as amended on March 24, 2020 (23)
10.6+	Form of Incentive Stock Option Agreement under 2013 Stock Incentive Plan (2)
10.7+	Form of Restricted Stock Agreement under 2013 Stock Incentive Plan (2)
10.8+	Form of Restricted Stock Unit Agreement under 2013 Stock Incentive Plan (18)
10.9+	2013 Employee Stock Purchase Plan (2)
10.10+	Executive Severance and Change in Control Plan (18)
10.11+	Employment Offer Letter between the Registrant and Robert Bazemore, dated August 5, 2015 (11)
10.12+	Employment Offer Letter between the Company and Matthew E. Ros, dated April 15, 2016 (13)
10.13+	Employment Offer Letter between the Registrant and Paolo Tombesi, dated July 1, 2019 (20)
10.14+	Employment Offer Letter between the Company and Shefali Agarwal, dated June 18, 2018 (17)
10.15+	Employment Offer Letter between the Company and Jeffery Kutok, dated February 21, 2020 (23)
10.16+	Employment Offer Letter between the Company and Victoria Vakiener, dated October 23, 2018 (25)
10.17	Form of Director and Officer Indemnification Agreement (2)
10.18†	Companion Diagnostics Agreement dated as of December 18, 2012 between the Registrant and Eisai Co., Ltd. on the one side and Roche Molecular Systems, Inc. on the other side (3)
10.19†	First Amendment to the Companion Diagnostics Agreement dated October 23, 2013 between the Registrant and Eisai Co. Ltd. on the one side and Roche Molecular Systems, Inc. on the other side (5)
10.20†	Second Amendment to the Companion Diagnostics Agreement dated November 16, 2015 between the Registrant and Eisai Co. Ltd. on the one side and Roche Molecular Systems, Inc. on the other side (12)
10.21†	Third Amendment to the Companion Diagnostics Agreement dated March 7, 2018 between the Registrant and Eisai Co. Ltd. on the one side and Roche Molecular Systems, Inc. on the other side (16)
10.22	Letter Agreement by and between the Registrant and Eisai Co., Ltd. dated as of December 21, 2012 relating to Companion Diagnostics Agreement (1)

Exhibit Number	Description of Exhibit
10.23	Amended and Restated Letter Agreement dated as of March 12, 2015 by and between the Registrant and Eisai Co., Ltd. relating to the Companion Diagnostics Agreement (10)
10.24□	Amended and Restated Collaboration and License Agreement dated as of March 12, 2015, by and between the Registrant and Eisai Co. Ltd. (25)
10.25	Lease Agreement dated as of June 15, 2012 between the Registrant and ARE-TECH Square, LLC (1)
10.26	Non-Employee Director Compensation Program, effective January 1, 2021 (25)
10.27	First Amendment to Lease Agreement dated as of September 30, 2013 between the Registrant and ARE-TECH Square, LLC (4)
10.28	Second Amendment to Lease Agreement dated as of May 18, 2016 between the Registrant and ARE-TECH Square, LLC (14)
10.29†	Collaboration and License Agreement dated as of January 8, 2011 by and between the Registrant and Glaxo Group Limited (3)
10.30†	Amendment to Collaboration and License Agreement dated as of July 23, 2013 by and between the Registrant and Glaxo Group Limited (6)
10.31†	Amendment to Collaboration and License Agreement dated as of February 24, 2014 by and between the Registrant and Glaxo Group Limited (7)
10.32†	Amendment to Collaboration and License Agreement dated as of March 18, 2014 by and between the Registrant and Glaxo Group Limited (7)
10.33†	Amendment to Collaboration and License Agreement dated as of April 17, 2014 by and between the Registrant and Glaxo Group Limited (8)
10.34†	Amendment to Collaboration and License Agreement dated as of October 1, 2014 by and between the Registrant and Glaxo Group Limited (9)
10.35	Third Amendment to Lease Agreement, entered into May 25, 2017 and effective May 18, 2017, by and between the Company and ARE-TECH Square, LLC (15)
10.36	Fourth Amendment to Lease Agreement, entered into May 25, 2017 and effective May 18, 2017, by and between the Company and ARE-TECH Square, LLC (15)
10.37	Fourth Amendment to the Companion Diagnostics Agreement dated July 26, 2019 between the Registrant and Eisai Co. Ltd. on the one side and Roche Molecular Systems, Inc. and Roche Sequencing Solutions, Inc. on the other side. (21)
10.38	Lease Agreement dated as of August 16, 2019 by and between the Registrant and BMR-Hampshire LLC. (21)
10.39	Amended and Restated Loan Agreement dated as of November 3, 2020 by and among the Registrant and BioPharma Credit Investments V (Master) LP, BPCR Limited Partnership and BioPharma Credit PLC (25)
10.40	Guaranty and Security Agreement dated as of November 18, 2019 by and between the Registrant and BioPharma Credit PLC (22)
10.41□	Purchase Agreement dated as of November 4, 2019 by and between the Registrant and RPI Finance Trust (22)
10.42	Warrant Agreement dated as of November 4, 2019 by and between the Registrant and RPI Finance Trust (22)
21.1	Subsidiaries of the Registrant (1)

Exhibit Number	Description of Exhibit
23.1	Consent of Ernst & Young LLP (25)
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. (25)
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. (25)
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 Paolo Tombesi, Chief Financial Officer of the Company. (25)
101	The following financial statements formatted in XBRL: (i) Consolidated Balance Sheets, (ii) Consolidated Statements of Net Income, (iii) Consolidated Statements of Comprehensive Income, (iv) Consolidated Statements of Changes in Stockholders' Equity, (v) Consolidated Statements of Cash Flows, and (vi) the Notes to the Consolidated Financial Statements.
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 Taxonomy Extension Schema Document
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	Inline XBRL Taxonomy Extension Labels Linkbase Document
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

+ Management compensatory agreement.

† Confidential treatment has been granted as to portions of the exhibit. Confidential materials omitted and filed separately with the Securities and Exchange Commission.

☐ Portions of this exhibit have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K. Certain portions of this exhibit have been omitted because they are not material and would likely cause competitive harm to the Registrant if disclosed.

(1) Incorporated by reference to the Registration Statement on Form S-1 (File No. 333-187982) filed with the Securities and Exchange Commission on April 18, 2013.

(2) Incorporated by reference to the Registration Statement on Form S-1/A (File No. 333-187892) filed with the Securities and Exchange Commission on April 26, 2013.

(3) Incorporated by reference to the Registration Statement on Form S-1/A (File No. 333-187982) filed with the Securities and Exchange Commission on May 13, 2013.

(4) Incorporated by reference to the Quarterly Report on Form 10-Q (File No. 001-35945) filed with the Securities and Exchange Commission on October 23, 2013.

(5) Incorporated by reference to the Registration Statement on Form S-1 (File No. 333-193569) filed with the Securities and Exchange Commission on January 27, 2014.

(6) Incorporated by reference to the Registration Statement on Form S-1/A (File No. 333-193569) filed with the Securities and Exchange Commission on January 28, 2014.

(7) Incorporated by reference to the Registrant's Current Report on Form 8-K (File No. 001-35945) filed with the Securities and Exchange Commission on April 22, 2014.

(8) Incorporated by reference to the Quarterly Report on Form 10-Q (File No. 001-35945) filed with the Securities and Exchange Commission on May 14, 2014.

(9) Incorporated by reference to the Registrant's Annual Report on Form 10-K (File No. 001-35945) filed with the Securities and Exchange Commission on March 12, 2015.

(10) Incorporated by reference to the Registrant's Current Report on Form 8-K (File No. 001-35945) filed with the Securities and Exchange Commission on March 16, 2015.

(11) Incorporated by reference to the Registrant's Current Report on Form 8-K (File No. 001-35945) filed with the Securities and Exchange Commission on August 6, 2015.

(12) Incorporated by reference to the Registrant's Annual Report on Form 10-K (File No. 001-35945) filed with the Securities and Exchange Commission on March 9, 2016.

(13) Incorporated by reference to the Registrant's Current Report on Form 8-K (File No. 001-35945) filed with the Securities and Exchange Commission on May 6, 2016.

(14) Incorporated by reference to the Quarterly Report on Form 10-Q (File No. 001-35945) filed with the Securities and Exchange Commission on August 8, 2016.

(15) Incorporated by reference to the Current Report on Form 8-K (File No. 001-35945) filed with the Securities and Exchange Commission on May 30, 2017.

(16) Incorporated by reference to the Quarterly Report on Form 10-Q (File No. 001-35945) filed with the Securities and Exchange Commission on May 8, 2018.

(17) Incorporated by reference to the Quarterly Report on Form 10-Q (File No. 001-35945) filed with the Securities and Exchange Commission on November 2, 2018

(18) Incorporated by reference to the Annual Report on Form 10-K (File No. 001-35945) filed with the Securities and Exchange Commission on February 26, 2019.

(19) Incorporated by reference to the Current Report on Form 8-K (File No. 001-35945) filed with the Securities and Exchange Commission on March 7, 2019.

(20) Incorporated by reference to the Quarterly Report on Form 10-Q (File No. 001-35945) filed with the Securities and Exchange Commission on August 9, 2019.

(21) Incorporated by reference to the Quarterly Report on Form 10-Q (File No. 001-35945) filed with the Securities and Exchange Commission on October 31, 2019.

(22) Incorporated by reference to the Annual Report on Form 10-K (File No. 001-35945) filed with the Securities and Exchange Commission on February 27, 2020.

(23) Incorporated by reference to the Quarterly Report on Form 10-Q (File No. 001-35945) filed with the Securities and Exchange Commission on May 4, 2020.

(24) Incorporated by reference to the Quarterly Report on Form 10-Q (File No. 001-35945) filed with the Securities and Exchange Commission on August 4, 2020.

(25) Filed with this Annual Report on Form 10-K.

Item 16. Form 10-K Summary

Not applicable.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) 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.

Epizyme, Inc.

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

Dated: February 23, 2021

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated:

Name	Title	Date
/s/ Robert B. Bazemore Robert B. Bazemore	President, Chief Executive Officer, Director *(Principal Executive Officer)*	February 23, 2021
/s/ Paolo Tombesi Paolo Tombesi	Chief Financial Officer *(Principal Financial Officer)*	February 23, 2021
/s/ Joseph Beaulieu Joseph Beaulieu	Corporate Controller and Treasurer *(Principal Accounting Officer)*	February 23, 2021
/s/ Andrew R. Allen Andrew R. Allen, M.D., Ph.D.	Director	February 23, 2021
/s/ Kenneth Bate Kenneth Bate	Director	February 23, 2021
/s/ Grant Bogle Grant Bogle	Director	February 23, 2021
/s/ Kevin T. Conroy Kevin T. Conroy	Director	February 23, 2021
/s/ Michael Giordano Michael Giordano, M.D.	Director	February 23, 2021
/s/ Carl Goldfischer Carl Goldfischer, M.D.	Director	February 23, 2021
/s/ Pablo Legorreta Pablo Legorreta	Director	February 23, 2021
/s/ David M. Mott David M. Mott	Director	February 23, 2021
/s/ Victoria Richon Victoria Richon	Director	February 23, 2021

EPIZYME, INC.
INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm	F-2
Consolidated Balance Sheets	F-4
Consolidated Statements of Operations and Comprehensive Loss	F-5
Consolidated Statements of Cash Flows	F-6
Consolidated Statements of Stockholders' Equity	F-7
Notes to Consolidated Financial Statements	F-8

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and the Board of Directors of Epizyme, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Epizyme, Inc. (the Company) as of December 31, 2020 and 2019, the related consolidated statements of operations and comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2020, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2020 and 2019, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2020, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2020, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework), and our report dated February 23, 2021, expressed an unqualified opinion thereon.

Adoption of New Accounting Standards

As discussed in Note 2 to the consolidated financial statements, the Company changed its method of accounting for leases in 2019 due to the adoption of Accounting Standards Update (ASU) No. 2016-02, *Leases* (ASC 842), and the related amendments.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matters

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of the critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Accrued and Prepaid Clinical Trial Expenses

Description of the Matter

The Company's total accrued expenses were $28.6 million at December 31, 2020, which included the estimated obligation for clinical trial expenses incurred as of December 31, 2020 but not paid as of that date. In addition, the Company's total prepaid expenses and other current assets were $17.9 million, which included amounts that were paid in advance of services incurred pursuant to clinical trials. As discussed in Note 2 to the consolidated financial statements, when vendors billing terms do not coincide with the Company's period-end, the Company is required to make estimates of its obligations to those vendors, including clinical trial and pharmaceutical development costs, contractual services costs and costs for supply of its product candidates incurred in a given accounting period and record accruals at the end of the period. The Company bases its estimates on its knowledge of the research and development programs, services performed for the period, past history for related activities and the expected duration of the vendor service contract, where applicable. Payments for these activities are based on the terms of the individual arrangements and may result in payment terms that differ from the pattern of costs incurred. There may be instances in which payments made to vendors will exceed the level of services provided and result in a prepayment of the clinical expense.

Auditing the Company's accrued and prepaid clinical trial expenses is especially challenging due to the large volume of information received from multiple vendors that perform service on the Company's behalf. While the Company's estimates of accrued and prepaid clinical trial expenses are primarily based on information received related to each study from its vendors, the Company may need to make an estimate for additional costs incurred. Additionally, due to the long duration of clinical trials and the timing of invoicing received from vendors, the actual amounts incurred are not typically known at the time the financial statements are issued.

How We Addressed the Matter in Our Audit

We evaluated and tested the design and operating effectiveness of internal controls over the Company's process used in determining the valuation and completeness of accrued and prepaid clinical trial expenses.

To evaluate the accrued and prepaid clinical trial expenses, our audit procedures included, among others, testing the accuracy and completeness of the underlying data used in determining the accrued and prepaid clinical trial expenses and evaluating the assumptions/estimates used by management to adjust the actual information received. To assess the nature and extent of the services incurred, we corroborated the progress of clinical trials with the Company's research and development personnel that oversee the clinical trials and obtained information directly from vendors of their costs incurred to date. To evaluate the completeness and valuation of the accrual, we also tested subsequent invoices received and inspected the Company's contracts with vendors and any pending change orders to assess the impact to the accrual.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2009.
Boston, Massachusetts
February 23, 2021

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

	December 31, 2020	December 31, 2019
ASSETS		
Current assets:		
Cash and cash equivalents	$ 168,215	$ 139,482
Marketable securities	205,391	241,605
Accounts receivable, net	3,105	2,567
Inventory	10,461	—
Prepaid expenses and other current assets	17,921	15,523
Total current assets	405,093	399,177
Property and equipment, net	2,152	2,219
Operating lease assets	17,305	21,206
Intangible assets, net	47,002	—
Restricted cash and other assets	2,021	1,987
Total assets	$ 473,573	$ 424,589
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 10,163	$ 8,782
Accrued expenses	28,572	22,565
Current portion of operating lease obligation	4,665	3,039
Total current liabilities	43,400	34,386
Operating lease obligation, net of current portion	15,409	19,120
Deferred revenue, net of current portion	—	3,806
Related party long-term debt, net of debt discount	215,670	23,309
Other long-term liabilities	21	38
Related party liability related to sale of future royalties	14,176	12,793
Commitments and contingencies		
Stockholders' equity:		
Preferred stock, $0.0001 par value; 5,000 shares authorized; 338 shares and 350 shares issued and outstanding, respectively (equivalent to 3,378 shares and 3,500 shares of common stock, respectively, upon conversion at a 10:1 ratio)	36,127	37,432
Common stock, $0.0001 par value; 150,000 shares and 125,000 shares, respectively, authorized; 101,627 shares and 97,783 shares issued and outstanding, respectively	10	10
Additional paid-in capital	1,137,470	1,050,695
Accumulated other comprehensive loss	3	19
Accumulated deficit	(988,713)	(757,019)
Total stockholders' equity	184,897	331,137
Total liabilities and stockholders' equity	$ 473,573	$ 424,589

See notes to consolidated financial statements.

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

	Year Ended December 31,		
	2020	2019	2018
Revenue:			
Product revenue, net	$ 11,469	$ —	$ —
Collaboration revenue	4,293	23,800	21,700
Total revenue	15,762	23,800	21,700
Operating expenses:			
Cost of product revenue	5,067	—	—
Research and development	110,933	132,639	105,833
Selling, general and administrative	125,178	68,303	43,972
Total operating expenses	241,178	200,942	149,805
Operating loss	(225,416)	(177,142)	(128,105)
Other (expense) income, net:			
Interest (expense) income, net	(4,682)	7,110	4,557
Other expense, net	(99)	(13)	(25)
Related party non-cash interest expense related to sale of future royalties	(1,383)	(192)	—
Other (expense) income, net	(6,164)	6,905	4,532
Loss before income taxes	(231,580)	(170,237)	(123,573)
Income tax provision	(114)	(58)	(57)
Net loss	$ (231,694)	$ (170,295)	$ (123,630)
Other comprehensive (loss) income:			
Unrealized gain (loss) on available for sale securities	(16)	73	(5)
Comprehensive loss	$ (231,710)	$ (170,222)	$ (123,635)
Reconciliation of net loss to net loss attributable to common stockholders:			
Net loss	$ (231,694)	$ (170,295)	$ (123,630)
Accretion of convertible preferred stock	—	(2,940)	—
Net loss attributable to common stockholders	$ (231,694)	$ (173,235)	$ (123,630)
Net loss per share attributable to common stockholders:			
Basic	$ (2.29)	$ (1.93)	$ (1.72)
Diluted	$ (2.29)	$ (1.93)	$ (1.72)
Weighted-average common shares outstanding used in net loss per share attributable to common stockholders:			
Basic	100,960	89,891	71,864
Diluted	100,960	89,891	71,864

See notes to consolidated financial statements.

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

	Year Ended December 31,		
	2020	**2019**	**2018**
CASH FLOWS FROM OPERATING ACTIVITIES:			
Net loss	$ (231,694)	$ (170,295)	$ (123,630)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	3,984	840	1,052
Stock-based compensation	27,609	18,016	12,004
Amortization of discount on investments	(93)	(3,175)	(1,556)
Amortization of debt discount	406	37	—
Loss on disposal of property and equipment	19	—	—
Non-cash interest expense associated with the sale of future royalties	1,383	192	—
Deferred income taxes	92	92	184
Changes in operating assets and liabilities:			
Accounts receivable	(538)	17,500	(19,686)
Inventory	(10,461)	—	—
Prepaid expenses and other current assets	(2,398)	(3,359)	(3,181)
Accounts payable	1,480	3,389	(2,404)
Accrued expenses	6,006	2,897	2,066
Deferred revenue	(3,806)	(13,300)	13,300
Operating lease assets	3,901	(9,921)	—
Operating lease liabilities	(2,085)	10,043	—
Other assets and liabilities	(141)	(124)	251
Net cash used in operating activities	**(206,336)**	**(147,168)**	**(121,600)**
CASH FLOWS FROM INVESTING ACTIVITIES:			
Purchases of available-for-sale securities	(276,404)	(504,981)	(298,670)
Maturities of available-for-sale securities	312,694	420,255	196,363
Purchase of intangible asset	(50,000)	—	—
Purchases of property and equipment	(880)	(594)	(299)
Net cash used in investing activities	**(14,590)**	**(85,320)**	**(102,606)**
CASH FLOWS FROM FINANCING ACTIVITIES:			
Proceeds from issuance of common stock, net of commissions	—	122,991	81,938
Proceeds from issuance of preferred stock, net of commissions	—	37,432	—
Payment of offering costs	(79)	(284)	(260)
Proceeds from the issuance of debt	195,000	25,000	—
Payment of debt issuance costs	(3,123)	(1,650)	—
Proceeds from the issuance of common stock, warrants, and sale of future royalties to RPI, net of offering costs	—	99,774	—
Proceeds from the issuance of common stock in connection with the exercise of the Put Option, net of financing costs	49,915	—	—
Payment under capital lease obligation	—	(16)	(129)
Proceeds from stock options exercised	6,692	2,358	1,885
Issuance of shares under employee stock purchase plan	1,254	741	779
Net cash provided by financing activities	**249,659**	**286,346**	**84,213**
Net increase (decrease) in cash, cash equivalents and restricted cash	28,733	53,858	(139,993)
Cash, cash equivalents, and restricted cash, beginning of period	140,991	87,133	227,126
Cash, cash equivalents, and restricted cash, end of period	$ 169,724	$ 140,991	$ 87,133
SUPPLEMENTAL CASH FLOW INFORMATION:			
Unpaid offering costs	$ —	$ 78	$ 75
Unpaid debt issuance costs	$ —	$ 78	$ —
Interest paid	$ 7,461	$ —	$ —
Property and equipment included in accounts payable or accruals	$ 60	$ 454	$ 194
Cash paid for income taxes	$ 64	$ 45	$ 48

See notes to consolidated financial statements

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

	Common Stock		Preferred Stock		Additional Paid-In	Accumulated	Accumulated Other Comprehensive	Total Stockholders'
	Shares	Amount	Shares	Amount	Capital	Deficit	Loss	Equity
Balance at December 31, 2017	69,301,691	$ 7	—	$ —	$ 723,510	$ (488,097)	$ (49)	$ 235,371
Cumulative catch up related to the adoption of ASU 2016-09 (Note 2)	—	—	—	—	—	25,003	—	25,003
Issuance of common stock (net of commissions and offering costs of $388)	9,583,334	1	—	—	81,601	—	—	81,602
Exercise of stock options and vesting of restricted stock units	215,156	—	—	—	1,885	—	—	1,885
Stock-based compensation	—	—	—	—	11,839	—	—	11,839
Issuance of shares of common stock in lieu of board fees	12,213	—	—	—	165	—	—	165
Issuance of shares under employee stock purchase plan	62,986	—	—	—	779	—	—	779
Unrealized loss on available for sale securities	—	—	—	—	—	—	(5)	(5)
Net loss	—	—	—	—	—	(123,630)	—	(123,630)
Balance at December 31, 2018	79,175,380	$ 8	—	$ —	$ 819,779	$ (586,724)	$ (54)	$ 233,009
Issuance of series A convertible preferred stock, net of commissions and beneficial conversion charge	—	—	350,000	34,492	2,940		—	37,432
Accretion of series A convertible preferred stock	—	—	—	2,940	(2,940)	—	—	—
Issuance of common stock (net of commissions and offering costs of $284)	11,500,000	1	—	—	122,707	—	—	122,708
Issuance of common stock to Royalty Pharma (net of commissions and offering costs of $304)	6,666,667	1	—	—	78,704	—	—	78,705
Issuance of warrant to Royalty Pharma	—	—	—	—	8,390	—	—	8,390
Exercise of stock options and vesting of restricted stock units	356,538	—	—	—	2,358	—	—	2,358
Stock-based compensation	—	—	—	—	17,875	—	—	17,875
Issuance of shares of common stock in lieu of board fees	12,156	—	—	—	141	—	—	141
Issuance of shares under employee stock purchase plan	72,735	—	—	—	741	—	—	741
Unrealized gain on available for sale securities	—	—	—	—	—	—	73	73
Net loss	—	—	—	—	—	(170,295)	—	(170,295)
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	1,097,280	—	—	—	6,692	—	—	6,692
Stock-based compensation	—	—	—	—	27,471	—	—	27,471
Issuance of shares of common stock in lieu of board fees	8,683	—	—	—	138	—	—	138
Issuance of shares under employee stock purchase plan	115,631	—	—	—	1,254	—	—	1,254
Unrealized loss on available for sale securities	—	—	—	—	—	—	(16)	(16)
Net loss	—	—	—	—	—	(231,694)	—	(231,694)
Balance at December 31, 2020	101,627,070	$ 10	337,800	$ 36,127	$ 1,137,470	$ (988,713)	$ 3	$ 184,897

See notes to 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 and other serious diseases through the discovery, development, and commercialization of novel epigenetic medicines. By focusing on the genetic drivers of disease, the Company's science seeks to match targeted medicines with the patients who need them.

Through December 31, 2020, in addition to revenues from product sales, the Company has raised, an aggregate of $1,527.4 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, $839.5 million from the sale of common stock and series A convertible preferred stock in the Company's public offerings and $76.0 million was from the sale of redeemable convertible preferred stock in private financings prior to the Company's initial public offering in May 2013. As of December 31, 2020, the Company had $373.6 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 $988.7 million through December 31, 2020 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 its product candidates, 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 of products.

2. Summary of Significant Accounting Policies

Basis of Presentation and Principles of Consolidation

The consolidated financial statements of the Company included herein have been prepared pursuant to the rules and regulations of the Securities and Exchange Commission, or the SEC, and in accordance with U.S. generally accepted accounting principles, or GAAP. Any reference in these notes to applicable guidance is meant to refer to the authoritative accounting principles generally accepted in the United States as found in the ASC and Accounting Standards Update, or ASU, of the Financial Accounting Standards Board, or FASB. The 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.

Use of Estimates

The preparation of these 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

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.

Subsequent Events

The Company considers events or transactions that occur after the balance sheet date but before the consolidated financial statements are issued to provide additional evidence relative to certain estimates or to identify matters that require additional disclosure. The Company evaluated all events and transactions through the date these financial statements were filed with the Securities and Exchange Commission.

Cash and cash equivalents

The Company considers all highly liquid securities with original final maturities of three months or less from the date of purchase to be cash equivalents. Cash and cash equivalents are comprised of demand deposit accounts, funds in money market accounts, commercial paper and corporate notes.

Marketable securities

The Company classifies marketable securities with a remaining maturity when purchased of greater than three months as available-for-sale. The Company considers all available-for-sale securities, including those with maturity dates beyond 12 months, as available to support current operational liquidity needs and therefore classifies all securities with maturity dates beyond 90 days at the date of purchase as current assets. Available-for-sale securities are maintained by the Company's investment managers and may consist of commercial paper, high-grade corporate notes, U.S. Treasury securities, and U.S. government agency securities. Available-for-sale securities are carried at fair value with the unrealized gains and losses included in other comprehensive loss as a component of stockholders' equity until realized. Any premium or discount arising at purchase is amortized and/or accreted to interest income and/or expense over the life of the instrument. Realized gains and losses are determined using the specific identification method and are included in other income (expense).

The aggregate fair value of securities held by the Company in an unrealized loss position for less than twelve months as of December 31, 2020 was $67.7 million, which consisted of 6 commercial paper securities, 7 corporate notes securities and 1 U.S. Treasury security. There were no marketable securities held by the Company for greater than twelve months as of December 31, 2020. The aggregate fair value of securities held by the Company in an unrealized loss position for less than twelve months as of December 31, 2019 was $116.7 million, which consisted of 3 commercial paper securities and 19 corporate notes securities. The aggregate fair value of securities held by the Company in an unrealized loss position for greater than twelve months as of December 31, 2019 was $4.0 million, which consisted of 1 U.S. government agency security.

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 there was no material change in the credit risk of the above investments, and as a result, the Company determined it did not hold any investments with an other-than-temporary impairment as of December 31, 2020 and 2019. 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 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

The following table summarizes the available for sale securities held at December 31, 2019 (in thousands):

Description	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Commercial paper	$ 96,952	$ 27	$ (16)	$ 96,963
Corporate notes	140,634	49	(41)	140,642
U.S. government agency securities and U.S. Treasuries	4,000	—	—	4,000
Total	$ 241,586	$ 76	$ (57)	$ 241,605

At December 31, 2020 and 2019, the Company had no securities and 1 security in an unrealized loss position for greater than twelve months, respectively, which the Company concluded was not impaired.

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.

All marketable securities held at December 31, 2020 have maturities of less than one year. The majority of marketable securities held at December 31, 2019 have maturities of less than one year, with the exception of one U.S. government agency security.

The amortized cost of available-for-sale securities is adjusted for amortization of premiums and accretion of discounts to maturity. At December 31, 2020, the balance in the Company's accumulated other comprehensive loss was composed mainly 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 year ended December 31, 2020 and December 31, 2019, respectively, and as a result, the Company did not reclassify any amounts out of accumulated other comprehensive loss for the same period.

Restricted Cash

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

	December 31,		
	2020	2019	2018
		(In thousands)	
Cash and cash equivalents	$ 168,215	$ 139,482	$ 86,671
Restricted cash, as part of other assets	1,509	1,509	462
Total cash, cash equivalents, and restricted cash shown in the consolidated statements of cash flows	$ 169,724	$ 140,991	$ 87,133

The $1.5 million in restricted cash is comprised of $0.5 million in a letter of credit as a security deposit for the 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 consolidated balance sheet. The restricted cash is classified as non-current based on the related lease terms.

Fair Value Measurements

The FASB Codification Topic 820, *Fair Value Measurements and Disclosures,* requires the use of valuation techniques that are consistent with the market approach, the income approach and/or the cost approach. The market approach uses prices and other relevant information generated by market transactions involving identical or comparable assets and liabilities. The income approach uses valuation techniques to convert future amounts, such as cash flows or earnings, to a single present amount on a discounted basis. The cost approach is based on the amount that currently would be required to replace the service capacity of an asset (replacement cost). Valuation techniques should be consistently applied. GAAP also establishes a fair value hierarchy which requires an entity to maximize the use of observable inputs, where available, and minimize the use of unobservable inputs when measuring fair value. The standard describes three levels of inputs that may be used to measure fair value:

Level 1 Quoted prices in active markets for identical assets or liabilities.
Level 2 Observable inputs other than Level 1 prices, such as quoted prices for similar assets or liabilities; quoted prices in markets that are not active; or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.
Level 3 Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

The Company's financial instruments as of December 31, 2020 and 2019 consisted primarily of cash and cash equivalents, marketable securities and accounts receivable and accounts payable. As of December 31, 2020 and December 31, 2019, the Company's financial assets recognized at fair value consisted of the following:

	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	$ —

	Fair Value as of December 31, 2019			
	Total	Level 1	Level 2	Level 3
	(In thousands)			
Cash equivalents	$ 132,193	$ 124,419	$ 7,774	$ —
Marketable securities:				
Commercial paper	96,963	—	96,963	—
Corporate notes	140,642	—	140,642	—
U.S. government agency securities and treasuries	4,000	—	4,000	—
Total	$ 373,798	$ 124,419	$ 249,379	$ —

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.

As of December 31, 2020, the fair value of the long-term debt, payable in installments through November 18, 2026, approximated its carrying value due to the proximity of the issuance of the Tranche D Loan date to December 31, 2020 (See Note 13, *Long-Term Debt*).

Amortization of Debt Discount and Issuance Costs

Long-term debt is initially recorded at its allocated proceeds, net of discounts and deferred costs. Debt discount and issuance costs, consisting of legal and other fees directly related to the debt, are offset against initial carrying value of the debt and are amortized to interest expense over the estimated life of the debt based on the effective interest method.

Liability Related to Sale of Future Royalties

The Company treats the liability related to sale of future royalties as a debt financing, as the Company has significant continuing involvement in the generation of the cash flows, to be amortized to interest expense using the effective interest rate method over the life of the related royalty stream.

The liability related to sale of future royalties and the related interest expense are based on the Company's current estimates of future royalties expected to be paid over the life of the arrangement. The Company will periodically assess the expected royalty payments using a combination of internal projections and forecasts from external sources. To the extent the Company's future estimates of royalty payments are greater or less than previous estimates or the estimated timing of such payments is materially different than its previous estimates, the Company will prospectively recognize related non-cash interest expense.

For further discussion of the sale of future royalties, refer to Note 12, *Sale of Future Royalties*.

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 analysis for the year ended December 31, 2020 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, and its existing debt service obligations. The Company also evaluated its forecasted product revenues from sales of TAZVERIK. Such estimates of future sales contain significant judgement as TAZVERIK was recently launched and there is little or no history with which to base such estimates. The Company expects its available cash, cash equivalents and marketable securities will be sufficient to fund current planned operations and capital expenditure requirements for at least the next twelve months from the filing date of this Annual Report on Form 10-K with the SEC. As a result, the Company concluded that it did not identify conditions or events that raise substantial doubt about the Company's ability to continue as a going concern within one year from the date these financial statements were issued. The Company's current operating plan is based on assumptions that may prove to be wrong, and the Company could use its capital resources sooner than it expects.

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.

Concentration of Credit Risk

Financial instruments that potentially subject the Company to concentrations of credit risk include cash, cash equivalents, marketable securities and accounts receivable. The Company attempts to minimize the risks related to cash, cash equivalents and marketable securities by working with highly rated financial institutions that invest in a broad and diverse range of financial instruments as defined by the Company. The Company has established guidelines relative to credit ratings and maturities intended to safeguard principal balances and maintain liquidity. The Company maintains its funds in accordance with its investment policy, which defines allowable investments, specifies credit quality standards and is designed to limit the Company's credit exposure to any single issuer.

Accounts receivable represent amounts due from customers and collaboration partners. The Company monitors economic conditions to identify facts or circumstances that may indicate that any of its accounts receivable are at risk of collection. For a further discussion of concentration of credit risk see Note 3, *Product Revenue, Net*.

Property and Equipment

The Company records property and equipment at cost. Property and equipment acquired under a capital lease is recorded at the lesser of the present value of the minimum lease payments under the capital lease or the fair value of the leased property at lease inception. The Company calculates depreciation and amortization using the straight-line method over the following estimated useful lives:

Asset Category	Useful Lives
Laboratory equipment	3 - 6 years
Computer and office equipment, and furniture	3 - 10 years
Leasehold improvements	3 - 6 years or term of respective lease, if shorter

Amortization of capital lease assets is included in depreciation expense. The Company capitalizes expenditures for new property and equipment and improvements to existing facilities and charges the cost of maintenance to expense. The Company eliminates the cost of property retired or otherwise disposed of, along with the corresponding accumulated depreciation, from the related accounts, and the resulting gain or loss is reflected in the results of operations.

Impairment of Long-Lived Assets

The Company reviews long-lived assets to be held and used, including property and equipment and intangible assets, for impairment whenever events or changes in circumstances indicate that the carrying amount of the assets or asset group may not be recoverable.

Evaluation of recoverability is based on an estimate of undiscounted future cash flows resulting from the use of the asset or asset group and its eventual disposition. In the event that such cash flows are not expected to be sufficient to recover the carrying amount of the asset or asset group, the assets are written down to their estimated fair values. No such impairments were recorded during 2020, 2019 or 2018.

Income Taxes

The Company records deferred income taxes to recognize the effect of temporary differences between tax and financial statement reporting. The Company calculates the deferred taxes using enacted tax rates expected to be in place when the temporary differences are realized and records a valuation allowance to reduce deferred tax assets if it is determined that it is more likely than not that all or a portion of the deferred tax asset will not be realized. The Company considers many factors when assessing the likelihood of future realization of deferred tax assets, including recent earnings results, expectations of future taxable income, carryforward periods available and other relevant factors. The Company records changes in the required valuation allowance in the period that the determination is made.

The Company assesses its income tax positions and records tax benefits for all years subject to examination based upon management's evaluation of the facts, circumstances and information available as of the reporting date. For

those tax positions where it is more likely than not that a tax benefit will be sustained, the Company records the largest amount of tax benefit with a greater than 50.0% likelihood of being realized upon ultimate settlement with a taxing authority having full knowledge of all relevant information. For those income tax positions where it is not more likely than not that a tax benefit will be sustained, the Company does not recognize a tax benefit in the financial statements. The Company records interest and penalties related to uncertain tax positions, if applicable, as a component of income tax expense. Refer to Note 8, *Income Taxes*, for additional information regarding the Company's income taxes.

Revenue Recognition – Collaboration Revenue

Under ASC 606, *Revenue from Contracts with Customers*, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the entity 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 entity satisfies a performance obligation. The Company only applies the five-step model to contracts when it is probable that the entity will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, the Company assesses the goods or services promised within each contract and determines those that are performance obligations, and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

The Company has entered into collaboration and license agreements, which are within the scope of ASC 606, to discover, develop, manufacture and commercialize product candidates. The terms of these agreements typically contain multiple promises or obligations, which may include: (i) licenses, or options to obtain licenses, to compounds directed to specific targets (referred to as "exclusive licenses") and (ii) research and development activities to be performed on behalf of the collaboration partner related to the licensed targets. Payments to the Company under these agreements may include non-refundable license fees, customer option exercise fees, payments for research activities, reimbursement of certain costs, payments based upon the achievement of certain milestones and royalties on any resulting net product sales.

The Company first evaluates license and/or collaboration arrangements to determine whether the arrangement (or part of the arrangement) represents a collaborative arrangement pursuant to ASC Topic 808, *Collaborative Arrangements,* based on the risks and rewards and activities of the parties pursuant to the contractual arrangement. The Company accounts for collaborative arrangements (or elements within the contract that are deemed part of a collaborative arrangement), which represent a collaborative relationship and not a customer relationship, outside the scope of ASC 606. The Company's collaborations primarily represent revenue arrangements. The Company uses judgment to determine whether milestones or other variable consideration, except for sales-based royalties, should be included in the transaction price as described further below. The transaction price is allocated to each performance obligation on a relative stand-alone selling price basis, for which the Company recognizes revenue as or when the performance obligations under the contract are satisfied. In determining the stand-alone selling price of a license to the Company's proprietary technology or a material right provided by a customer option, the Company considers market conditions as well as entity-specific factors, including those factors contemplated in negotiating the agreements as well as internally developed estimates that include assumptions related to the market opportunity, estimated development costs, probability of success and the time needed to commercialize a product candidate pursuant to the license. In validating its estimated stand-alone selling price, the Company evaluates whether changes in the key assumptions used to determine its estimated stand-alone selling price will have a significant effect on the allocation of arrangement consideration between performance obligations.

Amounts received prior to revenue recognition are recorded as deferred revenue. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified as current portion of deferred revenue in the accompanying consolidated balance sheets. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, net of current

portion. Amounts recognized as revenue, but not yet received or invoiced are generally recognized as contract assets.

Exclusive Licenses – If the license to the Company's intellectual property is determined to be distinct from the other promises or performance obligations identified in the arrangement, which generally include research and development services, the Company recognizes revenue from non-refundable, upfront fees allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. In assessing whether a license is distinct from the other promises, the Company considers relevant facts and circumstances of each arrangement, including the research and development capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. In addition, the Company considers whether the collaboration partner can benefit from the license for its intended purpose without the receipt of the remaining promises, whether the value of the license is dependent on the unsatisfied promises, whether there are other vendors that could provide the remaining promises, and whether it is separately identifiable from the remaining promises. For licenses that are combined with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition. The measure of progress, and thereby periods over which revenue should be recognized, are subject to estimates by management and may change over the course of the research and development and licensing agreement.

Research and Development Services – The promises under the Company's collaboration and license agreements generally include research and development services to be performed by the Company on behalf of the collaboration partner. For performance obligations that include research and development services, the Company generally recognizes revenue allocated to such performance obligations based on an appropriate measure of progress. The Company utilizes judgment to determine the appropriate method of measuring progress for purposes of recognizing revenue, which is generally an input measure such as costs incurred. The Company evaluates the measure of progress each reporting period as described under *Exclusive Licenses* above. Reimbursements from the partner that are the result of a collaborative relationship with the partner, instead of a customer relationship, such as co-development activities, are recorded as a reduction to research and development expense.

Customer Options – The Company's arrangements may provide a collaborator with the right to select a target for licensing either at the inception of the arrangement or within an initial pre-defined selection period, which may, in certain cases, include the right of the collaborator to extend the selection period. Under these agreements, fees may be due to the Company (i) at the inception of the arrangement as an upfront fee or payment, (ii) upon the exercise of an option to acquire a license or (iii) upon extending the selection period as an extension fee or payment. If an arrangement is determined to contain customer options that allow the customer to acquire additional goods or services, the goods and services underlying the customer options are not considered to be performance obligations at the outset of the arrangement, as they are contingent upon option exercise. The Company evaluates the customer options for material rights, or options to acquire additional goods or services for free or at a discount. If the customer options are determined to represent a material right, the material right is recognized as a separate performance obligation at the inception of the arrangement. The Company allocates the transaction price to material rights based on the relative stand-alone selling price, which is determined based on the identified discount and the probability that the customer will exercise the option. Amounts allocated to a material right are not recognized as revenue until, at the earliest, the option is exercised or expires.

Milestone Payments – At the inception of each arrangement that includes development milestone payments, the Company evaluates whether the milestones are considered probable of being achieved and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the control of the Company or the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. The Company evaluates factors such as the scientific, clinical, regulatory, commercial, and other risks that must be overcome to achieve the particular milestone in making this assessment. There is considerable judgment involved in determining whether it is probable that a significant revenue reversal would not occur. At the end of each subsequent reporting period, the Company reevaluates the

probability of achievement of all milestones subject to constraint and, if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenues and earnings in the period of adjustment. If a milestone or other variable consideration relates specifically to the Company's efforts to satisfy a single performance obligation or to a specific outcome from satisfying the performance obligation, the Company generally allocates the milestone amount entirely to that performance obligation once it is probable that a significant revenue reversal would not occur.

Royalties – For arrangements that include sales-based royalties, including milestone payments based on a level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) when the related sales occur or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, the Company has not recognized any royalty revenue resulting from any of its licensing arrangements.

For a complete discussion of accounting for collaboration revenues, see Note 11, *Collaborations*.

Revenue Recognition – Product Revenue

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*.

Research and Development Expenses

Research and development expenses are expensed as incurred. Research and development expenses are comprised of costs incurred in providing research and development activities, including salaries and benefits, facilities costs, overhead costs, contract research and development services, and other outside costs. Nonrefundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made.

External research and development expenses associated with the Company's programs include clinical trial site costs, clinical manufacturing costs, costs incurred for consultants and other outside services, such as data management and statistical analysis support, and materials and supplies used in support of the clinical and preclinical programs. Internal costs of the Company's clinical programs include salaries, stock-based compensation, and the portion of the Company's facility costs allocated to research and development expense. When vendors billing terms do not coincide with the Company's period-end, the Company is required to make estimates of its obligations to those vendors, including clinical trial and pharmaceutical development costs, contractual services costs and costs for supply of its product candidates incurred in a given accounting period and record accruals at the end of the period. The Company bases its estimates on its knowledge of the research and development programs, services performed for the period, past history for related activities and the expected duration of the vendor service contract, where applicable.

The Company generally accrues expenses related to research and development activities based on the services received and efforts expended pursuant to contracts with multiple contract research organizations that conduct and manage clinical trials, as well as other vendors that provide research and development services. Payments for these activities are based on the terms of the individual arrangements and may result in payment terms that differ from the pattern of costs incurred. There may be instances in which payments made to vendors will exceed the level of services provided and result in a prepayment of the clinical expense. Payments under some of these contracts depend on factors such as the successful enrollment of subjects and the completion of clinical trial milestones. In accruing service fees, the Company estimates the time period over which services will be performed and the level of effort to

be expended in each period. If the actual timing of the performance of services or the level of effort varies from estimates, the Company would adjust the accrual or prepaid accordingly in future periods.

Stock-Based Compensation

The Company measures employee and non-employee stock-based compensation based on the grant date fair value of the stock-based compensation award. The Company grants stock options at exercise prices equal to the fair value of the Company's common stock on the date of grant, based on observable market prices.

The Company recognizes employee stock-based compensation expense on a straight-line basis over the requisite service period of the awards. The Company recognizes forfeitures at the time they occur. The actual expense recognized over the vesting period will only represent those options that vest.

For awards with performance conditions in which the award does not vest unless the performance condition is met, the Company recognizes expense if, and to the extent that, the Company estimates that achievement of the performance condition is probable. If the Company concludes that vesting is probable, it recognizes expense from the date it reaches this conclusion through the estimated vesting date. For awards with performance conditions that accelerate vesting of the award, the Company estimates the likelihood of satisfaction of the performance conditions, which affects the period over which the expense is recognized, and recognizes the expense using the accelerated attribution model.

Refer to Note 15, *Employee Benefit Plans*, for additional information regarding the measurement and recognition of expense related to the Company's stock-based compensation awards.

Earnings (Loss) per Share

The Company computes basic earnings (loss) per share by dividing income (loss) attributable to common stockholders by the weighted average number of shares of common stock outstanding. During periods of income, the Company allocates participating securities a proportional share of income determined by dividing total weighted average participating securities by the sum of the total weighted average common shares and participating securities (the "two-class method"). The Company's restricted stock and Series A Convertible Preferred Stock par value of $0.0001 per share (the "Series A Preferred Stock") participate in dividends declared by the Company and are therefore considered to be participating securities. Participating securities have the effect of diluting both basic and diluted earnings per share during periods of income. During periods of loss, the Company allocates no loss to participating securities because they have no contractual obligation to share in the losses of the Company. The Company computes diluted earnings (loss) per share after giving consideration to the dilutive effect of stock options and warrants that are outstanding during the period, except where such non-participating securities would be anti-dilutive. Refer to Note 16, *Loss per Share*, for the Company's calculation of loss per share for the periods presented.

Segment Information

The Company currently operates as one reportable business segment: the discovery, development, and commercialization of novel epigenetic therapies for patients with cancer and other diseases.

Recently Adopted Accounting Pronouncements

Financial Instruments – Credit Losses

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments – Credit Losses*, or ASC 326, which requires earlier recognition of credit losses on financing receivables and other financial assets in scope. The new standard is effective for annual reporting periods beginning after December 15, 2019.

Effective January 1, 2020, the Company adopted ASC 326 using the required modified retrospective approach and utilizing the effective date as its date of initial application, for which prior periods are presented in accordance with the guidance in ASC 326. The FASB subsequently issued amendments to ASU 2016-13, which have the same effective date and transition date of January 1, 2020.

The adoption of these standards resulted in an immaterial allowance for credit losses on the Company's consolidated balance sheet. The adoption of these standards did not have a material effect on the Company's consolidated statements of operations and comprehensive loss or consolidated statements of cash flows.

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. 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 product 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 consolidated balance sheets net of accumulated amortization and impairments, if applicable. The amortization expense is recognized as cost of product revenue in the Company's 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 December 31, 2020 (in thousands):

	December 31, 2020	Estimated useful life (years)
In-licensed rights	$ 50,000	12.2
Less: accumulated amortization	(2,998)	
Total intangible asset, net	$ 47,002	

The Company recorded approximately $3.0 million in amortization expense related to intangible assets, using the straight-line methodology, during the year ended December 31, 2020. Estimated future amortization expense for intangible assets is approximately $4.2 million per each 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.

Leases

Adoption of Accounting Standards Codification Topic 842, Leases

Effective January 1, 2019, the Company adopted Accounting Standards Codification Topic 842, Leases (ASC 842), which requires lessees to recognize assets and liabilities on the balance sheet for the rights and obligations created by all leases with terms of more than 12 months. The Company elected to employ the transitionary relief offered by the FASB under ASU 2018-11 which allowed the new standard to be implemented without the restatement of comparative periods' financial information. The Company also elected to employ the package of practical expedients offered under ASC 842 and as a result did not assess (1) the presence of a lease in any expired or existing contracts, (2) the lease classification for any existing or expired leases, or (3) the initial direct costs for any existing leases. Additionally, the Company elected to account for the lease components and non-lease components as a single lease component. ASU-2018-11 also provides for recognizing the effects of applying ASC 842 as a cumulative-effect adjustment to retained earnings as of January 1, 2019; however, no such adjustment was recorded as of January 1, 2019.

The Company recorded the liability associated with the leases at the present value of the lease payments not yet paid, discounted using the discount rate for the leases established at the adoption date. As the discount rate implicit in the leases was typically not readily determinable, the Company utilized the fixed rate at which the Company could borrow on a collateralized basis the amount of the lease payments in the same currency, for a similar term, in a similar economic environment. incremental borrowing rate (IBR).

The adoption of this standard resulted in the recognition of operating lease liabilities and right-of-use assets of $11.5 million and $10.7 million, respectively, on the Company's consolidated balance sheet relating to its leases for its corporate headquarters and other office space in Cambridge, Massachusetts and other operating leases. The adoption of the standard did not have a material effect on the Company's consolidated statements of operation and comprehensive loss or consolidated statements of cash flows.

The lease liability will be reduced over the remaining lease term based on cash payments made offset by accretion of monthly interest calculated on the lease liability. The right-of-use (ROU) asset will be amortized over the remaining lease term in an amount equal to the difference between the calculated straight-line expense of the total lease payments less the monthly interest calculated on the remaining lease liability.

Subsequent Lease Recognition

At inception of a contract, we determine whether an arrangement is or contains a lease. For all leases, we determine the classification as either operating or financing. As of December 31, 2020, the Company does not have any leases that are classified as finance leases.

ROU assets represent our right to use an underlying asset for the lease term, and lease liabilities represent our obligation to make lease payments under the lease. Lease recognition occurs at the commencement date, and lease liability amounts are based on the present value of lease payments made during the lease term. Renewals are not assumed in the determination of the lease term unless they are deemed to be reasonably assured at the inception of the lease. Because our leases do not provide information to determine an implicit interest rate, we use our incremental borrowing rate in determining the present value of lease payments. ROU assets also include any lease payments made prior to the commencement date less lease incentives received. Operating lease expense is recognized on a straight-line basis over the lease term.

The Company has elected not to apply the recognition requirements to short-term leases with a term of 12 months or less. Instead, the Company recognizes the lease payments in the consolidated statements of operations and comprehensive loss on a straight-line basis over the lease term.

Pending Accounting Pronouncements

In November 2018, the Financial Accounting Standards Board, or the FASB, issued ASU 2018-18, *Collaborative Arrangements, or ASC 808,* which clarifies 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 ASU will be effective for the Company in the first quarter of fiscal 2021, with early adoption permitted. A retrospective adoption to the date the Company adopted ASC 606, *Revenue from Contracts with Customers*, is required by recognizing a cumulative-effect adjustment to the opening balance or retained earnings of the earliest period presented. The Company is currently evaluating the impact of the adoption of ASU 2018-18 and does not expect adoption to have a material effect on the Company's consolidated financial statements or disclosures.

In December 2019, the FASB issued ASU 2019-12, *Income Taxes*, or ASC 740, which simplifies the accounting for income taxes. The ASU will be effective for the Company in the first quarter of fiscal 2021, with early adoption permitted. The Company is currently evaluating the impact of the adoption of ASU 2019-12 and does not expect adoption to have a material effect on the Company's consolidated financial statements or disclosures.

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 year ended December 31, 2020:

	Chargebacks, Discounts, and Fees	Government and Other Rebates	Returns	Total
		(In thousands)		
Balance, January 1, 2020	$ —	$ —	$ —	$ —
Provision	802	1,046	67	1,915
Payments or credits	(669)	(618)	—	(1,287)
Balance, December 31, 2020	$ 133	$ 428	$ 67	$ 628

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 years ended December 31, 2020 and 2019, net product revenue was primarily accounted from four individual customers. Revenue earned from each customer as a percentage of net product revenue is as follows:

	Year Ended December 31,	
	2020	2019
Customer 1	45%	—
Customer 2	11%	—
Customer 3	20%	—
Customer 4	24%	—

There was no product revenue for the year ended December 31, 2019.

As of December 31, 2020, four individual customers accounted for a percentage of accounts receivable as follows:

	December 31, 2020	December 31, 2019
Customer 1	21%	—
Customer 2	14%	—
Customer 3	29%	—
Customer 4	36%	—

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

4. Property and Equipment, net

Property and equipment, net consists of the following:

	December 31,	
	2020	2019
	(In thousands)	
Laboratory equipment	$ 4,435	$ 4,273
Computer and office equipment, and furniture	4,636	5,113
Leasehold improvements	453	424
Construction in progress	34	560
Property and equipment	9,558	10,370
Less: accumulated depreciation and amortization	(7,406)	(8,151)
Property and equipment, net	$ 2,152	$ 2,219

Depreciation and amortization expense was $4.0 million, $0.8 million and $1.1 million for the years ended December 31, 2020, 2019, and 2018, respectively.

5. Inventory

All of the Company's inventory relates to the manufacturing of TAZVERIK. The following table sets forth the Company's inventory as of December 31, 2020 and December 31, 2019:

	December 31, 2020	December 31, 2019
	(In thousands)	
Raw materials	$ 1,068	$ —
Work in process	8,564	—
Finished goods	829	—
Total	$ 10,461	$ —

As of December 31, 2020, the Company has not capitalized inventory costs related to its other drug development programs.

6. Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets consisted of the following:

	December 31,	
	2020	2019
	(In thousands)	
Prepaid clinical and manufacturing costs	$ 12,646	$ 7,657
Interest receivable on available for sale securities	369	943
Other prepaid expenses and other receivables	4,906	6,923
Total prepaid expenses and other current assets	$ 17,921	$ 15,523

7. Accrued Expenses

Accrued expenses consisted of the following:

	December 31,	
	2020	2019
	(In thousands)	
Employee compensation and benefits	$11,921	$ 7,844
Research and development expenses	10,664	9,706
Professional services and other	5,970	4,999
Accrued expenses	$28,572	$22,565

8. Income Taxes

The Company's losses before income taxes consist solely of domestic losses.

The provision for (benefit from) income taxes for the years ended December 31, 2020, 2019, and 2018 is as follows:

	2020	2019	2018
		(In thousands)	
Current	$ 22	$ (34)	$ (127)
Deferred	92	92	184
Total	114	58	57
Income tax provision	$ 114	$ 58	$ 57

A reconciliation of the federal statutory income tax rate and the Company's effective income tax rate is as follows:

	Year Ended December 31,		
	2020	2019	2018
Federal statutory income tax rate	21.0%	21.0%	21.0%
State income taxes	6.1	6.0	5.7
Research and development and other tax credits	2.0	1.9	2.4
Permanent items	(0.6)	(0.7)	(0.7)
Change in valuation allowance	(27.9)	(27.5)	(28.3)
Other	(0.6)	(0.7)	(0.1)
Effective income tax rate	0.0%	0.0%	0.0%

Deferred Tax Assets (Liabilities)

The Company's deferred tax assets (liabilities) included in other assets in the consolidated balance sheets consist of the following:

	December 31,	
	2020	2019
	(In thousands)	
Deferred tax assets:		
Net operating loss carryforwards	$ 238,792	$ 180,877
Research and development and other credit carryforwards	34,205	29,774
Capitalized start-up costs	768	901
Deferred revenue	—	1,029
Accruals and allowances	2,949	1,922
Eisai license payment	11,935	12,840
Stock compensation	7,338	6,489
Other	452	442
Sale of royalty	3,857	3,458
Lease liability	5,462	5,990
Business interest	1,220	—
Gross deferred tax assets	306,978	243,722
Deferred tax asset valuation allowance	(302,137)	(237,858)
Total deferred tax assets	4,841	5,864
Deferred tax liabilities:		
Depreciation and other	(18)	(40)
Right of use asset	(4,709)	(5,732)
Total deferred tax liabilities	(4,727)	(5,772)
Net deferred tax asset (liability)	$ 114	$ 92

The Company evaluated the expected recoverability of its net deferred tax assets as of December 31, 2020 and 2019, and determined that, with the exception of the deferred tax asset related to alternative minimum tax ("AMT") credits, there was insufficient positive evidence to support the recoverability of these net deferred tax assets, concluding it is more likely than not that its net deferred tax assets would not be realized in the future; therefore, the Company provided a full valuation allowance against its net deferred tax asset balance as of December 31, 2020 and 2019, with the exception of the deferred tax asset related to the AMT credit. The AMT credit became refundable beginning in 2018 through no later than 2022 under the Tax Cuts and Jobs Act ("TCJA"), tax reform legislation, and as such, the related deferred tax asset will be able to be realized and the corresponding valuation allowance of $368,000 was reversed as of December 31, 2018 and recognized as a tax benefit. As of December 31, 2019, $184,000 of the deferred tax asset was reclassified to an income tax receivable. Fifty percent of the remaining AMT credit is refundable with the filing of the 2020 tax return. As such, as of December 31, 2020, $92,000 of the deferred tax asset was reclassified to an income tax receivable. There was no tax benefit or provision as a result of the asset reclassification on the consolidated balance sheet. Under the Coronavirus Aid, Relief, and Economic Security Act, or CARES, the AMT credit became 100% refundable with the filing of the Company's tax return for the year ended December 31, 2019. The Company re-classed the remaining deferred tax asset to an income tax receivable as part of the 2019 provision to return analysis. At December 31, 2020 there is no deferred tax asset related to AMT credits and the Company has a full valuation allowance against its net deferred tax assets.

As of December 31, 2020, the Company had operating loss carryforwards of approximately $877.8 million and $908.0 million available to offset future taxable income for United States federal and state income tax purposes, respectively. The U.S. federal tax operating loss carryforwards of $428.5 million will expire at various dates from 2029 through 2037. Approximately $449.2 million of the U.S. federal tax operating losses can be carried forward indefinitely. The state tax operating loss carryforwards expire commencing in 2030.

Additionally, as of December 31, 2020, the Company had research and development tax credit carryforwards of approximately $12.7 million and $4.8 million available to be used as a reduction of federal income taxes and state income taxes, respectively, which expire at various dates from 2028 through 2040, as well as federal orphan drug tax credit carryforwards of $17.7 million, which would expire at various dates from 2033 through 2040. The Company's ability to use its operating loss carryforwards and tax credits to offset future taxable income is subject to restrictions under Section 382 of the U.S. Internal Revenue Code of 1986, as amended (the "Internal Revenue Code"). These restrictions may limit the future use of the operating loss carryforwards and tax credits if certain ownership changes described in the Internal Revenue Code occur. Future changes in stock ownership may occur that would create further limitations on the Company's use of the operating loss carryforwards and tax credits. In such a situation, the Company may be required to pay income taxes, even though significant operating loss carryforwards and tax credits exist.

Uncertain Tax Positions

The following is a rollforward of the Company's unrecognized tax benefits:

	December 31,	
	2020	2019
	(In thousands)	
Unrecognized tax benefits - as of beginning of year	$ 6,328	$ 5,743
Gross increases - current period tax positions	832	585
Unrecognized tax benefits - as of end of year	$ 7,160	$ 6,328

None of the Company's unrecognized tax benefits would result in income tax expense or impact the Company's effective tax rate if recognized. The Company had no accrued tax-related interest or penalties as of December 31, 2020 or 2019.

The Company has generated research and development and orphan drug credits, but has not conducted a study to document the qualified activities. This study may result in an adjustment to the Company's reserve for uncertain tax positions, research and development credit, and orphan drug credit carryforwards.

The Company files income tax returns in the U.S. federal tax jurisdiction and various state tax jurisdictions. Since the Company is in a loss carryforward position, the Company is generally subject to examination by the U.S. federal, state and local income tax authorities for all tax years in which a loss carryforward is available.

9. Commitments and Contingencies

Commitments

In addition to commitments under leasing arrangements (Refer to Note 10, *Leases*), the Company committed to $10.4 million of development costs payable to Roche Molecular upon certain development and regulatory milestones, under the amended companion diagnostic agreement, 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. Through December 31, 2020, the Company has paid Roche Sequencing $9.4 million under the amended agreement, including developmental costs of $3.4 million paid in 2020, $4.0 million paid in 2019 and $2.0 million paid in 2018, respectively, upon the achievement of milestones under the amended agreement with Roche Sequencing. As of December 31, 2020, the Company is responsible for the remaining development costs of $1.0 million due under the agreement. The $0.9 million that Eisai has agreed to reimburse the Company related to a regulatory milestone for Japan that was achieved as of June 30, 2020 and payment received in the fourth quarter of 2020. In addition, the

Company paid $1.0 million to Roche Sequencing for the achievement of a development milestone in the fourth quarter of 2020.

Additionally, the Company enters into contracts in the normal course of business with clinical research organizations for clinical and preclinical research studies, external manufacturers for product for use in clinical trials, and other research supplies and other services as part of the Company's operations. These contracts generally provide for termination on notice, and therefore are cancelable contracts and not included in contractual commitments.

10. 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 consolidated balance sheet. In applying the ASC 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 years ended December 31, 2020 and 2019:

	Twelve months ended December 31, 2020	Twelve months ended December 31, 2019
Lease cost		
Operating lease cost	$ 6,155	$ 3,771
Variable lease cost	1,764	1,318
Total lease cost	$ 7,919	$ 5,089
Other information		
Operating cash flows used for operating leases	$ 4,374	$ 3,648
Weighted average remaining lease term	5.3 years	5.3 years
Weighted average discount rate	9.77%	9.60%

Rent expense was $3.5 million for the year ended December 31, 2018 under the previous guidance in ASC 840, *Leases*.

Future minimum lease payments under the Company's non-cancelable operating leases as of December 31, 2020 and 2019, are as follows:

	2020 (In thousands)
2021	$ 6,436
2022	6,256
2023	2,984
2024	3,053
Thereafter	6,966
Total lease payments	$ 25,695
Less: imputed interest	(5,621)
Total operating lease liabilities at December 31, 2020	$ 20,074

11. 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 December 31, 2020, 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 December 31, 2020, 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 consolidated statements of operations and comprehensive loss, including $20.0 million in milestone revenue in the year ended December 31, 2018. The Company did not recognize any collaboration revenue under the agreement in the years ended December 31, 2020 and 2019. The Company did not have any deferred revenue related to this agreement as of December 31, 2020 or December 31, 2019 and any future revenues 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 December 31, 2020 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.

In the second quarter of 2019, the Company submitted its first NDA to the FDA, for the treatment of patients with ES, triggering the payment of the first $10.0 million clinical development milestone to Eisai and the recording of this amount to research and development expense. The Company paid the $10.0 million clinical development milestone to Eisai in June 2019. In the fourth quarter of 2019, the Company submitted its second NDA to the FDA, for the treatment of patients with FL, triggering the payment of the second $10.0 million clinical development milestone to Eisai and the recording of this amount to research and development expense. The Company paid the $10.0 million clinical development milestone to Eisai in December 2019. In January 2020, the Company triggered the payment of the $25.0 million milestone payment upon regulatory approval of tazemetostat for ES, which was capitalized as an intangible asset on the Company's consolidated balance sheet as of December 31, 2020. In June 2020, the Company triggered the payment of the $25.0 million milestone payment upon regulatory approval of tazemetostat for FL, which was capitalized as an intangible asset on the Company's consolidated balance sheet as of December 31, 2020.

During the year ended December 31, 2020, Eisai purchased drug product from the Company at cost to facilitate development within Japan under the Eisai License Agreement and the Company recognized approximately $5.3 million, as a reduction to research and development expense. During the year ended December 31, 2019, Eisai purchased drug product from the Company at cost to facilitate development within Japan under the Eisai License Agreement and the Company recognized approximately $3.8 million as a reduction to research and development expense. During the year ended December 31, 2020, the Company recorded $1.7 million related to the worldwide royalties due under the Eisai License Agreement in cost of product revenue based on U.S. sales of TAZVERIK and as of December 31, 2020, $0.7 million in royalties were payable under the Eisai License Agreement. As of December 31, 2020, and 2019, the Company had accounts receivable of less than $0.1 million and $1.3 million, respectively, due from Eisai. For additional information regarding certain of the Eisai royalties, see Note 12, *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 December 31, 2020, 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.

Accounting Considerations of the Agreement

The Company assessed the arrangement in accordance with ASC 606 and concluded that the contract counterparty, Boehringer Ingelheim, is a customer based on the arrangement structure, through the satisfaction of each target's performance obligations. The Company identified the following performance obligations under the arrangement:

- the combination of the Epizyme license to the first undisclosed target inhibitor technology, associated research and development services through the research period and,
- the combination of the Epizyme license to the second undisclosed target inhibitor technology, associated research and development services through the research period.

The Company determined that each Epizyme license was not distinct from the associated research and development services due to the limited economic benefit that Boehringer Ingelheim would derive from the Epizyme license if the research services were not provided by the Company. Accordingly, the Epizyme licenses and associated research and development services, for each Target Project, are each accounted for as a combined performance obligation.

Under the agreement, the Company determined that the total transaction price at execution was $20.0 million, comprised of the following:

- $15.0 million total upfront payment received under the agreement; and
- $5.0 million research funding payment to be received in 2019.

In addition, during 2019, the Company achieved a $5.5 million development milestone for selection of a lead optimization candidate for the shared program targeting enzymes within helicase families, which was added to the transaction price.

The future potential milestone payments were excluded from the transaction price at inception, as the achievement of the milestone events are highly uncertain. As such, all milestone payments were fully constrained. The Company reevaluated the transaction price at the end of each reporting period and as uncertain events were resolved or other changes in circumstances occurred, it adjusted its estimate of the transaction price. The Company recognized a total of $23.8 million related to the two performance obligations through December 31, 2019.

During the year-ended 2020, the Company added $0.5 million in research funding for the shared program targeting enzymes within helicase families to the transaction price was recognized as the research performance obligation was performed prior to the end of 2020.

Collaboration Revenue

Through December 31, 2020, the Company has recognized $26.0 million in total collaboration revenue since the inception of this collaboration, including $0.5 million during the year ended December 31, 2020. The Company recognized $23.8 million and $1.7 million of revenue as of December 31, 2019 and 2018, respectively.

As of December 31, 2020 and 2019, the Company did not have any deferred revenue related to this agreement. As of December 31, 2020 and 2019, the Company had accounts receivable of $0.0 million and $1.3 million, respectively.

Celgene (a subsidiary of Bristol-Myers Squibb Company)

In April 2012, the Company entered into a collaboration and license agreement with Celgene Corporation, or Celgene. On July 8, 2015, the Company entered into an amendment and restatement of the collaboration and license agreement with Celgene, or the Celgene Collaboration Agreement.

All performance obligations, except for the three material rights were substantially satisfied as of the adoption of ASC 606 and therefore all of the transaction price allocated to those performance obligations has been recognized as revenue under ASC 606. Through December 31, 2020, the Company has recognized revenue of $99.2 million under

the agreement as collaboration revenue in the Company's consolidated statements of operations and comprehensive loss and in accumulated deficit as a result of the cumulative-effect recognition upon adoption of ASC 606. The amounts received that had previously not been recognized as revenue and were recorded in deferred revenue on the Company's consolidated balance sheet, relate to the material rights

On November 3, 2020, the Company received a notice of termination without cause of the Celgene Collaboration Agreement, and such termination became effective on January 2, 2021. As a result, deferred revenue related to the agreement of $3.8 million was recognized as revenue in the quarter ended December 31, 2020.

12. 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 December 31, 2020, the Company had borrowed an aggregate principal amount under the first tranche of $25.0 million (the "Tranche A Note Payable"), the second tranche of $25.0 million (the "Tranche B Note Payable"), and the third tranche of $20.0 million (the "Tranche C Note Payable") under the Loan Agreement. On November 3, 2020, the Company, the Collateral Agent and the Lenders amended and restated the Loan Agreement, (as amended and restated, the "Amended and Restated Loan Agreement"), to provide for, among other things, an additional secured term loan of $150.0 million, or the Tranche D Loan. On November 18, 2020, we borrowed the Tranche D Loan (See Note 13, *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 had 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 December 31, 2020 and 2019, RPI and its affiliates owned 9.0% and 6.8% 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.

The fair value for the liability related to the sale of future royalties at the time of the execution of the transaction was based on estimates of future royalties expected to be paid to RPI over the life of the arrangement, which are considered level 3 inputs.

The allocated fair value of the common stock and Common Stock Warrant have been recorded in additional paid-in-capital and the Tranche A Note Payable has been recorded as long-term debt (See Note 13, *Long-Term Debt*).

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 is responsible for any ongoing manufacturing and supply obligations agreed to by the Company and Eisai pursuant to the Eisai License Agreement related to 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. As of December 31, 2020, the Company's assessment of the estimated future royalty payments to RPI resulted in a current effective interest rate of approximately 13.4%.

The following table shows the activity of the Royalty Obligation since the transaction inception through December 31, 2020:

	Year Ended December 31, 2020
	(In thousands)
Proceeds from sale of future royalties	$ 12,601
Non-cash interest expense recognized	1,575
Liability related to the sale of future royalties - ending balance	$ 14,176

During the years ended December 31, 2020 and 2019 no non-cash royalties from net sales of tazemetostat in Japan were recorded and the Company recorded $1.4 million and $0.2 million, respectively, of related non-cash interest expense.

13. 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 origial $70.0 million committed facility amount in November 2019 and 2% of the $150.0 million Tranch 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 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 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 December 31, 2020 (in thousands):

	Year Ended December 31, 2020
2021	$ —
2022	—
2023	—
2024	70,000
2025	75,000
2026	75,000
Total minimum payments	220,000
Less amounts representing interest and discount	(4,330)
Less current portion	—
Long-term debt, net of current portion	$ 215,670

For the years ended December 31, 2020 and 2019, interest expense related to the Company's Loan Agreement was approximately $7.2 million and $0.3 million, respectively. The total carrying value of debt is classified as long-term on the consolidated balance sheet as of December 31, 2020 and 2019, respectively.

14. 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 "Charter Amendment"). At the Company's 2020 Annual Meeting of Stockholders, the stockholders of the Company approved the Charter Amendment, which was filed with the Secretary of State of the State of Delaware on May 29, 2020.

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

In 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. In March 2019, the Company issued 11,500,000 shares of Common Stock in connection with a public offering. In November 2019, the Company issued to RPI 6,666,667 shares of Common Stock pursuant to the RPI Purchase Agreement (for additional information refer to Note 12, *Sale of Future Royalties*). In October 2018, the Company issued, 9,583,334 shares of Common Stock in connection with a public offering.

The issuance of these shares contributed to significant increases in the Company's shares of common stock outstanding as of December 31, 2020 and 2019 and in the weighted average shares outstanding for the years ended December 31, 2020 and 2019 when compared to the comparable prior year periods.

As of December 31, 2020, a total of 20,405,623 shares of common stock were reserved for issuance upon (i) the exercise of outstanding stock options and the vesting of outstanding restricted stock units (ii) the issuance of additional stock awards under the Company's 2013 Stock Incentive Plan and 2013 Employee Stock Purchase Plan (iii) the issuance of common stock upon conversion of the outstanding Series A Preferred Stock and (iv) the issuance of common stock under the warrants.

Convertible Preferred Stock

On March 6, 2019, the Company entered into an Underwriting Agreement, (the "Preferred Stock Agreement"), that related to the public offering of 350,000 shares of Series A Convertible Preferred Stock, par value $0.0001 per share ("Series A Preferred Stock"), for a purchase price to the public of $115.00 per share. All of the Series A Preferred Stock was sold by the Company for net proceeds of $37.4 million.

Upon issuance, each share of Series A Preferred Stock included an embedded beneficial conversion feature because the market price of the Company's common stock on the date of issuance of the Series A Preferred Stock at $12.34 per share as compared to an effective conversion price of the Series A Preferred Stock of $11.50 per share. As a result, the Company recorded the intrinsic value of the beneficial conversion feature of $2.9 million as a discount on the Series A Preferred Stock at issuance. Because the Series A Preferred Stock is immediately convertible upon issuance and does not include mandatory redemption provisions, the discount on the Series A Preferred Stock was immediately accreted.

The Company evaluated the Series A Preferred Stock for liability or equity classification in accordance with the provisions of ASC 480, *Distinguishing Liabilities from Equity*, and determined that equity treatment was appropriate because the Series A Preferred Stock did not meet the definition of the liability instruments defined thereunder for convertible instruments. Specifically, the Series A Preferred Stock is not mandatorily redeemable and does not embody an obligation to buy back the shares outside of the Company's control in a manner that could require the transfer of assets. Additionally, the Company determined that the Series A Preferred Stock would be recorded as permanent equity, not temporary equity, based on the guidance of ASC 480 given that the holders of equally and more subordinated equity would be entitled to also receive the same form of consideration upon the occurrence of the event that gives rise to the redemption or events of redemption that are within the control of the Company.

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 our 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 refer to Note 12, *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 December 31, 2020.

15. Employee Benefit Plans

Stock Incentive Plans

In 2008, the Company's board of directors adopted and the Company's stockholders approved the 2008 Stock Incentive Plan (the "2008 Plan"), which provided for the granting of certain defined stock incentive awards to employees, members of the Company's board of directors and non-employee consultants, advisors or other service providers. In April 2013, the Company's board of directors adopted and the Company's stockholders approved the 2013 Stock Incentive Plan (the "2013 Plan"), which provides for the granting of certain defined stock incentive awards to employees, members of the Company's board of directors and non-employee consultants, advisors or other service providers. Additionally, in May 2013, the Company's board of directors adopted and the Company's stockholders approved the 2013 Employee Stock Purchase Plan (the "2013 ESPP"), which provides participating employees the option to purchase shares of the Company's common stock at defined purchase prices over six month offering periods.

Stock incentive awards granted under the 2013 Plan may be incentive stock options, non-qualified stock options, restricted stock awards, restricted stock units, stock appreciation rights and other stock-based awards under the applicable provisions of the Internal Revenue Code. Incentive stock options are granted only to employees of the Company. Non-qualified stock options and restricted stock and restricted stock units may be granted to officers, employees, consultants, advisors and other service providers. Incentive and non-qualified stock options granted to employees and generally vest over four years, with 25.0% vesting upon the one-year anniversary of the grant and the remaining 75.0% vesting monthly over the following three years. Restricted stock units granted to employees generally vest over four years in equal annual installments. Non-qualified stock options granted to consultants and other non-employees generally vest over the period of service to the Company. Initial non-qualified stock options granted to members of the Company's board of directors generally vest over four years, with 25% vesting upon the one-year anniversary of grant and the remaining 75% vesting monthly over the following three years. Annual non-qualified stock options granted to members of the Company's board of directors vest on the one-year anniversary of the grant. Incentive and non-qualified stock options expire ten years from the date of grant.

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 $27.6 million, $18.0 million, and $12.0 million for the years ended December 31, 2020, 2019, and 2018, respectively. Stock-based compensation expense is classified in the consolidated statements of operations and comprehensive loss as follows:

	Year Ended December 31,		
	2020	2019	2018
	(In thousands)		
Research and development	$ 9,093	$ 6,295	$ 4,083
General and administrative	18,516	11,721	7,921
Total	$ 27,609	$ 18,016	$ 12,004

Stock Options

The Company uses the Black-Scholes option-pricing model to measure the fair value of stock option awards. Weighted average assumptions used in this pricing model on the date of grant for options granted to employees are as follows:

	Year Ended December 31,		
	2020	2019	2018
Risk-free interest rate	0.9%	2.2%	2.6%
Expected life of options	5.99 years	6.0 years	6.0 years
Expected volatility of underlying stock	70.9%	72.0%	71.5%
Expected dividend yield	0.0%	0.0%	0.0%

There were no stock option awards granted to non-director, non-employees in the years ended December 31, 2020, December 31, 2019 or 2018.

The risk-free interest rate is based upon the U.S. Treasury yield curve in effect at the time of grant, with a term that approximates the expected life of the option. The Company calculates the expected life of options granted to employees using the simplified method as the Company has insufficient historical information to provide a basis for estimate. The Company determines the expected volatility using a blended approach encompassing its historical experience and the historical volatility of a peer group of comparable publicly traded companies with product candidates in similar stages of development to the Company's product candidates. The Company has applied an expected dividend yield of 0.0% as the Company has not historically declared a dividend and does not anticipate declaring a dividend during the expected life of the options.

The following is a summary of stock option activity for the year ended December 31, 2020:

	Number of Options	Weighted Average Exercise Price per Share	Weighted Average Remaining Contractual Term	Aggregate Intrinsic Value
	(In thousands)		(In years)	(In thousands)
Outstanding at December 31, 2019	8,087	$ 12.86		
Granted	3,522	18.70		
Exercised	(609)	10.98		
Forfeited or expired	(775)	15.71		
Outstanding at December 31, 2020	10,225	$ 14.77	7.8	$ 4,497
Exercisable at December 31, 2020	4,325	$ 13.66	6.6	$ 2,539

During the years ended December 31, 2020, 2019 and 2018, the Company granted stock options to purchase an aggregate of 3,522,258 shares, 4,222,693 shares, and 2,537,277 shares, respectively, at weighted-average grant date fair values per option share of $11.69, $6.99, and $9.49, respectively. The total grant date fair value of options that vested during the years ended December 31, 2020, 2019 and 2018 was $17.4 million, $13.2 million, and $12.1 million, respectively. The aggregate intrinsic value of stock options exercised was $5.5 million in 2020, $1.2 million in 2019 and $1.5 million in 2018.

As of December 31, 2020, there was $48.2 million in unrecognized stock-based compensation related to stock options that are expected to vest. These costs are expected to be recognized over a weighted average remaining vesting period of 2.6 years.

Restricted Stock Units

During the year-ended December 31, 2020, 541,431 restricted stock units ("RSUs") were granted to executives and employees. The awards were service-based. Assuming all service conditions are achieved, 25% of the RSUs would vest annually for four years.

	Number of Units	Weighted Average Grant Date Fair Value per Unit
	(In thousands except per share data)	
Outstanding at December 31, 2019	284	$ 9.34
Granted	541	19.64
Vested	(71)	10.59
Forfeited	(86)	13.33
Outstanding at December 31, 2020	668	$ 17.56

Compensation expense totaling $2.7 million and $0.5 million was recognized for the service-based RSUs for the years-ended December 31, 2020 and December 31, 2019, respectively.

As of December 31, 2020, there was $8.3 million of unrecognized compensation cost related to service-based RSUs that are expected to vest. These costs are expected to be recognized over a weighted average remaining vesting period of 2.7 years.

During 2019, the Company granted 604,000 RSUs to executives and employees, which contained performance conditions, 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.

	Number of Performance Based RSU Shares	Weighted Average Grant Date Fair Value per Unit
	(In thousands except per share data)	
Outstanding at December 31, 2019	443	$ 12.16
Granted	17	16.14
Vested	(432)	12.38
Forfeited	(28)	11.95
Outstanding at December 31, 2020	—	$ —

Compensation expense totaling $3.5 million was recognized for the performance-based RSUs for the year-ended December 31, 2020.

There was no unrecognized compensation cost as of December 31, 2020, related to performance-based RSUs, as all of the performance conditions have been achieved.

As of December 31, 2020, there were approximately 668,000 RSUs outstanding.

401(k) Savings Plan

The Company has a defined contribution 401(k) savings plan (the "401(k) Plan"). The 401(k) Plan covers substantially all employees, and allows participants to defer a portion of their annual compensation on a pretax basis. Company contributions to the 401(k) Plan may be made at the discretion of the board of directors. During the year ended December 31, 2014, the Company implemented a matching contribution to the 401(k) Plan, matching 50% of an employee's contribution up to a maximum of 3% of the participant's compensation. Company contributions to the 401(k) plan totaled $1.2 million, $0.6 million and $0.5 million in the years ended December 31, 2020, 2019 and 2018, respectively.

16. Loss per Share

As described in Note 2, *Summary of Significant Accounting Policies*, the Company computes basic and diluted earnings (loss) per share using a methodology that gives effect to the impact of outstanding participating securities (the "two-class method"). The two-class method was not applied for the years ended December 31, 2020, 2019, and 2018 due to the net loss recognized in each of those periods. In 2019 the net loss applicable to common stockholders did not equal net loss due to the accretion of the beneficial conversion feature of Series A Preferred Stock in the amount of $2.9 million. The beneficial conversion feature was initially recorded as a discount on the Series A Preferred Stock with a corresponding amount recorded to Additional Paid-in Capital. The discount on the Series A Preferred Stock was then immediately written off as a deemed dividend as the Series A Preferred Stock does not have a stated redemption date and is immediately convertible at the option of the holder.

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

	Year Ended December 31,		
	2020	2019	2018
	(In thousands except per share data)		
Net loss	$(231,694)	$(170,295)	$(123,630)
Accretion of Series A Preferred Stock	—	(2,940)	—
Net loss attributable to common stockholders	$(231,694)	$(173,235)	$(123,630)
Weighted average shares outstanding	100,960	89,891	71,864
Basic and diluted loss per share allocable to common stockholders	$ (2.29)	$ (1.93)	$ (1.72)

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:

	Year Ended December 31,		
	2020	2019	2018
	(In thousands)		
Stock options	10,225	8,087	5,153
Restricted stock units	669	757	—
Shares issuable under employee stock purchase plan	98	38	28
Series A Preferred Stock (if converted)	3,378	3,500	—
Warrants	2,500	2,500	—
	16,870	14,882	5,181

For the year ended December 31, 2019, the above table does not include the up to 6,250,000 shares subject to the Company's option to sell additional shares to RPI pursuant to the Put Option as the decision to exercise this option was within the Company's control. On December 30, 2019, the Company exercised its option to sell 2,500,000 shares of Common Stock to RPI for an aggregate of $50.0 million. The sale was effected on February 11, 2020.

17. Unaudited Quarterly Results

The results of operations on a quarterly basis for the years ended December 31, 2020 and 2019 are set forth below:

	Quarter Ended			
	March 31, 2020	June 30, 2020	September 30, 2020	December 31, 2020
	(In thousands, except per share data)			
Revenue:				
Product revenue, net	$ 1,284	$ 2,234	$ 3,445	$ 4,506
Collaboration revenue	70	233	121	3,869
Total revenue	1,354	2,467	3,566	8,375
Operating expenses:				
Cost of product revenue	614	1,022	1,608	1,823
Research and development	25,163	26,352	25,738	33,680
Selling, general and administrative	26,927	32,661	30,575	35,015
Total operating expenses	52,704	60,035	57,921	70,518
Operating loss	(51,350)	(57,568)	(54,355)	(62,143)
Other (expense) income, net:				
Interest (expense) income, net:	756	(569)	(1,364)	(3,505)
Other (expense), net	(48)	(15)	(42)	6
Non-cash interest expense related to sale of future royalties	(295)	(301)	(312)	(475)
Other (expense) income, net:	413	(885)	(1,718)	(3,974)
Income tax (provision)	—	2	—	(116)
Net loss	$(50,937)	$ (58,451)	$ (56,073)	$ (66,233)
Reconciliation of net loss to net loss attributable to common stockholders				
Net loss	$(50,937)	$ (58,451)	$ (56,073)	$ (66,233)
Accretion of convertible preferred stock	—	—	—	—
Net loss attributable to common stockholders	$(50,937)	$ (58,451)	$ (56,073)	$ (66,233)
Loss per share allocable to common stockholders:				
Basic	$ (0.51)	$ (0.58)	$ (0.55)	$ (0.65)
Diluted	$ (0.51)	$ (0.58)	$ (0.55)	$ (0.65)
Weighted-average common shares outstanding used in net loss per share attributable to common stockholders:				
Basic	99,616	101,104	101,512	101,596
Diluted	99,616	101,104	101,512	101,596

	Quarter Ended			
	March 31, 2019	June 30, 2019	September 30, 2019	December 31, 2019
	(In thousands, except per share data)			
Revenue:				
Product revenue, net	$ —	$ —	$ —	$ —
Collaboration revenue	7,891	5,900	5,715	4,294
Total revenue	7,891	5,900	5,715	4,294
Operating expenses:				
Cost of product revenue	—	—	—	—
Research and development	26,896	40,907	26,579	38,257
Selling, general and administrative	11,986	15,698	17,089	23,530
Total operating expenses	38,882	56,605	43,668	61,787
Operating loss	(30,991)	(50,705)	(37,953)	(57,493)
Other (expense) income, net:				
Interest income, net:	1,658	2,253	1,879	1,320
Other (expense) income, net	(6)	(13)	(15)	21
Non-cash interest expense related to sale of future royalties	—	—	—	(192)
Other income, net:	1,652	2,240	1,864	1,149
Income tax (provision)	—	—	—	(58)
Net loss	$(29,339)	$(48,465)	$ (36,089)	$ (56,402)
Reconciliation of net loss to net loss attributable to common stockholders				
Net loss	$(29,339)	$(48,465)	$ (36,089)	$ (56,402)
Accretion of convertible preferred stock	(2,940)	—	—	—
Net loss attributable to common stockholders	$(32,279)	$(48,465)	$ (36,089)	$ (56,402)
Loss per share allocable to common stockholders:				
Basic	$ (0.39)	$ (0.53)	$ (0.40)	$ (0.59)
Diluted	$ (0.39)	$ (0.53)	$ (0.40)	$ (0.59)
Weighted-average common shares outstanding used in net loss per share attributable to common stockholders:				
Basic	82,424	90,876	91,044	95,074
Diluted	82,424	90,876	91,044	95,074

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TRANSFER AGENT

The transfer agent is responsible, among other things, for handling stockholder questions regarding lost stock certificates, address changes, including duplicate mailings and changes in ownership or name in which shares are held. These requests may be directed to the transfer agent at the following addresses or telephone numbers:

Computershare Investor Services
P.O. Box 505000
Louisville, KY 40233-5005
877.373.6374 or 781.575.2879
www.computershare.com/investor

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INVESTOR RELATIONS

Bill Slattery, Jr.
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wslattery@realchemistry.com

ANNUAL MEETING

The Annual Meeting of Stockholders will be held at 10:00 a.m. ET on June 11, 2021

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NASDAQ: EPZM

CAUTIONARY NOTE ON FORWARD-LOOKING STATEMENTS

Any statements in this annual report to stockholders about future expectations, plans and prospects for Epizyme, Inc. and other statements containing the words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including: whether commercial sales of TAZVERIK for epithelioid sarcoma and follicular lymphoma in the approved indications will be successful; whether tazemetostat will receive marketing approval for epithelioid sarcoma or follicular lymphoma in other jurisdictions, full approval in the United States or approval in any other indication; whether results from preclinical studies or earlier clinical studies will be predictive of the results of future trials, such as the ongoing confirmatory trials; whether results from clinical studies will warrant meetings with regulatory authorities, submissions for regulatory approval or review by governmental authorities under the accelerated approval process; whether the company will receive regulatory approvals, including accelerated approval, to conduct trials or to market products; the impact of the COVID-19 pandemic on the company's business, results of operations and financial condition; whether the company's cash resources will be sufficient to fund the company's foreseeable and unforeseeable operating expenses and capital expenditure requirements; other matters that could affect the availability or commercial success of tazemetostat; and other factors discussed in the "Risk Factors" section of the company's annual report on Form 10-K for the year ended December 31, 2020 filed with the SEC and in the company's other filings from time to time with the SEC. In addition, the forward-looking statements included in this annual report to stockholders represent the company's views as of the date hereof and should not be relied upon as representing the company's views as of any date subsequent to the date hereof (provided that any such statements in the company's SEC filings represent the company's views as of the date of such filings). The company anticipates that subsequent events and developments will cause the company's views to change. However, while the company may elect to update these forward-looking statements at some point in the future, the company specifically disclaims any obligation to do so.

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NASDAQ: EPZM