

**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, 2018

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
(State or other jurisdiction of
incorporation or organization)

400 Technology Square, Cambridge, Massachusetts
(Address of principal executive offices)

26-1349956
(I.R.S. Employer
Identification No.)

02139
(Zip code)

617-229-5872

(Registrant's telephone number, including area code)

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

Common stock, \$0.0001 par value
(Title of each class)

Nasdaq Global Select Market
(Name of exchange on which registered)

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 if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

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 "accelerated filer," "large accelerated filer," "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act.

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

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

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

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, 2018, the last business day of the registrant's most recently completed second fiscal quarter, was approximately \$753.2 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 19, 2019 was 79,206,698.

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 2019 Annual Meeting of Stockholders are incorporated by reference into Part III of this Annual Report on Form 10-K to the extent stated herein.

Epizyme, Inc.
Annual Report on Form 10-K for the Fiscal Year Ended December 31, 2018

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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;
- 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;
- our ability to achieve anticipated milestones under our collaborations;
- the timing of and our ability to apply for, obtain and maintain regulatory approvals for our product candidates;
- the rate and degree of market acceptance and clinical utility of our products;
- our commercialization, marketing and manufacturing capabilities and strategy;
- 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. 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.

PART I

Item 1. Business

Overview

We are a late-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. We are developing our lead product candidate, tazemetostat, an oral, first-in-class, selective small molecule inhibitor of the EZH2 histone methyltransferase, or HMT, for the treatment of a broad range of cancer types in multiple treatment settings, and developing our novel G9a program, EZM8266, for the treatment of sickle cell disease, or SCD.

We have taken a “pipeline in a product” approach to developing tazemetostat with a broad clinical development program through company-sponsored studies and collaborations. This program is evaluating tazemetostat as both a monotherapy and combination treatment in hematological malignancies and solid tumors for both late and early lines of treatment. Tazemetostat has shown meaningful clinical activity as a monotherapy in multiple cancer indications and has been generally well-tolerated across clinical trials to date. Based on positive data in our two lead indications, epithelioid sarcoma and follicular lymphoma, or FL, and interactions with the United States Food and Drug Administration, or the FDA, we are planning to submit New Drug Applications, or NDAs, for accelerated approval of tazemetostat for each proposed indication in 2019, subject to the results of our ongoing trials in those indications.

In our hematological malignancy program, we are conducting a multi-cohort, global Phase 2 study evaluating tazemetostat’s treatment potential in patients with relapsed or refractory non-Hodgkin lymphoma, or NHL. Two cohorts are evaluating tazemetostat as a monotherapy for patients with relapsed or refractory FL, one of the most prevalent forms of NHL, both with and without EZH2 activating mutations. In December 2018, we completed target enrollment of FL patients in our study, with 54 patients with wild-type EZH2 and 45 patients with EZH2 activating mutations. Based on interactions with the FDA, we believe we have identified a path to submission for accelerated approval of tazemetostat in FL patients with either an EZH2 activating mutation or wild-type EZH2, whose disease has progressed following two or more lines of therapy. We are targeting submission of an NDA for accelerated approval for tazemetostat for FL in this population in the fourth quarter of 2019, subject to the results of our ongoing trial in this indication.

As part of an accelerated approval strategy, we will need to conduct a confirmatory clinical program to verify clinical benefit and support the full approval of tazemetostat. We intend to review our proposed confirmatory program with the FDA, and to finalize its design in the first half of 2019. We hope to leverage the confirmatory program to expand tazemetostat into the second-line treatment setting for patients with FL, both with and without EZH2 activating mutations. In addition, we plan to evaluate tazemetostat treatment in combination with other therapies. In mid-2019, we anticipate initiating a combination study that would compare tazemetostat plus rituximab and Revlimid, a chemotherapeutic-free treatment regimen referred to as R², versus R² with placebo in patients with relapsed or refractory FL, both with and without EZH2 activating mutations. In addition, we are finalizing plans for a trial of tazemetostat in combination with rituxan for the treatment of patients with relapsed and refractory FL. Based on clinical activity observed with tazemetostat in combination with R-CHOP as a front-line treatment for patients with diffuse large B-cell lymphoma, or DLBCL, we are evaluating the opportunity to investigate this combination as a front-line treatment for patients with FL. In collaboration with The Lymphoma Study Association, or LYSA, we are continuing to evaluate tazemetostat with R-CHOP as a front-line treatment for high-risk patients with DLBCL. In addition, Genentech Inc., or Genentech, is evaluating the combination of tazemetostat with its checkpoint inhibitor, Tecentriq (atezolizumab), for the treatment of patients with relapsed or refractory DLBCL, with preliminary data expected from that study in 2019.

In our solid tumor program, we are evaluating tazemetostat’s treatment potential in adults and children with molecularly defined solid tumors, including INI1- and SMARCA4-negative tumors, which we collectively refer to as INI1-negative tumors. We are conducting a multi-cohort global Phase 2 trial of tazemetostat in adults with INI1-negative tumors, including epithelioid sarcoma or chordoma. Based on positive data that we have observed in patients with epithelioid sarcoma in the ongoing Phase 2 study, we are targeting submission of our first NDA for

accelerated approval of tazemetostat for the treatment of epithelioid sarcoma in the second quarter of 2019. In connection with this submission, we will need to conduct a confirmatory program to verify clinical benefit and support the full approval of tazemetostat. We plan to explore with the FDA utilizing the natural history study in epithelioid sarcoma that we are conducting to serve as confirmatory evidence required in connection with any accelerated approval. The cohort of patients in the phase 2 study of chordoma patients is ongoing, and we are evaluating tazemetostat in the dose-expansion portion of a Phase 1 study in pediatric patients with INI1-negative tumors, with plans to report updated data in 2019.

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. We intend to build a focused field presence and marketing capabilities to commercialize tazemetostat for the epithelioid sarcoma and follicular lymphoma indications in the United States. We have begun building the infrastructure necessary to support the launch and marketing of tazemetostat for epithelioid sarcoma, and believe we can adequately address this patient population through a modest field force of less than 25 professionals. For geographies outside the United States, we are evaluating the most efficient path to reach patients, including through potential collaborations.

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, with or without activating EZH2 mutations, relapsed or refractory DLBCL with EZH2 activating mutations and metastatic or locally advanced epithelioid sarcoma 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 FL, 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.

Beyond tazemetostat, we are building an early pipeline to further support our leadership in epigenetics. We are developing our wholly-owned G9a candidate, EZM8266, for the treatment of people with sickle cell disease. We have completed IND-enabling studies for this program and plan to begin clinical evaluation with a safety and dose-finding study in the second half of 2019. In November 2018, we entered a strategic collaboration with Boehringer Ingelheim International GmbH, or Boehringer Ingelheim, focused on the research, development and commercialization of novel small molecule inhibitors, discovered by us, directed toward two previously unaddressed epigenetic targets as potential therapies for people with cancer. Specifically, these targets are enzymes within the helicase and histone acetyltransferase, or HAT, families that when dysregulated have been linked to the development of cancers that currently lack therapeutic options. We also have collaborations with Glaxo Group Limited (an affiliate of GlaxoSmithKline), or GSK, focused on the development of PRMT inhibitors discovered by us, and with Celgene Corporation and Celgene RIVOT Ltd., an affiliate of Celgene Corporation, which we collectively refer to as Celgene, focused on the development of pinometostat and small molecule inhibitors directed to three HMT targets.

Our Corporate Strategy

Our goal is to become a biopharmaceutical company developing and commercializing novel epigenetic therapies for people with cancer and other serious diseases.

The key elements of our corporate strategy are to:

- rapidly advance the clinical development of tazemetostat in solid tumors and hematological malignancies;
- collaborate closely with the FDA and other regulatory bodies to pursue the registration of tazemetostat with accelerated approval for epithelioid sarcoma and FL;
- expand the treatment utility for tazemetostat through a broad development program evaluating its benefit in different combinations, in both early- and late-lines of treatment and in additional indications;
- establish commercialization capabilities in the United States;

To better understand the potential risk of T-LBL in our trials, and the overall benefit-risk of tazemetostat across hematological malignancies and solid tumors in both adults and children, we conducted a comprehensive assessment of tazemetostat based on published literature and the clinical experience with tazemetostat to date. A panel of external scientific and medical experts reviewed and validated the findings for the assessment, and we submitted the assessment to the FDA as part of our complete response submission.

To resolve the partial clinical hold in the United States, we re-consented all patients in our clinical trials and updated our informed consent form based on the safety report. We also aligned with the FDA on certain amendments to our tazemetostat study protocols focused on increasing patient monitoring and putting in place risk-mitigation strategies designed to reduce the risk of potential future secondary malignancies.

In November 2018, Germany's Federal Institute for Drugs and Medical Devices lifted the partial clinical hold that it had imposed in Germany. The partial clinical hold in France remains in effect. We have re-activated clinical trial sites in the United States, resuming enrollment in our tazemetostat clinical trials at those sites, and are currently re-activating sites in Germany to resume enrollment there. We are engaging with regulators in France to work toward similar resolutions in that country.

Tazemetostat Clinical Program in Epithelioid Sarcoma and Other INI1-Negative Solid Tumors

Background on Epithelioid Sarcoma: 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 have a 5-year overall survival of less than 20 percent and there are no currently approved treatment options specifically indicated for epithelioid sarcoma. 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 disease that would be eligible for systemic therapy. However, because there are no treatments specifically indicated for epithelioid sarcoma, we believe the true prevalence of this disease is unknown.

Background on INI1-Negative Solid Tumors: INI1 and SMARCA4 are subunits of SWI/SNF, a chromatin modifying protein complex that opposes the activity of PRC2, the complex within which EZH2 resides. Loss of INI1 or SMARCA4 in specific cell backgrounds is believed to cause dysregulation in the balance between SWI/SNF and PRC2, and thus cause tumors to become sensitive to EZH2 inhibition. This effect was observed in a preclinical study of tazemetostat in a xenograft model of MRT in which tazemetostat caused a dose-dependent regression in INI1-negative tumors. INI1-negative tumors can appear in many different tissue types, and can present as epithelioid sarcoma, MRT, extraskeletal myxoid chondrosarcoma, peripheral nerve sheath tumor and myoepithelial carcinoma, among several others. SMARCA4-negative tumors can also appear as different tumor types, including MRTO.

INI1-negative or certain SMARCA4-negative tumors are typically aggressive cancers with few to no approved treatments, as with epithelioid sarcoma. INI1-negative tumors are most commonly seen in infants through young adults, while SMARCA4-negative tumors are most commonly seen in teenagers and young adults. It is estimated that approximately 2,000 new patients (adults and children) with INI1-negative tumors and certain SMARCA4-negative tumors are diagnosed annually in the United States and other major pharmaceutical markets; however, we believe that the actual number may be higher, as these types of molecularly defined cancers are significantly under-reported today.

Phase 2 Clinical Program in Adults: We are conducting a multi-cohort, global Phase 2 trial of tazemetostat in adults with INI1-negative tumors, including epithelioid sarcoma or chordoma. Patients in the Phase 2 trial are dosed at 800 mg twice daily with tablets taken orally.

This trial was designed to enroll up to 250 patients. The patients in the trial were previously stratified into one of five cohorts: epithelioid sarcoma (n=60), rhabdoid tumors (n=30), other INI1-negative tumors (n=30), renal medullary carcinoma (n=30) and synovial sarcoma (n=30). In 2017, we opened two additional cohorts: INI1-negative chordoma (n=30) and a cohort to explore the effect of tazemetostat treatment on immune responsiveness by obtaining paired tumor biopsies in epithelioid sarcoma patients (n=40). The primary endpoint for all cohorts, except synovial sarcoma and the paired biopsy cohort, is overall response rate. The primary endpoint for the synovial sarcoma cohort is disease control, defined as a complete response, partial response, or stable disease, at 16 weeks.

The primary endpoint for the paired biopsy cohort is assessment of pre- and post-dose biopsies for immune priming (e.g. PD-L1 and CD8 IHC).

Epithelioid Sarcoma Cohort: The epithelioid sarcoma cohort in our Phase 2 trial represents the largest prospective trial of epithelioid sarcoma with any approved or investigational treatment to date. The cohort was initially designed to enroll 30 patients and was expanded in December 2016 to enroll an additional 30 patients based on encouraging early activity.

We completed enrollment of the epithelioid sarcoma cohort in July 2017 with 24 treatment-naïve patients and 38 relapsed or refractory patients for a total of 62 patients. The primary endpoint of the cohort is overall response rate, or ORR, comprised of complete and partial responses as measured by Response Evaluation Criteria in Solid Tumors, or RECIST 1.1. We are enrolling up to an additional 40 patients in a new cohort to explore the effect of tazemetostat treatment on immune responsiveness by obtaining paired tumor biopsies in these patients.

In October 2018, interim data from the 62 patients in the ongoing epithelioid cohort of the Phase 2 study were presented during the European Society for Medical Oncology, or ESMO, Annual Congress. Interim data as of the August 21, 2018 data cut-off date showed that tazemetostat treatment demonstrated clinically meaningful activity in the trial, with durable objective responses and encouraging overall survival, and that tazemetostat was generally well-tolerated. As of the data cut-off date, eight patients had confirmed objective responses for an ORR of 13 percent in the overall intent-to-treat population. In the subset of 24 patients who were treatment-naïve, 5 patients had confirmed objective responses for an ORR of 21 percent, and in the subset of 38 relapsed or refractory patients, 3 patients had confirmed objective responses for an ORR of eight percent. Since the data cut-off, one additional patient in the treatment-naïve subgroup subsequently achieved an objective response, bringing the total to six responders in the treatment-naïve group, for an ORR of 24 percent, and to nine responders in the overall intent-to-treat population, for an ORR of 15 percent.

Key secondary endpoints include durability of response, overall survival and safety. As of the data cut-off date, in the intent-to-treat population, tazemetostat has demonstrated a median duration of response of 48 weeks and is still ongoing. In the treatment-naïve subset and the relapsed or refractory subset, tazemetostat demonstrated a median duration of response of 41 weeks and 48 weeks, respectively, and are still ongoing. The interim median overall survival for the intent-to-treat population was 82.4 weeks. For the subset of relapsed or refractory patients, the median overall survival was 47.4 weeks, and the median overall survival for the treatment-naïve patients had not yet been reached.

Other secondary endpoints that are markers of clinical activity are the disease control rate, or DCR, which is comprised of confirmed objective responses for any duration or disease stabilization of 32 weeks or more, and progression-free survival, or PFS. The DCR and the PFS rates in the intent-to-treat population were 24 percent and 16.1 weeks, respectively. The median PFS was 25.7 weeks in the treatment-naïve patients and 14.7 weeks in the relapsed or refractory patients. DCR for treatment-naïve patients was 38 percent and 16 percent in relapsed or refractory patients.

Tazemetostat was generally well-tolerated in epithelioid sarcoma patients, with no discontinuations or deaths due to treatment-related adverse events, or AE's. The majority of treatment-related AE's were grade 1 or 2, and only 13 percent of patients experienced a grade 3 or 4 treatment-related AE. Treatment-related events with an incidence of 10 percent or greater were fatigue, nausea, decreased appetite, vomiting, diarrhea and weight decrease, and anemia.

Due to a lack of treatment options and the severity of epithelioid sarcoma, we believe that this patient population may represent the fastest potential path to a first NDA submission, approval and commercial launch for tazemetostat. Based on positive data from the ongoing study, we plan to submit our first NDA to the FDA for accelerated approval of tazemetostat for epithelioid sarcoma in the second quarter of 2019. In connection with this submission and an accelerated approval, we would need to conduct a confirmatory program to verify clinical benefit and support full approval of tazemetostat. We plan to explore with the FDA utilizing the natural history study in epithelioid sarcoma that we are conducting to serve as confirmatory evidence required in connection with any accelerated approval. We are in the process of completing a multi-center study with a comprehensive benchmarking of current therapies, the clinical experience with those regimens, and treatment efficacy and safety in epithelioid sarcoma patients. We expect the data from this natural history study, which is largest of its kind in epithelioid sarcoma patients, will further contextualize the data observed with tazemetostat in epithelioid sarcoma patients and highlight the need for a meaningful new treatment option with therapeutic benefit over existing treatments. If our

planned NDA is submitted and granted accelerated approval in 2019, we anticipate that we could commercially launch tazemetostat as early as 2020.

Other IN11-Negative Tumor Cohorts: In November 2017, we reported that both the malignant rhabdoid tumor cohort and other IN11-negative tumor cohorts of the ongoing Phase 2 study surpassed their futility assessment with objective responses observed in both populations; however, the activity was not sufficient to warrant continued development in these cohorts. We added an additional cohort specifically for chordoma patients due to the previously observed high rate of enrollment of these patients in the other IN11-negative cohort of the Phase 2 study. Assessment of tazemetostat activity in this cohort remains ongoing.

Phase 1 Clinical Program in Children: We are conducting a global Phase 1 clinical trial of tazemetostat in approximately 110 children with IN11-negative solid tumors. We have completed the dose-escalation portion and have advanced to the dose-expansion stage of this trial. In the trial, we used 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. Enrollment is completed in all cohorts with the exception of the chordoma cohort and other IN11-negative solid tumors.

In May 2018 at the American Society of Pediatric Hematology/Oncology (ASPHO) Conference, data from the dose-escalation portion of the Phase 1 study were presented. Forty-six patients were treated with seven dose levels, ranging from 240 to 1200 mg/m² of twice-daily tazemetostat. Four patients who were treated at doses from 520 to 900 mg/m² demonstrated RECIST/RANO-confirmed objective responses.

Tazemetostat Clinical Program in Non-Hodgkin Lymphoma

We are executing a broad clinical development program for tazemetostat as both a monotherapy and combination treatment in relapsed or refractory and first-line NHL. We recently identified a path to submission for accelerated approval of tazemetostat in EZH2 mutant and wild-type FL patient populations, for patients whose disease has progressed following two or more lines of therapy. We also plan to seek to expand FL use into early lines of FL treatment through different combination regimens. We are also leveraging strategic collaborations to explore tazemetostat as a combination therapy in patients with DLBCL.

Background on NHL: Two types of NHL, FL and DLBCL of germinal center origin, are associated with oncogenic EZH2 mutations. In our preclinical studies, we observed that NHL cells were sensitive to EZH2 inhibitors such as tazemetostat and that NHL cells bearing EZH2 mutations were particularly responsive to such treatment. EZH2 plays a critical role at various stages in normal B-cell maturation, and a particularly important role during the stage of B-cell development known as the germinal center reaction. Recent research has demonstrated that EZH2 acts as a key gatekeeper for B-cell maturation and differentiation. Our own ongoing research suggests that it is a combination of stem or progenitor cell of origin together with specific genetic lesions that confer sensitivity of cancer cells to EZH2 inhibition. An analysis of patient samples with germinal center derived NHL has revealed a number of genetic alterations that impact EZH2 function in ways that may confer sensitivity to EZH2 inhibition. While FL remains our lead NHL target patient population for tazemetostat, our clinical and preclinical data suggest patients with other forms of B-cell NHL may also benefit from tazemetostat. We may explore the development of tazemetostat for those other forms of B-cell NHL.

Background on FL: The population of patients with FL is large and growing. 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 the number of treatment-eligible FL patients in the United States and five largest European Union countries as measured by population, or EU5, is approximately 36,000 patients and 30,000 patients, respectively. 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, salvage treatment regimens are typically other combinations of rituximab and other chemotherapy drugs or duvelisib, idealisib or copanlisib. There are no approved treatments specifically indicated for patients with FL with an EZH2 mutation.

Phase 2 Clinical Program: We are conducting a multi-cohort, global Phase 2 study evaluating tazemetostat's treatment potential in patients with relapsed or refractory NHL. Two cohorts are evaluating tazemetostat as a monotherapy for patients with relapsed or refractory FL, one with patients with EZH2 activating mutations and one with patients with wild-type EZH2. Two cohorts were evaluating tazemetostat as a monotherapy for patients with relapsed or refractory DLBCL, one with patients with EZH2 activating mutations and one with patients with wild-type EZH2, and an additional arm was evaluating tazemetostat as a combination agent with prednisone in patients with relapsed or refractory DLBCL.

Follicular Lymphoma Cohorts: We have completed target enrollment of both FL cohorts in the Phase 2 trial, including 45 patients with EZH2 activating mutations and 54 patients with wild-type EZH2. Patients in the trial are dosed with tazemetostat at 800 mg twice daily with tablets taken orally. The primary endpoint of the trial in these cohorts is overall response rate. Secondary endpoints include duration of response, progression free survival, overall survival, safety and population pharmacokinetics.

In June 2018, at the 23rd Congress of the European Hematology Association, we presented updated interim data of tazemetostat for the treatment of patients with FL. As of the May 1, 2018 data cut-off date, in 28 evaluable EZH2 mutation patients, we observed a confirmed objective response rate of 71 percent, with 11 percent of patients having achieved a complete response and 61 percent of patients having achieved a partial response. In addition, as of the data cut-off date, these patients had a median PFS of 49 weeks and a median duration of response of 32 weeks. Both endpoints have continued to mature since that cutoff. In the 54 evaluable wild-type EZH2 patients, we observed a confirmed objective response rate of 33 percent, with six percent of patients having achieved a complete response and 28 percent of patients having achieved a partial response. As of the data cut-off date, these patients had a median PFS of 30 weeks and a median duration of response of 76 weeks with the median duration of response continuing to mature, with more than half of the patients with responses still on therapy at the time. Notably, 100 percent of patients with an EZH2 activating mutation and 78 percent of patients with wild-type EZH2 experienced a reduction in tumor burden, an important measure of disease stabilization and clinical response in this unmet need population.

In addition, tazemetostat has been generally well-tolerated in this study. Interim safety results as of May 1, 2018 showed only six percent of FL patients discontinued treatment due to treatment-related adverse events. Adverse events of grade 3 or higher were reported across 17 percent of patients, the most frequent of which included thrombocytopenia, anemia, asthenia and fatigue.

We are conducting a natural history study of approximately 1000 FL patients to evaluate whether or not patients with EZH2 activating mutations are more likely to respond to any treatment than patients with wild-type EZH2. The data collection will occur from international lymphoma centers of excellence. Preliminary findings from this retrospective study showed a frequency of EZH2 mutations that is consistent with our estimated 20% regardless of the line of treatment; that patients with EZH2 activating mutations are not hyper-responsive to any treatment in any line of therapy; and that overall survival is equivalent for both FL patient populations when treated with currently available therapies. These data strengthen our belief that the benefits observed with tazemetostat in our Phase 2 study are due to tazemetostat treatment.

Based on interactions with the FDA, we believe we have identified a path to submission for accelerated approval of tazemetostat in FL patients with either EZH2 activating mutations or wild-type EZH2, whose disease has progressed following two or more lines of therapy. Based on this strategy, we anticipate submitting an NDA for this indication in the fourth quarter of 2019. As part of an accelerated approval strategy, we will need to conduct a confirmatory clinical program to verify clinical benefit and support the full approval of tazemetostat. We intend to review our proposed confirmatory program with the FDA, and to finalize its design in the first half of 2019. We continue to discuss with the FDA whether or not a companion or complementary diagnostic would be necessary. In parallel, we continue to collaborate with Roche Molecular Systems Inc. on the development of a companion or complementary diagnostic, if necessary. We hope to leverage the confirmatory program to expand tazemetostat into the second-line treatment setting for patients with FL, both with and without EZH2 activating mutations. In addition, we plan to evaluate the use of tazemetostat for the treatment of FL in combination with other therapies.

Based on interim data assessments in the Phase 2 study cohorts evaluating tazemetostat as a monotherapy and combination agent with prednisolone in relapsed or refractory patients with DLBCL, we determined that the activity

observed was not sufficient to warrant further development of tazemetostat for DLBCL as monotherapy or in combination with prednisolone.

Tazemetostat Combination Studies in NHL: In addition to evaluating tazemetostat as a monotherapy for FL, we are investigating the combination of tazemetostat with other cancer agents in both the relapsed or refractory and front-line settings of NHL.

- **FL Combinations.** We have seen extensive preclinical synergy of tazemetostat with a number of targeted agents and chemotherapies used for, or in development for the treatment of FL. Based on the monotherapy efficacy and safety data generated to-date, we plan to explore the potential of tazemetostat in earlier lines of FL as combination therapy. In 2019, we intend to initiate a study that would assess the activity of tazemetostat in combination with the chemotherapeutic-free treatment regimen of rituximab and Revlimid, known as R2, versus R2 with placebo in patients with relapsed or refractory FL. In addition, we are finalizing plans for a trial of tazemetostat in combination with rituxan for the treatment of patients with relapsed and refractory FL. Based on the clinical activity observed with tazemetostat in combination with R-CHOP as a front-line treatment for patients with DLBCL, we are considering opportunities to expand the evaluation of this combination into treatment-naïve, high-risk patients with FL.
- **DLBCL Combination with R-CHOP.** We are studying tazemetostat in combination with R-CHOP, in collaboration with LYSA, a premier cooperative group in France dedicated to clinical and translational research for lymphoma. This multi-center Phase 1b/2 trial in front-line, elderly high-risk patients with DLBCL is enrolling up to 133 patients. Primary endpoints in the trial include complete response rate, safety and tolerability of the combination. Secondary endpoints include ORR and 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.
- **Tecentriq (atezolizumab).** Based on preclinical evidence showing that EZH2 inhibition may enhance the activity of checkpoint inhibitors, we entered into a collaboration agreement with Genentech to conduct a global Phase 1b trial combining tazemetostat with atezolizumab, a PD-L1 inhibitor. The global trial was initiated in the fourth quarter of 2016 and is being conducted by Genentech. In March 2018, Genentech completed enrollment of the trial with 45 patients with relapsed or refractory DLBCL. Primary endpoints in the trial include safety and combination tolerability with the objective of establishing a recommended Phase 2 dose. Secondary and exploratory endpoints include overall response, objective response, duration of response, pharmacokinetics and preliminary biomarker assessment. Preliminary data from this study are anticipated to be reported in 2019.

Tazemetostat in Other Solid Tumors

We intend to expand the clinical investigation of tazemetostat to other solid tumors. This includes defining new monotherapy indications based on a strong scientific rationale and patient stratifications, and identifying key pathways for synergistic combinations that would enhance efficacy without compromising safety. We intend to do this by targeting specific patient populations where there is an unmet need, looking at indications for which there are efficient regulatory paths and areas where tazemetostat can be highly competitive.

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 castration-resistant prostate cancer, or CRPC; moderate to high EZH2 expression has been associated with worse failure-free survival; and, treatment with an EZH2 inhibitor after resistance to the standards-of-care results in recovery of sensitivity to these agents. We are planning to begin a clinical study in mid-2019 evaluating tazemetostat for people with resistant CRPC in combination with abiraterone or enzalutamide, the standard-of-care treatments for this disease.

Platinum-Resistant Solid Tumors: We are also 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. External research suggests that when DNA damage occurs, PARP enzymes catalyze modification of EZH2 which leads to decreased EZH2 enzyme activity. We believe that by adding an EZH2 inhibitor to a PARP inhibitor, certain cancer cell lines may have increased sensitivity and response to PARP inhibition. We plan to initiate a basket study in select tumor types in the second half of 2019.

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 plan to evaluate 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.

In July 2017, we announced that the NCI's Pediatric MATCH trial will include 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 will evaluate 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.

G9a Inhibitory Program for Sickle Cell Disease

Background on G9a: Elevation of fetal hemoglobin, which is normally silenced after birth, has been shown to have disease-modifying potential for patients with β -globinopathies, such as sickle cell disease, and β -thalassemia. Multiple academic groups previously identified that inhibition of G9a, an HMT, leads to increased levels of fetal hemoglobin in preclinical *in vitro* studies.

Background on Sickle Cell Disease: Sickle cell disease is an inherited red blood cell disorder. People with sickle cell disease have abnormal hemoglobin, called hemoglobin S or sickle hemoglobin, in their red blood cells. A monogenic disease, sickle cell disease is most common in people with African ancestry. Approximately 300,000 people have sickle cell disease globally, with an estimated 150,000 of those patients located in the United States and Europe. Potential complications include stroke, vaso-occlusive crises associated with pain attacks, acute chest syndrome and anemia. Recurrent acute pain crises and chronic long-term organ damage are the hallmarks for sickle cell disease. However, symptoms can vary significantly in different patients, and better treatments for sickle cell disease patients are needed. Life expectancy of sickle cell disease patients still lags the life expectancy of the general population.

EZM8266 Program: Building upon the industry's findings on the G9a target, our scientists leveraged our expertise in HMT drug discovery to generate potent, selective inhibitors of G9a with drug-like properties. We initially developed a tool compound that induced on-target elevation of fetal hemoglobin in cell culture assays, and elicited significant increases in mouse embryonic hemoglobin, which is the rodent developmental equivalent of human fetal hemoglobin. We believe these findings represent the first *in vivo* study to demonstrate reactivation of developmental hemoglobin with a G9a inhibitor. Following these efforts, we went on to identify the next product candidate in our pipeline, EZM8266, a potent, selective and orally bioavailable G9a inhibitor. Throughout 2018, we completed the necessary pre-IND work, including good laboratory practice and toxicology studies. We plan to submit and IND and initiate clinical development for EZM8266 for the treatment of people with sickle cell disease, beginning with a dose-finding and safety study in healthy volunteers in the second half of 2019. We hold worldwide development and commercialization rights to EZM8266.

Pinometostat for DOT1L Cancers

Background on 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.

Through external collaborators, the ability to enhance pinometostat's efficacy in leukemia through combinations with other anti-cancer agents is being explored in preclinical studies. We retain all U.S. rights to pinometostat and have granted Celgene an exclusive license to pinometostat outside of the United States. 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.

Other Pipeline Programs

In addition to tazemetostat, pinometostat and EZM8266, we also have a pipeline of drug discovery programs that target other prioritized chromatin modifying proteins, or CMPs. These programs are directed against both hematological malignancies and solid tumors and include approaches to patient stratifications.

In November 2018, we entered into a global collaboration with 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 histone acetyltransferase, or HAT, families that when dysregulated have been linked to the development of cancers that currently lack therapeutic options. We plan to work with Boehringer Ingelheim in 2019 on these two programs.

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.

Under our collaboration with Celgene, we are developing small molecule inhibitors directed to three HMT targets, in addition to pinometostat. Under the collaboration, we are responsible for all preclinical discovery work as well as Phase 1 clinical development for all three targets. Celgene has 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. We retain rights to develop and commercialize inhibitors directed at the third target in the United States.

Our Epigenetic Approach

Epigenetics refers to a broad regulatory system that controls gene expression without altering the makeup 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 chromatin modifying proteins, or 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.

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 the newer target classes, histone acetyltransferases, or HATs, and helicases, which are the subject of our 2018 collaboration with Boehringer Ingelheim. Beyond cancer, however, HMTs and other CMPs have been implicated as pathogenic drivers of a number of diseases with significant unmet medical need. At the end of 2017 we nominated our first development candidate, EZM8266, a HMT inhibitor targeting sickle cell disease. Targeting pathogenic CMPs affords us multiple opportunities to create, develop and commercialize novel therapeutics.

Our Collaborations

We have entered into several key strategic collaborations. These therapeutic collaborations have provided us with \$232.8 million in non-equity funding through December 31, 2018. Our Celgene, GSK, and Boehringer Ingelheim collaborations provide us with the potential for significant research, development, regulatory and sales-based milestone payments as well as royalties or profit sharing on net product sales. Our Boehringer Ingelheim collaboration provides for research funding and our Celgene and Boehringer Ingelheim collaborations also provide for potential development co-funding. In addition, we have entered into a collaboration to develop a companion diagnostic with Roche Molecular Systems, Inc., or Roche Molecular. Key terms of these collaborations are summarized below.

Celgene

Overview. In July 2015, we entered into an amendment and restatement of our collaboration and license agreement dated April 2012 with Celgene. Under the original agreement, we granted Celgene an exclusive license, for all countries other than the United States, to small molecule HMT inhibitors targeting the DOT1L HMT, including pinometostat, and an option, on a target-by-target basis, to exclusively license, for all countries other than the United States, rights to small molecule HMT inhibitors targeting any HMT targets, other than EZH2 HMT, including tazemetostat, and targets covered by our pre-existing collaboration and license agreement dated January 8, 2011 with GSK. Under the original agreement, Celgene's option was exercisable during an option period that would have expired in July 2015. Under the amended and restated collaboration and license agreement:

- Celgene retained its exclusive license to small molecule HMT inhibitors targeting DOT1L, including pinometostat,
- Celgene's other option rights were narrowed to small molecule HMT inhibitors targeting three predefined targets, which we refer to as the Option Targets,
- The exclusive licenses to HMT inhibitors targeting two of the Option Targets that Celgene may acquire were expanded to include the United States, with the exclusive license to HMT inhibitors targeting the third Option Target continuing to be for all countries other than the United States,
- Celgene's option period was extended for each of the Option Targets and Celgene's option is exercisable at the time of our investigational new drug application, or IND, filing for an HMT inhibitor targeting the applicable Option Target, upon the payment by Celgene at such time of a pre-specified development milestone-based license payment,
- Celgene's license may be maintained beyond the end of Phase 1 clinical development for each of the Option Targets, upon payment by Celgene at such time of a pre-specified development milestone-based license payment, and
- Our research and development obligations with respect to each Option Target under the amended agreement were extended for at least an additional three years, subject to Celgene exercising its option with respect to such Option Target at IND filing. Subject to our opt-out rights, our research and development obligations were expanded to include the completion of a Phase 1 clinical trial as to each Option Target following Celgene's exercise of its option at IND filing.

Through December 31, 2018, we have recognized \$99.2 million in total collaboration revenue. To date, we have received \$75.0 million in upfront payments (including \$10.0 million as part of the amended and restated agreement) and \$25.0 million from the sale of our series C preferred stock to an affiliate of Celgene, of which \$3.0 million was considered a premium and included as collaboration arrangement consideration for total upfront payments of \$78.0 million. In addition, we have received a \$25.0 million clinical development milestone payment in 2014 and \$7.0 million in global development co-funding through December 31, 2018. We are eligible to earn an aggregate of up to \$75.0 million in development milestones and license payments, up to \$365.0 million in regulatory milestone payments and up to \$170.0 million in sales milestone payments related to the three Option Targets. We are eligible to earn \$35.0 million in an additional clinical development milestone payment and up to \$100.0 million in regulatory milestone payments related to DOT1L.

We are also eligible to receive royalties as follows:

- As to DOT1L, we retain all product rights in the United States and are eligible to receive royalties at defined percentages ranging from the mid-single digits to the mid-teens on annual net product sales outside of the United States, subject to reductions in specified circumstances;
- As to the Option Target for which Celgene's option rights do not include the United States, if Celgene exercises its option as to such Option Target, we will retain all product rights in the United States and will be eligible to receive royalties, once an initial threshold of net product sales (for which we will not receive royalties) is exceeded, at defined percentages ranging from the mid-single digits to the low-double digits on net product sales outside of the United States, subject to reductions in specified circumstances; and
- As to the other two Option Targets, if Celgene exercises its option as to those Option Targets, we will be eligible to receive royalties, once an initial threshold of net product sales (for which we will not receive royalties) is exceeded, for each such Option Target at defined percentages ranging from the mid-single digits to the low-double digits on net product sales on a worldwide basis, subject to reductions in specified circumstances.

For DOT1L and, after Celgene's payment of the specified IND filing license payment for each Option Target, for each such Option Target, we are responsible for the conduct and funding of Phase 1 clinical trials, subject to our right to opt-out of such responsibilities as described below. Celgene may obtain a license to small molecule HMT inhibitors targeting each Option Target at the time of our IND filing for an HMT inhibitor for such target by exercising its option and paying us a specified license payment. Celgene may maintain its license with respect to an Option Target at the conclusion of the Phase 1 clinical trial of the Option Target by paying us a specified additional license payment. If Celgene does not elect to obtain a license during the option exercise period applicable to an Option Target, or to pay the specified IND license payment or end of Phase 1 license payment, we will retain worldwide rights to HMT inhibitors directed to the Option Target, other than HMT inhibitors that may be provided by Celgene if we were to agree to their introduction into the collaboration.

Research Obligations. We are primarily responsible for the research strategy under the collaboration. During each applicable option period we are required to use commercially reasonable efforts to carry out an agreed research plan for each Option Target, subject to our Opt-Out right described below. For the DOT1L target and each of the Option Targets, we are required to conduct and solely fund development costs of the Phase 1 clinical trials for HMT inhibitors directed to such targets, including for pinometostat. After completion of Phase 1 development, as to DOT1L and the Option Target for which we retain U.S. rights, we and Celgene will equally co-fund global development and each party will solely fund territory-specific development costs for its territory; and, as to the other two Option Targets, after completion of Phase 1 development, Celgene will solely fund all development costs on a worldwide basis.

Governance. Our collaboration with Celgene is guided by (a) a joint research committee, with authority over all activities performed under the research plan with respect to the two Option Targets as to which we granted worldwide rights; (b) a joint development committee, with authority over shared development activities with respect to DOT1L and the Option Target for which we retain U.S. rights; and (c) a joint commercialization committee, with authority over the commercialization of products developed under shared development programs with respect to DOT1L and the Option Target for which we retain U.S. rights. Subject to limitations specified in the amended and restated agreement, if the applicable governance committee is not able to make a decision by consensus and the

parties are not able to resolve the issue through escalation to specified senior executive officers of the parties, then (a) prior to Celgene's exercise of its option, we generally have final decision-making authority over research and development matters with respect to the Option Targets; (b) with respect to DOT1L and any Option Targets for which Celgene has exercised its option, Celgene generally has final decision-making authority over global development matters, including over global activities and related expenses that we are obligated to co-fund, unless we exercise our opt-out right as to such licensed program, and except that with respect to the Option Target for which we retain U.S. rights, the parties have mutual decision-making authority even after Celgene exercises its option as long as Celgene engages in a competitive development program with respect to such Option Target. Each party has final decision-making authority over commercialization matters in its respective territory.

Opt-Out Right. On an Option Target-by-Option Target basis, we have the right, in our sole discretion, to opt-out of further participation in any research and/or development activities after completion of the initial research plan and prior to the filing of an IND for an HMT inhibitor directed to the applicable Option Target, or the Pre-IND Opt-Out. Following exercise of a Pre-IND Opt-Out, if Celgene exercises its option as to the Option Target, Celgene will no longer be required, to the extent not already paid, to make the specified IND license payment or end of Phase 1 license payment to us, specified sales milestone payments will no longer be payable and all royalties on net product sales of applicable licensed products that become payable to us will be reduced by a specified percentage. Additionally, if Celgene exercises its option as to such Option Target, we are obligated to grant Celgene an exclusive worldwide license to HMT inhibitors directed to the applicable Option Target, even if we would otherwise retain U.S. rights to HMT inhibitors directed to the applicable Option Target. Additionally, on a licensed program-by-licensed program basis, we have the right, in our sole discretion, to opt-out of further participation in and co-funding of development, other than specified costs necessary to complete development activities in process at the time we exercise our opt-out right. We can exercise our licensed program opt-out right at specified times: (a) when the clinical trial stopping rules set forth in a clinical trial protocol for DOT1L or the Option Target for which we retain U.S. rights dictate that such clinical trial be stopped, or the Post-EOP1 Clinical Opt-Out; or (b) for any or no reason, in a licensed program for DOT1L or the Option Target for which we retain U.S. rights, during specified periods before the scheduled initiation of the first pivotal clinical trial or before the estimated date of filing of the first NDA for an HMT inhibitor directed to the licensed target or any time after regulatory approval of an HMT inhibitor directed to the licensed target, or the Late Stage Opt-Out. In the event of a Post-EOP1 Clinical Opt-Out, the royalties that become payable to us on net product sales of licensed products directed to DOT1L or the Option Target for which we retain U.S. rights, as applicable, will be reduced by a specified percentage. Following a Post-EOP1 Clinical Opt-Out or a Late Stage Opt-Out, we are no longer required to co-fund global development for the applicable program other than specified costs necessary to complete development activities in process at the time we exercise our opt-out right, and we are obligated to grant Celgene an exclusive license to HMT inhibitors directed to the applicable target in the United States. Following our exercise of a Post-EOP1 Clinical Opt-Out or a Late Stage Opt-Out, if any, we would be eligible to receive specified milestone payments and royalties based on net product sales in the United States of HMT inhibitors directed to the licensed target in the event that Celgene develops and commercializes a product in the United States.

Exclusivity Restrictions. Subject to exceptions specified in the amended agreement, during the option period, we may not research, develop or commercialize HMT inhibitors directed to DOT1L and the three Option Targets. Subject to exceptions specified in the amended agreement, following each applicable option period, we may not research, develop or commercialize HMT inhibitors directed to DOT1L or any target licensed by Celgene.

Right of First Negotiation. The amended and restated agreement eliminated the right of first negotiation that we had previously granted to Celgene under the original agreement with respect to business combination transactions that we may desire to pursue with third parties.

Term and Termination. The amended and restated agreement with Celgene will expire on a product-by-product and country-by-country basis on the date of the expiration of the applicable royalty term with respect to each licensed product in each country and 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 latest of expiration of specified patent coverage, specified regulatory exclusivity or 15 years following the first commercial sale in the applicable country. Celgene has the right to terminate the amended agreement in its entirety, upon 60 or 120 days' notice depending on the timing of such termination. The amended agreement may also be terminated in its

entirety during the option period, and on a licensed target-by-licensed target basis after the option period, by either Celgene or us in the event of a material breach by the other party. The amended agreement may be terminated on a licensed target-by-licensed target basis by either Celgene or us in the event the other party, or an affiliate or sublicensee of the other party, participates or actively assists in a legal challenge to specified patents of the terminating party or in its entirety in the event the other party becomes subject to specified bankruptcy, insolvency or similar circumstances.

GlaxoSmithKline

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 the option to obtain exclusive worldwide license rights to HMT inhibitors directed to three targets. In March 2014, we 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. Additionally, as part of the research collaboration provided for in the agreement, 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, or earlier if selection of a development candidate occurred.

Under the agreement, we have recognized as collaboration revenue a \$20.0 million upfront payment, a \$3.0 million payment upon the execution of the March 2014 agreement amendment, \$6.0 million in fixed research funding, \$9.0 million for research and development services and \$51.0 million in preclinical research and development milestone payments.

These preclinical and research and development milestone payments include a \$12.0 million milestone payment earned in 2018 relating to the first dosing of a patient in a Phase 2 clinical trial of GSK3326595, a PRMT5 inhibitor discovered by us and licensed to GSK under the collaboration agreement, as well as a \$8.0 million milestone payment earned in the fourth quarter of 2018 relating to the initiation of a patient dosing in a Phase 1 clinical trial of GSK3368715, a PRMT1 inhibitor discovered by us and licensed to GSK under the collaboration agreement.

In addition, a \$10.0 million milestone payment earned in May 2017 related to the second target in the collaboration, upon GSK's initiation of GLP toxicology studies, as well as a \$6.0 million clinical milestone recognized in the third quarter of 2016 following GSK's initiation of patient dosing in a Phase 1 clinical trial of a PRMT5 inhibitor that we discovered and licensed to GSK are included in the total of preclinical research and development milestone payments.

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 returns all rights to that target to us. The two other targets continue to be subject to the agreement and are not impacted by the termination.

As of December 31, 2018, 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.

For each selected target in the collaboration, we were primarily responsible for research until the earlier of selection of a development candidate for the target or January 8, 2015, and GSK is solely responsible for subsequent development and commercialization. GSK provided a fixed amount of research funding during the second and third years of the research term and was obligated to provide research funding equal to 100.0% of mutually agreed research and development costs, subject to specified limitations, for any research activities we conducted in the fourth year of the research term. At this stage, GSK is solely responsible for subsequent development and commercialization.

Exclusivity Provisions. Subject to exceptions specified in the agreement, during the term of the agreement, we may not 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.

Boehringer Ingelheim

Overview. In November 2018, we entered into a collaboration agreement with Boehringer Ingelheim to discover, research, develop and commercialize small molecule compounds that are inhibitors of an undisclosed histone acetyl transferase, or HAT target and an undisclosed helicase target, along with associated predictive biomarkers.

During a defined research period, we will perform research activities aimed at achieving certain criteria with respect to a HAT inhibiting compound and a helicase inhibiting compound. The research period will expire on December 31, 2019, unless Boehringer Ingelheim elects to extend the research period and we agree, which may be extended through December 31, 2020.

Following satisfaction of certain criteria with respect to a HAT inhibiting compound, Boehringer Ingelheim shall be solely responsible for the development and commercialization of such compound and products containing such compound throughout the world. BI shall bear the costs of such development and commercialization.

Following satisfaction of certain criteria with respect to the helicase inhibiting compound, Boehringer Ingelheim shall be responsible for the development and commercialization of such compound and products containing such compound in all countries throughout the world other than the United States, whereas we and Boehringer Ingelheim will work together through a joint steering committee to develop and commercialize the HAT inhibiting compound in the United States. With respect to commercializing the HAT inhibiting compound in the United States, we and Boehringer Ingelheim will equally share (50:50) such commercialization costs and activities.

Upon execution of the collaboration agreement, Boehringer Ingelheim agreed to pay us a \$15.0 million upfront payment. Boehringer Ingelheim also agreed to pay us research funding of \$5.0 million in calendar year 2019 and potentially additional research funding in calendar year 2020; up to \$280.5 million in development, regulatory, and sales milestone payments; and tiered royalties in the mid-single digits to low-double digits on sales of the HAT inhibiting compound throughout the world and on sales of the helicase inhibiting compound in all countries other than the United States. We will equally share profits and losses with Boehringer Ingelheim with respect to the helicase inhibiting compound in the United States.

Governance. We will work together with Boehringer Ingelheim through a joint steering committee to provide oversight over the research of the products during the research period, and oversight over the development and commercialization of the helicase inhibiting compound in the United States.

Exclusivity Provisions. Subject to exceptions specified in the agreement, neither we nor Boehringer Ingelheim may research, develop, manufacture or commercialize any product directed against the HAT or helicase targets that are the subject of the agreement, until a compound directed against the target that is developed under the agreement reaches a specified stage of development, other than pursuant to the agreement.

Opt out. We may opt-out of its participation in the development and commercialization of the joint product upon written notice to Boehringer Ingelheim, except under certain circumstances.

In the event that we elect to opt-out of the development and commercialization of the joint product or subject to a limited exception, detailed below, Boehringer Ingelheim elects to assume our development and commercialization rights with respect to the joint product in the United States following a change in control of our company, Boehringer Ingelheim will pay us tiered royalties in the mid-single digits to mid-teens, depending on the stage of development of the joint product at the time of such election, on sales of the joint product in the United States.

Following a change in control of our company, so long as the joint product has not reached a certain stage of development, Boehringer Ingelheim may, upon written notice to us, elect to assume our development and commercialization rights, responsibilities and obligations with respect to the joint product in the United States and we will be deemed to have given Boehringer Ingelheim an opt-out notice. However, if Boehringer Ingelheim elects to assume our development and commercialization rights with respect to the joint product in the United States following a change in control of Epizyme that occurs after a certain stage of development with respect to the joint product, then the sharing of costs and profits may continue.

Term and Termination. Generally, the collaboration agreement remains in effect, on a product-by-product basis, until the last to expire royalty term for a product, but the collaboration agreement shall remain in effect with respect to the joint product in the United States until both parties mutually agree to cease commercialization of the joint product in the United States. Either party may terminate the collaboration agreement for cause following notice and a failure to cure by the defaulting party, if the other party initiates a patent challenge against the other party's patents or if the other party becomes insolvent, and Boehringer Ingelheim may terminate the collaboration agreement without cause, subject to appropriate notice periods.

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 and waived the right of first negotiation for the rest of Asia. 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, 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 royalties at a percentage in the mid-teens on worldwide net sales of any EZH2 product, excluding net sales in Japan. 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 2019, we expect to trigger two \$10.0 million milestone payments upon the submission of the NDAs for accelerated approval of tazemetostat for epithelioid sarcoma and follicular lymphoma.

Under the original agreement, Eisai was solely responsible for funding all research, development and commercialization costs for licensed compounds. Under the amended 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 amendment and restatement of our collaboration and license agreement with Eisai, 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, and waived the right of first negotiation for the rest of Asia.

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 Epizyme retaining final decision-making authority with respect to global development.

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.

LYSA

In May 2016, we entered into a collaboration agreement with the Lymphoma Academic Research Organization, or LYSARC, to conduct a combination trial of tazemetostat with R-CHOP. LYSARC is the operational arm of LYSA. This multi-center Phase 1b/2 study is evaluating tazemetostat in combination with R-CHOP, as a first-line treatment in elderly, high-risk patients with DLBCL and is being sponsored by LYSARC. 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 overall response rate and PFS. The study was initiated in December 2016 and data from the Phase 1b evaluation were presented by LYSA at the 2018 American Society of Hematology meeting showing that the combination of tazemetostat and the R-CHOP regimen was generally well-tolerated, confirmed the recommended tazemetostat dose for the combination to be 800 mg twice-daily, and demonstrated clinical activity, with 87 percent of patients experiencing a metabolic complete response.

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 tazemetostat and Genentech's atezolizumab, when used in combination. The trial will evaluate this combination regimen for the treatment of patients with relapsed or refractory DLBCL. This trial was initiated in December 2016.

In June 2017, we announced an expansion of our clinical collaboration with Genentech to investigate the combination of tazemetostat with atezolizumab in a Phase 1b/2 clinical trial for the treatment of patients with relapsed or refractory metastatic NSCLC. The trial was part of MORPHEUS, Genentech's open-label, multi-center, randomized umbrella trial evaluating the efficacy and safety of multiple immunotherapy-based treatment combinations for metastatic NSCLC. This trial was initiated at the end of 2017, but before patients had been enrolled in the study, recruitment was halted due to the partial hold placed on tazemetostat studies. Due to the hold and strategic reprioritizations, in early 2019 the companies announced that they jointly opted not to move forward with the NSCLC combination study.

Under the agreement, each company supplies its respective anti-cancer agent to support the trials and shares equally in the trial costs. Genentech 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.

Companion Diagnostics

Roche Molecular

In December 2012, Eisai and we entered into an 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 entered into a second amendment to the companion diagnostic agreement with Roche Molecular. The agreement was further amended in March 2018. Before the additional amendment, we were responsible for the remaining development costs of \$10.5 million due under the agreement. Under the amended agreement, we are responsible for remaining development costs of \$10.4 million due under the agreement and Eisai has agreed to reimburse us \$0.9 million of this amount related to a regulatory milestone for Japan. We expect the remaining development costs under the amended agreement to be incurred and paid through 2020.

Under our agreement with Roche Molecular, Roche Molecular is obligated to use commercially reasonable efforts to develop and to make commercially available the companion diagnostic. Roche Molecular has exclusive rights to commercialize the companion diagnostic.

Our agreement with Roche Molecular will expire when we are no longer developing or commercializing tazemetostat. We may terminate the agreement by giving Roche Molecular 90 days' written notice if we discontinue development and commercialization of tazemetostat or determine, in conjunction with Roche Molecular, that the companion diagnostic is not needed for use with tazemetostat. Either we or Roche Molecular may also terminate the agreement in the event of a material breach by the 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, Roche Molecular 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 250 issued patents and allowed patent applications and over 525 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 histone acetyltransferases, or 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 38 additional U.S. patents and more than 200 foreign patents, expected to expire between 2031 and 2035, 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 35 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. Our patent applications in the EZH2 portfolio, if issued, would be expected to expire between 2031 and 2038, 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 13 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; and PCT applications that are eligible for filing in most 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 2036, 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. The portfolio includes PCT applications that are eligible for filing in most jurisdictions worldwide, and U.S. provisional applications that may be used as the basis for non-provisional U.S. and international applications. Patents, if issued from currently pending applications in the EHMT2 portfolio are expected to expire between 2037 and 2039.

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 40 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 2039. We have 18 granted US 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. In the future, if and when our 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 product candidates for preclinical and clinical development, as well as for commercial manufacture if our product candidates receive marketing approval. We have entered into clinical supply agreements with contract manufacturers for all products we have in clinical development, including tazemetostat, pinometostat, and EZM8266.

All of our product candidates are small molecules and are 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 US, EU, and ROW markets, meeting regulatory and compliance requirements as appropriate. We expect to continue to develop product candidates that can 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. We are currently collaborating with Roche Molecular for a diagnostic for its potential use with tazemetostat, and we expect to rely on Roche Molecular for the manufacture of the diagnostic it is developing. We may enter into similar agreements for the manufacture of other diagnostics.

Commercialization

We have recently begun to establish a commercial infrastructure in preparation for a potential future launch of tazemetostat and other product candidates that may receive marketing approval. We have retained commercial rights in the United States to all of our product candidates for which we may receive marketing approvals, except for two programs that are the subject of our collaboration with GSK, two of the preclinical programs that are the subject of our collaboration with Celgene, and the preclinical histone acetyltransferase inhibitor program that is the subject of

our collaboration with Boehringer Ingelheim. For the preclinical helicase inhibitor program, we will share U.S. commercialization responsibilities with Boehringer Ingelheim, with Boehringer Ingelheim assuming responsibility for commercialization outside of the U.S. We plan to retain commercialization rights in the United States and possibly in select foreign jurisdictions in connection with any future collaborations. We intend to build a focused field presence and marketing capabilities to commercialize any of our product candidates that receive regulatory approval in the United States, as well as the capabilities to lead global commercial strategy.

Subject to receiving marketing approvals, we expect to commence commercialization activities by building an 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 our clinical stage product candidates are being 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 Co. Ltd, or Eisai, holds the rights to develop and commercialize tazemetostat in Japan. We intend to build a focused field presence and marketing capabilities to commercialize tazemetostat for the epithelioid sarcoma and follicular lymphoma indications in the United States. We have begun building the infrastructure necessary to support the launch and marketing of tazemetostat for epithelioid sarcoma, and believe we can adequately address this patient population through a modest field force of less than 25 professionals. For geographies outside the United States, we are evaluating the most efficient path to reaching patients, including through potential collaborations.

We expect that our collaborators for any companion 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 Roche Molecular. 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.

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, Novartis AG, 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-1205, Phase 1/2 castration-resistant prostate cancer, solid tumors), Novartis AG, developing an EED inhibitor which indirectly blocks EZH2 (MAK683, Phase 1/2, advanced malignancies), Daiichi Sankyo, developing a EZH1/EZH2 dual inhibitor (valemestostat, DS-3201, Phase 1, relapsed or refractory non-Hodgkin lymphomas, AML, and ALL), and Pfizer, developing EZH2 inhibitor PF-06821497, Phase 1, relapsed or refractory SCLC, castration-resistant prostate cancer, follicular lymphoma 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, Merck & Co., Inc., Novartis AG, Spectrum Pharmaceuticals, and Eisai, 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 variety of available drug therapies marketed for cancer. In many cases, these drugs are administered in combination to enhance efficacy. While our product candidates may compete with many existing drugs and other therapies, to the extent they are ultimately used in combination with or as an adjunct to these therapies, our product candidates will not be competitive with them. Some of the currently approved drug therapies are branded and subject to patent protection, and others are available on a generic basis. Many of these approved drugs are well established therapies and are widely accepted by physicians, patients and third-party payors.

In addition to currently marketed therapies, there are also 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.

If our lead product candidates are approved for the indications for which we are currently undertaking clinical trials, they will compete with the therapies and currently marketed drugs discussed below.

Tazemetostat. The most common treatments for FL are chemotherapies, usually combined with the monoclonal antibody Rituxan, or more recently, in the case of FL, Gazyva, which is a next-generation antibody that acts against the same target as Rituxan, CD20. While Rituxan and a number of other widely used anti-cancer agents are labeled either broadly for NHL, 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.

No therapies are approved specifically for the treatment of INI1- and SMARCA4-negative tumors. 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 since there are no approved systemic therapies specifically indicated for this disease. To the best of our knowledge there are no competitive products in development for 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 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, animal studies and formulation studies in compliance with the FDA's GLP regulations;
- submission to the FDA of an IND which must become effective before human clinical trials may begin;
- manufacturing of the drug in compliance with the FDA's GMP 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;
- 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 to determine GCP compliance;
- 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; 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 efficacy. 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 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 clinical trials 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 effectiveness criteria to be evaluated. 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 plan 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, 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.

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.

On December 13, 2016, the 21st Century Cures Act established, and the 2017 Food and Drug Administration Reauthorization Act later amended, a requirement that sponsors of one or more investigational drugs for the treatment of a serious disease(s) or condition(s) make publicly available their policy for evaluating and responding to requests for expanded access for individual patients. Although these requirements were rolled out over time, they have now come into full effect. This provision requires drug and biologic companies to make publicly available their policies for expanded access for individual patient access to products intended for serious diseases. Sponsors are required to make such 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, 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 I 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 FDA 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 applications are subject to an application user fee, which for federal fiscal year 2019 is \$2,588,478 for an application requiring clinical data. The sponsor of an approved application is also subject to an annual program fee, which for fiscal year 2019 is \$309,915. 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. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan drug designation.

The FDCA 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 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 GCP and perform a sponsor-monitor audit if an audit has not been completed in the previous two years.

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. 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.

Breakthrough Drug Designation. FDA may grant breakthrough drug 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. 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.

Special FDA Expedited Review and Approval Programs. The FDA has various programs, including Fast Track designation, Accelerated Approval, Priority Review and Breakthrough 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.

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." 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. 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.

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.

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.

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 endpoint, 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 we believe will be more likely to respond to the product. 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 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, we believe that the FDA will require PMA approval of one or more *in vitro* companion diagnostics to identify patient populations suitable for our cancer therapies. The review of these *in vitro* companion diagnostics in conjunction with the review of our cancer treatments involves coordination of review by the FDA’s Center for Drug Evaluation and Research, or CDER, and by the FDA’s Center for Devices and Radiological Health, or CDRH, Office of In Vitro Diagnostics Device Evaluation and Safety.

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 2019, the standard fee for review of a PMA is \$322,147 and the small business fee is \$80,537.

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 to physicians and other health care providers or 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. The commercial success of our product candidates and our ability to commercialize any approved product candidates successfully will depend in part on the extent to which governmental authorities, private health insurers and other third-party payors provide coverage for and establish adequate reimbursement levels for our therapeutic product candidates and any related companion diagnostics. Government health administration authorities, private health insurers and other organizations generally decide which drugs they will pay for and establish reimbursement levels for healthcare. 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 2024 unless additional Congressional action is taken. 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.

With enactment of the Tax Cuts and Jobs Act of 2017, which was signed by the President 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, will become effective in 2019. According to the Congressional Budget Office, the repeal of the individual mandate will cause 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise. Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. The Congress will likely consider other legislation to replace elements of the ACA during the next Congressional session.

The Trump Administration has also taken executive actions to undermine or delay implementation of the ACA. Since January 2017, President Trump has signed two Executive Orders designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. One Executive Order directs federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA 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 ACA. Several state Attorneys General filed suit to stop the administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. In addition, CMS has recently proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. Further, on June 14, 2018, U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than \$12 billion in ACA risk corridor payments to third-party payors who argued were owed to them. The effects of this gap in reimbursement on third-party payors, the viability of the ACA marketplace, providers, and potentially our business, are not yet known. Further, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted state 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. For example, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted state 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. At the federal level, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. For example, on May 11, 2018, the Administration issued a plan to lower drug prices. Under this blueprint for action, the Administration indicated that the Department of Health and Human Services (HHS) will: take steps to end the gaming of regulatory and patent processes by drug makers to unfairly protect monopolies; advance biosimilars and generics to boost price competition; evaluate the inclusion of prices in drug makers' ads to enhance price competition; speed access to and lower the cost of new drugs by clarifying policies for sharing information between insurers and drug makers; avoid excessive pricing by relying more on value-based pricing by expanding outcome-based payments in Medicare and Medicaid; work to give Part D plan sponsors more negotiation power with drug makers; examine which Medicare Part B drugs could be negotiated for a lower price by Part D plans, and improving the design of the Part B Competitive Acquisition Program; update Medicare's drug-pricing dashboard to increase transparency; prohibit Part D contracts that include "gag rules" that prevent pharmacists from informing patients when they could pay less out-of-pocket by not using insurance; and require that Part D plan members be provided with an annual statement of plan payments, out-of-pocket spending, and drug price increases.

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 a patent infringement lawsuit 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.

We intend to seek orphan drug designation and exclusivity for our products whenever it is available. We have been granted orphan drug designation in the United States and the European Union for pinometostat, and orphan drug designation in the United States for tazemetostat for the treatment of patients with FL, MRT, soft tissue sarcoma and mesothelioma.

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.

The 21st Century Cures Act. On December 13, 2016, President Obama signed the Cures Act into law. The Cures Act is designed to modernize and personalize healthcare, spur innovation and research, and streamline the discovery and development of new therapies through increased federal funding of particular programs. It authorizes increased funding for the FDA to spend on innovation projects. The new law also amends the Public Health Service Act to reauthorize and expand funding for the National Institutes of Health. The Act establishes the NIH Innovation Fund to pay for the cost of development and implementation of a strategic plan, early stage investigators and research. It also charges NIH with leading and coordinating expanded pediatric research. Further, the Cures Act directs the Centers for Disease Control and Prevention to expand surveillance of neurological diseases.

With amendments to the FDCA and the Public Health Service Act, or PHSA, Title III of the Cures Act seeks to accelerate the discovery, development, and delivery of new medicines and medical technologies. To that end, and among other provisions, the Cures Act reauthorizes the existing priority review voucher program for certain drugs intended to treat rare pediatric diseases until 2020; creates a new priority review voucher program for drug applications determined to be material national security threat medical countermeasure applications; revises the FDCA to streamline review of combination product applications; requires the FDA to evaluate the potential use of “real world evidence” to help support approval of new indications for approved drugs; provides a new “limited population” approval pathway for antibiotic and antifungal drugs intended to treat serious or life-threatening infections; and authorizes the FDA to designate a drug as a “regenerative advanced therapy,” thereby making it eligible for certain expedited review and approval designations.

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 28 EU Member States without the need for any national implementing legislation, and will become applicable no earlier than 2020. 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 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.

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, a Pediatric Investigation Plan, or a request for waiver or deferral, is required for submission 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 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, and provide early and enhanced support to optimize the development of eligible medicines speed up their evaluation and contribute 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 European Union, which is commonly referred to as Brexit. Thereafter, on March 29, 2017, the country formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. The United Kingdom has a period of a maximum of two years from the date of its formal notification to negotiate the terms of its withdrawal from, and future relationship with, the European Union. If no formal withdrawal agreement is reached between the United Kingdom and the European Union, then it is expected the United Kingdom's membership in the European Union will automatically terminate two years after the submission of the notification of the United Kingdom's intention to withdraw from the European Union. Discussions between the United Kingdom and the European Union focused on finalizing withdrawal issues and transition agreements are ongoing. However, limited progress to date in these negotiations and ongoing uncertainty within the UK Government and Parliament sustains the possibility of the United Kingdom leaving the European Union on March 29, 2019 without a withdrawal agreement and associated transition period in place, which is likely to cause significant market and economic disruption. 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 European Union directives and regulations, Brexit could materially impact the future regulatory regime which applies to products and the approval of product candidates in the United Kingdom. It remains to be seen how, if at all, Brexit will impact regulatory requirements for product candidates and products in the United Kingdom.

Employees

As of February 15, 2019, we had 124 full-time employees, 74 of whom were primarily engaged in research and development activities.

Executive Officers of the Company

The following table sets forth the name, age and position of each of our executive officers as of February 26, 2019.

Name	Age	Position
Robert B. Bazemore	51	President, Chief Executive Officer and Director
Shefali Agarwal	45	Chief Medical Officer
Matthew E. Ros	52	Chief Strategy and Business Officer

Robert B. Bazemore has served as a director and our President and Chief Executive Officer since joining us in September 2015. Prior to joining us, from September 2014 to July 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 March 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. He received a B.S. in biochemistry from the University of Georgia.

Dr. Shefali Agarwal has served as our Chief Medical Officer since joining us in June 2018. 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 Kamataka 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 Chief Strategy and Business Officer since September 2018 and initially joined Epizyme 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. Prior to that role, Mr. Ros served in the rare disease business of Genzyme, a Sanofi company, where he served as Vice President and Franchise Head of its Pompe disease unit from September 2012 to December 2014. 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 1990-2007. 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.

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, 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, Cambridge, Massachusetts 02139.

Item 1A. 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.

Risks Related to the Discovery and Development of Our Product Candidates

We are dependent on the successful development and commercialization of our lead product candidate, tazemetostat. If we are unable to develop, obtain marketing approval for or successfully commercialize this product candidate, either alone or through a collaboration, or if we experience significant delays in doing so, our business could be harmed.

We currently have no products approved for sale and are investing a significant portion of our efforts and financial resources to fund the development of our lead product candidate, tazemetostat. We have another product candidate in clinical trials that we are developing—pinometostat, and Glaxo Group Limited (an affiliate of GlaxoSmithKline), or GSK, has initiated a Phase 2 clinical trial for a PRMT5 inhibitor that it has licensed from us. In addition, we plan to commence clinical testing in the second half of 2019 of EZM8266, our investigational agent for the treatment of sickle cell disease. However, these development programs are early stage, and all of our other 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 develop, obtain marketing approval for and successfully commercialize tazemetostat in one or more disease indications. The success of tazemetostat and any other product candidate will depend on several factors, including the following:

- successful enrollment in, and completion of, clinical trials;
- safety, tolerability and efficacy profiles that are satisfactory to the U.S. Food and Drug Administration, or FDA, the European Medicines Agency, or EMA, or any comparable foreign regulatory authority for marketing approval;
- timely receipt of marketing approvals from applicable regulatory authorities and the patient populations for which the approvals are granted;
- the extent of any required post-marketing approval commitments to applicable regulatory authorities;
- making arrangements with third-party manufacturers for, or establishing, clinical and commercial manufacturing capabilities;
- launching commercial sales of the products, if and when approved, whether alone or in collaboration with others;

- acceptance of the products, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies;
- obtaining and maintaining healthcare coverage and adequate reimbursement;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates;
- protecting our rights in our intellectual property portfolio; and
- maintaining a continued acceptable safety profile of the products following approval.

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 or any other product candidate, we may not be able to successfully develop or commercialize our product candidates on a timely basis or at all, which would materially harm our business.

Clinical drug development involves 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 our product candidates.

We are conducting multiple clinical trials of tazemetostat. In addition, GSK's PRMT5 and PRMT1 inhibitors are in clinical development. The risk of failure for each of these product candidates is high. It is impossible to predict when or if any of our product candidates 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 and then conduct extensive clinical trials to demonstrate the safety and efficacy of our 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 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 follicular lymphoma, or FL, at the time of the IND 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 April 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 issued a partial clinical hold on new enrollment of patients in our ongoing clinical trials of tazemetostat. In the second quarter of 2018, the French National Agency for Medicines and Health Products Safety and Germany's Federal Institute for Drugs and Medical Devices each placed a comparable partial clinical hold on new patient enrollment. In September 2018, the FDA lifted the partial clinical hold on new patient enrollment in the United States and in November 2018, Germany's Federal Institute for Drugs and Medical Devices lifted the partial clinical hold in Germany. However, the partial clinical hold in France remains in effect. Following the event, we proactively re-consented all patients in our clinical trials and updated our informed consent form based on the safety report. We also aligned with the FDA and regulators in Germany on certain amendments to our tazemetostat study protocols focused on increasing patient monitoring and putting in place risk-mitigation strategies designed to reduce the risk of potential future secondary malignancies. We have re-activated clinical trial sites in the United States, resuming enrollment in our tazemetostat clinical trials at those sites, and are currently re-activating sites in Germany to resume enrollment there. We are currently engaging with French regulators to work toward a similar resolution regarding the partial clinical hold in France. We have responded to queries from the French regulators for which our responses are currently under final review. We are also working closely with our collaborators to reach a similar resolution for their respective trials in which tazemetostat is being studied in combination with other therapies. If we or our collaborators are unable to fully and adequately address the partial clinical hold to the satisfaction of these regulatory authorities, and other matters such as these when they arise, we may be unable to conduct clinical trials of our 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. In our FL program, we have engaged in discussions with the FDA regarding the classification of FL patients as EZH2 mutant or wild-type patients. If the FDA does not agree with our classification of patients, particularly the wild-type patients in our studies, the FDA may disagree with our data in our patient population subsets, which could affect our ability to obtain regulatory approval of tazemetostat for one or both of the FL patient populations.

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 our 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 participants 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 participants 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 participants 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.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our 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 our 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, because certain of our product candidates may be focused on specific patient populations, our ability to enroll eligible patients may be limited or may result in slower enrollment than we anticipate. In addition, some of our competitors have ongoing clinical trials for product candidates that may treat the broader patient populations within which our product candidates are being developed for the treatment of a subset of identifiable patients with cancer and other diseases, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates. For instance, our ongoing clinical trials of tazemetostat in adult and pediatric patients with INI1-negative tumors are targeting rare patient populations. In addition, our Phase 2 clinical trial of tazemetostat in patients with non-Hodgkin lymphoma, or NHL, has two arms targeting patients with EZH2 activating mutations in their tumors, one in diffuse large B-cell lymphoma, or DLBCL, and one in follicular lymphoma, or FL. Based on the aggregate scientific literature, we believe that patients with these mutations represent approximately 20% of the total GCB DLBCL and FL population in the United States and other major reimbursable markets. In any clinical study, the actual percentage of patients enrolled with these EZH2 mutations may vary from the range suggested by the literature.

Patient enrollment is affected by other factors including:

- the severity 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; and
- the ability to identify specific patient population for molecularly defined study cohort(s).

In April 2018, following a safety report of a pediatric patient who developed a secondary T-cell lymphoma, the FDA issued a partial clinical hold on new enrollment of patients in our ongoing clinical trials of tazemetostat. In the second quarter of 2018, the French National Agency for Medicines and Health Products Safety and Germany's Federal Institute for Drugs and Medical Devices each took similar actions. In September 2018, the FDA lifted the partial clinical hold on new patient enrollment in the United States and in November 2018, Germany's Federal Institute for Drugs and Medical Devices lifted the partial clinical hold in Germany. However, the partial clinical hold in France remains in effect. We have responded to queries from the French regulators for which our responses are currently under final review. The safety event may adversely affect enrollment in trials of tazemetostat following resumption of enrollment.

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 our 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.

If serious adverse or unacceptable side effects are identified during the development of our product candidates, we may need to abandon or limit our development of some of our product candidates.

If our product candidates are associated with undesirable side effects in preclinical testing or clinical trials or have characteristics that are unexpected in clinical trials or preclinical testing, we may need to abandon their development or limit development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. 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.

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 and may never lead to marketable products.

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 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 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, to date no company has translated these biological observations into systematic drug discovery that has yielded a drug that has received marketing approval. We believe that our first three inhibitors of histone methyltransferases, or HMTs, in the clinic 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 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 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 a particular 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 diagnostic and if we or our collaborators are unable to successfully develop diagnostics for our 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 our 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 Molecular to develop and commercialize a diagnostic for use with tazemetostat for NHL patients with EZH2 activating mutations. Companion 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 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 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 use and expand our proprietary drug discovery platform to build a pipeline of small molecule inhibitors of HMT and other CMP targets and progress these product candidates through clinical development for the treatment of a variety of different types of cancer and other diseases. Although our research and development efforts to date have resulted in a pipeline of programs directed to specific HMT and other CMP targets, 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.

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 \$123.6 million for the year ended December 31, 2018, \$134.3 million for the year ended December 31, 2017, and \$110.2 million for the year ended December 31, 2016. As of December 31, 2018, we had an accumulated deficit of \$586.7 million. To date, we have financed our operations primarily through our collaborations, our public offerings, and private placements of our preferred stock. All of our revenue to date has been collaboration revenue. We have devoted substantially all of our financial resources and efforts to research and development, including clinical and preclinical studies. We are still in the early to middle stages of development of our product candidates, and we have not completed development of any 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 our expenses will continue to increase over the next several years if and as we:

- continue our Phase 2 clinical trial of tazemetostat for the treatment of patients with NHL, including relapsed or refractory FL cohorts in the trial;
- continue our Phase 2 clinical trial of tazemetostat for the treatment of adult patients with certain molecularly defined solid tumors, including the epithelioid sarcoma cohort in the trial;
- continue our Phase 1 clinical trial of tazemetostat for the treatment of pediatric patients with certain molecularly-defined solid tumors;

- continue our Phase 2 clinical trial of tazemetostat in relapsed or refractory patients with mesothelioma characterized by BAP1 loss-of-function;
- continue our clinical trials of tazemetostat in combination with R-CHOP in first line elderly patients with DLBCL and in combination with Genentech Inc.'s anti-PD-L1 cancer immunotherapy, atezolizumab, in patients with relapsed or refractory DLBCL being conducted by our collaborators;
- design and conduct a new combination trial of tazemetostat in FL;
- pay any milestone payments provided for and achieved under the amended and restated collaboration and license agreement with Eisai Co Ltd, or Eisai;
- complete IND-enabling studies for EZM8266, a G9a inhibitor designed to treat patients with sickle cell disease, and prepare for a Phase 1 study;
- conduct research and development under our collaboration and license agreements with Celgene and Boehringer Ingelheim International GmbH or Boehringer Ingelheim;
- continue the research and development of our other product candidates, as well as for Celgene Corporation, or Celgene, under our amended and restated collaboration and license agreement;
- 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;
- establish a sales, marketing and distribution infrastructure and scale up external manufacturing capabilities to commercialize any products for which we may obtain regulatory approval;
- grow our medical affairs organization to support the commercialization efforts of any product candidate that is approved;
- 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 succeed in developing, and eventually commercializing, a product or products that generate significant revenue. The ability to achieve this success will require us to be effective in a range of challenging activities, including completing preclinical testing and clinical trials of our product candidates, discovering additional product candidates, obtaining regulatory approval for these product candidates and manufacturing, marketing and selling any products for which we may obtain regulatory approval. We are only in the preliminary stages of most of these 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 associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. If we are required by the FDA, the EMA, or other regulatory authorities to perform studies in addition to those currently expected, or if there are any delays in completing our clinical trials or the development of any of our product candidates, our expenses could increase.

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 to fund our tazemetostat development program; make any milestone payments provided for and achieved under the amended and restated collaboration and license agreement with Eisai; continue our collaboration with Celgene; and continue research and development and initiate clinical trials of, and seek regulatory approval for, any future product candidates. In addition, if we obtain regulatory approval for any of our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. Accordingly, we will 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 any future commercialization efforts.

Based on our research and development plans and our timing expectations related to the progress of our programs, we expect that our existing cash, cash equivalents and marketable securities as of December 31, 2018, will be sufficient to fund our planned operating expenses and capital expenditure requirements into the second quarter of 2020, without giving effect to milestone payments we may receive under our collaboration agreements. We have based these expectations on assumptions that may prove to be wrong, and we could use our capital resources sooner than we expect. Our future capital requirements will depend on many factors, including:

- 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 may pursue, including the scope, progress, results and costs of discovery research, preclinical development, laboratory testing and clinical trials for such product candidates;
- our ongoing collaboration with Celgene;
- the costs, timing and outcome of regulatory review of our product candidates;
- milestones, option exercise fees, license fees, and other collaboration-based revenues, if any;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution for any of our product candidates for which we receive marketing approval;
- 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 and defending any intellectual property-related claims; and
- the extent to which we acquire or in-license other products and technologies.

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 we may never generate the necessary data or results required to obtain regulatory approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Commercial revenues, if any, will not be derived until and unless we can achieve sales of commercially available products. Accordingly, we will 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. 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. 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 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 future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Our limited operating history may make it difficult to evaluate the success of our business to date and to assess our future viability.

We commenced active operations in early 2008, and our operations to date have been limited to organizing and staffing our company, business planning, raising capital, developing our technology, identifying potential product candidates, undertaking preclinical studies and, beginning in 2012, conducting clinical trials. All but four of the product candidates discovered by us are still in preclinical development. We have not yet demonstrated our ability to obtain regulatory approvals, manufacture a commercial scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Consequently, any predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history.

In addition, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We will need to transition at some point from a company with a research and development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

We expect our financial condition and operating results to continue to fluctuate significantly from quarter-to-quarter and year-to-year due to a variety of factors, many of which are beyond our control. Accordingly, the results of any quarterly or annual periods should not be relied upon as indications of future operating performance.

Risks Related to the Commercialization of Our Product Candidates

We may be unable to obtain, or may be delayed in obtaining, marketing approval for our product candidates.

Based on interactions with the FDA, we have identified a potential path for accelerated approval in epithelioid sarcoma and we are targeting submission of our first new drug application, or NDA, to the FDA for tazemetostat for this indication in the second quarter of 2019. In addition, based on recent interactions with the FDA, we believe we have identified a potential path for accelerated approval of tazemetostat as a monotherapy for relapsed or refractory FL in both EZH2 mutant and wild-type FL patient populations, where patients' disease has progressed following two or more lines of therapy. Subject to the results of the FL cohorts in our ongoing global Phase 2 study of tazemetostat in NHL, we are targeting submission of an NDA for tazemetostat for this indication in the fourth quarter of 2019.

It is possible that the FDA or any other regulatory authority may refuse to accept our applications for substantive review, or that the FDA or other regulatory authority may conclude after review of our data that our application is insufficient to obtain marketing approval of tazemetostat on an accelerated basis or at all. If the FDA does not agree that we have sufficient data to seek accelerated approval or does not accept or approve one or more of our planned

NDA for tazemetostat, we may be required to study tazemetostat in additional patients or conduct additional clinical trials, preclinical studies or manufacturing validation studies and submit that data to regulators before our application can be resubmitted or will be reconsidered. Even if the FDA grants accelerated approval for either of our planned NDAs, we may need to conduct a confirmatory program in each indication, which may involve Phase 3 trials that may be expensive and time-consuming and may not confirm such benefit and subject the NDAs to withdrawal.

Moreover, we are planning to submit an NDA for tazemetostat for relapsed or refractory FL in both EZH2 mutant and wild-type FL patient populations. If the FDA only accepts or approves our application for the mutant FL patient population, we may be required to study tazemetostat in additional wild-type FL patients or conduct additional clinical trials or preclinical studies and submit that data to regulators and resubmit an application for that patient population. Depending on the extent of these or any other required trials or studies, submission of our planned NDAs or acceptance or approval of these NDAs for tazemetostat may be delayed by several years, or may require us to expend more resources than we have available. It is also possible that additional trials or studies, if performed and completed, may not be considered sufficient by the FDA to accept or approve the planned NDAs for tazemetostat. Any delay in obtaining, or an inability to obtain, marketing approvals would prevent us from commercializing tazemetostat in the United States and/or abroad, generating revenue and achieving and sustaining profitability. If any of these outcomes occurs, either to tazemetostat 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.

Even if any of our product candidates receives marketing approval, it 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 any of our product candidates receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. If our product candidates do 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 our product candidates, if approved for commercial sale, 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.

If we are unable to establish sales, marketing and distribution capabilities, we may not be successful in commercializing our product candidates if and when they are approved.

We do not have a sales or marketing infrastructure and have no experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any product for which we have obtained marketing approval, we will need to establish a sales and marketing organization.

We have recently begun building the infrastructure necessary to support the successful commercial launch and marketing of tazemetostat and other product candidates that may receive marketing approval. There are risks involved with establishing our own sales, marketing and distribution capabilities. For example, recruiting and training a sales force is expensive and time consuming and could delay any product launch. 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 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 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 establish our own sales, marketing and distribution capabilities and enter into arrangements with third parties to perform these services, our product revenues and our profitability, if any, are likely to be lower than if we were to market, sell and distribute any products that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell, market and distribute our 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 and market our products effectively. If we do not establish sales, marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our 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 our current product candidates, 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 disease indications for which we are developing our product candidates. 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. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

Specifically, 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, Novartis AG, 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-1205, Phase 1/2 castration-resistant prostate cancer, solid tumors), Novartis AG, developing an EED inhibitor which indirectly blocks EZH2 (MAK683, Phase 1/2, advanced malignancies), Daiichi Sankyo, developing a EZH1/EZH2 dual inhibitor (valemestostat, DS-3201, Phase 1, relapsed or refractory non-Hodgkin lymphomas, AML, and ALL), and Pfizer, developing EZH2 inhibitor PF-06821497, Phase 1, relapsed or refractory SCLC, castration-resistant prostate cancer, follicular lymphoma and diffuse large B-cell lymphoma. In July 2017, GSK discontinued their EZH2 inhibitor program, GSK2816126, which had been in

Phase 1 development in solid tumors and hematological malignancies. In addition, many companies are developing cancer therapeutics that work by targeting epigenetic mechanisms other than HMTs, and some including Celgene, Merck & Co., Inc., Novartis AG, Spectrum Pharmaceuticals, and Eisai, are now marketing cancer treatments that work by targeting epigenetic mechanisms other than HMTs. There are a number of companies currently evaluating investigational agents in the relapsed and refractory follicular lymphoma patient setting. To the best of our knowledge there are no competitive products in development for epithelioid sarcoma

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 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. If our product candidates achieve marketing approval, we expect that they will 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.

Even if we are able to commercialize any product candidates, the products 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 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 commercialize any product candidates successfully also will depend in part on the extent to which 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 reimbursement levels. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted 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. 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 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.

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 of our product candidates in human clinical trials and will face an even greater risk if we commercially sell any products that we may develop. 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;
- 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 \$20.0 million in product liability insurance coverage in the aggregate, with a per incident limit of \$20.0 million, which may not be adequate to cover all liabilities that we may incur. We may need to increase our insurance coverage as we expand our clinical trials or if we commence commercialization of our product candidates. 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.

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 do not yet have any capability for sales, marketing or distribution. Accordingly, we have entered into therapeutic collaborations with other companies that we believe can provide such capabilities, including our collaboration and license agreements with Celgene, GSK, and Boehringer Ingelheim. We also rely on Genentech to manage our combination trial of tazemetostat and atezolizumab in relapsed or refractory DLBCL, and on the Lymphoma Study Association to manage our combination study of tazemetostat and R-CHOP in newly diagnosed, elderly, high risk patients with DLBCL. With our reacquisition of tazemetostat rights under our amended and restated collaboration and license agreement with Eisai, we do not have access to Eisai's capabilities for tazemetostat except with Eisai in Japan. 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;
- 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, 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 agreement with us, we may not receive any future research funding or milestone or royalty payments under the collaboration. 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 engaging in activities that are the subject of the collaboration with third parties for specified periods of time. For example, under our collaboration agreement with Celgene, subject to specified exceptions, we may not, during the option period, research, develop or commercialize inhibitors directed to DOT1L and the three option targets covered by the agreement outside of the collaboration. 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.

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 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, or increase our expenditures and undertake development or commercialization activities at our own expense. 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 fail to enter into collaborations and 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, we are 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, we may rely on Roche Molecular to develop a companion diagnostic for detecting activating mutations in EZH2 in the tazemetostat in NHL program. Our collaborators:

- may not perform their obligations as expected or have difficulty responding to accelerated approval time lines 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 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 and plan to rely on third-party clinical research organizations or third-party research collaborative groups to conduct our planned clinical trials. We do not plan to independently conduct clinical trials of 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 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 rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors 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 our product candidates for preclinical and clinical testing and expect to continue to do so 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 if any of our product candidates receive marketing approval. 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 also expect to rely on third-party manufacturers or third-party collaborators for the manufacture of commercial supply of any other product candidates for which our collaborators or we obtain marketing approval. We may be unable to establish any agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on 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.

Our product candidates and any products 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. We do not currently have arrangements in place for redundant supply or a second source for bulk drug substance. If our current contract manufacturers cannot perform as agreed, we may be required to replace such manufacturers. Although we believe that there are several potential alternative manufacturers who could manufacture our product candidates, we may 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 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.

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. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our novel technologies and product candidates.

The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. 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 patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

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 laws of foreign countries 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. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we 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 or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection.

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. In the future, if and when our product candidates receive FDA approval, we expect to apply for patent term extensions on patents covering those product candidates. We intend to seek patent term extensions for any of our issued patents in any jurisdiction where they 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 such extensions.

Patent reform legislation such as the Leahy-Smith America Invents Act, or the Leahy-Smith Act, could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. 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 U.S. Patent and Trademark Office during patent prosecution and additional procedures to attack the validity of a patent at U.S. Patent and Trademark Office administered post-grant proceedings, including post-grant review, *inter partes* review, and derivation proceedings. In addition, under the Leahy-Smith Act, the United States transitioned to a first inventor to file system in which, assuming that the other statutory requirements 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. As such, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

Moreover, we may be subject to a third-party preissuance submission of prior art to the U.S. Patent and Trademark Office, 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 products without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Even if our owned and 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.

Our competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and 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 freedom to operate 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. 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. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

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

Competitors may infringe our issued patents or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement 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 their patents. In addition, in a patent infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly.

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, including patent rights, that are important or necessary to the development of our products. It may be necessary for us to use the patented or proprietary technology of third parties to commercialize our products, in which case we may be required to obtain a license from these third parties on commercially reasonable terms, or our business could be harmed, possibly materially.

Third parties may initiate legal proceedings alleging that we are infringing 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 product candidates and use our proprietary technologies without infringing 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 regarding intellectual property rights with respect to our products and technology. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future. For example, with respect to tazemetostat, we are aware of U.S. patents held by a third party, which could be construed to cover tazemetostat and its use in certain clinical indications.

In the event that an owner of one or more of these patents were to bring an infringement action against us, we believe we have defenses that we could assert in such event, and additionally in the U.S. Patent & Trademark Office, 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 these third party'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 and marketing our products and technology. 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. We could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

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, diligence, development and commercialization timelines, milestone payment, royalty, insurance and other obligations on us. Under our existing licensing and funding agreements, we are obligated to pay royalties on net product sales of product candidates or related technologies to the extent they are covered by the agreements. We also had diligence and development obligations under those agreements that we have satisfied. 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 market 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 product candidate 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.

We may be subject to claims by third parties asserting that our employees or we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Many of our employees 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 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 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 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 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. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to management.

Intellectual property litigation 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. Uncertainties resulting from the initiation and continuation of patent 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 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, 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 manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. 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 would be harmed.

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

Even if we complete the necessary preclinical studies and clinical trials, 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 our product candidates, and our ability to generate revenue will be materially impaired.

Our product candidates 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. We have not submitted an application for or received marketing approval for any of our product candidates in the United States or in any other jurisdiction.

However, we plan to submit an NDA to the FDA for tazemetostat for the treatment of epithelioid sarcoma in the second quarter of 2019 and to submit an NDA to the FDA for tazemetostat for the treatment of relapsed and refractory FL in the fourth quarter of 2019, subject to the results of our ongoing trials in those indications. Failure to obtain marketing approval for tazemetostat or any other product candidate will prevent us from commercializing the product candidate. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to 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 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. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. 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 plan to submit our NDAs for accelerated approval of tazemetostat in patients with epithelioid sarcoma and in patients with relapsed or refractory FL in both EZH2 mutant and wild-type FL patient populations. In order to obtain accelerated approval, we must demonstrate that tazemetostat provides meaningful therapeutic benefit over existing treatments. In addition, as a condition of accelerated approval, we will need to perform post-marketing confirmatory study(ies) to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical endpoints, and if the studies are unsuccessful, tazemetostat may be subject to accelerated withdrawal procedures. In the case of our planned FL submission, if tazemetostat is approved in both EZH2 mutant and wild-type FL patient populations, the FDA could use these post-marketing studies to withdraw our approval if the confirmatory studies demonstrate a clinical benefit.

If we experience delays in obtaining approval or if we fail to obtain approval of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenues will be materially impaired.

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 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 these product candidates for other indications, or for any other future clinical candidates we may develop.

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 USC 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 17, 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. Follicular lymphoma 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.

A Fast Track designation by the FDA, such as the Fast Track designation we received for tazemetostat, may not lead to a faster development or regulatory review or approval process.

We have announced that we have received Fast Track designation from the FDA for tazemetostat for patients with relapsed or refractory FL, with or without activating EZH2 mutations, relapsed or refractory DLBCL with EZH2 activating mutations, and metastatic or locally advanced epithelioid sarcoma 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. 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. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular product candidate is eligible for this designation, we cannot assure that the FDA would decide to grant it. Even if we do receive Fast Track designation, as we have for tazemetostat, we may not experience a faster development process, review or approval compared to conventional FDA procedures. We or the FDA may withdraw Fast Track designation if it believes that the designation is no longer supported by data from our clinical development program.

A breakthrough therapy designation by the FDA for our product candidates may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that our product candidates will receive marketing approval.

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.

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. Even if we receive breakthrough therapy designation, the receipt of such designation for a product candidate may not result in a faster development process, review or approval compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that the products no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

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 our products in the European Union 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, on June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. On March 29, 2017, the country formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty and is scheduled to withdraw from the European Union on March 29, 2019. Since a significant proportion of the regulatory framework in the United Kingdom is derived from European Union directives and regulations, the referendum could materially impact the regulatory regime with respect to the approval of our product candidates in the United Kingdom or the European Union and could prevent or delay our marketing approval in the European Union or United Kingdom in addition to delaying the pricing arrangements or reimbursements for any approved product candidates. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the United Kingdom and/or the European Union and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom and/or 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 diagnostic in connection with approval of a candidate therapeutic product, and we do not obtain or 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 diagnostic is not also approved or cleared for that indication. Under the Federal Food, Drug, and Cosmetic Act, companion diagnostics are regulated as medical devices, and the FDA has generally required companion 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 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. 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.

Any 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.

Any 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 study(ies) 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. 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 any of our product candidates 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. 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.

Non-compliance with European Union and United Kingdom 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.

Similarly, failure to comply with the European Union's and the United Kingdom's requirements regarding the protection of personal information can also lead to significant penalties and sanctions. 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 U.S., 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 our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with our European activities.

Our relationships with healthcare providers, physicians and third-party payors will be 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, physicians and third-party payors will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our future arrangements with healthcare providers, physicians 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;
- 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 \$5,500 to \$11,000 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 and foreign 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. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

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 European Union. The provision of benefits or advantages to physicians is governed by the national anti-bribery laws of European Union Member States, such as the U.K. Bribery Act 2010. Infringement of these laws could result in substantial fines and imprisonment.

Payments made to physicians in certain European Union 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 European Union Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct applicable in the European Union Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

Efforts to ensure that our business with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. We do not have a fully developed compliance program and are in the process of establishing a more robust compliance infrastructure to address our needs in this area. We may fail to establish appropriate compliance measures, and even with a stronger program in place, it is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Recently enacted 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 enacted 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 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.

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.

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, will become effective in 2019. According to the Congressional Budget Office, the repeal of the individual mandate will cause 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise. Further, each chamber of the Congress has put forth multiple bills designed to repeal or replace portions of the PPACA. Although none of these measures has been enacted by Congress to date, Congress may consider other legislation to repeal and replace elements of the PPACA. The Congress will likely consider other legislation to replace elements of the PPACA, during the next Congressional session.

The Trump Administration has also taken executive actions to undermine or delay implementation of the ACA. Since January 2017, President Trump has signed two Executive Orders designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. One Executive Order directs federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA 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 ACA. Several state Attorneys General filed suit to stop the administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. In addition, CMS has recently proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. Further, on June 14, 2018, U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than \$12 billion in ACA risk corridor payments to third-party payors who argued were owed to them. The effects of this gap in reimbursement on third-party payors, the viability of the ACA marketplace, providers, and potentially our business, are not yet known.

The costs of prescription pharmaceuticals in the United States has also been the subject of considerable discussion in the United States, and members of Congress and the Trump administration have stated that they will address such costs through new legislative and administrative measures. To date, there have been several recent U.S. congressional inquiries and proposed 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.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. Increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

Governments outside of the United States tend to impose strict price controls, which may adversely affect our revenues, if any.

In some countries, particularly the countries 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. 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.

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 employees may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation.

We are exposed to the risk of employee fraud or other misconduct, including intentional failures to comply with FDA regulations or similar regulations of comparable foreign regulatory authorities, provide accurate information to the FDA or comparable foreign regulatory authorities, comply with manufacturing standards we have established, comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities, report financial information or data accurately or disclose unauthorized activities to us. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, standards 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 and results of operations, including the imposition of significant fines 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 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 cyber-attacks by malicious third parties over the Internet or through other mechanisms. Cyber-attacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cyber-attacks 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. Cyber-attacks also could include phishing attempts or e-mail fraud to cause payments or information to be transmitted to an unintended recipient.

While we have not experienced any such 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. 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.

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, 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 have terminated 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 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 and regulatory capabilities and implement 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 significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug development, regulatory affairs and, if any of our product candidates receives marketing approval, 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 and our bylaws 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, 2016 until February 25, 2019, the sale price of our common stock as reported on the Nasdaq Global Select Market ranged from a high of \$28.48 to a low of \$5.14. The market price for our common stock may be influenced by many factors, including:

- 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 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; 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.

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 and delay the development of our product candidates. 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.

The Tax Cuts and Jobs Act of 2017 could adversely affect our business and financial condition.

On December 22, 2017, President Trump signed into law the Tax Cuts and Jobs Act of 2017, which significantly revised the Internal Revenue Code of 1986, as amended. The newly enacted federal income tax law, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitation of the tax deduction for interest expense to 30% of adjusted earnings (except for certain small businesses), limitation of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, one time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifying or repealing many business deductions and credits. Notwithstanding the reduction in the corporate income tax rate, the overall impact of the new federal tax law is uncertain and our business and financial condition could be adversely affected. The impact of this tax reform on holders of our common stock is also uncertain and could be adverse. We urge our stockholders to consult with their legal and tax advisors with respect to this legislation and the potential tax consequences of investing in or holding our common stock.

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

As a public company, and particularly now that we are no longer an emerging growth company as of January 1, 2019, we will continue to 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. Moreover, these rules and regulations will increase our legal and financial compliance costs and make some activities more time-consuming and costly.

We cannot predict or estimate the amount of additional 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. Now that we are no longer an emerging growth company, 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. 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.

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 Cambridge lease expires November 30, 2022. In addition, we occupy approximately 6,830 square feet of office space in Durham, North Carolina. The term of the Durham lease expires on November 30, 2020. In January 2019, we entered into a sublease agreement to lease all of our office space in North Carolina to a subtenant through a lease term that expires on November 29, 2020.

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 the Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

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. The following table sets forth the high and low sale prices per share of our common stock, as reported on the Nasdaq Global Select Market, for the periods indicated:

	Market Price	
	High	Low
Year ended December 31, 2018:		
Fourth quarter	\$ 11.00	\$ 5.14
Third quarter	\$ 14.25	\$ 8.61
Second quarter	\$ 18.70	\$ 12.56
First quarter	\$ 21.40	\$ 12.35
Year ended December 31, 2017:		
Fourth quarter	\$ 20.45	\$ 11.35
Third quarter	\$ 20.00	\$ 11.15
Second quarter	\$ 18.50	\$ 9.30
First quarter	\$ 17.80	\$ 9.45

As of February 15, 2019, the number of holders of record of our common stock was 16. This number does not include beneficial owners whose shares are held in street name.

Dividends

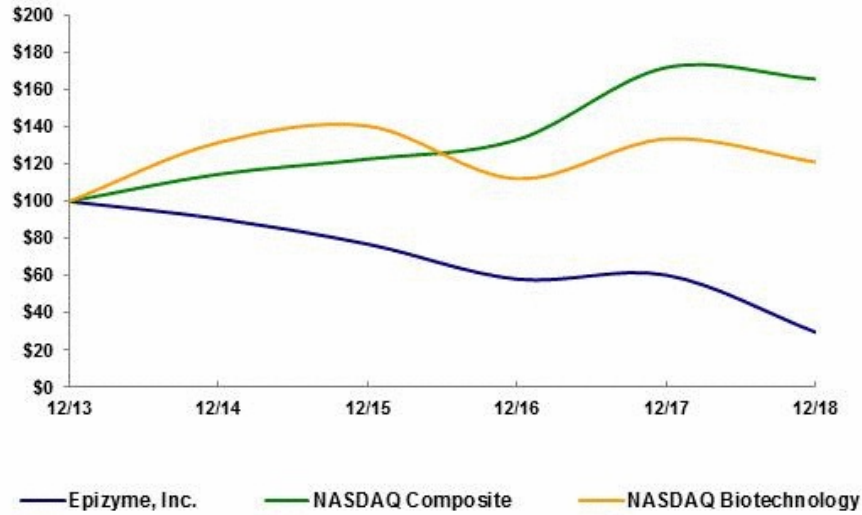
We have never declared or paid cash dividends on our capital stock. We intend to retain all of our future earnings, if any, to finance the growth and development of our business. We do not intend to pay cash dividends to our stockholders in the foreseeable future.

Stock Performance Graph

The following graph shows a comparison from December 31, 2013 through December 31, 2018 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.

COMPARISON OF 5 YEAR CUMULATIVE TOTAL RETURN*

Among Epizyme, Inc., the NASDAQ Composite Index
and the NASDAQ Biotechnology Index



*\$100 invested on 12/31/13 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. Selected Financial Data

The following selected financial data has been derived from our consolidated financial statements. The information set forth below should be read in conjunction with Item 7. *Management's Discussion and Analysis of Financial Condition and Results of Operations* and with our consolidated financial statements and notes thereto included elsewhere in this document.

	Year Ended December 31,				
	2018	2017	2016	2015	2014
	(In thousands, except per share data)				
Consolidated Statements of Operations Data:					
Collaboration revenue	\$ 21,700	\$ 10,000	\$ 8,007	\$ 2,560	\$ 41,411
Operating expenses:					
Research and development	105,833	109,661	91,461	111,209	75,595
General and administrative	43,972	37,181	28,372	23,900	20,866
Total operating expenses	149,805	146,842	119,833	135,109	96,461
Operating loss	(128,105)	(136,842)	(111,826)	(132,549)	(55,050)
Other income, net	4,532	2,197	1,614	173	154
Income tax benefit (expense)	(57)	336	—	—	(109)
Net loss	\$(123,630)	\$(134,309)	\$(110,212)	\$(132,376)	\$(55,005)
Basic and diluted loss per share allocable to common stockholders	\$ (1.72)	\$ (2.18)	\$ (1.93)	\$ (3.32)	\$ (1.67)
Basic and diluted weighted average shares outstanding	71,864	61,471	57,126	39,839	33,027
	As of December 31,				
	2018	2017	2016	2015	2014
	(In thousands)				
Consolidated Balance Sheets Data:					
Cash and cash equivalents	\$ 86,671	\$ 226,664	\$ 77,895	\$ 208,323	\$ 190,095
Marketable securities	153,633	49,775	164,297	—	—
Total assets	275,501	289,359	252,441	217,903	199,203
Deferred revenue	17,106	28,809	28,809	30,709	23,151
Total stockholders' equity	233,009	235,371	201,700	169,532	160,282

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.

Overview

We are a late-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. We are developing our lead product candidate, tazemetostat, an oral, first-in-class, selective small molecule inhibitor of the EZH2 histone methyltransferase, or HMT, for the treatment of a broad range of cancer types in multiple treatment settings, and developing our novel G9a program, EZM8266, for the treatment of sickle cell disease, or SCD.

We have taken a "pipeline in a product" approach to developing tazemetostat with a broad clinical development program through company-sponsored studies and collaborations. This program is evaluating tazemetostat as both a monotherapy and combination treatment in hematological malignancies and solid tumors for both late and early lines of treatment. Tazemetostat has shown meaningful clinical activity as a monotherapy in multiple cancer indications and has been generally well-tolerated across clinical trials to date. Based on positive data in our two lead indications, epithelioid sarcoma and follicular lymphoma, or FL, and interactions with the United States Food and Drug Administration, or the FDA, we are planning to submit New Drug Applications, or NDAs, for accelerated approval of tazemetostat for each proposed indication in 2019, subject to the results of our ongoing trials in those indications.

In our hematological malignancy program, we are conducting a multi-cohort, global Phase 2 study evaluating tazemetostat's treatment potential in patients with relapsed or refractory non-Hodgkin lymphoma, or NHL. Two cohorts are evaluating tazemetostat as a monotherapy for patients with relapsed or refractory FL, one of the most prevalent forms of NHL, both with and without EZH2 activating mutations. In December 2018, we completed target enrollment of FL patients in our study, with 54 patients with wild-type EZH2 and 45 patients with EZH2 activating mutations. Based on interactions with the FDA, we believe we have identified a path to submission for accelerated approval of tazemetostat in FL patients with either an EZH2 activating mutation or wild-type EZH2, whose disease has progressed following two or more lines of therapy. We are targeting submission of an NDA for accelerated approval for tazemetostat for FL in this population in the fourth quarter of 2019, subject to the results of our ongoing trial in this indication.

As part of an accelerated approval strategy, we will need to conduct a confirmatory clinical program to verify clinical benefit and support the full approval of tazemetostat. We intend to review our proposed confirmatory program with the FDA, and to finalize its design in the first half of 2019. We hope to leverage the confirmatory program to expand tazemetostat into the second-line treatment setting for patients with FL, both with and without EZH2 activating mutations. In addition, we plan to evaluate tazemetostat treatment in combination with other therapies. In mid-2019, we anticipate initiating a combination study that would compare tazemetostat plus rituximab and Revlimid, a chemotherapeutic-free treatment regimen referred to as R², versus R² with placebo in patients with relapsed or refractory FL, both with and without EZH2 activating mutations. In addition, we are finalizing plans for a trial of tazemetostat in combination with rituxan for the treatment of patients with relapsed and refractory FL. Based on clinical activity observed with tazemetostat in combination with R-CHOP as a front-line treatment for

patients with diffuse large B-cell lymphoma, or DLBCL, we are evaluating the opportunity to investigate this combination as a front-line treatment for patients with FL. In collaboration with The Lymphoma Study Association, or LYSA, we are continuing to evaluate tazemetostat with R-CHOP as a front-line treatment for high-risk patients with DLBCL. In addition, Genentech Inc., or Genentech, is evaluating the combination of tazemetostat with its checkpoint inhibitor, Tecentriq (atezolizumab), for the treatment of patients with relapsed or refractory DLBCL, with preliminary data expected from that study in 2019.

In our solid tumor program, we are evaluating tazemetostat's treatment potential in adults and children with molecularly defined solid tumors, including INI1- and SMARCA4-negative tumors, which we collectively refer to as INI1-negative tumors. We are conducting a multi-cohort global Phase 2 trial of tazemetostat in adults with INI1-negative tumors, including epithelioid sarcoma or chordoma. Based on positive data that we have observed in patients with epithelioid sarcoma in the ongoing Phase 2 study, we are targeting submission of our first NDA for accelerated approval of tazemetostat for the treatment of epithelioid sarcoma in the second quarter of 2019. In connection with this submission, we will need to conduct a confirmatory program to verify clinical benefit and support the full approval of tazemetostat. We plan to explore with the FDA utilizing the natural history study in epithelioid sarcoma that we are conducting to serve as confirmatory evidence required in connection with any accelerated approval. The cohort of patients in the phase 2 study of chordoma patients is ongoing, and we are evaluating tazemetostat in the dose-expansion portion of a Phase 1 study in pediatric patients with INI1-negative tumors, with plans to report updated data in 2019.

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. We intend to build a focused field presence and marketing capabilities to commercialize tazemetostat for the epithelioid sarcoma and follicular lymphoma indications in the United States. We have begun building the infrastructure necessary to support the launch and marketing of tazemetostat for epithelioid sarcoma, and believe we can adequately address this patient population through a modest field force of less than 25 professionals. For geographies outside the United States, we are evaluating the most efficient path to reach patients, including through potential collaborations.

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, with or without activating EZH2 mutations, relapsed or refractory DLBCL with EZH2 activating mutations and metastatic or locally advanced epithelioid sarcoma 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 FL, 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.

Beyond tazemetostat, we are building an early pipeline to further support our leadership in epigenetics. We are developing our wholly-owned G9a candidate, EZM8266, for the treatment of people with sickle cell disease. We have completed IND-enabling studies for this program and plan to begin clinical evaluation with a safety and dose-finding study in the second half of 2019. In November 2018, we entered a strategic collaboration with Boehringer Ingelheim International GmbH, or Boehringer Ingelheim, focused on the research, development and commercialization of novel small molecule inhibitors, discovered by us, directed toward two previously unaddressed epigenetic targets as potential therapies for people with cancer. Specifically, these targets are enzymes within the helicase and histone acetyltransferase, or HAT, families that when dysregulated have been linked to the development of cancers that currently lack therapeutic options. We also have collaborations with Glaxo Group Limited (an affiliate of GlaxoSmithKline), or GSK, focused on the development of PRMT inhibitors discovered by us, and with Celgene Corporation and Celgene RIVOT Ltd., an affiliate of Celgene Corporation, which we collectively refer to as Celgene, focused on the development of pinometostat and small molecule inhibitors directed to three HMT targets.

Through December 31, 2018, we have raised an aggregate of \$988.2 million to fund our operations, of which \$232.8 million was non-equity funding through our collaboration agreements, \$679.4 million was from the sale of common stock in our public offerings and \$76.0 million was from the sale of redeemable convertible preferred stock. As of December 31, 2018, we had \$240.3 million in cash, cash equivalents and marketable securities.

We commenced active operations in early 2008, and since inception, have incurred significant operating losses. As of December 31, 2018, our accumulated deficit totaled \$586.7 million. As a late stage company, 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, including our continued execution on our clinical development and commercialization plans for tazemetostat.

Collaborations

Refer to Item 1, *Business--Our Collaborations* and Note 9, *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 Boehringer Ingelheim, Eisai, Celgene and GSK, as well as the related accounting and revenue recognition considerations.

Results of Operations for the Years Ended December 31, 2018, 2017 and 2016

Collaboration Revenue

The following is a comparison of collaboration revenue for the years ended December 31, 2018, 2017, and 2016:

	<u>Year Ended December 31,</u>		<u>Change</u>	<u>%</u>
	<u>2018</u>	<u>2017</u>		
	(In millions)			
Collaboration revenue	\$ 21.7	\$ 10.0	\$ 11.7	117.0%

	<u>Year Ended December 31,</u>		<u>Change</u>	<u>%</u>
	<u>2017</u>	<u>2016</u>		
	(In millions)			
Collaboration revenue	\$ 10.0	\$ 8.0	\$ 2.0	25.0%

Our revenue consists of collaboration revenue, including 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, 2018, 2017, and 2016:

Collaboration Partner	<u>Year Ended December 31,</u>		<u>Change</u>	<u>%</u>
	<u>2018</u>	<u>2017</u>		
	(In millions)			
GSK:	\$ 20.0	\$ 10.0	\$ 10.0	100.0%
BI:	1.7	—	1.7	100.0%
	<u>\$ 21.7</u>	<u>\$ 10.0</u>	<u>\$ 11.7</u>	<u>117.0%</u>

	Year Ended December 31,		Change	%
	2017	2016		
(In millions)				
Collaboration Partner				
GSK:	\$ 10.0	\$ 6.0	\$ 4.0	66.7%
Celgene:	—	1.9	(1.9)	-100.0%
Other	—	0.1	(0.1)	-100.0%
	<u>\$ 10.0</u>	<u>\$ 8.0</u>	<u>\$ 2.0</u>	<u>25.0%</u>

Collaboration revenue for the year ended December 31, 2018 increased \$11.7 million as compared to the year ended December 31, 2017, primarily as a result of 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, as compared to the achievement of a \$10.0 million milestone with GSK in 2017. Collaboration revenue for the year ended December 31, 2017 increased \$2.0 million as compared to the year ended December 31, 2016, primarily as a result of the achievement of a \$10.0 million milestone under our agreement with GSK during 2017 as compared to the achievement of a \$6.0 million milestone under our agreement with GSK during 2016 and the recognition of \$1.9 million in upfront revenue under our agreement with Celgene in 2016.

GSK. Through December 31, 2018, we have earned a total of \$89.0 million under the GSK agreement, which we recognized as collaboration revenue in the consolidated statements of operations and comprehensive loss, including \$12.0 million in preclinical and research and development milestone revenue earned in 2018 upon GSK's dosing of a patient in a Phase 2 clinical trial of GSK3326595, a PRMT5 inhibitor discovered by us and licensed to GSK under the collaboration agreement, and \$8.0 million in research and development milestone revenue earned in the fourth quarter of 2018 related to the second target in the collaboration, upon GSK's dosing of a patient in a Phase 1 clinical trial, both for a first-in-class methyltransferase inhibitor discovered by us and licensed to GSK. In the year ended December 31, 2017, revenue attributable to the GSK collaboration reflects the \$10.0 million in preclinical and research and development milestone revenue earned in May 2017 related to the second target in the collaboration, upon GSK's initiation of good laboratory practices toxicology studies for a first-in-class methyltransferase inhibitor discovered by us and licensed to GSK. In the year ended December 31, 2016, revenue attributable to the GSK collaboration reflects the \$6.0 million milestone earned upon GSK's initiation of patient dosing in a Phase 1 clinical trial of GSK3326595, a PRMT5 inhibitor discovered by us and licensed to GSK under the collaboration agreement. Since we have no further performance obligations under the GSK collaboration, future revenues under the collaboration will relate to milestone payments and royalties received under the agreement, if any.

Boehringer Ingelheim. In the year ended December 31, 2018, we recognized \$1.7 million in collaboration revenue as part of our Boehringer Ingelheim collaboration. 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 will receive \$5.0 million in research funding in 2019. The \$1.7 million in revenue was recognized as the Company performed research services. The remaining consideration will be recognized in 2019 as services are performed.

Celgene. In the years ended December 31, 2017 and 2018, no collaboration revenue was recognized as part of our Celgene collaboration. Collaboration revenue attributed to the Celgene collaboration in the year ended December 31, 2016 reflects the recognition of \$1.9 million in deferred revenue as upfront revenue recognized under the agreement.

As of December 31, 2018, we have total deferred revenue of \$17.1 million, of which \$13.3 million is in current liabilities on our consolidated balance sheet and relates to the upfront payment received under our Boehringer Ingelheim collaboration agreement and \$3.8 million is in noncurrent liabilities on our consolidated balance sheet and relates to our Celgene collaboration, attributable to options for the non-pinometostat targets that are subject to the collaboration. We satisfied all of our obligations related to pinometostat under the collaboration as of December 31, 2016. As a result of the adoption of the new revenue accounting guidance, ASC 606, *Revenue From Contracts with Customers*, in the first quarter of 2018, as described in Note 2, *Summary of Significant Accounting Policies—Recent 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, our noncurrent deferred revenue balance changed from the year ended December 31, 2017.

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, such as our Celgene collaboration, 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, 2018, 2017, and 2016:

	<u>Year Ended December 31,</u>		<u>Change</u>	<u>%</u>
	<u>2018</u>	<u>2017</u>		
	(In millions)			
Research and development	\$ 105.8	\$ 109.7	\$ (3.9)	-3.6%

	<u>Year Ended December 31,</u>		<u>Change</u>	<u>%</u>
	<u>2017</u>	<u>2016</u>		
	(In millions)			
Research and development	\$ 109.7	\$ 91.5	\$ 18.2	19.9%

During the year ended December 31, 2018, total research and development expenses decreased by \$3.9 million compared to the year ended December 31, 2017, primarily due to decreases in our discovery research activities due to a greater focus on our most advanced programs and decreases in clinical trial expenses, offset by greater tazemetostat manufacturing costs.

During the year ended December 31, 2017 total research and development expenses increased by \$18.2 million compared to the year ended December 31, 2016, primarily due to increased tazemetostat manufacturing activities, tazemetostat clinical development, expansion of activities related to our drug platform and target families, and research activities related to advancing our next development candidate.

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

Product Program	Year Ended December 31,		Change	%
	2018	2017		
	(In millions)			
External research and development expenses:				
Tazemetostat and related EZH2 programs	\$ 49.5	\$ 54.2	(4.7)	-8.7%
Pinometostat and related DOT1L programs	0.0	0.8	(0.8)	-100.0
Discovery and preclinical stage product programs, collectively	16.0	17.9	(1.9)	-10.6
Unallocated personnel and other expenses	40.3	36.8	3.5	9.5
Total research and development expenses	<u>\$ 105.8</u>	<u>\$ 109.7</u>	<u>\$ (3.9)</u>	<u>-3.6%</u>

Product Program	Year Ended December 31,		Change	%
	2017	2016		
	(In millions)			
External research and development expenses:				
Tazemetostat and related EZH2 programs	\$ 54.2	\$ 39.9	\$ 14.3	35.8%
Pinometostat and related DOT1L programs	0.8	2.6	(1.8)	-69.2
Discovery and preclinical stage product programs, collectively	17.9	18.9	(1.0)	-5.3
Unallocated personnel and other expenses	36.8	30.1	6.7	22.3
Total research and development expenses	<u>\$ 109.7</u>	<u>\$ 91.5</u>	<u>\$ 18.2</u>	<u>19.9%</u>

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 \$4.7 million for the year ended December 31, 2018 compared to the year ended December 31, 2017. The decrease in tazemetostat related spending in the year ended December 31, 2018 is primarily a result of a decreased clinical spending as a result of the partial clinical holds on the enrollment of new patients in the United States, France and Germany, offset by an increase in tazemetostat manufacturing costs.

External research and development expenses for tazemetostat and related EZH2 programs increased \$14.3 million for the year ended December 31, 2017 compared to the year ended December 31, 2016. The increase in tazemetostat related spending in the year ended December 31, 2017 is primarily a result of a significant increase in tazemetostat manufacturing and clinical trial activities in 2017 as compared to 2016.

External research and development expenses for pinometostat and related DOT1L programs for the year ended December 31, 2018 decreased \$0.8 million when compared to the year ended December 31, 2017. There were no costs incurred related to pinometostat in 2018. The costs incurred related to pinometostat in the year ended December 31, 2017 were primarily associated with costs attributed to the CRADA with the NCI. External research and development expenses for pinometostat decreased by \$1.8 million for the year ended December 31, 2017 compared to 2016. The decline in program spending reflects our completion of the pinometostat Phase 1 clinical trials during the fourth quarter of 2016 and the associated reduction in costs. The costs incurred related to pinometostat in year ended December 31, 2016 are primarily associated with study closeout and final reporting activities on the Phase 1 clinical trials, as well as costs attributed to the CRADA with the NCI entered into in October 2016.

External research and development expenses for discovery and preclinical stage product programs decreased \$1.9 million for the year ended December 31, 2018 compared to the year ended December 31, 2017, primarily related to decreased spending for discovery research activities, offset by increased development activities related to our novel G9a program, EZM8266, for the potential treatment of sickle cell disease. External research and development expenses for discovery and preclinical stage product programs decreased \$1.0 million for the year ended December 31, 2017 compared to the year ended December 31, 2016, primarily related to a greater focus on more mature existing targets and reduced efforts on the discovery of new chemical matter.

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, 2018 increased \$3.5 million compared to the year ended December 31, 2017. The increase in unallocated personnel and other expenses was primarily due to growth in our internal development functions and the associated third-party costs to support tazemetostat and the anticipated submission of our first NDA in the second quarter of 2019. Unallocated personnel and other expenses for the year ended December 31, 2017 increased \$6.7 million compared to the year ended December 31, 2016. The increase in unallocated personnel and other expenses in the year ended December 31, 2017 was primarily due to the expansion of our development organization to support expanded tazemetostat clinical trials, chemistry, manufacturing and controls, translational medicine, data analytics and regulatory activities. Costs incurred in 2016 related to the expansion of our development organization to support expanded tazemetostat clinical trials, chemistry, manufacturing and controls, translational medicine, data analytics and regulatory activities.

We expect research and development expenses will remain consistent in 2019, as we continue our clinical trial expenses for tazemetostat and focus on our most advanced discovery stage research programs.

General and Administrative

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 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 general and administrative expenses for the years ended December 31, 2018, 2017, and 2016:

	<u>Year Ended December 31,</u>		<u>Change</u>	<u>%</u>
	<u>2018</u>	<u>2017</u>		
	(In millions)			
General and administrative	\$ 44.0	\$ 37.2	\$ 6.8	18.3%

	<u>Year Ended December 31,</u>		<u>Change</u>	<u>%</u>
	<u>2017</u>	<u>2016</u>		
	(In millions)			
General and administrative	\$ 37.2	\$ 28.4	\$ 8.8	31.0%

For the year ended December 31, 2018, our general and administrative expenses increased \$6.8 million compared to the year ended December 31, 2017, primarily due to an increase in medical affairs and commercial costs as a result of organizational development in preparation for commercialization of tazemetostat. For the year ended December 31, 2017, our general and administrative expenses increased \$8.8 million compared to the year ended December 31, 2016, primarily due to an increase in consulting services as a result of rapid organizational development, including preparation for commercialization, and increased intellectual property legal fees associated with potential drug research candidates. General and administrative costs incurred in 2016 primarily related to higher compensation-related expenses associated with additions to the senior leadership team in the first half of 2016, as well as increased investment in business development activities and pre-commercial activities related to tazemetostat.

We expect that general and administrative expenses will increase in 2019, as we plan to increase our commercial activities, including the continued build out of our medical affairs and commercial organizations.

Other Income, Net

The following is a comparison of other income, net for the years ended December 31, 2018, 2017, and 2016:

	<u>Year Ended December 31,</u>		<u>Change</u>	<u>%</u>
	<u>2018</u>	<u>2017</u>		
	<u>(In millions)</u>			
Other income, net				
Interest income, net	\$ 4.6	\$ 2.2	2.4	109.1%
Other income, net	—	—	—	0.0
Other income, net	<u>\$ 4.6</u>	<u>\$ 2.2</u>	<u>\$ 2.4</u>	<u>109.1%</u>
	<u>Year Ended December 31,</u>		<u>Change</u>	<u>%</u>
	<u>2017</u>	<u>2016</u>		
	<u>(In millions)</u>			
Other income, net				
Interest income, net	\$ 2.2	\$ 1.5	\$ 0.7	46.7%
Other income, net	—	0.1	(0.1)	-100.0
Other income, net	<u>\$ 2.2</u>	<u>\$ 1.6</u>	<u>\$ 0.6</u>	<u>37.5%</u>

Other 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, and other income recorded from a tax incentive award received in 2013. Other income is mainly comprised of net interest income, which increased \$2.4 million for the year ended December 31, 2018 compared to the year ended December 31, 2017, primarily due to active management of our investment portfolio, an increase in investment yields, and an increased cash balance as a result of the October 2018 follow-on offering. Net interest income increased \$0.7 million for the year ended December 31, 2017 compared to the year ended December 31, 2016, primarily due to an increased cash balance as a result of the September 2017 follow-on offering. Net interest income in the year ended December 31, 2016 reflects an increased cash balance as a result of the January 2016 follow-on offering and the purchases of short term interest bearing securities in 2016.

Income Tax Benefit

We evaluated the expected recoverability of our net deferred tax assets as of December 31, 2018 and 2017, 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. Fifty percent of the deferred tax asset related to the AMT Credit is refundable with the filing of the 2018 tax return. As such, as of December 31, 2018, \$184,000 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.

Liquidity and Capital Resources

Through December 31, 2018, we have raised an aggregate of \$988.2 million to fund our operations, of which \$232.8 million was non-equity funding through our collaboration agreements, \$679.4 million was from the sale of common stock in our public offerings and \$76.0 million was from the sale of redeemable convertible preferred stock. As of December 31, 2018, we had \$240.3 million in cash, cash equivalents and marketable securities.

In October 2018, we raised approximately \$81.6 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 9,583,334 shares of our common stock in a public offering at a price of \$9.00 per share.

In September 2017, we raised \$151.3 million, net of underwriting discounts and commissions, but before direct and incremental costs from the sale of 10,557,000 shares of our common stock in a public offering at a price to the public of \$15.25 per share.

On April 15, 2016, we entered into a Sales Agreement with Cowen and Company, LLC, or Cowen, to sell, from time to time, shares of our common stock having an aggregate sales price of up to \$50.0 million through an “at the market offering” as defined in Rule 415 under the Securities Act of 1933, as amended, under which Cowen would act as sales agent, which we refer to as the ATM Offering. Through March 10, 2017, we sold 155,834 shares of common stock under the Sales Agreement, resulting in net proceeds of \$1.9 million related to the ATM Offering. We terminated the Sales Agreement with Cowen, effective March 10, 2017.

In addition to our existing cash, cash equivalents and marketable securities, we may receive research and development co-funding and are eligible to earn a significant amount of option exercise and 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 preparation for commercialization, compensation and related expenses, laboratory and related supplies, our potential future milestone payment obligations to Eisai and Roche Molecular under the amended Eisai collaboration agreement and Roche Molecular companion diagnostic agreement, legal and other regulatory expenses and general overhead costs.

Because our product candidates are in various stages of clinical and preclinical development and the outcome of these efforts is uncertain, we cannot estimate the actual amounts necessary to successfully complete the development and commercialization of our product candidates or 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 research and development plans and our timing expectations related to the progress of our programs, we expect that our existing cash, cash equivalents and marketable securities as of December 31, 2018, will be sufficient to fund our planned operating expenses and capital expenditure requirements into the second quarter of 2020, without giving effect to any potential option exercise fees or milestone payments we may receive under our collaboration agreements. We have based this estimate on assumptions that may prove to be wrong, particularly as the process of testing product 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, 2018, 2017 and 2016:

	Year Ended December 31,		Change	%
	2018	2017		
	(In millions)			
Net cash used in operating activities	\$ (121.6)	\$ (120.4)	(1.2)	1.0%
Net cash (used in) provided by investing activities	(102.6)	113.3	(215.9)	190.6
Net cash provided by financing activities	84.2	155.9	(71.7)	46.0

	Year Ended December 31,		Change	%
	2017	2016		
	(In millions)			
Net cash used in operating activities	\$ (120.4)	\$ (96.4)	(24.0)	24.9%
Net cash provided by (used in) investing activities	113.3	(165.4)	278.7	-168.5
Net cash provided by financing activities	155.9	131.4	24.5	18.6

Net Cash Used in Operating Activities

Net cash used in operating activities was \$121.6 million during the year ended December 31, 2018 compared to \$120.4 million during the year ended December 31, 2017. The increase in net cash used in operating activities primarily relates to the decrease in net loss in the period compared to 2017, a net increase in non-cash stock-based compensation, partially offset by a decrease in net depreciation and amortization and changes in working capital. The most significant items affecting working capital in the year ended December 31, 2018 includes accounts receivable related to the milestone revenue recognized under the GSK agreement and current deferred revenue associated with the BI Agreement.

Net cash used in operating activities was \$120.4 million during the year ended December 31, 2017 compared to \$96.4 million during the year ended December 31, 2016. The increase in net cash used in operating activities primarily relates to the increase in net loss in the period compared to 2016, partially offset by changes in working capital.

Net Cash Used in Investing Activities

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 investing activities during the year ended December 31, 2017 reflects \$126.4 million of purchases of available-for-sale securities and \$1.0 million of purchases of property and equipment, offset by maturities of available-for-sale securities of \$240.7 million.

Net cash used in investing activities during the year ended December 31, 2016 reflects \$229.9 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 \$65.1 million.

We enter into contracts in the normal course of business with CROs 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 the table of contractual obligations and 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 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. We believe the critical accounting policies used in the preparation of our financial statements which require significant estimates and judgments are as follows:

Revenue Recognition

Effective January 1, 2018, we adopted Accounting Standards Codification, or 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 HMT 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 HMT 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 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 promise, whether the value of the license is dependent on the unsatisfied promise, whether there are other vendors that could provide the remaining promise, and whether it is separately identifiable from the remaining promise. 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 the Company 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. 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. 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 control of the licensee, 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 9, *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.

Stock-Based Compensation

We issue stock-based compensation awards to employees, including stock options and restricted stock, and offer an employee stock purchase plan. We measure stock-based compensation expense related to these awards based on the fair value of the award on the date of grant and recognize stock-based compensation expense on a straight-line basis over the requisite service period of the awards, which generally equals the vesting period. We have selected the Black-Scholes option pricing model to determine the fair value of stock option awards which requires the input of various assumptions that require management to apply judgment and make assumptions and estimates, including:

- the expected life of the stock option award, which we calculate using the simplified method as we have insufficient historical information regarding our stock options to provide a basis for estimate;
- the expected volatility of the underlying common stock, which we estimate using a blended approach encompassing our historical experience and the historical volatility of a peer group of comparable publicly traded companies with product candidates in similar stages of development;
- the expected risk-free interest rate based on the U.S. Treasury zero coupon rate with a remaining term approximating the expected term; and
- the expected dividend yield of zero.

Our assumptions may differ from those used in prior periods, and changes in the assumptions may have a significant impact on the fair value of future equity awards, which could have a material impact on our consolidated financial statements.

We recognize forfeitures for employee and non-employee grants at the time they occur. The actual expense recognized over the vesting period will only represent those options that vest.

Since our initial public offering, the exercise price per share of all option grants has been set at the closing price of our common stock on The Nasdaq Global Select Market on the applicable date of grant, which our board of directors believes represents the fair value of our common stock.

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 research and development plans and our timing expectations related to the progress of our programs, we expect that our existing cash, cash equivalents and marketable securities as of December 31, 2018, will be sufficient to fund our planned operating expenses and capital expenditure requirements into the second quarter of 2020, without giving effect to any potential option exercise fees or milestone payments we may receive under our collaboration agreements.

Recent 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—Recent 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, 2018, we had cash equivalents and available for sale securities of \$240.3 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, 2018 by \$0.3 million.

We contract with CROs 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.

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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, 2018. 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, 2018, 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, 2018. 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, 2018, 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, 2018, which report is included herein.

Report of Independent Registered Public Accounting Firm

To the Stockholders and 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, 2018, 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, 2018, 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, 2018 and 2017, 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, 2018, and the related notes and our report dated February 26, 2019 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 26, 2019

Changes in Internal Control over Financial Reporting

We use a third-party, cloud-based software service provider in connection with certain aspects of our financial reporting. In the fourth quarter of 2018, this service provider made changes to its internal controls to address deficiencies in its own information technology change management controls relating to its cloud-based software services.

Other than these third-party changes, no change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the three months ended December 31, 2018 that has materially affected, or is 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 2019 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 2019 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 2019 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 2019 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 2019 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:¹

Exhibit Number	Description of Exhibit
3.1	Restated Certificate of Incorporation of the Registrant (1)
3.2	Amended and Restated Bylaws of the Registrant (2)
4.2	Amended and Restated Investor Rights Agreement dated as of April 2, 2012 (4)
10.1+	2008 Stock Incentive Plan (4)
10.2+	Form of Incentive Stock Option Agreement under 2008 Stock Incentive Plan (4)
10.3+	Form of Nonstatutory Stock Option Agreement under 2008 Stock Incentive Plan (4)
10.4+	Form of Restricted Stock Agreement under 2008 Stock Incentive Plan (4)
10.5+	2013 Stock Incentive Plan (2)
10.6+	Form of Incentive Stock Option Agreement under 2013 Stock Incentive Plan (2)
10.7+	Form of Nonstatutory Stock Option Agreement under 2013 Stock Incentive Plan (2)
10.8+	Form of Restricted Stock Agreement under 2013 Stock Incentive Plan (2)
10.9+	Form of Restricted Stock Unit Agreement under 2013 Stock Incentive Plan (21)
10.10+	2013 Employee Stock Purchase Plan (2)
10.11+	Executive Severance and Change in Control Plan (21)
10.12+	Employment Offer Letter dated between the Registrant and Robert Bazemore, dated August 5, 2015 (12)
10.13+	Employment Offer Letter between the Company and Matthew E. Ros, dated April 15, 2016 (15)
10.14+	Employment Offer Letter between the Company and Susan Graf, dated April 25, 2016 (17)
10.15+	Employment Offer Letter between the Company and Shefali Agarwal, dated June 18, 2018 (20)
10.16	Form of Director and Officer Indemnification Agreement (2)

Exhibit Number	Description of Exhibit
10.17†	<u>Collaboration and License Agreement dated as of April 1, 2011 by and between the Registrant and Eisai Co., Ltd. (3)</u>
10.18†	<u>License and Collaboration Agreement dated as of April 2, 2012 by and between the Registrant and Celgene International Sàrl and Celgene Corporation (3)</u>
10.19†	<u>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)</u>
10.20†	<u>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 (6)</u>
10.21†	<u>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 (14)</u>
10.22†	<u>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 (19)</u>
10.23	<u>Letter Agreement by and between the Registrant and Eisai Co., Ltd. dated as of December 21, 2012 relating to Companion Diagnostics Agreement (4)</u>
10.24	<u>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 (11)</u>
10.25†	<u>Amended and Restated Collaboration and License Agreement dated as of March 12, 2015, by and between the Registrant and Eisai Co. Ltd. (11)</u>
10.26	<u>Lease Agreement dated as of June 15, 2012 between the Registrant and ARE-TECH Square, LLC (4)</u>
10.27	<u>Non-Employee Director Compensation Program (21)</u>
10.28	<u>First Amendment to Lease Agreement dated as of September 30, 2013 between the Registrant and ARE-TECH Square, LLC (5)</u>
10.29	<u>Second Amendment to Lease Agreement dated as of May 18, 2016 between the Registrant and ARE-TECH Square, LLC (16)</u>
10.30†	<u>Amended and Restated Collaboration and License Agreement dated as of July 8, 2015 by and between the Registrant and Celgene Corporation and Celgene RIVOT Ltd. (13)</u>
10.31†	<u>Collaboration and License Agreement dated as of January 8, 2011 by and between the Registrant and Glaxo Group Limited (3)</u>
10.32†	<u>Amendment to Collaboration and License Agreement dated as of July 23, 2013 by and between the Registrant and Glaxo Group Limited (7)</u>
10.33†	<u>Amendment to Collaboration and License Agreement dated as of February 24, 2014 by and between the Registrant and Glaxo Group Limited (8)</u>
10.34†	<u>Amendment to Collaboration and License Agreement dated as of March 18, 2014 by and between the Registrant and Glaxo Group Limited (8)</u>
10.35†	<u>Amendment to Collaboration and License Agreement dated as of April 17, 2014 by and between the Registrant and Glaxo Group Limited (9)</u>
10.36†	<u>Amendment to Collaboration and License Agreement dated as of October 1, 2014 by and between the Registrant and Glaxo Group Limited (10)</u>

Exhibit Number	Description of Exhibit
10.37	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 (18)
10.38	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 (18)
10.39	<input type="checkbox"/> Collaboration Agreement dated as of November 14, 2018 by and between the Registrant and Boehringer Ingelheim International GmbH (21)
21.1	Subsidiaries of the Registrant (4)
23.1	Consent of Ernst & Young LLP (21)
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. (21)
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. (21)
32.1	Certifications pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of The Sarbanes-Oxley Act of 2002, by Robert B. Bazemore, President and Chief Executive Officer of the Company, and Matthew Ros, Chief Strategy & Business Officer of the Company. (21)
101.INS	XBRL Instance Document
101.SCH	XBRL Schema Document
101.CAL	XBRL Calculation Linkbase Document
101.LAB	XBRL Labels Linkbase Document
101.PRE	XBRL Presentation Linkbase Document
101.DEF	XBRL Definition Linkbase 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.

Confidential treatment requested as to portions of the exhibit. Confidential materials omitted and filed separately with the Securities and Exchange Commission.

(1) 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 June 7, 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 Registration Statement on Form S-1 (File No. 333-187982) filed with the Securities and Exchange Commission on April 18, 2013.

(5) 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.

(6) 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.

- (7) 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.
- (8) 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.
- (9) 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.
- (10) 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.
- (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 March 16, 2015.
- (12) 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.
- (13) Incorporated by reference to the Registrant's Quarterly Report on Form 10-Q (File No. 001-35945) filed with the Securities and Exchange Commission on August 6, 2015.
- (14) 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.
- (15) 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.
- (16) 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.
- (17) Incorporated by reference to the Annual Report on Form 10-K (File No. 001-35945) filed with the Securities and Exchange Commission on March 3, 2017.
- (18) 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.
- (19) 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.
- (20) 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.
- (21) Filed with this Annual Report on Form 10-K.

EPIZYME, INC.
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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and 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, 2018 and 2017, 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, 2018, 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, 2018 and 2017, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2018, 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, 2018, 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 26, 2019, expressed an unqualified opinion thereon.

Adoption of New Accounting Standard

As discussed in Note 2 to the consolidated financial statements, the Company changed its method of accounting for revenue in 2018 due to the adoption of Accounting Standards Update (ASU) No. 2014-09, *Revenue from Contracts with Customers* (Topic 606), 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.

/s/ Ernst & Young LLP

We have served the Company's auditor since 2009.
Boston, Massachusetts
February 26, 2019

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

	December 31, 2018	December 31, 2017
ASSETS		
Current assets:		
Cash and cash equivalents	\$ 86,671	\$ 226,664
Marketable securities	153,633	49,775
Accounts receivable	20,067	382
Prepaid expenses and other current assets (Note 4)	12,164	8,983
Total current assets	272,535	285,804
Property and equipment, net (Note 3)	2,057	2,527
Restricted cash and other assets	909	1,028
Total assets	<u>\$ 275,501</u>	<u>\$ 289,359</u>
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	\$ 4,780	\$ 7,001
Accrued expenses (Note 5)	19,700	17,549
Current portion of capital lease obligation	16	110
Current portion of deferred revenue	13,300	—
Other current liabilities	37	4
Total current liabilities	37,833	24,664
Capital lease obligation, net of current portion	53	—
Deferred revenue	3,806	28,809
Other long-term liabilities	800	515
Commitments and contingencies (Note 7)		
Stockholders' equity:		
Preferred stock, \$0.0001 par value; 5,000 shares authorized; no shares issued and outstanding	—	—
Common stock, \$0.0001 par value; 125,000 shares authorized; 79,175 shares and 69,302 shares issued and outstanding, respectively	8	7
Additional paid-in capital	819,779	723,510
Accumulated other comprehensive loss	(54)	(49)
Accumulated deficit	(586,724)	(488,097)
Total stockholders' equity	233,009	235,371
Total liabilities and stockholders' equity	<u>\$ 275,501</u>	<u>\$ 289,359</u>

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,		
	2018	2017	2016
Collaboration revenue	\$ 21,700	\$ 10,000	\$ 8,007
Operating expenses:			
Research and development	105,833	109,661	91,461
General and administrative	43,972	37,181	28,372
Total operating expenses	<u>149,805</u>	<u>146,842</u>	<u>119,833</u>
Operating loss	(128,105)	(136,842)	(111,826)
Other income, net:			
Interest income, net	4,557	2,165	1,531
Other (expense) income, net	(25)	32	83
Other income, net	<u>4,532</u>	<u>2,197</u>	<u>1,614</u>
Loss before income taxes	(123,573)	(134,645)	(110,212)
Income tax (provision) benefit	(57)	336	—
Net loss	<u>\$ (123,630)</u>	<u>\$ (134,309)</u>	<u>\$ (110,212)</u>
Other comprehensive loss:			
Unrealized (loss) gain on available for sale securities	(5)	57	(106)
Comprehensive loss	<u>\$ (123,635)</u>	<u>\$ (134,252)</u>	<u>\$ (110,318)</u>
Loss per share allocable to common stockholders:			
Basic	\$ (1.72)	\$ (2.18)	\$ (1.93)
Diluted	\$ (1.72)	\$ (2.18)	\$ (1.93)
Weighted average shares outstanding:			
Basic	71,864	61,471	57,126
Diluted	71,864	61,471	57,126

See notes to consolidated financial statements.

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

	Year Ended December 31,		
	2018	2017	2016
	<i>(as revised)*</i>		
CASH FLOWS FROM OPERATING ACTIVITIES:			
Net loss	\$ (123,630)	\$ (134,309)	\$ (110,212)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	1,052	1,639	1,589
Stock-based compensation	12,004	11,431	10,568
Amortization of discount on investments	(1,556)	265	(51)
Deferred income taxes	184	(368)	—
Changes in operating assets and liabilities:			
Accounts receivable	(19,686)	(359)	239
Prepaid expenses and other current assets	(3,181)	(2,525)	(1,542)
Accounts payable	(2,404)	1,967	341
Accrued expenses	2,066	1,523	4,673
Deferred revenue	13,300	—	(1,900)
Other assets	(66)	(17)	106
Other long-term liabilities	317	320	(182)
Net cash used in operating activities	(121,600)	(120,433)	(96,371)
CASH FLOWS FROM INVESTING ACTIVITIES:			
Purchases of marketable securities	(298,670)	(126,356)	(229,887)
Proceeds from sales/maturities of marketable securities	196,363	240,670	65,097
Purchases of property and equipment	(299)	(984)	(624)
Net cash (used in) provided by investing activities	(102,606)	113,330	(165,414)
CASH FLOWS FROM FINANCING ACTIVITIES:			
Proceeds from public offering of common stock, net of commissions	81,938	152,922	130,438
Payment of common stock offering costs	(260)	(388)	(483)
Payment under capital lease obligation	(129)	(620)	(561)
Proceeds from stock options exercised	1,885	3,281	1,589
Issuance of shares under employee stock purchase plan	779	677	374
Net cash provided by financing activities	84,213	155,872	131,357
Net (decrease) increase in cash and cash equivalents	(139,993)	148,769	(130,428)
Cash, cash equivalents, and restricted cash, beginning of period	227,126	78,357	208,785
Cash, cash equivalents, and restricted cash, end of period	<u>\$ 87,133</u>	<u>\$ 227,126</u>	<u>\$ 78,357</u>
SUPPLEMENTAL DISCLOSURES OF CASH FLOW INFORMATION:			
Unpaid offering costs	\$ 75	\$ —	\$ —
Cumulative catch up related to the adoption of ASU 2016-09	\$ —	\$ 115	\$ —
Property and equipment included in accounts payable or accruals	\$ 194	\$ 58	\$ —
Cash paid for income taxes	\$ 48	\$ 33	\$ —

See notes to consolidated financial statements.

* Revised as a result of the adoption of ASU 2016-18

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

	Common Stock		Additional Paid-In Capital	Accumulated Deficit	Accumulated Other Comprehensive Loss	Total Stockholders' Equity
	Shares	Amount				
Balance at December 31, 2015	41,785,774	\$ 4	\$ 412,989	\$ (243,461)	\$ —	\$ 169,532
Issuance of common stock (net of commissions and offering costs of \$483)	15,420,220	2	129,953	—	—	129,955
Exercise of stock options	788,097	—	1,589	—	—	1,589
Stock-based compensation	—	—	10,568	—	—	10,568
Issuance of shares under employee stock purchase plan	56,189	—	374	—	—	374
Unrealized loss on available for sale securities	—	—	—	—	(106)	(106)
Net loss	—	—	—	(110,212)	—	(110,212)
Balance at December 31, 2016	58,050,280	\$ 6	\$ 555,473	\$ (353,673)	\$ (106)	\$ 201,700
Cumulative catch up related to the adoption of ASU 2016-09 (Note 2)	—	—	115	(115)	—	—
Issuance of common stock (net of commissions and offering costs of \$388)	10,689,253	1	152,533	—	—	152,534
Exercise of stock options and vesting of restricted stock units	478,471	—	3,281	—	—	3,281
Stock-based compensation	—	—	11,431	—	—	11,431
Issuance of shares under employee stock purchase plan	83,687	—	677	—	—	677
Unrealized gain on available for sale securities	—	—	—	—	57	57
Net loss	—	—	—	(134,309)	—	(134,309)
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 2014-09 (Note 2)	—	—	—	25,003	—	25,003
Issuance of common stock (net of commissions and offering costs of \$260)	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
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

See notes to consolidated financial statements.

EPIZYME, INC.

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 late-stage biopharmaceutical company that is committed to rewriting treatment for 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. The Company is developing its lead product candidate, tazemetostat, an oral, first-in-class selective inhibitor of the EZH2 histone methyltransferase, or HMT, in a broad range of cancer types and settings, and developing its lead development candidate in its novel G9a program, EZM8266, for the treatment of sickle cell disease, or SCD.

Through December 31, 2018, the Company has raised, including amounts received under collaboration agreements, an aggregate of \$988.2 million to fund its operations, of which \$232.8 million was non-equity funding through its collaboration agreements, \$679.4 million was from the sale of common 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, 2018, the Company had \$240.3 million in cash, cash equivalents and marketable securities.

The Company commenced active operations in early 2008. Since its inception, the Company has generated an accumulated deficit of \$586.7 million through December 31, 2018 and will require substantial additional capital to fund its research and development. The Company is subject to risks common to companies in the biotechnology industry, including, but not limited to, risks of failure of 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, 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

Principles of Consolidation

The consolidated financial statements include the accounts of the Company 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 collaboration 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 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 within the consolidated balance sheets. 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, 2018 was \$139.2 million, which consisted of 19 commercial paper securities and 29 corporate notes securities. The aggregate fair value of securities held by the Company in an unrealized loss position for less than twelve months as of December 31, 2017 was \$42.8 million, which consisted of 4 commercial paper securities, 14 corporate notes securities, and 1 U.S. government agency security. If any adjustment to fair value reflects a decline in value of the investment, the Company considers all available evidence to evaluate the extent to which the decline is "other-than-temporary" and, if so, mark the investment to market through a charge to the Company's statement of operations and comprehensive loss.

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, 2018 and 2017.

The following table summarizes the available for sale securities held at December 31, 2018 (in thousands):

Description	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Commercial paper	\$ 73,110	\$ —	\$ (22)	\$ 73,088
Corporate notes	80,575	—	(30)	80,545
U.S. government agency securities and U.S. Treasuries	—	—	—	—
Total	<u>\$ 153,685</u>	<u>\$ —</u>	<u>\$ (52)</u>	<u>\$ 153,633</u>

The following table summarizes the available for sale securities held at December 31, 2017 (in thousands):

Description	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Commercial paper	\$ 16,964	\$ —	\$ (6)	\$ 16,958
Corporate notes	31,610	—	(43)	31,567
U.S. government agency securities and U.S. Treasuries	1,250	—	—	1,250
Total	<u>\$ 49,824</u>	<u>\$ —</u>	<u>\$ (49)</u>	<u>\$ 49,775</u>

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, 2018 and 2017 have maturities of less than one year.

The amortized cost of available-for-sale securities is adjusted for amortization of premiums and accretion of discounts to maturity. At December 31, 2018, 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, 2018 and as a result, the Company did not reclassify any amounts out of accumulated other comprehensive loss for the same period.

The aggregate fair value of available-for-sale securities held by the Company in an unrealized loss position for less than twelve months as of December 31, 2018 was \$139.2 million. The aggregate unrealized loss for those securities in an unrealized loss position for less than twelve months as of December 31, 2018 was less than \$0.1 million. The Company determined that there was no material change in the credit risk of any of its investments. As a result, the Company determined it did not hold any investments with any other-than-temporary impairment as of December 31, 2018. The weighted-average maturity of the Company's portfolio was approximately two months at December 31, 2018.

Fair Value Measurements

The Financial Accounting Standards Board, or 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, 2018 and 2017 consisted primarily of cash and cash equivalents, marketable securities and accounts receivable and accounts payable. As of December 31, 2018 and December 31, 2017, the Company's financial assets recognized at fair value consisted of the following:

	Fair Value as of December 31, 2018			
	Total	Level 1	Level 2	Level 3
	(In thousands)			
Cash equivalents	\$ 79,225	\$ 50,785	\$ 28,440	\$ —
Marketable securities:				
Commercial paper	73,088	—	73,088	—
Corporate notes	80,545	—	80,545	—
U.S. government agency securities and treasuries	—	—	—	—
Total	\$ 232,858	\$ 50,785	\$ 182,073	\$ —

	Fair Value as of December 31, 2017			
	Total	Level 1	Level 2	Level 3
	(In thousands)			
Cash equivalents	\$ 207,251	\$ 207,251	\$ —	\$ —
Marketable securities:				
Commercial paper	16,958	—	16,958	—
Corporate notes	31,567	—	31,567	—
U.S. government agency securities and treasuries	1,250	—	1,250	—
Total	\$ 257,026	\$ 207,251	\$ 49,775	\$ —

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. 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.

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 the current cash, cash equivalent and marketable security balances. After considering the Company's current research and development plans and the timing expectations related to the progress of its programs, and after considering its existing cash, cash equivalents and marketable securities as of December 31, 2018, the Company 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.

Accounts Receivable

Accounts receivable are amounts due from collaboration partners as a result of research and development services provided, reimbursements under equally co-funded global development arrangements or milestones achieved but not yet paid. The Company considered the need for an allowance for doubtful accounts and has concluded that no allowance was needed as of December 31, 2018 or 2017, as the estimated risk of loss on its accounts receivable was determined to be minimal.

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 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.

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:

<u>Asset Category</u>	<u>Useful Lives</u>
Laboratory equipment	5 - 10 years
Office furniture and equipment	3 - 10 years
Leasehold improvements	3 - 10 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, 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 2018, 2017 or 2016.

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 6, *Income Taxes*, for additional information regarding the Company's income taxes.

On December 22, 2017, the President of the United States signed into law the Tax Cuts and Jobs Act ("TCJA"). This legislation makes broad and complex changes to the U.S. tax code, including, but not limited to, (i) reducing the U.S. federal statutory tax rate from 35% to 21%; (ii) eliminating the corporate alternative minimum tax (AMT) and changing how existing AMT credits can be realized; (iii) changing rules related to uses and limitations of net operating loss carryforwards created in tax years beginning after December 31, 2017, (iv) modifying the officer's compensation limitation, (v) changing rules related to the deductibility of entertainment expenses beginning in 2018, and (vi) changing rules related to the deductibility of qualified transportation benefits beginning in 2018. The Company recognizes the effects of changes in tax law, including the TCJA, in the period the law is enacted. Accordingly, the effects of the TCJA have been recognized in the financial statements as applicable for the years ended December 31, 2017 and December 31, 2018.

In December 2017, the SEC staff issued Staff Accounting Bulletin, or SAB, No. 118 to address the application of GAAP in situations when a registrant does not have the necessary information available, prepared, or analyzed (including computations) in reasonable detail to complete the accounting for certain income tax effects of TCJA. As of December 31, 2017, the effects of the TCJA were recorded on a provisional basis. As of December 31, 2018, the Company finalized its accounting for the TCJA and no measurement adjustments were recorded.

Revenue Recognition

Effective January 1, 2018, the Company adopted Accounting Standards Codification, or 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. 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. 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, the Company performs 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) the Company satisfies each performance obligation. As part of the accounting for these arrangements, the Company 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. 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 9, *Collaborations*.

Revenue Recognition Prior to Adoption of ASC 606 – Prior to the adoption of ASC 606, the Company recognized revenue when all of the following criteria were met: persuasive evidence of an arrangement exists; delivery has occurred or services have been rendered; the Company’s price to the customer is fixed or determinable and collectability is reasonably assured.

The Company has entered into collaboration and license agreements to discover, develop, manufacture and commercialize compounds directed to specific HMT targets. The terms of these agreements typically contain multiple deliverables, which may include: (i) licenses, or options to obtain licenses, to compounds directed to specific HMT 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 HMT targets. Payments to the Company under these agreements may include non-refundable license fees, option fees, exercise fees, payments for research activities, payments based upon the achievement of certain milestones and royalties on any resulting net product sales.

Multiple-Element Revenue Arrangements. The Company’s collaborations primarily represented multiple-element revenue arrangements. To account for these transactions, the Company determined the elements, or deliverables, included in the arrangement and allocated arrangement consideration to the various elements based on each element’s relative selling price. The identification of individual elements in a multiple-element arrangement and the estimation of the selling price of each element involved significant judgment, including consideration as to whether each delivered element had standalone value to the collaborator. The Company determined the estimated selling price for deliverables within each agreement using vendor-specific objective evidence (“VSOE”) of selling price, if available, or third-party evidence of selling price if VSOE was not available, or the Company’s best estimate of selling price, if neither VSOE nor third-party evidence was available. Determining the best estimate of selling price for a deliverable required significant judgment. The Company typically used its best estimate of a selling price to estimate the selling price for licenses to its proprietary technology, since it often did not have VSOE or third-party evidence of selling price for these deliverables. In those circumstances where the Company applied its best estimate of selling price to determine the estimated selling price of a license to its proprietary technology, it considered 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 best estimate of selling price, the Company evaluated whether changes in the key assumptions used to determine its best estimate of selling price would have a significant effect on the allocation of arrangement consideration between deliverables. The Company recognized consideration allocated to an individual element when all other revenue recognition criteria were met for that element.

Our multiple-element revenue arrangements generally included the following:

- ***Exclusive Licenses.*** The deliverables under our collaboration agreements generally included exclusive licenses to discover, develop, manufacture and commercialize compounds with respect to one or more specified HMT targets. To account for this element of the arrangement, we evaluated whether the exclusive license had standalone value from the undelivered elements to the collaboration partner based on the consideration of the relevant facts and circumstances of each arrangement, including the research and development capabilities of the collaboration partner and other market participants. Arrangement consideration allocated to licenses may be recognized upon delivery of the license if facts and circumstances indicate that the license has standalone value apart from the undelivered elements, which generally include research and development services. Arrangement consideration allocated to licenses is deferred if facts and circumstances indicate that the delivered license does not have standalone value from the undelivered elements.

We have determined that some of our exclusive licenses lack standalone value apart from the related research and development services, and in those circumstances we recognized collaboration revenue from non-refundable exclusive license fees on a straight-line basis over the contracted or estimated period of performance, which is generally the period over which the research and development services are to be provided.

- **Research and Development Services.** The deliverables under our collaboration and license agreements generally include deliverables related to research and development services to be performed on behalf of the collaboration partner. As the provision of research and development services is a part of our central operations, when we are principally responsible for the performance of these services under the agreements, we recognized revenue on a gross basis for research and development services as those services were performed.
- **Option Arrangements.** 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 at the inception of the arrangement as an upfront fee or payment, upon the exercise of an option to acquire a license or upon extending the selection period as an extension fee or payment.

The accounting for option arrangements is dependent on the nature of the options granted to the collaboration partner. Options are considered substantive if, at the inception of the arrangement, we are at risk as to whether the collaboration partner will choose to exercise the options to secure exclusive licenses. Factors that are considered in evaluating whether options are substantive include the overall objective of the arrangement, the benefit the collaborator might obtain from the arrangement without exercising the options, the cost to exercise the options relative to the total upfront consideration and the additional financial commitments or economic penalties imposed on the collaborator as a result of exercising the options. For arrangements under which the option to secure licenses is considered substantive, we did not consider the licenses to be deliverables at the inception of the arrangement. For arrangements where the option to secure licenses is not considered substantive, we considered the license to be a deliverable at the inception of the arrangement and, upon delivery of the license, applied the multiple-element revenue arrangement criteria to the license and any other deliverables to determine the appropriate revenue recognition. None of the options to secure exclusive licenses included in our collaborative arrangements have been determined to be substantive.

Milestone Revenue. Our collaboration and license agreements generally include contingent milestone payments related to specified preclinical research and development milestones, clinical development milestones, regulatory milestones and sales-based milestones. Preclinical research and development milestones are typically payable upon the selection of a compound candidate for the next stage of research and development. Clinical development milestones are typically payable when a product candidate initiates or advances in clinical trial phases or achieves defined clinical events, such as proof-of-concept. Regulatory milestones are typically payable upon submission for marketing approval with regulatory authorities, upon receipt of actual marketing approvals for a compound or for additional indications or upon the first commercial sale. Sales-based milestones are typically payable when annual sales reach specified levels.

At the inception of each arrangement that included milestone payments, we evaluated whether each milestone was substantive and at risk to both parties on the basis of the contingent nature of the milestone. This evaluation included an assessment of whether:

- the consideration is commensurate with either the entity's performance to achieve the milestone or the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from the entity's performance to achieve the milestone;
- the consideration relates solely to past performance; and
- the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement.

We evaluated factors such as the scientific, regulatory, commercial and other risks that must be overcome to achieve the respective milestone, the level of effort and investment required to achieve the respective milestone and whether the milestone consideration is reasonable relative to all deliverables and payment terms in the arrangement in making this assessment.

Non-refundable preclinical research and development, clinical development and regulatory milestones that were expected to be achieved as a result of our efforts during the period of our performance obligations under the collaboration and license agreements were generally considered to be substantive and were recognized as revenue upon the achievement of the milestone, assuming all other revenue recognition criteria are met. If not considered to be substantive, revenue from achievement of milestones was initially deferred and recognized over the remaining term of our performance obligations. Milestones that were not considered substantive because we did not contribute effort to their achievement are recognized as revenue upon achievement, assuming all other revenue recognition criteria are met, as there are no undelivered elements remaining and no continuing performance obligations on our part.

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 third-party service providers' billing terms do not coincide with the Company's period-end, the Company is required to make estimates of its obligations to those third parties, 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 third-party 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. 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 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 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.

Refer to Note 10, *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) allocable 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 participates 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 that are outstanding during the period, except where such non-participating securities would be anti-dilutive. Refer to Note 11, *Loss per Share*, for the Company’s calculation of loss per share for the periods presented.

Segment Information

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

Pending Accounting Pronouncements

In February 2016, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or ASU, 2016-02, *Leases (Topic 842)*, which requires lessees to recognize a right-of-use asset and lease liability for most lease arrangements. The new standard is effective for annual reporting periods beginning after December 15, 2018. A modified retrospective transition approach is required to be applied to leases existing as of, or entered into after, the beginning of the earliest comparative period presented in the financial statements, with certain practical expedients available.

Currently, the Company is gathering information, reviewing its portfolio of existing leases, and continuing to evaluate the potential changes to the Company’s future financial reporting and disclosures that may result from adopting this ASU. The Company plans to elect the practical expedient which will allow it to not apply the amended lease accounting guidance to comparative periods that will be presented. The Company expects that all of its lease commitments will be subject to the new standard with the cumulative effect of adoption recognized to retained earnings on January 1, 2019.

In June 2018, the FASB issued ASU No. 2018-07, *Compensation—Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting*, or ASU 2018-07. The guidance in this ASU expands the scope of Topic 718 to include share-based payment transactions for acquiring goods and services from nonemployees. The new standard is effective for annual reporting periods beginning after December 15, 2018, including interim reporting periods within each annual reporting period. The adoption of ASU 2018-07 is not expected to have an impact on the Company’s consolidated financial statements, as the Company currently has not issued share-based payments to non-employees.

In November 2018, the FASB issued ASU 2018-18, *Collaborative Arrangements (Topic 808)*, which clarifies that certain transactions between collaborative arrangement participants should be accounted for as revenue when the collaborative arrangement participant is a customer in the context of a unit of account and precludes recognizing as revenue consideration received from a collaborative arrangement participant if the participant is not a customer. The 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 is required by recognizing a cumulative-effect adjustment to the opening balance of retained earnings of the earliest annual period presented. The Company is currently evaluating the impact of the adoption of this standard on its financial statements.

Recently Adopted Accounting Pronouncements

Revenue Recognition

In May 2014, the FASB, issued ASU, 2014-09, *Revenue From Contracts With Customers*. ASU 2014-09 amends Accounting Standards Codification, or ASC, 605, *Revenue Recognition* (“ASC 605”), by outlining a single comprehensive model for entities to use in accounting for revenue arising from contracts with customers. In addition, the FASB issued ASUs 2016-10 and 2016-12, which provide clarifying amendments to ASU 2014-09. ASU 2014-09 and its related amendments were effective for the Company for interim and annual periods in 2018. The new standards are codified under ASC 606. The Company adopted this new standard on January 1, 2018 using the modified retrospective approach. The Company has elected to use the following practical expedient that is permitted under the rules of the adoption, which has been applied consistently to all contracts: the Company has not retrospectively restated its contracts that have been amended at each amendment date as is generally required under ASC 606. Instead, upon adoption, an entity may reflect the aggregate effect of all modifications that occurred before the beginning of the earliest period presented when identifying the satisfied and unsatisfied performance obligations; determining the transaction price; and allocating the transaction price to the satisfied and unsatisfied performance obligations.

As a result of adopting ASC 606 on January 1, 2018, the Company recorded a cumulative-effect credit to opening accumulated deficit of \$25.0 million as of January 1, 2018 and a corresponding decrease to deferred revenue, net of current portion.

The cumulative-effect change relates principally to the Company’s treatment of option rights under its agreement with Celgene Corporation, or “Celgene”, and the identification of more performance obligations under ASC 606 in comparison with identified units of accounting under ASC 605. The adoption did not impact the previous accounting for the Company’s agreements with Glaxo Group Limited, or “GSK” and Eisai Co. Ltd., or Eisai. Pursuant to ASC 605, the Company had deemed Celgene’s options to license the three small molecule HMT inhibitors targeting three predefined targets, or the Option Targets, as non-substantive and therefore included the services that it would be required to perform upon option exercise as deliverables. ASC 606 provides that only options that are deemed to be material rights are a performance obligation and that any goods or services required upon exercise of the option be excluded from the evaluation of performance obligations until the option is exercised. As a result of this change to the guidance, (1) the pre-IND research services performed by the Company for each of the three Option Targets were deemed to be distinct performance obligations whereas each had previously been combined into one unit of accounting with the respective license that is subject to the exercise of the option and (2) a lesser amount of transaction price was allocated to the options. For further discussion of the change and the adoption of this standard, see Note 9, *Collaborations*.

For the twelve months ended December 31, 2018, we recognized \$21.7 million in collaboration revenue in accordance with ASC 606, which was materially consistent with what we would have recorded under ASC 605. Deferred revenue as of December 31, 2018 was \$17.1 million under ASC 606, as compared to a balance of \$42.1 million, which would have resulted under ASC 605.

Cash

As of January 1, 2018, the Company adopted ASU 2016-15, *Statement of Cash Flows (Topic 230): Classification of Certain Cash Receipts and Cash Payments*. The new standard clarifies certain aspects of the statement of cash flows, including the classification of debt prepayment or debt extinguishment costs, settlement of zero-coupon debt instruments or other debt instruments with coupon interest rates that are insignificant in relation to the effective interest rate of the borrowing, contingent consideration payments made after a business combination, proceeds from the settlement of insurance claims, proceeds from the settlement of corporate-owned life insurance policies, distributions received from equity method investees and beneficial interests in securitization transactions. The new standard also clarifies that an entity should determine each separately identifiable source or use within the cash receipts and cash payments on the basis of the nature of the underlying cash flows. In situations in which cash receipts and payments have aspects of more than one class of cash flows and cannot be separated by source or use, the appropriate classification should depend on the activity that is likely to be the predominant source or use of cash flows for the item. The adoption of this standard did not have a material impact on the Company’s consolidated statements of cash flows.

As of January 1, 2018, the Company adopted ASU 2016-18, *Restricted Cash*, or ASU 2016-18, which requires an entity to reconcile and explain the period-over-period change in total cash, cash equivalents and restricted cash within its statements of cash flows. The Company adopted the standard using the retrospective approach. The adoption of the standard did not have a material impact on the Company's consolidated financial statements or disclosures; however, prior period restricted cash was added to beginning and ending cash and cash equivalents in the consolidated statements of cash flows to conform to the current period presentation.

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,		
	2018	2017	2016
	(In thousands)		
Cash and cash equivalents	\$ 86,671	\$ 226,664	\$ 77,895
Restricted cash, as part of other assets	462	462	462
Total cash, cash equivalents, and restricted cash shown in the consolidated statements of cash flows	\$ 87,133	\$ 227,126	\$ 78,357

The \$0.5 million relates to a letter of credit as a security deposit for the office and laboratory lease at Technology Square in Cambridge, Massachusetts. The Company has recorded cash held to secure this letter of credit as restricted cash in restricted cash and other assets on the consolidated balance sheet.

Share-Based Payment

As of January 1, 2018, the Company adopted ASU 2017-09, *Compensation-Stock Compensation (Topic 718): Scope of Modification Accounting*, which clarifies when to account for a change to the terms or conditions of a share-based payment award as a modification. The new standard does not change the accounting for modifications but clarifies that modification accounting guidance should only be applied if the fair value, vesting conditions, or classification of the award changes as a result of the change in terms or conditions. The adoption of this standard did not materially impact the Company's stock-based compensation expense as no awards were modified during the year ended December 31, 2018.

3. Property and Equipment, net

Property and equipment, net consists of the following:

	December 31,	
	2018	2017
	(In thousands)	
Laboratory equipment	\$ 4,132	\$ 4,138
Computer and office equipment, furniture (1)	5,040	4,807
Leasehold improvements	414	354
Construction in progress	271	71
Property and equipment	9,857	9,370
Less: accumulated depreciation and amortization	(7,800)	(6,843)
Property and equipment, net	\$ 2,057	\$ 2,527

- (1) In 2015, the Company acquired \$1.7 million in computer hardware and equipment, pursuant to a capital lease, the term of which expires in February 2018. In April 2018, the Company acquired \$0.1 million of equipment pursuant to a capital lease, the term of which expires in April 2023. Accumulated depreciation related to these assets totaled \$0.0 million and \$1.6 million as of December 31, 2018 and 2017, respectively.

Depreciation and amortization expense was \$1.1 million, \$1.6 million and \$1.6 million for the years ended December 31, 2018, 2017, and 2016, respectively.

4. Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets consisted of the following:

	December 31,	
	2018	2017
	(In thousands)	
Prepaid clinical and manufacturing costs	\$ 6,295	\$ 5,724
Interest receivable on available for sale securities	679	249
Other prepaid expenses and other receivables	5,190	3,010
Total prepaid expenses and other current assets	<u>\$ 12,164</u>	<u>\$ 8,983</u>

5. Accrued Expenses

Accrued expenses consisted of the following:

	December 31,	
	2018	2017
	(In thousands)	
Employee compensation and benefits	\$ 5,509	\$ 4,628
Research and development expenses	11,272	11,658
Professional services and other	2,919	1,263
Accrued expenses	<u>\$ 19,700</u>	<u>\$ 17,549</u>

6. 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, 2018, 2017, and 2016 is as follows:

	2018	2017	2016
		(In thousands)	
Current	\$ (127)	\$ 32	\$ —
Deferred	184	(368)	—
Total	<u>57</u>	<u>(336)</u>	<u>—</u>
Income tax provision (benefit)	<u>\$ 57</u>	<u>\$ (336)</u>	<u>\$ —</u>

A reconciliation of the federal statutory income tax rate and the Company's effective income tax rate is as follows:

	Year Ended December 31,		
	2018	2017	2016
Federal statutory income tax rate	21.0%	34.0%	34.0%
State income taxes	5.7	4.8	4.5
Research and development and other tax credits	2.4	4.2	3.3
Permanent items	(0.7)	(2.0)	(1.9)
Change in valuation allowance	(28.3)	5.7	(40.1)
Return-to-provision adjustments	(0.1)	(0.7)	—
Change in deferred taxes	—	—	0.2
Rate Change	—	(45.7)	—
Effective income tax rate	0.0%	0.3%	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,	
	2018	2017
	(In thousands)	
Deferred tax assets:		
Net operating loss carryforwards	\$ 147,586	\$ 116,869
Research and development and other credit carryforwards	26,731	24,257
Capitalized start-up costs	1,031	1,175
Deferred revenue	1,021	7,766
Accruals and allowances	1,522	1,250
Eisai license payment	8,225	8,985
Other	5,172	4,738
Gross deferred tax assets	191,288	165,040
Deferred tax asset valuation allowance	(191,070)	(164,607)
Total deferred tax assets	218	433
Deferred tax liabilities:		
Depreciation and other	(34)	(65)
Total deferred tax liabilities	(34)	(65)
Net deferred tax asset (liability)	\$ 184	\$ 368

The Company evaluated the expected recoverability of its net deferred tax assets as of December 31, 2018 and 2017, 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, 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, 2018 and 2017, 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 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, 2017 and recognized as a tax benefit. Fifty percent of the deferred tax asset related to the AMT Credit is refundable with the filing of the 2018 tax return. As such, as of December 31, 2018, \$184,000 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.

As a result of the enacted law, the Company was required to revalue deferred tax assets and liabilities at 21 percent as of December 31, 2017. This revaluation resulted in a provision of \$61.6 million to income tax expense in continuing operations related to the reduction in the carrying value of the Company's deferred tax assets, offset by a corresponding reduction in the valuation allowance in 2017.

As of December 31, 2018, the Company had operating loss carryforwards of approximately \$542.6 million and \$535.4 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 \$114.1 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, 2018, the Company had research and development tax credit carryforwards of approximately \$9.1 million and \$2.9 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 2038, as well as federal orphan drug tax credit carryforwards of \$15.2 million, which would expire at various dates from 2033 through 2038, and a \$0.2 million federal alternative minimum tax credit carryforward, which represents the remaining AMT credit to be refunded with the filing of the 2019-2022 tax returns. 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,	
	2018	2017
	(In thousands)	
Unrecognized tax benefits - as of beginning of year	\$ 5,223	\$ 4,206
Gross increases - current period tax positions	520	1,017
Unrecognized tax benefits - as of end of year	<u>\$ 5,743</u>	<u>\$ 5,223</u>

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, 2018 or 2017.

The Company files income tax returns in the U.S. federal tax jurisdiction and Colorado, Indiana, Massachusetts, and North Carolina 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.

In December 2017, the SEC staff issued SAB 118 to address the application of GAAP in situations when a registrant does not have the necessary information available, prepared, or analyzed (including computations) in reasonable detail to complete the accounting for certain income tax effects of TCJA. The Company did not record any adjustments in the year ended December 31, 2018 to provisional amounts that were material to its financial statements. As of December 31, 2018, the Company's accounting treatment is complete.

7. Commitments and Contingencies

Commitments

The Company leases office and laboratory space at Technology Square in Cambridge, Massachusetts under a Lease Agreement, dated as of June 15, 2012, as amended (the "Lease") with ARE-TECH Square, LLC, a Delaware limited liability company (the "Landlord"), with a term that originally continued through May 31, 2018, and a Company option to extend the term of the lease at the then-current market rent, as defined in the Lease, through November 30, 2022.

In May 2017, the Company entered into a Third Amendment to Lease (the "Third Amendment") with the Landlord, and a Fourth Amendment to Lease with the Landlord (the "Fourth Amendment," and, together with the Third Amendment, the "Amendments").

Under the Amendments, the Company extended the term of the lease to November 30, 2022 but retained the right to terminate the Lease effective as of December 31, 2018, by giving written notice to the Landlord by December 31, 2017 and paying an early termination fee. The Company did not exercise this right. Under the Lease as amended, the Company has 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 December 1, 2021.

The Company has a \$0.5 million letter of credit as a security deposit for this lease and has recorded cash held to secure this letter of credit as restricted cash in restricted cash and other assets on the consolidated balance sheet. The Company recognizes rent expense, including escalation charges, on a straight-line basis over the initial term of the lease agreement.

In addition, the Company has a capital lease related to computer hardware equipment, an operating lease for storage space in Colorado and an operating lease for office space in North Carolina.

Rent expense was \$3.5 million, \$3.3 million and \$2.8 million for the years ended December 31, 2018, 2017, and 2016, respectively.

The Company's contractual commitments under these leases, excluding common area maintenance charges and real estate taxes, as of December 31, 2018 are as follows:

	Total	2019	2020	2021	2022	2023
	(In thousands)					
Operating leases	\$ 14,099	\$ 3,552	\$ 3,641	\$ 3,574	\$ 3,332	\$ —
Capital lease, including amounts representing interest	69	16	17	18	18	—
Total commitments	<u>\$ 14,168</u>	<u>\$ 3,568</u>	<u>\$ 3,658</u>	<u>\$ 3,592</u>	<u>\$ 3,350</u>	<u>\$ —</u>

In addition to commitments under leasing arrangements, as of December 31, 2018, the Company has committed to \$8.4 million of remaining development costs payable to Roche Molecular Systems Inc, ("Roche Molecular") upon certain development and regulatory milestones, under the amended companion diagnostic agreement, and Eisai has agreed to reimburse the Company \$0.9 million of this amount related to a regulatory milestone for Japan. The Company expects the remaining development costs under the amended agreement to be incurred and paid through 2020. Developmental costs of \$2.0 million and \$1.5 million were paid in 2018 and 2017, respectively, upon the achievement of milestones under the companion diagnostic agreement with Roche Molecular. In addition, the contractual commitments table above does not include potential future milestones or royalties that the Company may be required to make under license and collaboration agreements, including potential future milestones or royalties payable to Eisai under the amended collaboration and license agreement, due to the uncertainty of the occurrence of the events requiring payment under these agreements. Refer to Note 9, *Collaborations*.

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 the contractual commitments table above.

8. Stockholders' (Deficit) Equity

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 October 2018, September 2017 and January 2016, the Company issued 9,583,334, 10,557,000 and 15,333,334 shares of Common Stock, respectively, in connection with public offerings. The issuance of these shares contributed to significant increases in the Company's shares outstanding as of December 31, 2018 and 2017 and in the weighted average shares outstanding for the years ended December 31, 2018 and 2017 when compared to the comparable prior year periods.

The Company sold 132,253 shares and 23,581 shares, of Common Stock during the years ended December 31, 2017 and December 31, 2016, respectively, under an "at the market" program ("ATM Facility") with Cowen and Company, LLC ("Cowen") acting as sales agent under a sales agreement that the Company and Cowen entered into in April 2016. Cowen was compensated at a fixed commission rate of 3.0%. Transactions under the ATM Facility resulted in net proceeds of \$1.6 million and \$0.3 million in the years ended December 31, 2017 and 2016, respectively. The Company also incurred other issuance related costs of \$0.1 million associated with the ATM Facility in the fourth quarter of 2017, which have been accounted for as an offset to additional paid in capital. Through March 10, 2017, including sales in the year ended December 31, 2017, the Company sold 155,834 shares of Common Stock under the sales agreement with Cowen. The Company terminated the sales agreement with Cowen, effective March 10, 2017.

As of December 31, 2018, a total of 11,090,646 shares of common stock were reserved for issuance upon (i) the exercise of outstanding stock options and vesting of restricted stock units and (ii) the issuance of stock awards under the Company's 2013 Stock Incentive Plan and 2013 Employee Stock Purchase Plan.

9. Collaborations

Celgene

In April 2012, the Company entered into a collaboration and license agreement with Celgene. On July 8, 2015, the Company entered into an amendment and restatement of the collaboration and license agreement with Celgene.

Original Agreement Structure

Under the original agreement, the Company granted Celgene an exclusive license, for all countries other than the United States, to small molecule HMT inhibitors targeting the DOT1L HMT, including pinometostat, and an option, on a target-by-target basis, to exclusively license, for all countries other than the United States, rights to small molecule HMT inhibitors targeting any HMT targets, other than the EZH2 HMT, including tazemetostat, and targets covered by the Company's collaboration and license agreement dated January 8, 2011 with GlaxoSmithKline, or GSK. Under the original agreement, Celgene's option was exercisable during an option period that would have expired on July 9, 2015.

Under the original agreement, the Company received a \$65.0 million upfront payment and \$25.0 million from the sale of its series C redeemable convertible preferred stock to an affiliate of Celgene, of which \$3.0 million was considered a premium and included as collaboration arrangement consideration for a total upfront payment of \$68.0 million. In addition, the Company has received a \$25.0 million clinical development milestone payment and \$7.0 million in global development co-funding through December 31, 2018. The Company was also eligible to receive \$35.0 million in an additional clinical development milestone payment and up to \$100.0 million in regulatory milestone payments related to DOT1L as well as up to \$65.0 million in payments, including a combination of clinical development milestone payments and an option exercise fee for each available target to which Celgene had the right to exercise its option during an initial option period that would have ended in July 2015 but was extended pursuant to the amended and restated agreement as discussed below under “Amended and Restated Agreement Structure” (each a “selected target”), and up to \$100.0 million in regulatory milestone payments for each selected target. As to DOT1L and each selected target, the Company retained all product rights in the United States and was eligible to receive royalties for each target at defined percentages ranging from the mid-single digits to the mid-teens on net product sales outside of the United States subject to reduction in specified circumstances.

The Company was obligated to conduct and solely fund research and development costs of the Phase 1 clinical trials for pinometostat. For all remaining DOT1L program development costs, Celgene and the Company were to equally co-fund global development and each party was to solely fund territory-specific development costs for its territory.

Amended and Restated Agreement Structure

Under the amended and restated collaboration and license agreement:

- Celgene retained its exclusive license to small molecule HMT inhibitors targeting DOT1L, including pinometostat,
- Celgene’s other option rights were narrowed to small molecule HMT inhibitors targeting three predefined targets (the “Option Targets”),
- The exclusive licenses to HMT inhibitors targeting two of the Option Targets that Celgene may acquire were expanded to include the United States, with the exclusive license to HMT inhibitors targeting the third Option Target continuing to be for all countries other than the United States,
- Celgene’s option period was extended for each of the Option Targets and Celgene’s option is exercisable at the time of the Company’s investigational new drug application, or IND, filing for an HMT inhibitor targeting the applicable Option Target, upon the payment by Celgene at such time of a pre-specified development milestone-based license payment,
- Celgene’s license may be maintained beyond the end of Phase 1 clinical development for each of the Option Targets, upon payment by Celgene at such time of a pre-specified development milestone-based license payment, and
- The Company’s research and development obligations with respect to each Option Target under the amended and restated agreement were extended for at least an additional three years, subject to Celgene exercising its option with respect to such Option Target at IND filing. Subject to the Company’s opt-out rights, the Company’s research and development obligations were expanded to include the completion of a Phase 1 clinical trial as to each Option Target following Celgene’s exercise of its option at IND filing.

Under the amended and restated agreement, the Company received a \$10.0 million upfront payment in exchange for the Company's extension of Celgene's option rights to the Option Targets and the Company's research and development obligations. In addition, the Company is eligible to earn an aggregate of up to \$75.0 million in development milestones and license payments, up to \$365.0 million in regulatory milestone payments and up to \$170.0 million in sales milestone payments related to the three Option Targets. The Company is also eligible to receive royalties on each of the Option Targets as specified in the amended and restated agreement. The Company is also eligible to earn \$35.0 million in an additional clinical development milestone payment and up to \$100.0 million in regulatory milestone payments related to DOT1L. 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 Celgene. Due to the varying stages of development of each target, the Company is not able to determine the next milestone that might be earned, if any.

The amended and restated agreement eliminated the right of first negotiation that the Company had granted to Celgene under the original agreement with respect to business combination transactions that the Company may desire to pursue with third parties.

The Company is primarily responsible for the research strategy under the collaboration. During each applicable option period the Company is required to use commercially reasonable efforts to carry out a mutually agreed-upon research plan for each Option Target. Subject to the Company's opt-out right, for the DOT1L target and each of the Option Targets, the Company is required to conduct and solely fund development costs of the Phase 1 clinical trials for HMT inhibitors directed to such targets, including for pinometostat. After the completion of Phase 1 development, as to DOT1L and the Option Target for which the Company retains U.S. rights, Celgene and the Company will equally co-fund global development and each party will solely fund territory-specific development costs for its respective territory; and, as to the other two Option Targets, after the completion of Phase 1 development, Celgene will solely fund all development costs on a worldwide basis.

Accounting Considerations of the Amended and Restated Agreement

The Company assessed the amended arrangement in accordance with ASC 606 and concluded that the contract counterparty, Celgene, is a customer based on the arrangement structure, through the satisfaction of each target's performance obligations. As of the amendment, the Company identified the following performance obligations under the arrangement, whether satisfied or not:

- an exclusive license to small molecule HMT inhibitors targeting DOT1L, including pinometostat, combined with pre-IND research services for DOT1L;
- post-IND research and development services for DOT1L through a Phase 1 clinical trial;
- pre-IND research services for each Option Target; and
- material rights related to each of Celgene's options at the time of an IND filing to license HMT inhibitors targeting each Option Target.

The Company determined that the DOT1L license and pre-IND research and development activities for DOT1L were not distinct from one another, due to the limited economic benefit that Celgene would derive from the DOT1L license if it did not obtain the research services. After IND effectiveness, the Company concluded that the DOT1L license would be distinct apart from any remaining research and development services because Celgene, or other market participants, would have the ability to execute human clinical trials on the identified compound. Accordingly, the DOT1L license and pre-IND research services for DOT1L were accounted for as a combined performance obligation. The post-IND research and development services for DOT1L have been accounted for as a separate performance obligation.

The pre-IND research services for each Option Target were the only performance obligations not subject to the exercise of a customer option at the time of the amendment for each Option Target and therefore represent three separate performance obligations (one for each Option Target).

The Company evaluated the option rights at the time of an IND filing to determine whether they provide Celgene with material rights. The Company concluded that the options were issued at a discount, and therefore provide material rights. As such, the option rights at the time of an IND filing for each Option Target represent three separate performance obligations (one for each Option Target) as of the amendment of the arrangement. The license to each HMT inhibitor targeting each respective Option Target, the Company's research and development obligations through the completion of a Phase 1 clinical trial for each Option Target, and the option to maintain the license beyond the end of Phase 1 clinical development for each Option Target are all subject to Celgene's exercise of the option rights at the time of an IND filing and, therefore, are not considered performance obligations as of the amendment.

Under the agreement, the Company determined that the total transaction price was \$103.0 million as of the amendment of the arrangement, comprised the following:

- \$68.0 million total upfront payment received under the original agreement, as described above;
- \$25.0 million clinical development milestone payment for DOT1L; and
- \$10.0 million upfront payment under the amended and restated agreement.

The option exercise fees of \$75.0 million in the aggregate, for the options at the time of IND and completion of Phase 1, that may be received are excluded from the transaction price until each customer option is exercised. The future potential milestone payments were excluded from the transaction price, as all milestone amounts were fully constrained. The Company reevaluates the transaction price at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur, and, if necessary, adjust its estimate of the transaction price.

The transaction price was allocated to the performance obligations based on the estimated stand-alone selling prices at the time of the amendment. For the DOT1L performance obligation that includes the license and pre-IND research services, the stand-alone selling price was determined considering the stage and status of the program and the technology involved and the level of development expected, as well as the expected cost and margin for the research services. For the post-IND research and development services for DOT1L and the pre-IND research services for each Option Target, the stand-alone selling price was determined considering the expected cost and a reasonable margin for the respective services. The material rights from the option rights at the time of an IND filing for each Option Target were valued based on the estimated discount at which the option is priced and the Company's estimated probability of the options' exercise as of the time of the amendment. The Company believes that a change in the assumptions used to determine its stand-alone selling price for the performance obligations most likely would not have a significant effect on the allocation of consideration received (or receivable) to the performance obligations that were not satisfied as of the adoption of ASC 606.

The Company allocated the following amounts of the total transaction price to the performance obligations as of the amendment date:

- \$65.1 million, including the \$25.0 million clinical development milestone payment for DOT1L, to the two DOT1L performance obligations, which were satisfied prior to the ASC 606 adoption date;
- \$34.1 million to the three Pre-IND research services performance obligations related to the Option Targets, which were substantially satisfied as of the ASC 606 adoption date; and
- \$3.8 million to the three material rights related to Celgene's option rights at the time of an IND filing for each Option Target, which will not be satisfied until the option is exercised or one of the parties opts out of the arrangement.

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, 2018, 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 have not yet been recognized as revenue, relate to the material rights, and are recorded in deferred revenue on the Company's consolidated balance sheet. Deferred revenue related to the agreement amounted to \$3.8 million as of December 31, 2018, all of which is included in noncurrent liabilities.

GSK

In January 2011, the Company entered into a collaboration and license agreement with 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 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 a \$20.0 million upfront payment, a \$3.0 million payment upon the execution of the March 2014 agreement amendment, \$6.0 million in fixed research funding, \$9.0 million for research and development services and \$51.0 million in preclinical research and development milestone payments. The preclinical and research and development milestone payments total includes a \$10.0 million milestone payment earned in May 2017 related to the second target in the collaboration, upon GSK's initiation of good laboratory practices toxicology studies, as well as a \$6.0 million clinical milestone following GSK's initiation of patient dosing in a Phase 1 clinical trial of a PRMT5 inhibitor that the Company discovered and licensed to GSK. In 2018 we recognized a \$12.0 million milestone earned in 2018 relating to the first dosing of a patient in a Phase 2 clinical trial of GSK3326595, a PRMT5 inhibitor discovered by us and licensed to GSK under the collaboration agreement, as well as a \$8.0 million milestone payment earned in the fourth quarter of 2018 relating to the initiation of a patient dosing in a Phase 1 clinical trial of GSK3368715, a PRMT1 inhibitor discovered by us and licensed to GSK under the collaboration agreement. As of December 31, 2018, 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, 2018, the Company has earned a total of \$89.0 million under 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 and \$10.0 million in milestone revenue in the year ended December 31, 2017. The Company did not have any deferred revenue related to this

agreement as of December 31, 2018 or December 31, 2017 and any future revenues will relate to any milestone payments and royalties received under the agreement with respect to the two remaining targets.

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, under which the Company reacquired worldwide rights, excluding Japan, to its EZH2 program, including tazemetostat. Under the amended and restated 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 waived the right of first negotiation for the rest of Asia.

Under the original agreement, Eisai was solely responsible for funding all research, development and commercialization costs for EZH2 compounds. Under the amended and restated 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 Roche Molecular companion diagnostic agreement, and 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 amended and restated agreement with Eisai 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 has also agreed to pay Eisai up to \$20.0 million in clinical development milestone payments, including 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, 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 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.

LYSA

In May 2016, the Company entered into a collaboration agreement with the Lymphoma Academic Research Organisation, or LYSARC, for the first planned 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, the standard of care first line combination treatment for diffuse large B-cell lymphoma, or DLBCL, as a first line treatment in elderly, high-risk patients with DLBCL and is being sponsored by LYSARC. LYSA is managing the study operations for the trial, and the Company is recognizing its share of the related expenses as those costs are incurred over the duration of the trial.

Genentech

In June 2016, the Company entered into a collaboration agreement with Genentech Inc. (“Genentech”), a member of the Roche Group, to conduct a Phase 1b clinical trial to investigate the anti-cancer effects of the Company’s EZH2 inhibitor, tazemetostat, and Genentech’s anti-PD-L1 cancer immunotherapy, atezolizumab, when used in combination. The trial is evaluating this combination regimen for the treatment of patients with relapsed or refractory DLBCL. Under the agreement, each company is supplying its respective anti-cancer agent to support the trial and sharing equally in the trial costs. Genentech is managing the study operations for the trial, and the Company is recognizing its share of the related expenses as those costs are incurred over the duration of the trial.

In June 2017, the Company announced an expansion of the clinical collaboration with Genentech to investigate the combination of tazemetostat with atezolizumab in a Phase 1b/2 clinical trial for the treatment of patients with relapsed or refractory metastatic non-small cell lung cancer, or NSCLC. The trial will be part of MORPHEUS, Genentech’s open-label, multi-center, randomized umbrella trial evaluating the efficacy and safety of multiple immunotherapy-based treatment combinations for metastatic NSCLC. Under the agreement, each company is supplying its respective anti-cancer agent to support the trial and sharing equally in the trial costs. Genentech is managing the study operations for the trial, and the Company is recognizing its share of the related expenses as those costs are incurred over the duration of the trial.

Roche Molecular

In December 2012, Eisai and the Company entered into an 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 entered into a second amendment to the companion diagnostic agreement with Roche Molecular. The agreement was further amended in March 2018. Under the amended agreement, the Company is responsible for remaining development costs of \$10.4 million due under the agreement as of March 2018 and Eisai has agreed to reimburse the Company \$0.9 million of this amount related to a regulatory milestone for Japan. As of December 31, 2018, the Company is responsible for the remaining development costs of \$8.4 million due under the agreement. We expect the remaining development costs under the amended agreement to be incurred and paid through 2020.

Under the agreement with Roche Molecular, Roche Molecular is obligated to use commercially reasonable efforts to develop and to make commercially available the companion diagnostic. Roche Molecular has exclusive rights to commercialize the companion diagnostic.

The agreement with Roche Molecular will expire when the Company is no longer developing or commercializing tazemetostat. The Company may terminate the agreement by giving Roche Molecular 90 days’ written notice if the Company discontinues development and commercialization of tazemetostat or determines, in conjunction with Roche Molecular, that the companion diagnostic is not needed for use with tazemetostat. Either the Company or Roche Molecular may also terminate the agreement in the event of a material breach by the 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, Roche Molecular 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 acetyl transferase, 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, world-wide license to the undisclosed target inhibitors technology. The agreement also includes reciprocal licenses to utilize each other’s know-how, patents and technologies for activities under the agreement. Further, each party is granted the license to develop, manufacture, commercialize and otherwise exploit any compound or product that successfully achieves start of lead optimization (“SoLO”). The Company is 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 contractual term of the contract. The parties will jointly research and develop the first target program and will share commercialization activities within the United States. Boehringer Ingelheim will assume responsibility for commercialization outside of the United States. Boehringer Ingelheim is responsible for worldwide development and commercialization of the second target program.

Agreement Structure

Under the terms of the agreement, the Company received a \$15.0 million upfront payment and will receive \$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 has the option to extend the research period by up to one year, subject the Company’s agreement to the specified research activities and additional research funding. The Company is eligible to receive up to \$80.5 million in clinical development milestone payments, up to \$106.5 million in regulatory milestone payments and up to \$93.5 million in sales-based milestone payments. In addition, Boehringer Ingelheim is required to pay the Company tiered royalties, on a product by product, and country by country basis, at percentages ranging from the mid-single digits to low-double digits. Royalties will be payable on net product sales for therapies directed at the second target both in the United States and the rest of the world and net product sales outside of the United States for therapies directed at the first target. The next potential milestone payment that the Company might be entitled to receive under this agreement is a \$5.5 million milestone, for each Target Project, for the SoLO Approval for a compound, as defined in the agreement. 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 or royalty payments from Boehringer Ingelheim.

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 license 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 is \$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

The future potential milestone payments are excluded from the transaction price, as the achievement of the milestone events are highly uncertain. As such, all milestone payments are fully constrained. The Company will reevaluate the transaction price at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur, and, if necessary, adjust its estimate of the transaction price.

The Company determined that a 50/50 allocation of transaction price between the two performance obligations is appropriate considering the following factors: (i) R&D components' standalone selling price estimated using the cost plus margin approach; based on cost-plus 10%; (ii) the license rights granted for each program (world-wide or ex-US only) and their potential market opportunities; (iii) the total potential milestone payments for each program; and (iv) the expected revenue recognition pattern for each program, which is expected to be relatively consistent. Therefore, \$10.0 million is allocated to the first undisclosed target license and associated research services and \$10.0 million is allocated to the second undisclosed target license and associated research services and will be recognized through December 31, 2019.

The allocation of the variable consideration, the development milestones, will be allocated to each performance obligation as described in the contract. The milestone payments are defined by program and are directly attributable to distinct achievements in each program. The recognition of revenue for each milestone will be based on progress to date in satisfying the applicable performance obligation.

Collaboration Revenue

Through December 31, 2018, the Company has recognized \$1.7 million in total collaboration revenue since the inception of this collaboration. As of December 31, 2018, the Company had deferred revenue of \$13.3 million related to this agreement.

The Company will reevaluate the likelihood of achieving future milestones at the end of each reporting period. If the performance obligations have not been satisfied at the point at which the risk of significant revenue reversal is resolved, the transaction price will be adjusted and a cumulative catch up based on performance to date will be recorded. If performance obligations that have been satisfied, the milestone revenue from the arrangement will be recognized as revenue in the period the risk of significant reversal is relieved.

10. 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 may be granted to officers, employees, consultants, advisors and other service providers. Incentive and non-qualified stock options and restricted stock granted to employees 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. 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 the recipient's term of board service. 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

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

	Year Ended December 31,		
	2018	2017	2016
	(In thousands)		
Research and development	\$ 4,083	\$ 5,613	\$ 5,352
General and administrative	7,921	5,818	5,216
Total	\$ 12,004	\$ 11,431	\$ 10,568

Stock Options

The Company uses the Black-Scholes option-pricing model to measure the fair value of stock option awards. Key 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,		
	2018	2017	2016
Risk-free interest rate	2.6%	1.8%	1.2%
Expected life of options	6.0 years	6.0 years	6.0 years
Expected volatility of underlying stock	71.5%	74.2%	78.5%
Expected dividend yield	0.0%	0.0%	0.0%

There were no stock option awards granted to non-employees in the years ended December 31, 2018, 2017 or 2016.

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, 2018:

	<u>Number of Options</u> (In thousands)	<u>Weighted Average Exercise Price per Share</u>	<u>Weighted Average Remaining Contractual Term</u> (In years)	<u>Aggregate Intrinsic Value</u> (In thousands)
Outstanding at December 31, 2017	4,576	\$ 14.57		
Granted	2,537	14.66		
Exercised	(215)	8.76		
Forfeited or expired	(1,745)	15.70		
Outstanding at December 31, 2018	<u>5,153</u>	\$ 14.48	7.7	\$ 513
Exercisable at December 31, 2018	2,126	\$ 15.33	6.1	\$ 513

During the years ended December 31, 2018, 2017 and 2016, the Company granted stock options to purchase an aggregate of 2,537,277 shares, 2,331,500 shares, and 2,212,668 shares, respectively, at weighted average grant date fair values per option share of \$9.49, \$8.85, and \$6.42, respectively. The total grant date fair value of options that vested during the years ended December 31, 2018, 2017 and 2016 was \$12.1 million, \$12.0 million, and \$12.0 million, respectively. The aggregate intrinsic value of stock options exercised was \$1.5 million in 2018, \$4.1 million in 2017 and \$7.1 million in 2016.

As of December 31, 2018, there was \$23.4 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 2.7 years.

Restricted Stock Units

As of December 31, 2018, there were no restricted stock units outstanding.

In February 2016, the Company granted 80,732 restricted stock units with a grant date fair value of \$9.29 per unit, in accordance with a former chief financial officer's employment agreement. Of the total restricted stock unit awards granted, 73,779 shares vested through the termination of the officer's employment in August 2017. As of December 31, 2018, there was no unrecognized compensation cost related to restricted stock units, which were cancelled upon termination for the remaining unvested awards. The intrinsic value of restricted stock that vested during the years ended December 31, 2018, 2017 and 2016 was \$0.0 million, \$0.3 million and \$0.5 million, respectively.

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 \$0.5 million, \$0.5 million and \$0.4 million in the years ended December 31, 2018, 2017 and 2016, respectively.

11. 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, 2018, 2017, and 2016 due to the net loss recognized in each of those periods.

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

	Year Ended December 31,		
	2018	2017	2016
	(In thousands except per share data)		
Net loss	\$(123,630)	\$(134,309)	\$(110,212)
Weighted average shares outstanding	71,864	61,471	57,126
Basic and diluted loss per share allocable to common stockholders	<u>\$ (1.72)</u>	<u>\$ (2.18)</u>	<u>\$ (1.93)</u>

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 antidilutive:

	Year Ended December 31,		
	2018	2017	2016
	(In thousands)		
Stock options	5,153	4,576	4,059
Unvested restricted stock	—	—	64
Shares issuable under employee stock purchase plan	28	23	46
	<u>5,181</u>	<u>4,599</u>	<u>4,169</u>

12. Related Party Transactions

Celgene has made a series of equity investments in the Company, owning 3,674,640 shares of common stock representing 4.6% of the Company’s outstanding common stock as of December 31, 2018. Refer to Note 9, *Collaborations*, for additional information regarding the Company’s original agreement with Celgene entered into in April 2012 and the amended and restated agreement with Celgene entered into in July 2015.

Under the Celgene collaboration agreement, the Company recognized \$1.9 million and \$1.1 million in collaboration revenue in the years ended December 31, 2017 and 2016, respectively. The Company recognized no revenue under the Celgene collaboration agreement for the year ended December 31, 2018. As of December 31, 2018, and 2017 the Company had \$3.8 million and \$28.8 million in deferred revenue related to the Celgene collaboration arrangement, respectively. Additionally, in the years ended December 31, 2018, 2017 and 2016, the Company recorded \$0.0 million, \$0.0 million and \$0.1 million, respectively, in global development co-funding from Celgene. As of December 31, 2018 and 2017, the Company had no accounts receivable for either period, respectively, related to this collaboration arrangement.

13. Unaudited Quarterly Results

The results of operations on a quarterly basis for the years ended December 31, 2018 and 2017 are set forth below:

	Quarter Ended			
	March 31, 2018	June 30, 2018	September 30, 2018	December 31, 2018
	(In thousands, except per share data)			
Collaboration revenue	\$ —	\$ 12,000	\$ —	\$ 9,700
Operating expenses:				
Research and development	25,622	31,346	27,027	21,838
General and administrative	9,360	10,914	11,528	12,170
Total operating expenses	<u>34,982</u>	<u>42,260</u>	<u>38,555</u>	<u>34,008</u>
Operating loss	(34,982)	(30,260)	(38,555)	(24,308)
Other income, net	917	1,132	1,063	1,420
Income tax benefit	—	—	—	(57)
Net loss	<u>\$ (34,065)</u>	<u>\$ (29,128)</u>	<u>\$ (37,492)</u>	<u>\$ (22,945)</u>
Loss per share allocable to common stockholders:				
Basic	\$ (0.49)	\$ (0.42)	\$ (0.54)	\$ (0.29)
Diluted	\$ (0.49)	\$ (0.42)	\$ (0.54)	\$ (0.29)
Weighted average shares outstanding:				
Basic	69,386	69,490	69,539	78,962
Diluted	69,386	69,490	69,539	78,962

	Quarter Ended			
	March 31, 2017	June 30, 2017	September 30, 2017	December 31, 2017
	(In thousands, except per share data)			
Collaboration revenue	\$ —	\$ 10,000	\$ —	\$ —
Operating expenses:				
Research and development	24,695	27,292	28,741	28,933
General and administrative	8,269	11,170	9,311	8,431
Total operating expenses	<u>32,964</u>	<u>38,462</u>	<u>38,052</u>	<u>37,364</u>
Operating loss	(32,964)	(28,462)	(38,052)	(37,364)
Other income, net	442	438	455	862
Income tax benefit	—	—	—	336
Net loss	<u>\$ (32,522)</u>	<u>\$ (28,024)</u>	<u>\$ (37,597)</u>	<u>\$ (36,166)</u>
Loss per share allocable to common stockholders:				
Basic	\$ (0.56)	\$ (0.48)	\$ (0.63)	\$ (0.52)
Diluted	\$ (0.56)	\$ (0.48)	\$ (0.63)	\$ (0.52)
Weighted average shares outstanding:				
Basic	58,219	58,377	59,899	69,287
Diluted	58,219	58,377	59,899	69,287

EPIZYME, INC.
RESTRICTED STOCK UNIT AWARD AGREEMENT (the "Agreement")

Epizyme, Inc. (the "Company") has selected you to receive an award of restricted stock units ("RSUs") pursuant to the Company's 2013 Stock Incentive Plan (the "Plan"). The terms and conditions attached hereto are also a part hereof. Terms used in this Agreement which are not defined in this Agreement shall have the meanings used or defined in the Plan.

Notice of Grant

Name of recipient (the " <u>Participant</u> "):	
Grant Date (the " <u>Grant Date</u> "):	
Number of RSUs	
Vesting Start Date:	
Vesting Schedule:	
All vesting is dependent on the Participant remaining an Eligible Participant, as provided herein.	

Please confirm your acceptance of this restricted stock unit award and of the terms and conditions of this Agreement by signing a copy of this Agreement where indicated below.

EPIZYME, INC.

By: _____

Name: Robert B. Bazemore

Title: President and CEO

Accepted and Agreed:

 Signature of Participant

 Street Address

 City/State/Zip Code

EPIZYME, INC.

Restricted Stock Unit Award Agreement
Incorporated Terms and Conditions

The award of RSUs granted to the Participant hereunder is made pursuant to the Plan. The terms and conditions of the award of RSUs made to the Participant, as set forth in the Notice of Grant that forms part of this Agreement (the "Notice of Grant"), are as follows:

1. Grant of Restricted Stock Units.

The RSUs are issued to the Participant, effective as of the Grant Date set forth in the Notice of Grant, in consideration of services to be rendered by the Participant to the Company.

2. Vesting Schedule. Unless otherwise provided in this Agreement or in the Plan, the RSUs shall vest in accordance with the vesting schedule set forth in the Notice of Grant. Any fractional shares that would otherwise vest as of a particular date will be rounded down and carried forward to the next vesting date until a whole share can be issued. Upon the vesting of this award, the Company shall deliver, for each RSU that becomes vested, one (1) share of Common Stock (as defined in the Plan). The Common Stock shall be delivered as soon as practicable following each vesting date or event set forth in the Notice of Grant, but in any case, within thirty (30) days after such date or event.

3. Termination of Relationship.

Notwithstanding any other provision of the Plan to the contrary, if the Participant ceases to be an employee, director or officer of, or consultant or advisor to, the Company or any other entity the employees, officers, directors, consultants, or advisors of which are eligible to receive restricted stock unit awards under the Plan (an "Eligible Participant") for any reason or no reason, with or without cause, all of the RSUs that are unvested as of the time of such cessation shall be forfeited immediately and automatically to the Company, without the payment of any consideration to the Participant, effective as of such cessation. The Participant shall have no further rights with respect to any RSUs that are so forfeited. If the Participant provides services to a subsidiary of the Company, any references in this Agreement to employment by or a relationship with the Company shall instead be deemed to refer to employment by or a relationship with such subsidiary.

Notwithstanding any other provision of the Plan, this Agreement or any other agreement (written or oral) to the contrary, the Participant shall not be entitled (and by entering into this Agreement, hereby irrevocably waives any such entitlement) to any payment or other benefit to compensate the Participant for the loss of any rights under the Plan as a result of the termination or expiration of an award in connection with any termination of the Participant's relationship with the Company.

4. Transfer Restrictions.

Except as set forth in the Plan, this award may not be sold, assigned, transferred, pledged or otherwise encumbered by the Participant, either voluntarily or by operation of law or otherwise.

5. Rights as a Stockholder.

The Participant shall have no rights as a stockholder of the Company with respect to any shares of Common Stock underlying or relating to any award until the issuance of such Common Stock to the Participant in respect of such award.

6. Provisions of the Plan.

This Agreement is subject to the provisions of the Plan, a copy of which is furnished to the Participant with this Agreement.

7. Tax Obligations.

(a) Acknowledgments; No Section 83(b) Election. The Participant acknowledges that he or she is responsible for obtaining the advice of the Participant's own tax advisors with respect to the award of RSUs and the Participant is relying solely on such advisors and not on any statements or representations of the Company or any of its agents with respect to the tax consequences relating to the RSUs. The Participant understands that the Participant (and not the Company) shall be responsible for the Participant's tax liability that may arise in connection with the acquisition, vesting and/or disposition of the RSUs. The Participant acknowledges that no election under Section 83(b) of the Internal Revenue Code, as amended, is available with respect to RSUs.

(b) Withholding. The Participant acknowledges and agrees that the Company has the right to deduct from payments of any kind otherwise due to the Participant any federal, state, local or other taxes of any kind required by law to be withheld with respect to the vesting of the RSUs. The Participant acknowledges that on each vesting date, the Company shall retain from the number of shares of Common Stock otherwise deliverable to the Participant a number of shares having a fair market value (as determined by the Company, in its sole discretion) equal to the Company's statutory minimum tax withholding obligations.

8. Miscellaneous.

(a) No Right to Continued Relationship. The Participant acknowledges and agrees that, notwithstanding the fact that the vesting of the RSUs is contingent upon his/her continued relationship with the Company, this Agreement does not constitute an express or implied promise of a continued relationship or confer upon the Participant any rights with respect to a continued relationship with the Company.

(b) Governing Law. This Agreement shall be construed, interpreted and enforced in accordance with the internal laws of the State of Delaware without regard to any applicable conflicts of laws provisions.

(c) Participant's Acknowledgments. The Participant acknowledges that he or she has read this Agreement, has received and read the Plan, and understands the terms and conditions of this Agreement and the Plan.

EPIZYME, INC.
Severance and Change in Control Plan
(as amended through January 24, 2019)

Section I: Establishment and Purpose of Plan

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

Section II: Definitions

For purposes of this Plan:

“Participant” means:

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

“Cause” means any of the following:

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

(b) with respect to a termination upon or during the twelve (12) month period following a Change in Control (i) the Participant’s conviction of, or plea of guilty or nolo contendere to, any felony; (ii) the willful and continued failure by the Participant (other than any such failure resulting from the Participant’s incapacity due to physical or mental illness) to perform substantially the duties and

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

"Change in Control" means any of the following:

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

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

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

“Good Reason” means the occurrence, without the Participant’s prior written consent, of any of the following events:

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

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

Section III: Severance Benefits

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

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

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

- (b) **Severance Benefits Contingent on a Change in Control.** If, upon or within twelve (12) months following a Change in Control, a Participant’s employment is terminated by the Company without Cause or by the Participant for Good Reason, and provided the Participant abides by the conditions set forth in Section IV below, the Participant shall be eligible to receive the following severance benefits:
 - (i) the Company will pay to the Participant as severance pay an aggregate amount equivalent to (a) in the case of the Chief Executive Officer, eighteen months of his or her then current base salary, (b) in the case of a Senior Executive level Participant, twelve months of his or her then current base salary, (c) in the case of a Senior Vice President level Participant, twelve months of his or her then current base salary, (d) in the case of a Vice President level Participant, nine months of his or her then current base salary, (e) in the case of a Director level Participant, six months of his or her then current base salary, (f) in the case of a Manager level Participant, four months of his or her then current base salary, or (g) in the case of a Participant below the Manager level, three months of his or her then current base salary, in each case, less all applicable taxes and withholdings. The foregoing severance pay will be paid ratably in installments in accordance with the Company’s normal payroll practices, but in no event shall payment begin earlier than the eighth day after the Participant’s execution and timely return of the Severance Agreement;

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

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

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

- (iv) in the case of the Chief Executive Officer, or a Senior Executive level Participant, or a Senior Vice President level Participant, or a Vice President level Participant, any unvested stock options or restricted stock unit awards (or, in the case of restricted stock awards, any such awards that remain subject to repurchase by the Company) the Participant may have as of his or her termination date will not terminate upon such termination of employment and shall immediately vest (or become free from repurchase) and, if applicable, become exercisable in full upon the effectiveness of the Severance Agreement.

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

Section IV: Severance Agreement and Release

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

Section V: Miscellaneous Provisions

1. No Employment Rights. Nothing in this Plan shall be construed to provide any Participant with a guarantee of employment or shall supersede the Company's policy of employment at will.
2. Governing Law. The Plan and the rights of all persons under the Plan shall be construed in accordance with and under applicable provisions of ERISA, and the regulations thereunder, and the laws of the Commonwealth of Massachusetts (without regard to conflict of laws provisions) to the extent not preempted by federal law.
3. No Limitation upon Rights of Company. The Plan shall not affect in any way the right or power of the Company to make adjustments, reclassifications or changes of its capital or business structure; to merge or consolidate; to dissolve or liquidate; or to sell or transfer all or any part of its business or assets.
4. Indemnification. To the extent permitted by law, the Plan Administrator (as defined in Appendix A) and all employees, officers, directors, agents and representatives of the Plan Administrator will be indemnified by the Company and held harmless against any claims and the expenses of defending against such claims, resulting from any action or conduct relating to the administration of the Plan except to the extent that such claims arise from gross negligence, willful neglect, or willful misconduct.
5. Plan Name and Type. The name of the Plan is the Epizyme, Inc. Severance and Change in Control Plan. The Plan is intended to constitute an "Employee Welfare Benefits Plan" under Department of Labor Regulation 2510.3-2(b) and other applicable regulations and statutes. The Plan must be construed and interpreted in a manner consistent with the foregoing intent.

6. Funding. The Plan is unfunded and all payments under the Plan will be made from the Company's general assets.
7. Name and Address of Employer. The Plan is sponsored by:

Epizyme, Inc.
400 Technology Square
4th Floor
Cambridge, MA 02139
8. Employer and Plan Identification Number. The Internal Revenue Service has assigned the Company the following employer identification number: 26-1349956. The ERISA plan number assigned to this program is 502.
9. Agent for Service of Legal Process. Legal process with respect to claims under the Plan may be served on the Plan Administrator.
10. ERISA. The provisions set forth in Appendix A are incorporated herein and made a part of this Plan.
11. Fiscal Year of the Plan. The Plan and its records are kept on a calendar-year basis. The first plan year will be a short plan year beginning on March 22, 2013 and ending on December 31, 2013. Subsequent plan years are the 12-month period beginning January 1 and ending December 31.
12. Entire Agreement. This Plan supersedes any and all severance or equity acceleration plans, policies, and provisions applying to the Participants, including, without limitation, any provision in any Participant's offer letter, employment agreement, or equity agreement providing the Participant with any pay, benefits, or equity acceleration following a change in control of the Company and/or termination of his or her employment for any reason (including termination due to death or disability). To the extent any such plan, policy, or provision contradicts the Plan, the terms of the Plan shall govern.
13. Successor and Assigns. The Company shall require any successor (whether direct or indirect, by purchase, merger, consolidation or otherwise) to all or substantially all of the business and/or assets of the Company to expressly assume and agree to perform the Company's obligations under the Plan in the same manner and to the same extent that the Company would be required to perform such obligations if no such succession had taken place.
14. Severability. In case any one or more of the provisions of this Plan (or part thereof) shall be held to be invalid, illegal or unenforceable in any respect, such invalidity, illegality or unenforceability shall not affect the other provisions hereof, and this Plan shall be construed as if such invalid, illegal or unenforceable provisions (or part thereof) never had been contained herein.

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

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

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

Section VI: Section 409A

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

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

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

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

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

APPENDIX A

Plan Administration

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

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

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

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

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

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

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

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

Statement of ERISA Rights

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

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

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

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

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

If an employee is successful, the court may order the person sued to pay costs and fees. If the employee loses, the court may order the employee to pay these fees (for example, if the claim is frivolous). Employees should contact the Plan Administrator concerning questions about the Plan. Employees who have any questions about this statement or rights under ERISA should contact the nearest area office of the Employee Benefits Security Administration, U.S. Department of Labor listed in the telephone directory or the Division of Technical Assistance and Inquiries, Employee Benefits Security Administration, U.S. Department of Labor, 200 Constitution Avenue, N.W., Washington, DC 20210.

Claims Procedure

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

EPIZYME, INC.Non-Employee Director Compensation Program

Under Epizyme, Inc.'s (the "Company") director compensation program, the Company pays its non-employee directors retainers in cash. Each non-employee director receives a cash retainer for service on the board of directors and for service on each committee on which the director is a member, as well as additional fees for service as chairman of the board or chairman of each committee. These fees are payable in arrears in four equal quarterly installments on the last day of each quarter and are as follows:

	Member Annual Fee	Chairman Additional Annual Fee
Board of Directors	\$ 40,000	\$ 35,000
Audit Committee	\$ 7,500	\$ 15,000
Compensation Committee	\$ 6,250	\$ 12,500
Nominating and Corporate Governance Committee	\$ 4,500	\$ 9,000

The Company also reimburses its non-employee directors for reasonable travel and out-of-pocket expenses incurred in connection with attending its board of director and committee meetings.

The Company's non-employee director compensation program also includes a stock-for-fees policy, under which directors have the right to elect to receive common stock in lieu of cash fees. The stock will be issued on the date of the annual meeting, and the number of shares to be issued to participating directors will be determined by dividing the expected cash fees to be paid for the full year by the closing price of the Company's common stock on the day of the annual meeting.

In addition, under the Company's director compensation program, each non-employee director receives, upon his or her initial election to its board of directors, an option to purchase the number of shares of the Company's common stock that have a Black-Scholes value as of the date of grant equal to \$300,000; provided, that, in no event shall the number of shares of common stock issuable upon any such initial election exceed 50,000. Each of these options will vest as to 25% of the shares of common stock underlying such option on the one-year anniversary of the grant date and as to an additional 2.0833% of the shares of common stock underlying such option at the end of each successive month following the first anniversary of the grant date until the fourth anniversary of the grant date, subject to the non-employee director's continued service as a director. Further, under the Company's director compensation program, on the date of each annual meeting of stockholders, each non-employee director that had served on its board of directors for at least six months will receive an option to purchase the number of shares of Company's common stock that have a Black-Scholes value as of the date of grant equal to \$150,000; provided, that, in no year shall the number of shares of common stock issuable upon such option exceed 25,000. Each of these options will vest in full on the one-year anniversary of the grant date, subject to the non-employee director's continued service as a director. All options issued to the Company's non-employee directors under its director compensation program will become exercisable in full upon a change in control of the Company. The exercise price of these options will be equal to the fair market value of the Company's common stock on the date of grant.

Confidential Materials omitted and filed separately with the
Securities and Exchange Commission. Double asterisks denote omissions.

COLLABORATION AGREEMENT

between

BOEHRINGER INGELHEIM INTERNATIONAL GMBH

and

EPIZYME, INC.

Dated as of Wednesday November 14, 2018

BII Contract Number []**

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COLLABORATION AGREEMENT

This Collaboration Agreement (this “**Agreement**”) is made and entered into as of Wednesday November 14, 2018 (the “**Effective Date**”) by and between Boehringer Ingelheim International GmbH, a German corporation, with its principal place of business at Binger Strasse 173, 55216 Ingelheim am Rhein, Germany (“**BII**”), and Epizyme, Inc., a Delaware corporation, with its principal place of business at 400 Technology Square, 4th Floor, Cambridge, Massachusetts 02139, USA (“**Epizyme**”). BII and Epizyme may each be referred to herein as a “**Party**” and, collectively, as the “**Parties**.”

RECITALS

WHEREAS, BII is a global pharmaceutical company with experience in the research, development, manufacture and commercialization of pharmaceutical products;

WHEREAS, Epizyme is a clinical stage biopharmaceutical company engaged in the research, development and manufacture of novel epigenetic medicines for patients with cancer and other diseases; and

WHEREAS, subject to the terms and conditions of this Agreement, BII and Epizyme now desire to collaborate with respect to researching and developing small molecule compounds that are inhibitors of the [**] (a histone acetyl transferase) and [**] (a helicase) targets, along with associated predictive biomarkers therefor, and commercializing products containing such compounds.

NOW, THEREFORE, in consideration of the premises and the mutual promises and conditions hereinafter set forth, and other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties, intending to be legally bound, do hereby agree as follows:

ARTICLE 1 DEFINITIONS

Unless otherwise specifically provided herein, the following terms will have the following meanings:

1.1 “**Additional Cure Period**” has the meaning set forth in Section 13.2.1 (Termination of Agreement for Cause).

1.2 “**Affiliate**” means, with respect to a Party, any Person that, directly or indirectly, through one or more intermediaries, controls, is controlled by or is under common control with such Party. For purposes of this definition, “control” and, with correlative meanings, the terms “controlled by” and “under common control with” means: (a) the possession, directly or indirectly, of the power to direct the management or policies of a Person, whether through the ownership of voting securities, by contract relating to voting rights or corporate governance, or otherwise; or (b) the ownership, directly or indirectly, of at least fifty percent (50%) of the voting securities or other ownership interest of a Person (or, with respect to a limited partnership or other similar entity, its general partner or controlling entity). The Parties acknowledge that in the

case of certain entities organized under the laws of certain countries outside of the United States, the maximum percentage ownership permitted by law for a foreign investor may be less than fifty percent (50%), and that in such case such lower percentage will be substituted in the preceding sentence; *provided that* such foreign investor has the power to direct the management or policies of such entity.

1.3 “**Agreement**” has the meaning set forth in the Preamble.

1.4 “**Alliance Manager**” has the meaning set forth in Section 2.2.4 (Alliance Manager).

1.5 “**Allowable Expenses**” means the following expenses that are specifically identifiable and directly attributable to the Commercialization of Joint Products in the United States:

1.5.1 Sales and Marketing Costs;

1.5.2 Distribution Costs;

1.5.3 Manufacturing Costs;

1.5.4 Medical Affairs Costs, including (for clarity) Phase IV Costs;

1.5.5 Patient Assistance Program Costs;

1.5.6 Third Party Payments, including the appropriate allocable portion of upfront payments;

1.5.7 Diagnostic Third Party Payments;

1.5.8 Trademark Costs;

1.5.9 Recall Costs;

1.5.10 Product Liability Costs; and

1.5.11 Product Insurance Costs.

1.6 “**ANDA Act**” has the meaning set forth in Section 8.3.5 (Generic Competition).

1.7 “**Applicable Law**” means federal, state, local, national and supra-national laws, statutes, rules and regulations, including any rules, regulations, regulatory guidelines or other requirements of the Regulatory Authorities, major national securities exchanges or major securities listing organizations, that may be in effect from time to time during the Term and applicable to a particular activity or country hereunder.

1.8 “**ArbnErfG**” has the meaning set forth in Section 8.1.6 (German Statute).

1.9 “**Bankruptcy Code**” has the meaning set forth in Section 13.2.5 (Termination for Insolvency).

1.10 “**BII**” has the meaning set forth in the Preamble.

1.11 “**BII Compound**” has the meaning set forth in Section 5.1.1 (BII Products Report).

1.12 “**BII Controlled Project**” means the Target Project directed to the [**] target.

1.13 “**BII Indemnitees**” has the meaning set forth in Section 12.2 (Indemnification of BII).

1.14 “**BII Know-How**” means all Information that is: (a) Controlled by BII or any of its Affiliates on the Effective Date or during the Term, (b) not generally known, (c) reasonably necessary or useful for performing Research Activities or for the Development, Manufacture or Commercialization of a Compound, Product or Diagnostic Product and (d) arose from or was actually applied in (i) the performance of Research Activities or (ii) the Development, Manufacture or Commercialization of a Compound, Product or Diagnostic Product, but excluding any Information comprising Joint Know-How.

1.15 “**BII Patents**” means all of the Patents that: (a) are Controlled by BII or any of its Affiliates on the Effective Date or during the Term, (b) Covers subject matter that is reasonably necessary or useful (or, with respect to patent applications, would be reasonably necessary or useful if such patent applications were to issue as patents) for performing Research Activities or for the Development, Manufacture or Commercialization of a Compound, Product or Diagnostic Product and (c) arose from or was actually applied in (i) the performance of Research Activities or (ii) the Development, Manufacture or Commercialization of a Compound, Product or a Diagnostic Product, but excluding any Joint Patents.

1.16 “**BII Product**” has the meaning set forth in Section 5.1.1 (BII Products Report).

1.17 “**BII Product Infringement**” has the meaning set forth in Section 8.3.3 (Enforcement of BII Patents).

1.18 “**BII Product Patents**” has the meaning set forth in Section 8.2.3 (BII Patents).

1.19 “**BII Product Prosecuted Infringements**” has the meaning set forth in Section 8.3.3 (Enforcement of BII Patents).

1.20 “**BII Products Report**” has the meaning set forth in Section 5.1.1 (BII Products Report).

1.21 “**BII Research Compounds**” means all compounds that are identified by BII and arising under this Agreement, including any modifications, variations or derivatives thereof, including any metabolite, salt, ester, hydrate, solvate, isomer, enantiomer, free acid form, free base form, crystalline form, co-crystalline form, amorphous form, pro-drug (including ester pro-drug) form, racemate, polymorph, chelate, stereoisomer, tautomer, optically active form or any derivatives; *provided that*, following cross-screening of such compounds by BII or by Epizyme in accordance with the Research Plan using its helicase or histone acetyl transferase cross-screening panels, BII will have the right to exclude up to [**] Compounds that are shown through such cross-screening to be [**] inhibitors and up to [**] Compounds that are shown through such cross-screening to be [**] inhibitors from the definition of BII Research Compounds upon written notice to Epizyme (such written notices, collectively, the “**Excluded Compound List**”); *provided further* that BII may periodically update the Excluded Compound List with other Compounds upon written notice to Epizyme (but in no event may the Excluded Compound List identify more than [**] inhibitors and [**] inhibitors at any time) and, upon each such update (i) Compounds that were previously included in the Excluded Compound List but that BII removes from the Excluded Compound List, shall be deemed to be BII Research Compounds and (ii) Compounds that were not previously included in the Excluded Compound List but that BII adds to the Excluded Compound List, shall be excluded from the definition of BII Research Compounds.

1.22 “**BII SoD Committee**” has the meaning set forth in Section 4.2.2(a) (Satisfaction of SoD Criteria).

1.23 “**BII SoLO Committee**” has the meaning set forth in Section 4.1.2(a) (Satisfaction of SoLO Criteria).

1.24 “**BII Technology**” means, collectively, the BII Know-How and BII Patents.

1.25 “**Board of Directors**” has the meaning set forth in the definition of “Change in Control.”

1.26 “**Business Day**” means a day other than a Saturday or Sunday on which banking institutions in Boston, Massachusetts and Ingelheim am Rhein, Germany are open for business.

1.27 “**Calendar Quarter**” means each successive period of three (3) calendar months commencing on January 1, April 1, July 1 and October 1, except that the first Calendar Quarter of the Term will commence on the Effective Date and end on the day immediately prior to the first to occur of January 1, April 1, July 1 or October 1 after the Effective Date, and the last Calendar Quarter will end on the last day of the Term.

1.28 “**Calendar Year**” means each successive period of twelve (12) calendar months commencing on January 1 and ending on December 31, except that the first Calendar Year of the Term will commence on the Effective Date and end on December 31 of the year in which the Effective Date occurs, and the last Calendar Year of the Term will commence on January 1 of the year in which the Term ends and end on the last day of the Term.

1.29 “**Centralized Approval Procedure**” means the procedure through which a MAA filed with the EMA results in a single marketing authorization valid throughout the European Union.

1.30 “**Change in Control**” means, with respect to a Party, the occurrence of any of the following after the Effective Date:

1.30.1 any “person” or “group” (as such terms are defined below): (a) is or becomes the “beneficial owner” (as defined below), directly or indirectly, of shares of capital stock or other interests (including partnership interests) of such Party then outstanding and normally entitled (without regard to the occurrence of any contingency) to vote in the election of the directors, managers or similar supervisory positions (“**Voting Stock**”) of such Party representing fifty percent (50%) or more of the total voting power of all outstanding classes of Voting Stock of such Party; or (b) has the power, directly or indirectly, to elect a majority of the members of the Party’s board of directors, or similar governing body (“**Board of Directors**”); or

1.30.2 such Party enters into a merger, consolidation or similar transaction with another Person (whether or not such Party is the surviving entity) and as a result of such merger, consolidation or similar transaction (a) the members of the Board of Directors of such Party immediately prior to such transaction constitute less than a majority of the members of the Board of Directors of such Party or such surviving Person immediately following such transaction; or (b) the Persons that beneficially owned, directly or indirectly, the shares of Voting Stock of such Party immediately prior to such transaction cease to beneficially own, directly or indirectly, shares of Voting Stock of such Party representing at least a majority of the total voting power of all outstanding classes of Voting Stock of the surviving Person in substantially the same proportions as their ownership of Voting Stock of such Party immediately prior to such transaction; or

1.30.3 such Party sells or transfers to any Third Party, in one or more related transactions, properties or assets representing all or substantially all of such Party’s consolidated total assets to which this Agreement relates; or

1.30.4 the holders of capital stock of such Party approve a plan or proposal for the liquidation or dissolution of such Party.

For the purpose of this definition of “Change in Control,” (a) “person” and “group” have the meanings given such terms under Section 13(d) and 14(d) of the United States Securities Exchange Act of 1934 and the term “group” includes any group acting for the purpose of acquiring, holding or disposing of securities within the meaning of Rule 13d-5(b)(1) under the said Act; (b) a “beneficial owner” will be determined in accordance with Rule 13d-3 under the aforesaid Act; and (c) the terms “beneficially owned” and “beneficially own” will have meanings correlative to that of “beneficial owner.”

1.31 “**Clinical Trials**” means, collectively, First In-Human Clinical Trials, Non-Pivotal Clinical Trials and Pivotal Clinical Trials, and such other tests and studies in human subjects or patients that are required by Applicable Law, or otherwise recommended by the Regulatory Authorities, to obtain or maintain Regulatory Approvals for a Product for one or

more Indications, including tests or studies that are intended to expand the Product Labeling for such Product with respect to one or more such Indications or are otherwise deemed useful with respect to the continued Development of a Compound and/or Product. For clarity, Phase IV Studies are not part of Clinical Trials.

1.32 “**Collaboration Technology**” means, collectively, the BII Technology, the Epizyme Technology and the Joint Technology.

1.33 “**Combination Product**” means a Product that is sold in the form of a combination product, whether in a fixed dose combination or in the same packaging, containing both a Compound and one or more independently therapeutically active pharmaceutical or biologic products.

1.34 “**Commercialization**” means any and all activities directed to the preparation for sale of, offering for sale of or sale of a Product, including activities related to marketing, promoting, distributing, importing and exporting such Product, and interacting with Regulatory Authorities regarding any of the foregoing, and in all cases, which do not constitute Development activities. When used as a verb, “**to Commercialize**” and “**Commercializing**” means to engage in Commercialization, and “**Commercialized**” has a corresponding meaning.

1.35 “**Commercialization Overrun**” has the meaning set forth in Section 5.2.2(c)(iv) (Commercialization Overruns).

1.36 “**Commercially Reasonable Efforts**” means, with respect to the performance of Development and Commercialization activities with respect to any Compound, Product or Diagnostic Product by a Party, the carrying out of such activities in a sustained manner using efforts and resources, in good faith, consistent with reasonable practices and expended in a manner and timing consistent with the exercise of prudent scientific and business judgment that a similarly situated company within the biopharmaceutical or pharmaceutical industry, as the case may be, would reasonably devote in a given market for the development and commercialization of a pharmaceutical product having similar market potential as a particular Compound, Product or Diagnostic Product at a similar stage in development or product life, taking into account all scientific, commercial, and other factors that such company would take into account, including issues of safety and efficacy, expected and actual cost and time to develop, expected and actual profitability, expected and actual competitiveness of alternative products [**] (including generic or biosimilar products), the nature and extent of expected and actual market exclusivity (including Patent coverage and regulatory exclusivity), the expected likelihood of Regulatory Approval, the expected and actual reimbursability and pricing, and the expected and actual amounts of marketing and promotional expenditures required.

1.37 “**Committed Costs**” means, with respect to the Joint Product, (a) (i) the next [**] of expenses not yet incurred, as set forth in the firm budget portion of the then-current Joint Development Plan and Budget or Joint Commercialization Plan and Budget for such Joint Product or (ii) if less than [**] remain with respect to the firm budget portion of the then-current Joint Development Plan and Budget or Joint Commercialization Plan and Budget for such Joint Product, the expenses not yet incurred and associated with the months remaining in the firm budget portion of the then-current Joint Development Plan and Budget or Joint

Commercialization Plan and Budget for such Joint Product and (b) [**] costs associated with Clinical Trials for the Joint Product that have been Initiated as of the effective date of the termination of this Agreement or date of the Epizyme Opt-Out Notice with respect to such Joint Product.

1.38 “**Companion Diagnostic Product**” means a medical device, often an *in vitro* device (IVD), that provides Information that is essential for the safe and effective use of a Compound or Product.

1.39 “**Complementary Diagnostic Product**” means a test that aids in the benefit-risk decision-making about the use of a Compound or Product, where the difference in benefit-risk is clinically meaningful.

1.40 “**Compound**” means, with respect to each Target Project, all small molecule [**] inhibitors and [**] inhibitors that meet the criteria set forth on Schedule 1.40 and are (a) Controlled by Epizyme as of the Effective Date of this Agreement or (b) Controlled by Epizyme or BII following the Effective Date and discovered or identified by or on behalf of a Party in performing its activities under this Agreement or, with respect to (a)-(b), (i) any modifications, variations or derivatives thereof that meet the criteria set forth on Schedule 1.40 or (ii) regardless of whether they meet the criteria set forth on Schedule 1.40 (A) any salt, ester, hydrate, solvate, enantiomer, free acid form, free base form, crystalline form, co-crystalline form, amorphous form, pro-drug (including ester pro-drug) form, racemate, polymorph, chelate, tautomer or optically active form thereof or (B) any metabolite, isomer, stereoisomer or isotopic derivatives thereof that are useful for Development and, with respect to each of the foregoing (i)-(ii), that are discovered identified or created by or on behalf of a Party during the Term; *provided that* any [**] inhibitor or [**] inhibitor that achieves SoLO Approval or SoD Approval shall be considered a Compound irrespective of whether such [**] inhibitor or [**] inhibitor meets the criteria set forth on Schedule 1.40.

1.41 “**Conduct**” means, with respect to any Clinical Trial, to (a) sponsor, support or perform, directly or indirectly through a Third Party, such Clinical Trial; or (b) provide to a Third Party funding for, or clinical supplies (including placebo (to the extent required by Clinical Trial design)) for use in, such Clinical Trial.

1.42 “**Confidential Information**” means any Information or data provided orally, visually, in writing or other form by or on behalf of one Party (or an Affiliate or representative of such Party) to the other Party (or to an Affiliate or representative of such Party) in connection with this Agreement, whether prior to, on or after the Effective Date, including Information relating to the terms of this Agreement, any Compound, Product or Diagnostic Product, any Exploitation of any Compound, Product or Diagnostic Product, any know-how with respect thereto developed by or on behalf of the disclosing Party or its Affiliates or the scientific, regulatory or business affairs or other activities of either Party.

1.43 “**Contractor**” means a Third Party to whom a Party has subcontracted any of its activities under this Agreement pursuant to Section 6.5 (Subcontracting).

1.44 “**Control**” means, with respect to any item of Information, material, Patent or other property right, the possession of the right, whether directly or indirectly, and whether by ownership, license, covenant not to sue or otherwise, to grant a license, sublicense or other right to or under such Information, material, Patent or other property right as provided for herein without violating the terms of any agreement or other arrangement with any Third Party. Notwithstanding the foregoing, a Party and its Affiliates will not be deemed to “Control” any item of Information, material, Patent or other property right that, prior to or following the consummation of a Change in Control of such Party, is owned or in-licensed by a Third Party that becomes an Affiliate of such acquired Party after the Effective Date as a result of such Change in Control unless (a) prior to the consummation of such Change in Control, such acquired Party or any of its Affiliates also Controlled such item of Information, material, Patent or other property right or (b) the item of Information, material, Patent or other property right owned or in-licensed by the applicable Third Party were not used in the performance of activities under this Agreement prior to the consummation of such Change in Control, but after the consummation of such Change in Control, such acquired Party or any of its Affiliates determines to use or uses any such item of Information, material, Patent or other property right in the performance of its obligations or exercise of its rights under this Agreement, in each of which cases ((a) and (b)), such item of Information, material, Patent or other property right will be “Controlled” by such Party for purposes of this Agreement.

1.45 “**Counter Screen**” means an enzymatic or cellular assay used to determine the activity of a compound as an inhibitor or activator of helicase or histone acetyl transferase activity.

1.46 “**Cover**” means, with respect to a particular subject matter at issue and a relevant Patent, that the manufacture, use, sale, offer for sale or importation of such subject matter would fall within the scope of a claim in such Patent.

1.47 “[**]” means [**].

1.48 “[**]” means [**].

1.49 “**Defaulting Party**” has the meaning set forth in Section 13.2.1 (Termination of Agreement for Cause).

1.50 “**Detail**” means, with respect to a Joint Product in the United States, a face-to-face or virtual/digital contact between a sales representative and a physician or other medical professional licensed to prescribe drugs, during which a primary position detail or a secondary position detail is made to such Person, in each case, as measured by each Party’s internal recording of such activity and always consistent with then-current Joint Commercialization Plan and Budget; *provided that* such meeting is consistent with and in accordance with the requirements of Applicable Law, the PhRMA Code on Interactions with Healthcare Professionals and this Agreement. When used as a verb, “**Detail**” or “**Detailing**” means to engage in a Detail. For clarity, Detail shall exclude discussions at conventions, trade shows and similar forums or meetings.

1.51 “**Detail Costs**” means those costs incurred in accordance with the Joint Commercialization Plan and Budget and specifically identifiable and directly attributable to Detailing the Joint Product in the United States, which shall be determined in accordance with Section 5.2.2(c)(ii) (FTE Records and Calculation).

1.52 “**Development**” means all activities related to research, pre-clinical and other non-clinical testing, test method development and stability testing, toxicology, formulation, process development, Manufacturing scale-up, qualification and validation, quality assurance/quality control, Clinical Trials, including Manufacturing in support thereof, statistical analysis and report writing, the preparation and submission of Drug Approval Applications, regulatory affairs with respect to the foregoing and all other activities necessary or reasonably useful or otherwise requested or required by a Regulatory Authority as a condition or in support of obtaining or maintaining a Regulatory Approval. When used as a verb, “**Develop**” means to engage in Development, and “**Developed**” means to have engaged in Development. For purposes of clarity, Development will include any submissions and activities required in support thereof, required by Applicable Laws or a Regulatory Authority as a condition or in support of obtaining a pricing or reimbursement approval for an approved Compound, Product or Diagnostic Product.

1.53 “**Development Costs**” means the FTE Costs (charged in accordance with Section 5.2.1(d)(ii) (FTE Records and Calculation)) incurred and the out-of-pocket costs recorded as an expense in accordance with GAAP, by or on behalf of a Party or any of its Affiliates, after the Effective Date and during the Term, that are incurred in accordance with the Joint Development Plan and Budget and specifically identifiable and directly attributable to the following Development activities with respect to a Product in the Territory, as applicable:

(a) pre-clinical and non-clinical activities such as toxicology and formulation development, test method development, stability testing, quality assurance, quality control development and statistical analysis;

(b) Clinical Trials for a Compound, Product or Diagnostic Product, including: (i) the preparation for and Conduct of Clinical Trials; (ii) data collection and analysis and report writing; (iii) clinical laboratory work; (iv) regulatory activities in direct connection with such studies, including adverse event recording and reporting; and (v) advisory meetings in connection with a Compound, Product or Diagnostic Product;

(c) the preparation of a regulatory dossier to the extent necessary to obtain any Regulatory Approval for a Product in the Territory and filing fees in connection with the filing of applications for Regulatory Approvals;

(d) (i) Manufacturing of Compound, Product or Diagnostic Product for use in Clinical Trials or other Development activities for such Compound, Product or Diagnostic Product; (ii) the Manufacture, purchase or packaging of comparators or placebo (to the extent required by Clinical Trial design) for use in Clinical Trials for a Compound, Product or Diagnostic Product (with the manufacturing costs for comparators or placebo (to the extent required by Clinical Trial design) to be determined in the same manner as Manufacturing Costs are determined for such Compound, Product or Diagnostic Product); and (iii) costs and expenses of disposal of drugs and other supplies used in such Clinical Trials or other Development activities;

payments;

(e) Third Party Payment, including the appropriate allocable portion of upfront

(f) Diagnostic Third Party Payments;

(g) maintaining the Global Safety Database (and, if applicable, the parallel safety database) pursuant to Section 9.2 (Global Safety Database); and

(h) costs for the establishment of the Manufacturing process for a Compound, Product or Diagnostic Product, scale-up, Manufacturing process validation, including validation batches, Manufacturing improvements and qualification and validation of Third Party contract manufacturers, but not including the purchase or construction of capital equipment, capital assets or real estate for the purposes of building manufacturing facilities and capabilities.

1.54 “**Development Overrun**” has the meaning set forth in Section 5.2.1(d)(iii) (Development Overruns).

1.55 “**Diagnostic Products**” means Companion Diagnostic Products or Complementary Diagnostic Products.

1.56 “**Diagnostic Third Party Payments**” means all payments of any kind, including upfront payments, milestone payments, royalties or other amounts paid by a Party to a Third Party after the Effective Date and during the Term of this Agreement that are in consideration of the supply of Diagnostic Products to the Parties or a license of Patents that Cover or Information that is used in the making, using, offering to sell, selling, importing or exporting of Diagnostic Products in the Territory.

1.57 “**Distribution Costs**” means the FTE Costs (charged in accordance with Section 5.2.2(c)(ii) (FTE Records and Calculation)) incurred, and the out-of-pocket costs recorded as an expense in accordance with GAAP, by a Party or any of its Affiliates after the Effective Date and during the Term that are incurred in accordance with the Joint Commercialization Plan and Budget and specifically identifiable and directly attributable to the commercial distribution of a Joint Product to a Third Party in the U.S., including:

1.57.1 handling and transportation to fulfill orders (excluding such costs, if any, treated as a deduction in the definition of Net Sales);

1.57.2 customer services, including order entry, billing and adjustments, inquiry and credit and collection; and

1.57.3 direct cost of storage and distribution of such Joint Product.

The Parties may, if appropriate, agree that Distribution Costs be determined on the basis of a specified annual charge or as a percentage of Net Sales.

1.58 “**Dollars**” or “**\$**” means United States Dollars.

1.59 “**Drug Approval Application**” means any New Drug Application (“**NDA**”), as defined in the FDCA, or any corresponding foreign applications in the Territory, including (a) with respect to the European Union, a Marketing Authorization Application (a “**MAA**”) filed with the EMA pursuant to the Centralized Approval Procedure or with the applicable Regulatory Authority of a country in Europe with respect to the mutual recognition or any other regional or national approval procedure or (b) with respect to Japan, an MAA filed with the PMDA.

1.60 “**Effective Date**” has the meaning set forth in the Preamble.

1.61 “**EMA**” means the European Medicines Agency and any successor agency(ies) or authority having substantially the same function.

1.62 “**Epizyme**” has the meaning set forth in the Preamble.

1.63 “**Epizyme Carve-Out Patents**” has the meaning set forth in Section 8.2.5(a) (Joint Patents and Epizyme Product Patents).

1.64 “**Epizyme Indemnitees**” has the meaning set forth in Section 12.1 (Indemnification of Epizyme).

1.65 “**Epizyme Know-How**” means all Information that is (a) Controlled by Epizyme or any of its Affiliates on the Effective Date or during the Term, (b) not generally known and (c) reasonably necessary or useful for performing Research Activities or for the Development, Manufacture or Commercialization of a Compound, Product or a Diagnostic Product, but excluding any Information comprising Joint Know-How or to the extent related to any active ingredient in a Product that is not a Compound.

1.66 “**Epizyme Patents**” means all of the Patents that (a) are Controlled by Epizyme or any of its Affiliates on the Effective Date or during the Term and (b) Covers subject matter that is reasonably necessary or useful (or, with respect to patent applications, would be reasonably necessary or useful if such patent applications were to issue as patents) for performing Research Activities or for the Development, Manufacture or Commercialization of a Compound, Product or a Diagnostic Product, but excluding any Joint Patents or any Patents solely to the extent Covering any active ingredient in a Product that is not a Compound.

1.67 “**Epizyme Product Patents**” means any Epizyme Patent that Covers a Compound (including the composition of matter), Product or a method of use of a Compound or Product; *provided that*, with respect to Epizyme Patents that Cover the Manufacture of a Compound or Product, such Patents shall only be Epizyme Product Patents if such Patents are specifically and solely related to a Compound or Product.

1.68 “**Epizyme Technology**” means, collectively, the Epizyme Know-How and Epizyme Patents.

1.69 “**European Union**” or “**E.U.**” means the economic, scientific and political organization of member states known as the European Union, as its membership may be altered from time to time, and any successor thereto.

1.70 “**Excluded Claim**” has the meaning set forth in Section 14.7.2(f) (ADR; Arbitration).

1.71 “**Excluded Compound List**” has the meaning set forth in the definition of BII Research Compounds.

1.72 “**Exploit**” or “**Exploitation**” means to make, have made, import, export, use, have used, sell, have sold, or offer for sale, including to Develop, Commercialize, register, modify, enhance, improve, Manufacture, have Manufactured, hold or keep (whether for disposal or otherwise), formulate, optimize, transport, distribute, promote or otherwise dispose of. When used as a verb, “**to Exploit**” and “**Exploiting**” means to engage in Exploitation, and “**Exploited**” has a corresponding meaning.

1.73 “**FDA**” means the United States Food and Drug Administration and any successor agency(ies) or authority having substantially the same function.

1.74 “**FDCA**” means the United States Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 301 et seq., as amended from time to time, together with any rules, regulations and requirements promulgated thereunder (including all additions, supplements, extensions, and modifications thereto).

1.75 “**Field**” means any and all uses, including the diagnostic, prophylactic and therapeutic treatment of humans and animals.

1.76 “[**]” has the meaning set forth in Section 5.2.1(b)(ii) (Revisions).

1.77 “**First Commercial Sale**” means, with respect to a Product and a country, the first sale for monetary value in an arm’s-length transaction for use or consumption by the end user of such Product in such country after Regulatory Approval for such Product has been obtained in such country. Sales prior to receipt of Regulatory Approval for a Product, such as so-called “treatment IND sales,” “named patient sales,” and “compassionate use sales,” will not be construed as a First Commercial Sale.

1.78 “**First In-Human Clinical Trial**” means the first human clinical trial of a Product that is Conducted in any country in the Territory in accordance with GCP (whether a standalone trial or a stage of a “Phase 1/2” clinical trial described in the protocol as the Phase 1 portion) that: (a) is intended to initially evaluate the safety, tolerability, pharmacokinetic and sometimes pharmacological effect of a Product (including evaluating such Product in target tissues, collecting biologic materials from human subjects or patients and evaluating such biologic materials for signs of pharmacodynamic activity of such Product) and determine the maximum tolerated dose, biologically optimal dose or recommended dose of a Product for subsequent human clinical trials; or (b) that would otherwise satisfy requirements of 21 C.F.R. § 312.21(a), or its foreign equivalent. For clarity, a First In-Human Clinical Trial may include an efficacy component so long as such efficacy component is not the principal purpose of such First In-Human Clinical Trial, and inclusion of such efficacy component will not result in a First In-Human Clinical Trial being considered to be a Non-Pivotal Clinical Trial or Pivotal Clinical Trial.

1.79 “FTE” means the equivalent of the work of one employee full time for one Calendar Year (consisting of at least a total of [**] working hours per Calendar Year, and always excluding vacation, holiday, sick, personal, or other like time). No additional payment will be made with respect to any Person who works more than [**] hours per Calendar Year and any Person who devotes less than [**] hours per Calendar Year will be treated as an FTE on a pro rata basis based upon the actual number of hours worked divided by [**].

1.80 “FTE Cost” means, with respect to a Party for any period, the applicable FTE Rate multiplied by the applicable number of FTEs of such Party performing activities during such period.

1.81 “FTE Rate” means the rate set forth on Schedule 1.81 (FTE Rate).

1.82 “GAAP” means (i) for BII, the maintenance of records and books of accounts in accordance with Handelsgesetzbuch (HGB), which standards or principles are currently used at the relevant time, and consistently applied by BII and (ii) for Epizyme, the maintenance of records and books of accounts in accordance with Generally Accepted Accounting Principles in the United States, which standards or principles are currently used at the relevant time, and consistently applied by Epizyme.

1.83 “Generic Competition” means, on a country-by-country and Product-by-Product basis, the unit volume of Generic Products sold in a country by one or more Third Parties in a Calendar Quarter is at least [**] percent ([**]%) of the aggregate unit volume of Products sold in such country by BII, its Affiliates and Sublicensees (or its or their distributors) and all Generic Products sold in such country, based on data provided by IQVIA (formerly, Quintiles IMS Holdings, Inc.) or, if such data is not available, such other reliable data source as agreed upon by the Parties (such agreement not to be unreasonably withheld).

1.84 “Generic Product” means, on a country by country basis with respect to a Product, any generic product such as a product that contains the Compound as an active ingredient; and is approved in reliance, in whole or in part, on the prior approval (or on safety or efficacy data submitted in support of the prior approval) of such Product as determined by the applicable Regulatory Authority, including any product authorized for sale (i) in the U.S. pursuant to Section 505(b)(2) or Section 505(j) of the FDCA (21 U.S.C. 355(b)(2) and 21 U.S.C. 355(j), respectively), (ii) in the E.U. pursuant to a provision of Articles 10, 10a or 10b of Parliament and Council Directive 2001/83/EC as amended (including an application under Article 6.1 of Parliament and Council Regulation (EC) No 726/2004 that relies for its content on any such provision), or (iii) in any other country or jurisdiction pursuant to all equivalents of such provisions, including any amendments and successor statutes with respect to the subsections (i) through (iii) thereto. A Product marketed under the same Drug Approval Application as that of BII or any of its Affiliates but with the same or different trade name (i.e., commonly known as an authorized generic product) will not constitute a Generic Product.

1.85 “Good Clinical Practice” or “GCP” means, with respect to any applicable jurisdiction, the then-current standards, practices and procedures for clinical trials for pharmaceuticals promulgated or endorsed by the applicable Regulatory Authority in such jurisdiction (including, with respect to the United States, the FDA) as set forth in the Applicable

Laws of such jurisdiction, including, with respect to the United States, the guidelines titled “Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance” and related regulatory requirements imposed by the FDA, and with respect to jurisdictions outside the United States, comparable regulatory standards, practices and procedures promulgated by the EMA, PMDA or other Regulatory Authority, as applicable, including any applicable quality guidelines promulgated under the International Conference on Harmonization (“ICH”), in each case as they may be updated from time to time.

1.86 “**Good Laboratory Practice**” or “**GLP**” means, with respect to any applicable jurisdiction, the then-current standards, practices and procedures for laboratory activities for pharmaceuticals promulgated or endorsed by the applicable Regulatory Authority in such jurisdiction (including, with respect to the United States, the FDA) as set forth in the Applicable Laws of such jurisdiction, including, with respect to the United States, 21 C.F.R. Part 58 and related regulatory requirements imposed by the FDA, and with respect to jurisdictions outside the United States, comparable regulatory standards, practices and procedures promulgated by the EMA, PMDA or other Regulatory Authority, as applicable, including any applicable quality guidelines promulgated under the ICH, in each case as they may be updated from time to time.

1.87 “**Good Manufacturing Practice**” or “**GMP**” means, with respect to any applicable jurisdiction, the then-current good manufacturing practices for the manufacture and testing of pharmaceutical materials required by the applicable Regulatory Authority in such jurisdiction (including, with respect to the United States, the FDA) as set forth in the Applicable Laws of such jurisdiction, including, with respect to the United States, the FDCA, as amended, and the regulations promulgated thereunder, and with respect to applicable jurisdictions outside the United States, comparable regulatory standards, practices and procedures promulgated by the EMA, PMDA or other Regulatory Authority, as applicable, including the guidelines promulgated by the ICH designated ICH Q7A, titled “Q7A Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients” and the regulations promulgated thereunder, in each case as they may be updated from time to time.

1.88 “**ICC**” means the International Chamber of Commerce.

1.89 “**ICH**” has the meaning set forth in the definition of “Good Clinical Practice.”

1.90 “**IND**” means an application filed with a Regulatory Authority for authorization to commence Clinical Trials, including: (a) an Investigational New Drug Application as defined in the FDCA or any successor application or procedure filed with the FDA; (b) any equivalent of a United States IND in other countries or regulatory jurisdictions (i.e., clinical trial application); and (c) all supplements, amendments, variations, extensions and renewals thereof that may be filed with respect to any of the foregoing.

1.91 “**Indemnified Party**” has the meaning set forth in Section 12.3 (Procedure).

1.92 “**Indemnifying Party**” has the meaning set forth in Section 12.3 (Procedure).

1.93 “**Indication**” means a separate and distinct disease or medical condition in humans and non-humans. For clarity, with respect to oncologic diseases, Non-Small Cell Lung Cancer (“**NSCLC**”) is a separate and distinct disease from, for example, Small Cell Lung Cancer, Breast Cancer, Colorectal Cancer, and Melanoma and any similarly described conditions, however, any indication that would allow for the treatment of patients who have NSCLC (or Colorectal Cancer, or Breast Cancer, etc.) in a first line setting and/or a second line setting and/or a third line setting (or any of these), such treatment lines would not constitute a separate and distinct disease or medical condition.

1.94 “**Information**” means all technical, scientific, business and other know-how, information, trade secrets, knowledge, technology, means, methods, processes, practices, formulae, instructions, skills, techniques, procedures, experiences, ideas, technical assistance, designs, drawings, assembly procedures, computer programs, apparatuses, specifications, data, results and other material, including biological, chemical, pharmacological, toxicological, pharmaceutical, physical and analytical, pre-clinical, clinical, safety, regulatory, Manufacturing and quality control data and information, including study designs and protocols, reagents (e.g., plasmids, proteins, cell lines, assays and compounds) and biological methodology; in each case (whether or not confidential, proprietary, patented or patentable, of commercial advantage or not) in written, electronic or any other form now known or hereafter developed.

1.95 “**Initiation**” or “**Initiate**” means, with respect to a Clinical Trial, the first dosing of the first human subject or patient in such Clinical Trial.

1.96 “**Intellectual Property**” has the meaning set forth in Section 13.2.5 (Termination for Insolvency).

1.97 “**Invoice**” means an original invoice sent by Epizyme to BII with respect to any payment due hereunder that contains the Information within Schedule 1.97.

1.98 “**IRB**” means an institutional review board, ethics committee or other similar body.

1.99 “**JCC**” or “**Joint Commercialization Committee**” has the meaning set forth in Section 2.4.2 (Joint Commercialization Committee).

1.100 “**Joint Commercialization Plan and Budget**” has the meaning set forth in Section 5.2.2(a)(i) (Joint Commercialization Plan and Budget).

1.101 “**Joint Compound**” has the meaning set forth in Section 5.2.1(b)(i) (Initial Development Plan and Budget).

1.102 “**Joint Counsel**” has the meaning set forth in Section 8.2.4 (Joint Patents and Epizyme Product Patents).

- 1.103** “**Joint Counsel Patent Rights**” has the meaning set forth in Section 8.2.4 (Joint Patents and Epizyme Product Patents).
- 1.104** “**Joint Development Plan and Budget**” has the meaning set forth in Section 5.2.1(b)(i) (Initial Development Plan and Budget).
- 1.105** “**Joint Know-How**” has the meaning set forth in Section 8.1.2 (Ownership of Joint Technology).
- 1.106** “**Joint Patents**” has the meaning set forth in Section 8.1.2 (Ownership of Joint Technology).
- 1.107** “**Joint Product**” has the meaning set forth in Section 5.2.1(b)(i) (Initial Development Plan and Budget).
- 1.108** “**Joint Product Infringement**” has the meaning set forth in Section 8.3.1 (Enforcement of Epizyme’s Patents and Joint Patents).
- 1.109** “**Joint Product Patents**” means any Joint Patent that Covers a Compound (including the composition of matter), Product, or a method of use of a Compound or Product.
- 1.110** “**Joint Product Prosecuted Infringement**” has the meaning set forth in Section 8.3.1 (Enforcement of Epizyme’s Patents and Joint Patents).
- 1.111** “**Joint Technology**” has the meaning set forth in Section 8.1.2 (Ownership of Joint Technology).
- 1.112** “**Jointly Controlled Project**” means the Target Project directed to the [**] target but, for the avoidance of doubt, [**].
- 1.113** “**JSC**” or “**Joint Steering Committee**” has the meaning set forth in Section 2.1.1 (Formation).
- 1.114** “**Losses**” has the meaning set forth in Section 12.1 (Indemnification of Epizyme).
- 1.115** “**MAA**” has the meaning set forth in the definition of “Drug Approval Application”.
- 1.116** “**Major Markets**” means each of the [**].
- 1.117** “**Manufacture**” and “**Manufacturing**” means all activities related to the synthesis, making, production, processing, purifying, formulating, filling, finishing, packaging, testing and release, labeling, shipping, handling, storing and holding of a Compound, any Product or any intermediate thereof, including process development, process qualification and validation, scale-up, pre-clinical, clinical and commercial production and analytic development, product characterization, stability testing, quality assurance and quality control.

1.118 “**Manufacturing Costs**” means the FTE Costs (charged in accordance with Section 5.2.2(c)(ii) (FTE Records and Calculation)) incurred, and the out-of-pocket costs recorded as an expense in accordance with GAAP, by or on behalf of a Party or any of its Affiliates after the Effective Date and during the Term that are incurred in accordance with the Joint Commercialization Plan and Budget and specifically identifiable and directly attributable to the following Manufacturing activities with respect to Joint Products in the U.S. for Commercialization purposes:

- Product;
- 1.118.1** synthesis, making, production, processing, purifying, formulating a Compound or Joint
 - 1.118.2** filling, finishing, packaging and labelling;
 - 1.118.3** testing and releasing, shipping, handling storing and holding; and
 - 1.118.4** stability testing, quality assurance and quality control.

provided that, in no event will Manufacturing Costs include the purchase or construction of capital equipment, capital assets or real estate for the purposes of building manufacturing facilities and capabilities.

1.119 “**Materials**” has the meaning set forth in Section 4.3.1(a) (Provision of Materials).

1.120 “**Medical Affairs Activities**” means, with respect to a Joint Product in the U.S., the coordination of medical Information requests and field based medical scientific liaisons with respect to such Joint Product, including activities designed to ensure or improve appropriate medical use of, conduct medical education of, or further research regarding such Joint Product, including (a) conducting service based medical activities (including providing input and assistance with consultancy meetings, recommending investigators for Clinical Trials and providing input in the design of such trials and other research related activities), (b) delivering non-promotional communications and conducting non-promotional activities (including presenting new Clinical Trial data and other scientific Information), (c) reviewing grants to support continuing medical education or symposia related to the Joint Product, (d) development, publication and dissemination of publications relating to the Joint Product and relevant disease states in the United States, (e) conducting advisory board meetings or other consultant programs, (f) supporting investigator-initiated trials, (g) managing relationships with cooperative groups, physician/hospital networks and advocacy groups, (h) establishing and implementing risk, evaluation and mitigation strategies pertaining to the Joint Product and (i) Conducting Phase IV Studies.

1.121 “**Medical Affairs Costs**” means the FTE Costs (charged in accordance with Section 5.2.2(c)(ii) (FTE Records and Calculation)) incurred, and the out-of-pocket costs recorded as an expense in accordance with GAAP, by or on behalf of a Party or its Affiliates after the Effective Date and during the Term that are incurred in accordance with the Joint Commercialization Plan and Budget and specifically identifiable and directly attributable to Medical Affairs Activities with respect to any Joint Product sold in the United States, including Phase IV Costs.

1.122 “**Milestone Event**” has the meaning set forth in Section 7.3 (Milestone Payments).

1.123 “**Milestone Payment**” has the meaning set forth in Section 7.3 (Milestone Payments).

1.124 “**Net Losses**” has the meaning set forth in the definition of “Net Profits.”

1.125 “**Net Profits**” and, with correlative meaning, “**Net Losses,**” means, with respect to a Joint Product, Net Sales of such Joint Product in the United States, less Allowable Expenses (to the extent not already deducted from Net Sales and with respect to the Joint Product in the United States).

1.126 “**Net Sales**” means, with respect to a certain time period, the gross invoiced sales charged for Product(s) sold by or for BII, its Affiliates and Sublicensees in arm’s-length transactions to Third Parties (but not including sales relating to transactions between BII, its Affiliates or their respective Sublicensees) during such time period, less the total of the following charges or expenses as determined in accordance with GAAP (as defined in this Agreement), consistently applied across all products sold by BII and its Affiliates, in each case without duplication:

1.126.1 sales returns and allowances actually paid, granted or accrued, including trade, quantity, prompt payment and cash discounts and any other adjustments, including those granted on account of price adjustments or billing errors;

1.126.2 credits or allowances actually granted for rejected goods, damaged or defective goods, recalls and returns;

1.126.3 rebates, chargeback rebates, compulsory rebates, reimbursements or similar payments granted or given to wholesalers or other distributors, buying groups, health care insurance carriers or other institutions (e.g. managed care entities) and compulsory payments to governmental authorities and any other governmental charges imposed upon the sale of such Product to Third Parties;

1.126.4 retroactive price reductions applicable to sales of such Product;

1.126.5 adjustments actually made in accordance with consumer discount programs or other similar programs;

1.126.6 the actual acquisition cost of devices used for dispensing or administering the Product that are shipped with the Product and included in the gross invoiced sales price;

1.126.7 non-collectable receivables related to Product;

1.126.8 customs or excise duties, sales tax, consumption tax, VAT and other taxes (except income taxes); and

1.126.9 charges for packing, freight, shipping and insurance (to the extent that BII, its Affiliates or Sublicensees bear the cost for Product).

BII and its Affiliates and Sublicensees shall not incur discounts, allowances, credits, rebates or other deductions on the Product in order to advantage other products of BII, its Affiliates or Sublicensees, such that the Product would bear a disproportionate portion of such deductions (i.e., the Product would serve as a loss leader for the benefit of other products). All defined deductions in this section shall be consistent with BII's, its Affiliates' or its Sublicensees', as applicable, audited financial statements.

For the sake of clarity and avoidance of doubt, sales by BII and its Affiliates or Sublicensees of a Product to a Recognized Agent of such Product in a given country shall be considered a sale to a Third Party customer (the term "**Recognized Agent**" used in this sentence shall mean any Third Party who distributes Products directly to customers in countries where BII has no Affiliate or Sublicensee).

Any disposal of Product for promotional or advertising purposes, or use of Products in pre-clinical trials or Clinical Trials, given as free samples, or transferred to Third Parties as part of an expanded access program, compassionate sales or use program, an indigent program, or distributed at no charge to patients unable to purchase Product shall not be included in Net Sales. Donations for charity reasons shall also not be part of Net Sales.

Upon any sale or other disposal of any Product that should be included in Net Sales for any consideration other than an exclusively monetary consideration on bona fide arm's-length terms, then for purposes of calculating the Net Sales under this Agreement, such Product shall be deemed to be sold exclusively for money at the average sales price charged for such Product during the applicable reporting period achieved for such Product in the country in which such sale or other disposal occurred when such Product is sold alone and not with other products. In the event no sales price is available for the Product alone in such country during the applicable reporting period, then such Product shall be deemed to be sold exclusively for money at the arithmetic mean sales price charged for such Product during the applicable reporting period generally achieved for such Product in all countries in which such sale or other disposal occurred when such Product is sold alone and not with other products; *provided, however, that* if such Product is not sold alone in any country, then BII shall calculate in good faith an estimated market price for the Product, allocating the same proportion of costs, overhead and profit as are then allocated to all similar products then being made and marketed by BII and having an ascertainable market price, and shall provide Epizyme with a written summary of the methodology used by BII in arriving at such estimated market price.

If a Product is sold in the form of a Combination Product, then the Net Sales of such Product for the purpose of calculating payments owed under this Agreement for sales of such Product shall be determined as described below. Notwithstanding the foregoing, Net Sales shall not include amounts (whether actually existing or deemed to exist for purposes of calculation) for Product distributed for use in Clinical Trials. In the event a Product is sold as a Combination Product, Net Sales of the Combination Product will be calculated as follows:

1.126.10 If the Combination Product, the Product and the other product are sold separately, Net Sales of the Product portion of Combination Products will be calculated by multiplying the total Net Sales of the Combination Product by the fraction $A/(A+B)$, where A is the average gross selling price in the applicable country in the Territory of the Product sold separately in the same formulation and dosage, and B is the sum of the average gross selling prices in the applicable country in the Territory of all other therapeutically or prophylactically active ingredients or products in the Combination Product sold separately in the same formulation and dosage, during the applicable Calendar Quarter.

1.126.11 If the Combination Product and the Product are sold separately, but the average gross selling price of the other product(s) cannot be determined, Net Sales of the Combination Product shall be equal to the Net Sales of the Combination Product multiplied by the fraction A/C wherein A is the average gross selling price of the Product and C is the average gross selling price of the Combination Product.

1.126.12 If the Combination Product and the other product(s) are sold separately, but the average gross selling price of the Product cannot be determined, Net Sales of the Combination Product shall be equal to the Net Sales of the Combination Product multiplied by the following formula: one (1) minus B/C wherein B is the average gross selling price of the other product(s) and C is the average gross selling price of the Combination Product.

1.126.13 If the Combination Product are sold but the average gross selling price of neither the Product nor the other product(s) can be determined, Net Sales of the Combination Product shall be equal to Net Sales of the Combination Product multiplied by a mutually agreed percentage.

The average gross selling price for such other product(s) contained in the Combination Product shall be calculated for each Calendar Year by dividing the sales amount by the units of such other product(s), as published by IQVIA or another mutually agreed independent source.

In the initial Calendar Year during which a Combination Product is sold, a forecasted average gross selling price shall be used for the Product, other product(s), or Combination Product. Any overpayment or underpayment due to a difference between forecasted and actual average gross selling prices shall be paid or credited in the second royalty payment of the following Calendar Year. In the following Calendar Year, the average gross selling price of the previous Calendar Year shall apply from the second royalty payment on.

1.127 “**Non-Defaulting Party**” has the meaning set forth in Section 13.2.1 (Termination of Agreement for Cause).

1.128 “**Non-Pivotal Clinical Trial**” means a human clinical trial of a Product that is Conducted in any country in the Territory (whether a standalone trial or a stage of a “Phase 1/2” clinical trial described in the protocol as the Phase 2 portion, or a stage of a “Phase 2/3” clinical trial described in the protocol as the Phase 2 portion) the principal purpose of which is: (a) to evaluate the clinical efficacy, safety, pharmacodynamics or biological activity of such Product (itself or other biological materials) in the target patient population as its primary endpoint and is prospectively designed to generate sufficient data that may permit commencement of a Pivotal Clinical Trial; or (b) that would otherwise satisfy the requirements of 21 C.F.R. § 312.21(b), or its foreign equivalent.

1.129 “**Off-Cycle Amendment**” has the meaning set forth in Section 5.2.1(b)(ii) (Revisions).

1.130 “**Opt-Out Notice**” has the meaning set forth in Section 5.2.5 (Epizyme Opt-Out).

1.131 “**Opt-Out Royalties**” has the meaning set forth in Section 5.2.5 (Epizyme Opt-Out).

1.132 “**Party**” and “**Parties**” has the meaning set forth in the Preamble.

1.133 “**Patent Liaisons**” has the meaning set forth in Section 8.2.1 (Patent Liaisons).

1.134 “**Patents**” means: (a) all national, regional and international patents and patent applications, including provisional patent applications; (b) all patent applications filed either from such patents, patent applications or provisional applications or from an application claiming priority from either of these, including divisionals, continuations, continuations-in-part, provisionals, converted provisionals and continued prosecution applications; (c) any and all patents that have issued or in the future issue from the foregoing patent applications ((a) and (b)), including utility models, petty patents and design patents and certificates of invention; and (d) any and all extensions or restorations by existing or future extension or restoration mechanisms, including revalidations, reissues, re-examinations and extensions (including any supplementary protection certificates and the like) of the foregoing patents or patent applications ((a), (b) and (c)).

1.135 “**Patient Assistance Program Costs**” means the FTE Costs (charged in accordance with Section 5.2.2(c)(ii) (FTE Records and Calculation)) incurred, and the out-of-pocket costs recorded as an expense in accordance with GAAP, by or on behalf of a Party or any of its Affiliates after the Effective Date and during the Term that are incurred in accordance with the Joint Commercialization Plan and Budget and specifically identifiable to operating patient assistance programs that aim to provide low-income or uninsured patients with free or low-cost medications.

1.136 “**Person**” means an individual, sole proprietorship, partnership, limited partnership, limited liability partnership, corporation, limited liability company, business trust, joint stock company, trust, unincorporated association, joint venture or other similar entity or organization, including a government or political subdivision, department or agency of a government.

1.137 “**Phase IV Costs**” means the FTE Costs (charged in accordance with Section 5.2.2(c)(ii) (FTE Records and Calculation)) incurred, and the out-of-pocket costs recorded as an expense in accordance with GAAP, by or on behalf of a Party or any of its Affiliates after the Effective Date, during the Term of and pursuant to this Agreement, that are specifically identifiable and directly attributable to Phase IV Studies, wherever conducted, of a Joint Product in support of Commercialization of such Joint Product in the U.S. and always consistent with then-current Joint Commercialization Plan and Budget.

1.138 “**Phase IV Study**” means a post-marketing human clinical study for a Product with respect to any Indication as to which Regulatory Approval has been received or for a use that is the subject of an investigator-initiated study program.

1.139 “**Pivotal Clinical Trial**” means a human clinical trial of a Product that is Conducted in any country in the Territory (whether a standalone trial or a stage of a multiple-stage clinical trial): (a) with a defined dose or a set of defined doses of such Product designed to establish statistically significant efficacy and safety of such Product for the purpose of enabling the preparation and submission of a Drug Approval Application to the competent Regulatory Authorities in a country of the Territory; (b) where the results of such clinical trial are intended (if successful) to be used to establish both safety and efficacy of such Product in patients which are the subject of such trial and serve as the basis for initial or supplemental marketing authorization of such Product in at least one Major Market; or (c) that would otherwise satisfy requirements of 21 C.F.R. § 312.21(c), or its foreign equivalent. For the avoidance of doubt, a Non-Pivotal Clinical Trial will be considered a Pivotal Clinical Trial if the results of such Non-Pivotal Clinical Trial ultimately serve as the basis for a Drug Approval Application, regardless of original intent.

1.140 “**PMDA**” means Japan’s Pharmaceuticals and Medical Devices Agency and any successor agency(ies) or authority having substantially the same function.

1.141 “**Product**” means any and all preparations in final form containing Compound for use in the Field in the Territory, including BII Products and Joint Products.

1.142 “**Product Insurance Costs**” means the out-of-pocket costs recorded as an expense in accordance with GAAP, by or on behalf of a Party or any of its Affiliates after the Effective Date and during the Term that are incurred in accordance with the Joint Commercialization Plan and Budget and specifically identifiable and directly attributable to the premiums paid for Product liability insurance.

1.143 “**Product Labeling**” means, with respect to a Product in a country in the Territory: (a) the Regulatory Authority-approved full prescribing Information for such Product for such country, including any required patient Information; and (b) all labels and other written, printed, or graphic matter upon a container, wrapper or any package insert utilized with or for such Product in such country.

1.144 “**Product Liability Costs**” means the out-of-pocket costs (including reasonable attorney’s fees) and awards recorded as an expense in accordance with GAAP, by or on behalf of a Party or any of its Affiliates after the Effective Date and during the Term of and pursuant to this Agreement that are specifically identifiable and directly attributable to the costs of Product liability that are not otherwise covered by insurance pursuant to Section 12.5 (Insurance) and otherwise not subject to indemnification pursuant to ARTICLE 12 (Indemnity).

1.145 “**Product Marks**” has the meaning set forth in Section 8.1.5 (Ownership of Product Marks).

1.146 “**Prosecution and Maintenance**” means, with respect to a Patent, preparation, filing, prosecution and maintenance of such Patent, as well as post grant review proceedings, reexaminations, reissues and the like with respect to such Patent, together with the conduct of interferences, the defense of oppositions and other similar proceedings with respect to the particular Patent; and “**Prosecute and Maintain**” shall have the correlative meaning.

1.147 “**Publication Policies**” has the meaning set forth in Section 10.6 (Publications).

1.148 “**Recall Costs**” means the FTE Costs (charged in accordance with Section 5.2.2(c)(ii) (FTE Records and Calculation)) incurred, and the out-of-pocket costs recorded as an expense in accordance with GAAP, by or on behalf of a Party or any of its Affiliates after the Effective Date and during the Term of and pursuant to this Agreement that are specifically identifiable and directly attributable to conducting recalls, market suspensions or market withdrawals for the Joint Product pursuant to Section 5.4 (Recalls).

1.149 “**Regulatory Approval**” means, with respect to a country in the Territory, any and all approvals (including Drug Approval Applications that have been approved by a Regulatory Authority), licenses, registrations or authorizations of any Regulatory Authority necessary to Commercialize a Product in such country, excluding separate pricing or reimburseability approvals that may be required or useful to Commercialize a Product.

1.150 “**Regulatory Authority**” means any applicable supra-national, federal, national, regional, state, provincial or local governmental or regulatory authority, agency, department, bureau, commission, council or other entities (e.g., the FDA, EMA and PMDA) regulating or otherwise exercising authority with respect to activities contemplated in this Agreement, including the Exploitation of Compounds or Products in the Territory.

1.151 “**Remedial Plan**” has the meaning set forth in Section 4.1.2(b) (Satisfaction of SoLO Criteria).

1.152 “**Replacement Product**” has the meaning set forth in Section 7.3 (Milestone Payments).

1.153 “**Research Activities**” means those research and other activities undertaken by the Parties pursuant to the Research Plan with respect to discovering, characterizing, identifying and optimizing Compounds directed to (a) the [**] target and (b) the [**] target.

1.154 “**Research Funding**” has the meaning set forth in Section 7.2 (Research Funding).

1.155 “**Research Period**” has the meaning set forth in Section 3.2.1 (Initial Research Period).

1.156 “**Research Plan**” means the Research and Development Plan and Budget attached hereto as Schedule 1.156 (Research Plan) and described in Section 3.1 (Research Plan), including the SoLO Criteria and SoD Criteria, as may be amended from time to time pursuant to Section 3.3 (Amendments to Research Plan).

1.157 “**ROW**” means all countries of the world other than the U.S.

1.158 “**Royalty Term**” means, with respect to each Product and each country in the Territory, the period beginning on the date of the First Commercial Sale of such Product in such country, and ending on the [**] to occur of: (a) subject to Section 8.2.5 (Patent Term Extensions), the expiration, invalidation or abandonment date of the last Epizyme Patent, BII Patent or Joint Patent that includes a Valid Claim that claims the composition of matter of the Compound for such Product; or (b) the [**] anniversary of the First Commercial Sale of such Product in such country.

1.159 “**Sales and Marketing Costs**” means the FTE Costs (charged in accordance with Section 5.2.2(c) (ii) (FTE Records and Calculation)) incurred, and the out-of-pocket costs recorded as an expense, by a Party or any of its Affiliates in accordance with GAAP after the Effective Date and during the Term that are incurred in accordance with the Joint Commercialization Plan and Budget and specifically identifiable and directly attributable to the sales and marketing of a Joint Product in the United States. Sales and Marketing Costs shall include amounts paid by a Party to Third Parties that are specifically identifiable and directly attributable to the Commercialization of a Joint Product by such Third Party in the U.S. Subject to the foregoing, Sales and Marketing Costs include costs incurred in connection with the following activities (but in each case only to the extent specifically identifiable and directly attributable to the sales and marketing of a Joint Product in the United States):

1.159.1 activities directed to the advertising and marketing of Joint Products in the United States;

1.159.2 launch meetings;

1.159.3 advertising and public relations agencies, including development and distribution of selling and advertising and promotional materials relating to the use of a Joint Product, field literature, direct-to-consumer advertising campaigns, media/journal advertising, distribution of such advertising and promotional materials by a Party to its sales force personnel, exhibiting at seminars and conventions, convention costs, and promotional premiums;

1.159.4 speakers programs, including training of such speakers;

1.159.5 developing, obtaining, and providing educational and training packages for Joint Products, promotional literature, promotional materials, and other selling materials, including shipment costs of the same to a Party’s central distribution facility and from a Party’s central distribution facility to its sales force personnel;

1.159.6 transporting, housing and maintaining sales representatives for training and the costs of all training materials used for such purpose;

1.159.7 developing and performing market research;

1.159.8 developing Information and data specifically intended for national accounts, managed care organizations, governmental agencies (e.g., federal, state and local), and other group purchasing organizations, including pull-through activities;

1.159.9 developing Product Trademarks, including style guides;

1.159.10 Detail Costs; and

1.159.11 operation and maintenance of the sales representatives that promote a Joint Product in the U.S., sales bulletins and other communications, sales meetings, specialty sales forces, call reporting and other monitoring/tracking costs, district and regional sales management, home office personnel who support the sales force, development and copying of training, motivational and communications materials relating to Joint Products, and other services ancillary to the foregoing.

1.160 “**SEC Filing**” has the meaning set forth in Section 10.5 (Agreement Redactions).

1.161 “[**]” has the meaning set forth in Section 5.2.1(b)(ii) (Revisions).

1.162 “**Senior Officers**” means, with respect to BII, [**], or a designee nominated by such individual, and with respect to Epizyme, its Chief Executive Officer (or his or her designee).

1.163 “[**]” means [**].

1.164 “[**]” means [**].

1.165 “[**]” means [**].

1.166 “**SoD**” or “**Start of Development**” means, with respect to a Compound, that such Compound has demonstrated sufficient characteristics in pre-clinical Development to warrant activities with respect to such Compound directed toward the start of clinical Development of such Compound, which is expected to occur prior to the initiation of IND-enabling toxicity studies of such Compound.

1.167 “**SoD Approval**” has the meaning set forth in Section 4.2.2(b) (Satisfaction of SoD Criteria).

1.168 “**SoD Criteria**” has the meaning set forth in Section 3.1 (Research Plan).

1.169 “**SoLO**” or “**Start of Lead Optimization**” means, with respect to a Compound, that such Compound has demonstrated sufficient characteristics in pre-clinical Development to warrant the start of lead optimization of such Compound.

1.170 “**SoLO Approval**” has the meaning set forth in Section 4.1.2(b) (Satisfaction of SoLO Criteria).

1.171 “**SoLO Criteria**” has the meaning set forth in Section 3.1 (Research Plan).

1.172 “**Sublicensee**” has the meaning set forth in Section 6.4.2 (Sublicenses).

1.173 “**Target Projects**” means, collectively, the two (2) projects conducted by the Parties pursuant to the Research Plan related to the discovery and research of Compounds that are inhibitors to (a) the [**] target and (b) the [**] target, and the corresponding and resulting Joint Compound or Joint Product on the one hand, and BII Compound or BII Product on the other hand, as these are further Developed and Commercialized by the Parties or by BII under this Agreement. When used in the singular, “**Target Project**” means either the [**] target project (including any Joint Compound or Joint Product) or the [**] target project (including any BII Compound or BII Product), as the context requires.

1.174 “**Term**” has the meaning set forth in Section 13.1.1 (Term).

1.175 “**Territory**” means ROW and the United States.

1.176 “[**]” has the meaning set forth in Section 5.2.1(b)(ii) (Revisions).

1.177 “**Third Party**” means any Person other than Epizyme and its Affiliates and BII and its Affiliates.

1.178 “**Third Party Claims**” has the meaning set forth in Section 12.1 (Indemnification of Epizyme).

1.179 “**Third Party Payments**” means all upfront payments, milestone payments or royalties paid by a Party to a Third Party after the Effective Date and during the Term of and pursuant to this Agreement that are in consideration of a license of Patents that Cover, or Information that is used in, the making, using, offering to sell, selling, importing or exporting of a Compound or Product in the Territory.

1.180 “**Trademark**” means any word, name, symbol, color, designation or device or any combination thereof that functions as a source identifier, including any trademark, trade dress, brand mark, service mark, trade name, brand name, logo, business symbol or domain names, whether or not registered.

1.181 “**Trademark Costs**” means those out-of-pocket costs (including the reasonable fees and expenses paid to outside counsel and other Third Parties, and filing and maintenance fees paid to governmental authorities) recorded as an expense by a Party or any of its Affiliates in accordance with GAAP after the Effective Date, during the Term of and pursuant to this Agreement, (a) in connection with the prosecution and maintenance of rights, including filing and registration fees with respect to the Trademark(s) for the Joint Products in the U.S. and (b) the costs of litigation (enforcement or defense) or other proceedings, under the Trademark(s) for the Joint Products in the U.S., only to the extent not reimbursed by a Third Party.

1.182 “**Transition Agreement**” has the meaning set forth in Section 13.3.2(f) (Transition Agreement).

1.183 “**United States**” or “**U.S.**” means the United States of America and its territories and possessions (including the District of Columbia and Puerto Rico).

1.184 “**Valid Claim**” means, as applicable, a claim in any (a) unexpired and issued Patent that has not been disclaimed, revoked or held invalid by a final non-appealable decision of a court of competent jurisdiction or government agency or (b) a pending Patent application that has not been finally abandoned, finally rejected or expired (after exhaustion of all appeals); *provided that*, if a claim of a pending Patent application shall not have been issued within [**] after the earliest filing date from which such claim takes priority, such claim shall not constitute a Valid Claim for the purposes of this Agreement unless and until a Patent issues with respect to such claim.

1.185 “**VAT**” has the meaning set forth in Section 7.7 (Taxes; Withholding Taxes).

1.186 “**Voting Stock**” has the meaning set forth in the definition of “Change in Control.”

1.187 “**Working Group**” has the meaning set forth in Section 2.4.1 (Working Groups – Generally).

ARTICLE 2 COLLABORATION MANAGEMENT

2.1. Joint Steering Committee.

2.1.1 Formation. Within [**] of the Effective Date (or such later date as may be agreed to by the Parties), the Parties will establish a joint steering committee (the “**JSC**”). The JSC shall consist of an equal number of representatives from each of the Parties, each of whom will have the requisite experience and seniority to enable such Person to make decisions on behalf of the Parties with respect to the issues falling within the jurisdiction of the JSC. Each Party shall select from its representatives a chairperson for the JSC. From time to time, each Party may substitute one or more of its representatives to the JSC upon written notice (including by email or otherwise) to the other Party.

2.1.2 Specific Responsibilities. Subject to the limitations on its authority imposed by Section 2.1.3 (Limitations on Authority), the JSC shall provide oversight and decision-making for all matters arising in connection with this Agreement, including by serving as a forum for planning, reviewing and coordinating activities related to Target Projects, Compounds, Products and Diagnostic Products. In particular, the JSC will be responsible for:

(a) establishing Working Groups from time to time pursuant to Section 2.4 (Working Groups);

(b) periodically reviewing and, as necessary, approving proposed amendments to the Research Plan pursuant to Section 3.3 (Amendments to the Research Plan);

(c) overseeing Epizyme's undertaking of characterization, validation and identification activities (if any) pursuant to Section 4.1.1 (SoLO Performance Obligation) that are necessary for SoLO Approval;

(d) determining whether to nominate a [**] inhibitor or [**] inhibitor to BII for SoLO Approval pursuant to Section 4.1.2(a) (Satisfaction of SoLO Criteria) and to nominate a Compound to BII for SoD Approval pursuant to Section 4.2.2(a) (Satisfaction of SoD Criteria);

(e) determining whether to re-nominate a [**] inhibitor or [**] inhibitor to BII for SoLO Approval upon completing a Remedial Plan with respect thereto pursuant to Section 4.1.2 (Satisfaction of SoLO Criteria) and to re-nominate a Compound to BII for SoD Approval upon completing a Remedial Plan with respect thereto pursuant to Section 4.2.2(b) (Satisfaction of SoD Criteria);

(f) approving the (i) Joint Development Plan and Budget pursuant to Section 5.2.1(b) (i) (Initial Development Plan and Budget) and (ii) Joint Commercialization Plan and Budget pursuant to Section 5.2.2(a)(i) (Initial Commercialization Plan and Budget), with respect to (i)-(ii), including all revisions and all amendments thereto;

(g) (i) monitoring the Development of Joint Products for the United States and serving as the decision-making forum with respect to decisions impacting the Development of the Joint Product for the United States, including with respect to determining (A) the specific Clinical Trials to be Conducted (including those that are committed and those that are conditioned based upon the results of ongoing Clinical Trials), (B) the anticipated timelines for such Clinical Trials and (C) the Clinical Trial activities to be assigned to each Party and (ii) monitoring the Development of the Joint Product for the ROW and serving as a forum for the Parties with respect to discussing matters affecting the Development of the Joint Product for the ROW and U.S. and Information sharing with respect thereto, with respect to (i)-(ii), pursuant to Section 5.2.1(c) (JSC Development Responsibility);

(h) (i) monitoring the Commercialization of Joint Products in the United States and serving as the decision-making forum with respect to strategic decisions impacting the Commercialization of the Joint Product in the United States, including with respect to establishing (A) a general Commercialization strategy (including life-cycle plans), (B) anticipated timelines for launch, (C) pricing and reimbursement strategy, (D) branding strategy, (E) supply chain and distribution strategy, (F) packaging and labeling, (G) advertising and public relations agencies of record, (H) market research strategy, (I) sales force strategy, (J) sizing and alignment, planned physician detail equivalents, deployment and incentive compensation guidelines, (K) revenue forecasts, (L) sales objectives, (M) Medical Affairs Activities and (N) allocating specific accounts or geographies to a Party and (ii) serving as a forum for the Parties with respect to discussing matters affecting the Commercialization of the Joint Product for the ROW and U.S. and Information sharing with respect thereto, with respect to (i)-(ii), pursuant to Section 5.2.2(b) (JSC Commercialization Responsibility);

(i) following notice from Epizyme pursuant to Section 5.2.3 (Adverse Actions), discussing (i) Epizyme's concerns that BII's proposed regulatory or Commercialization activities in a ROW country could adversely affect a Product's Development or Commercialization in the U.S. and (ii) whether BII should amend its proposed regulatory or Commercialization activities based on Epizyme's concerns;

(j) establishing the pre-clinical, clinical and commercial supply strategy for Joint Compounds and Joint Products in the U.S. pursuant to Section 5.3.1 (Supply Plans);

(k) developing and approving Publication Policies and reviewing abstracts, manuscripts and presentations pursuant to Section 10.6 (Publications); and

(l) performing such other functions as are set forth in this Agreement or as the Parties may mutually agree in writing, except where in conflict with any provision of this Agreement.

2.1.3 Limitations on Authority.

(a) For the BII Controlled Project, the scope of the JSC's oversight and decision-making authority shall be limited to those activities set forth in the Research Plan that occur prior to SoD Approval for the BII Controlled Project.

(b) For the Jointly Controlled Project, the scope of the JSC's oversight and decision-making authority shall extend to all matters arising in connection with this Agreement; *provided that*, other than serving as a forum for the coordination of ROW matters and Information sharing with respect thereto, the JSC will have no authority to direct Development, regulatory or Commercialization matters that pertain specifically to ROW.

(c) The JSC will not have the power to amend, modify or waive compliance with this Agreement (including the SoLO Criteria and SoD Criteria set forth in the Research Plan), which may only be amended or modified as provided in Section 14.9 (Entire Agreement; Amendments) or compliance with which may only be waived as provided in Section 14.12 (Waiver and Non-Exclusion of Remedies).

(d) Each Party will retain the rights, powers and discretion granted to it under this Agreement and no such rights, powers or discretion will be delegated to or vested in the JSC unless such delegation or vesting of rights is expressly provided for in this Agreement or the Parties expressly so agree in writing.

2.1.4 Disbandment.

(a) In the event that Epizyme provides BII with an Opt-Out Notice pursuant to Section 5.2.5 (Epizyme Opt-Out), unless otherwise mutually agreed in writing by the Parties, the JSC shall be disbanded upon the effective date of the Opt-Out Notice as set forth in Section 5.2.5 (Epizyme Opt-Out).

(b) In the event that BII elects, pursuant to Section 14.2.1 (U.S. Commercialization Rights), to terminate Epizyme's Development and Commercialization rights, responsibilities and obligations with respect to the Joint Compound and Joint Product in the U.S. and to vest all such rights, responsibilities and obligations for the Joint Compound and Joint Product in BII, then, unless otherwise mutually agreed in writing by the Parties, the JSC shall be disbanded as set forth in the transition plan agreed to by the Parties pursuant to Section 14.2.1 (U.S. Commercialization Rights). If the JSC is disbanded as set forth in this Section 2.1.4(b), then at least [**] prior to the start of the [**], BII will provide Epizyme (or its successor) with a non-binding, good faith, written estimate of the Development Costs and Allowable Expenses that BII reasonably expects to incur (or have incurred on its behalf) for the remainder of the [**] in which the JSC was disbanded, which estimate will be provided on a [**] basis. Contemporaneously with delivery of the foregoing estimate, BII will also provide Epizyme (or its successor) with a non-binding, good faith, written estimate of the Development Costs and Allowable Expenses that BII reasonably expects to incur (or have incurred on its behalf) for the [**] following the [**] in which the JSC is disbanded, which estimate will be provided on a [**] basis. Thereafter, BII will provide revised estimates to Epizyme (or its successor) [**] so that Epizyme (or its successor) always has a written estimate of the Development Costs and Allowable Expenses that BII reasonably expects to incur (or have incurred on its behalf) during the ensuing [**] period, which estimates will be provided (i) on a [**] basis with respect to the [**] of such [**] period and (ii) on a [**] basis, with respect to the [**] of such [**] period. For the avoidance of doubt, any such estimates provided by BII to Epizyme (or its successor) are non-binding and BII shall in its sole discretion determine and conduct Development and Commercialization activities (always subject to Commercially Reasonable Efforts) for which Development Costs or Allowable Expenses are incurred in any such period, regardless of whether such actual costs and expenses incurred deviate substantially more or less from those Development Costs or Allowable Expenses reflected in such estimates.

(c) In the event the JSC is disbanded pursuant to this Section 2.1.4 (Disbandment) with respect to [**], all rights, responsibilities and obligations assigned to the JSC pursuant to this Agreement for [**] shall instead be deemed to be assigned to BII and BII shall have sole decision-making authority with respect thereto.

2.2. General Provisions Applicable to Joint Committees.

2.2.1 Meetings and Minutes. The JSC will meet [**], and more frequently should the chairpersons mutually agree. The location of such meetings will alternate between locations designated by Epizyme and locations designated by BII. Both Party's chairpersons shall initially establish the schedule of JSC meetings, and such schedule shall be continually updated to provide for the meetings times and locations for the next [**]. Each Party will make all proposals for agenda items and will provide all appropriate Information with respect to such proposed items at least [**] in advance of the applicable meeting; *provided that*, under exigent circumstances requiring input by the JSC, a Party may provide its agenda items to the other Party within a shorter period of time in advance of the meeting, or may propose that there not be a specific agenda for a particular meeting, so long as the other Party consents to such later addition of such agenda items or the absence of a specific agenda for such meeting, such consent not to be unreasonably withheld or delayed. The JSC will designate an individual to prepare and circulate for review and approval of the Parties minutes of each meeting [**] after the meeting. The Parties will agree on the minutes of each meeting promptly, but in no event later than [**] after the meeting, and a representative of each Party will execute such agreed minutes.

2.2.2 Procedural Rules. The JSC will have the right to adopt such standing rules as will be necessary for its work, to the extent that such rules are not inconsistent with this Agreement. A quorum of the JSC will exist whenever there is present (for clarity, in accordance with the participation options given in the immediately following sentence) at a meeting at least [**] appointed by each Party. Each Party's JSC representatives may attend a meeting either in person or by telephone, video conference or similar means in which each participant can hear what is said by, and be heard by, the other participants. The JSC will take action by consensus of the representatives present at a meeting at which a quorum exists, with each Party having a single vote irrespective of the number of representatives of such Party in attendance, or by a written resolution signed by at least one representative appointed by each Party. Alliance Managers and, with the prior consent of the other Party (not to be unreasonably withheld or delayed) and on a need to participate basis, other employees or consultants of either Party who are not representatives of such Party on the JSC, may attend meetings of the JSC; *provided that* such attendees: (a) will not vote in the decision-making process of the JSC; and (b) are bound by obligations of confidentiality and non-disclosure equivalent at least as protective of the other Party as to those set forth in ARTICLE 10 (Confidentiality and Non-Disclosure).

2.2.3 Disagreement Resolution. If the JSC cannot, or does not, reach consensus on an issue that is within the scope of its responsibilities at any JSC meeting or within a period of [**] thereafter, then the disagreement will first be referred to the Senior Officers of the Parties, who will confer in good faith on the resolution of the issue. Any final decision mutually agreed to by the Senior Officers will be conclusive and binding on the Parties. If the Senior Officers are not able to agree on the resolution of any such issue within [**] after such issue was first referred to them, then (a) with respect to disagreements related to the BII Controlled Project, the Senior Officer of [**] shall have final decision-making authority with respect thereto, without recourse to the dispute resolution process set forth in Section 14.7 (Dispute Resolution) and (b) with respect to disputes related to the Jointly Controlled Project, (i) the Senior Officer of [**] shall have final decision-making authority with respect to all matters arising prior to [**] for the Jointly Controlled Project and (ii) the Senior Officer of [**] shall have final decision-making authority with respect to all matters that arise following [**] for the Jointly Controlled Project, with respect to (i)-(ii), without recourse to the dispute resolution process set forth in Section 14.7 (Dispute Resolution); *provided that*, with respect to (a)-(b), each Party shall exercise its final decision-making authority in good faith. Notwithstanding the foregoing, in no event (A) may BII exercise its final decision-making authority to impose on Epizyme an obligation to perform a Development, Manufacturing or Commercialization activity with respect to the Jointly Controlled Project without Epizyme's consent, (B) may either Epizyme or BII exercise its final decision-making authority to amend the SoLO Criteria or SoD Criteria, (C) may BII exercise its final decision-making authority to force the Parties to share a Development Overrun pursuant to Section 5.2.1(d)(iii) (Development Overruns) or (D) may BII exercise its final decision-making authority to force the Parties to share a Commercialization Overrun pursuant to Section 5.2.2(c)(iv) (Commercialization Overruns).

2.2.4 Alliance Manager. Each Party will appoint one employee of such Party who will oversee contact between the Parties for all matters between meetings of each JSC and will have such other responsibilities as the Parties may agree in writing after the Effective Date (each, an “**Alliance Manager**”). Each Party may replace its Alliance Manager at any time by notice in writing (including by email or otherwise) to the other Party. The Alliance Managers will work together to manage and facilitate the communication between the Parties under this Agreement, including the resolution (in accordance with the terms of this Agreement) of issues between the Parties that arise in connection with this Agreement.

2.3. Interactions Between JSC and Internal Teams. The Parties recognize that each Party possesses an internal structure (including various committees, teams and review boards) that will be involved in administering such Party’s activities under this Agreement. Nothing contained in this ARTICLE 2 (Collaboration Management) will prevent a Party from making routine day-to-day decisions relating to the conduct of those activities for which it has a performance or other obligations hereunder, in each case in a manner consistent with the then-current Research Plan or, as applicable, and the terms and conditions of this Agreement.

2.4. Working Groups.

2.4.1 Generally. From time to time, the JSC may establish and delegate duties to subcommittees or directed teams (each, a “**Working Group**”) on an “as-needed” basis to oversee particular projects or activities (e.g., a Development Working Group responsible for clinical efforts in the Territory). Each such Working Group will be constituted and will operate as the JSC determines; *provided that* each Working Group will have equal representation from each Party, unless otherwise mutually agreed. Working Groups may be established on an ad hoc basis for purposes of a specific project or on such other basis as the JSC may determine. Each Working Group and its activities will be subject to the oversight, review and approval of, and will report to, the JSC. In no event will the authority of the Working Group exceed that specified by the JSC for such Working Group. All decisions of a Working Group will be by consensus. Any disagreement between the designees of BII and Epizyme with respect to a Working Group will be referred to the JSC for resolution.

2.4.2 Joint Commercialization Committee. Upon the earlier of (a) [**] for a Joint Product in the Territory or (b) [**] prior to the anticipated First Commercial Sale of a Joint Product in the U.S., the JSC shall establish a Working Group responsible for overseeing the Commercialization of the Joint Product in the U.S. (the “**JCC**” or “**Joint Commercialization Committee**”) and shall specify the specific responsibilities of the JCC (which may include responsibilities of the JSC described in Section 2.1.2 (Specific Responsibilities)). The JCC will generally operate in accordance with Section 2.1.1 (Formation), Section 2.2.1 (Meetings and Minutes) and Section 2.2.2 (Procedural Rules), as applicable. Disputes that cannot be resolved at the JCC will be referred to the JSC for resolution in accordance with Section 2.2.3 (Disagreement Resolution).

2.5. Expenses. Each Party will be responsible for all travel and related costs and expenses for its members and other representatives to attend meetings of, and otherwise participate on, the JSC or other Working Group.

ARTICLE 3
RESEARCH PLAN; RESEARCH PERIOD

3.1. Research Plan. As more fully set forth in this Agreement, BII and Epizyme shall conduct Research Activities allocated to such Party for each Target Project pursuant to the Research Plan. The Research Plan shall set forth (a) the overall objectives of each Target Project, (b) a list of criteria to be used to determine SoLO (the “**SoLO Criteria**”) and a list of criteria to be used to determine SoD (the “**SoD Criteria**”) for such Target Project, (c) the Research Activities to be conducted by the Parties in connection with such Target Project, including the work packages to be generated by the Parties in connection with its Research Activities, (d) the resources to be allocated by each Party in connection with such Target Project and (e) the budget for such Target Project.

3.2. Research Period.

3.2.1 Initial Research Period. With respect to a Target Project, the term of the Research Plan for such Target Project shall commence on the Effective Date and continue (unless sooner terminated pursuant to ARTICLE 13 (Term and Termination)) until the earlier to occur of (a) December 31, 2019 (unless extended pursuant to Section 3.2.2 (Extension)) or (b) [**] (the “**Research Period**”).

3.2.2 Extension. If BII believes, acting reasonably and in good faith, that [**] will likely not be achieved by December 31, 2019, then BII, in its sole discretion, may elect to extend the initial Research Period for such Target Project by providing written notice to Epizyme of such election no later than [**], which notice shall set forth the duration of such extension (not to exceed an additional twelve (12) month period). Upon receipt of such extension notice provided by BII pursuant to this Section 3.2.2 (Extension), the Parties shall, upon mutual written agreement, promptly amend the Research Plan to include (a) the additional Research Activities (including Research Activities that may have been set forth in the existing Research Plan that Epizyme did not complete by December 31, 2019) to be performed by the Parties on account of such extension, (b) any additional work packages (including work packages that may have been set forth in the existing Research Plan that Epizyme did not generate by December 31, 2019) to be generated by the Parties on account of such extension, (c) any additional resources (including resources that may be required to complete the activities or generate the work packages set forth in subclause (a) or (b) above) to be allocated by the Parties on account of such extension and (d) pursuant to Section 7.2.2 (Research Funding – Calendar Year 2020), the additional Research Funding to be paid to Epizyme on account of such extension, which additional Research Funding shall be appropriate and commercially reasonable with respect to the additional Research Activities to be performed and resources to be expended. The Research Period for such Target Project shall be deemed extended by the period set forth in any notice provided by BII pursuant to this Section 3.2.2 (Extension) upon the mutual agreement of the Parties with respect to the matters set forth in the immediately preceding sentence. If the Parties are unable to reach mutual agreement with respect to such matters by [**], then BII may solely decide to perform, at its sole expense, any additional research activities from January 1, 2020 onwards with respect to the applicable Target Project, subject to JSC oversight as applicable, and with BII having final decision making with respect to any JSC decisions notwithstanding the provisions found in Section 2.2.3 (Disagreement Resolutions).

3.3. Amendments to the Research Plan. Either Party may, acting through its representatives on the JSC, propose amendments to the Research Plan at any time. The JSC may amend the Research Plan provided such amendments are mutually agreed to by the JSC representatives of each Party (without reference to the tie-breaking provisions of Section 2.2.3 (Disagreement Resolution)) and in no event may the JSC amend the SoLO Criteria or SoD Criteria, unless such amendments are mutually agreed to by the Parties as provided in Section 14.9 (Entire Agreement; Amendments).

ARTICLE 4 RESEARCH PROGRAM

4.1. Prior to SoLO.

4.1.1 SoLO Performance Obligation. Following the Effective Date, Epizyme shall, in accordance with the Research Plan, use Commercially Reasonable Efforts to (a) further characterize and validate the [**] target and [**] target (if further efforts are needed) and (b) conduct research to identify and characterize [**] inhibitors and [**] inhibitors for BII to determine, acting reasonably and in good faith, whether a [**] inhibitor and [**] inhibitor has satisfied the SoLO Criteria for a Target Project. Subject to BII's obligation to provide Research Funding to Epizyme pursuant to the Section 7.2 (Research Funding), Epizyme shall bear the costs of all Research Activities undertaken by Epizyme pursuant to this Section 4.1.1 (SoLO Performance Obligation).

4.1.2 Satisfaction of SoLO Criteria.

(a) If Epizyme believes that a [**] inhibitor or [**] inhibitor has met all of the SoLO Criteria for the applicable Target Project, then it shall notify the JSC. The JSC shall discuss and review the Research Plan results that pertain to such inhibitors and criteria, and decide whether the SoLO Criteria have been met. If the JSC representatives of each Party mutually agree in good faith (without reference to the tie-breaking provisions of Section 2.2.3 (Disagreement Resolution)) that the SoLO Criteria have been met, then the JSC shall so notify BII in writing, which notice shall be accompanied by a report containing Information in sufficient detail to demonstrate that the SoLO Criteria have been achieved for such [**] inhibitor or [**] inhibitor, as applicable. Upon BII's receipt of such written notice and report, BII will promptly inform its [**] (collectively, the "**BII SoLO Committee**") of the JSC's belief that the relevant [**] inhibitor or [**] inhibitor should be considered for SoLO Approval and will initiate a process for the BII SoLO Committee to determine whether or not such [**] inhibitor or [**] inhibitor should receive SoLO Approval. For the avoidance of doubt, the JSC may always decide to nominate a [**] inhibitor or [**] inhibitor prior to such [**] inhibitor or [**] inhibitor, as applicable, meeting all of the SoLO Criteria for the applicable Target Project provided the members of the JSC of each Party mutually agree (without reference to the tie-breaking provisions of Section 2.2.3 (Disagreement Resolution)).

(b) Within [**] of BII's receipt of such report, the BII SoLO Committee shall notify the JSC in writing that SoLO has occurred for the Target Project with respect to such [**] inhibitor or [**] inhibitor (the "**SoLO Approval**"), unless the BII SoLO Committee, acting reasonably and in good faith, has a scientific or commercial reason for

withholding SoLO Approval for such [**] inhibitor or [**] inhibitor. In the event that the BII SoLO Committee has such a reason for withholding SoLO Approval for a [**] inhibitor or [**] inhibitor, the BII SoLO Committee (or its designee) shall provide the JSC with written notice of its reasons and a plan aimed at remedying such concerns (each, a “**Remedial Plan**”) with respect to such nominated [**] inhibitor or [**] inhibitor, which Remedial Plan may include the performance or re-performance of Research Activities that were set forth in the existing Research Plan or performance of additional Research Activities not set forth in the existing Research Plan and, if such Remedial Plan does include the performance of additional Research Activities not set forth in the then existing Research Plan, then such Remedial Plan shall include a reasonable timeline for completing such additional Research Activities. Subject to Section 3.2.2 (Extension), with respect to Research Activities set forth in the Remedial Plan, Epizyme will bear the costs of conducting any such Research Activities that were set forth in the existing Research Plan that were not completed at the time the [**] inhibitor or [**] inhibitor was nominated for SoLO Approval consideration pursuant to Section 4.1.2(a) (Satisfaction of SoLO Criteria), while the costs of any such Research Activities not set forth in the existing Research Plan (i.e., additional Research Activities) shall be at (i) BII’s cost if (A) the Remedial Plan requires that BII perform any additional research activities with respect to any [**] inhibitor or [**] inhibitor, (B) the entirety of the SoLO Criteria were met for a [**] inhibitor or [**] inhibitor, but the BII SoLO Committee nevertheless withholds SoLO Approval for such [**] inhibitor or [**] inhibitor or (C) the work contemplated in the Remedial Plan is intended to produce results or data that is not included in the SoLO Criteria (and not already covered under the existing Research Plan) and (ii) Epizyme’s costs if the JSC members mutually agreed (without reference to the tie-breaking provisions of Section 2.2.3 (Disagreement Resolution)) to nominate a [**] inhibitor or [**] inhibitor for SoLO Approval prior to such [**] inhibitor or [**] inhibitor meeting all of the SoLO Criteria for the applicable Target Project.

(c) Upon completion of the Remedial Plan, the JSC shall notify BII in writing, which notice shall be accompanied by a report containing Information in sufficient detail to demonstrate that the Remedial Plan was completed. Upon BII’s receipt of such written notice and report, BII will promptly inform the BII SoLO Committee. Within [**] of BII’s receipt of such report, the BII SoLO Committee will provide the JSC with SoLO Approval with respect to the applicable [**] inhibitor or [**] inhibitor, unless BII has further scientific or commercial reasons for withholding SoLO Approval for such [**] inhibitor or [**] inhibitor. If BII has further scientific or commercial reasons for withholding SoLO Approval, then Epizyme shall continue to perform in accordance with the Research Plan and BII may solely decide to perform any additional research related activities not set forth in the Research Plan with respect to achieving SoLO Approval for a Target Project or Compound, subject to JSC oversight as applicable, and with BII having final decision making with respect to any JSC decisions with respect to such additional research related activities notwithstanding the provisions found in Section 2.2.3 (Disagreement Resolutions).

4.1.3 Allocation of Responsibilities Following SoLO Approval. Following SoLO Approval for a Target Project but prior to SoD for such Target Project, as more fully set forth in the Research Plan and Section 4.2 (Following SoLO But Prior to SoD), (a) with respect to the BII Controlled Project, BII shall be primarily responsible for and assume the operational activities concerning such Target Project; *provided that* Epizyme shall assist BII as set forth in the Research Plan or as may be mutually agreed to by the Parties and (b) with respect

to the Jointly Controlled Project, Epizyme shall be primarily responsible for and assume the operational activities concerning such Target Project; provided that BII shall assist Epizyme as set forth in the Research Plan or as may be mutually agreed to by the Parties.

4.2. Following SoLO but Prior to SoD

4.2.1 Research Performance Obligation. Following SoLO Approval for a particular Target Project, each Party shall use Commercially Reasonable Efforts to perform its Research Activities under the Research Plan for each Target Project during the applicable Research Period applicable to such Target Project to achieve the SoD Criteria for each Target Project. Subject to BII's obligation to provide Research Funding to Epizyme pursuant to the Section 7.2 (Research Funding), Epizyme shall bear the costs of all Research Activities undertaken by Epizyme pursuant to this Section 4.2.1 (Research Performance Obligation).

4.2.2 Satisfaction of SoD Criteria.

(a) If Epizyme believes that a Compound has met all of the SoD Criteria for the applicable Target Project, then it shall notify the JSC. The JSC shall discuss and review the Research Plan results that pertain to such inhibitors and criteria, and decide whether the SoD Criteria have been met. If the JSC representatives of each Party mutually agree in good faith (without reference to the tie-breaking provisions of Section 2.2.3 (Disagreement Resolution)) that the SoD Criteria have been met, then the JSC shall so notify BII in writing, which notice shall be accompanied by a report containing Information in sufficient detail to demonstrate that the SoD Criteria have been achieved for such Compound. Upon BII's receipt of such written notice and report, BII will promptly inform its [**] (collectively, the "**BII SoD Committee**") of the JSC's belief that the relevant Compound should be considered for SoD Approval and will initiate a process for the BII SoD Committee to determine whether or not such Compound should receive SoD Approval. For the avoidance of doubt, the JSC may always decide to nominate a Compound prior to such Compound meeting all of the SoD Criteria for the applicable Target Project provided the members of the JSC of each Party mutually agree (without reference to the tie-breaking provisions of Section 2.2.3 (Disagreement Resolution)).

(b) Within [**] of BII's receipt of such report, the BII SoD Committee shall notify the JSC in writing that SoD has occurred for the Target Project with respect to such Compound (the "**SoD Approval**"), unless the BII SoD Committee, acting reasonably and in good faith, has a scientific or commercial reason for withholding SoD Approval for such Compound. In the event that the BII SoD Committee has such a reason for withholding SoD Approval for a Compound, the BII SoD Committee (or its designee) shall provide the JSC with written notice of its reasons and a Remedial Plan with respect to such nominated Compound, which Remedial Plan may include the performance or re-performance of Research Activities that were set forth in the existing Research Plan or performance of additional Research Activities not set forth in the existing Research Plan and, if such Remedial Plan does include the performance of additional Research Activities not set forth in the then existing Research Plan, shall include a reasonable timeline for completing such additional Research Activities. Subject to Section 3.2.2 (Extension), with respect to Research Activities set forth in the Remedial Plan, Epizyme will bear the costs of conducting any such Research Activities that were set forth in the existing Research Plan that were not completed at the time the Compound

was nominated for SoD Approval consideration pursuant to Section 4.2.2(a) (Satisfaction of SoD Criteria), while the costs of any such Research Activities not set forth in the existing Research Plan (i.e., additional Research Activities) shall be at (i) BII's cost if (A) the Remedial Plan requires that BII perform any additional research activities with respect to any Compound, (B) the entirety of the SoD Criteria were met for a Compound, but the BII SoD Committee nevertheless withholds SoD Approval for such Compound or (C) the work contemplated in the Remedial Plan is intended to produce results or data that is not included in the SoD Criteria (and not already covered under the existing Research Plan) and (ii) Epizyme's costs if the JSC members mutually agreed (without reference to the tie-breaking provisions of Section 2.2.3 (Disagreement Resolution)) to nominate a Joint Compound for SoD Approval prior to such Joint Compound meeting all of the SoD Criteria for the applicable Target Project.

(c) Upon completion of the Remedial Plan, the JSC shall notify BII in writing, which notice shall be accompanied by a report containing Information in sufficient detail to demonstrate that the Remedial Plan was completed. Upon BII's receipt of such written notice and report, BII will promptly inform the BII SoD Committee. Within [**] of BII's receipt of such report, the BII SoD Committee will provide the JSC with SoD Approval with respect to the applicable Compound, unless BII has further scientific or commercial reasons for withholding SoD Approval for such Compound. If BII has further scientific or commercial reasons for withholding SoD Approval, Epizyme shall continue to perform in accordance with the Research Plan, including conducting any Research Activities set forth in the Research Plan, and BII may solely decide to perform any additional research related activities not set forth in the Research Plan with respect to achieving SoD Approval for a Target Project or Compound, subject to JSC oversight as applicable, and with BII having final decision making with respect to any JSC decisions with respect to such additional research related activities notwithstanding the provisions found in Section 2.2.3 (Disagreement Resolutions).

4.3. Materials, Compound Transfer, and Customs Related Topics.

4.3.1 Provision of Materials.

(a) In order to facilitate the Research Plan and Research Activities, each Party shall, as set forth in the Research Plan, provide to the other Party certain tangible biological and chemical materials, including Compounds (collectively, "**Materials**"). All Materials provided by one Party to the other Party remain the sole property of the supplying Party.

(b) Epizyme will not ship any Materials to BII without the prior written request of BII and BII shall request such Materials through a written purchase order issued to Epizyme, which will outline the specific amount and price (if any) assigned to such Materials and the requested date of delivery, as agreed to between the Parties. Epizyme shall monitor the synthesis, production and shipment of Materials provided to BII under this Agreement. Epizyme shall share information related to the synthesis, production and shipment of such Materials and send such information to BII upon shipment of the applicable Materials to BII. Epizyme agrees to reasonably cooperate with BII to determine whether Epizyme may become an approved exporter in a country that has a Reciprocal Preferential Trade Agreement with the E.U. in place, and therefore all Materials meet preferential origin status. Epizyme shall

declare the country of origin for each shipment of Materials and correspond and fulfill the rules of origin for preferential trade with the E.U. Epizyme shall use reasonable efforts to make available to BII any additional information required by the relevant customs authorities to prove that each shipment of Materials corresponds and fulfills the rules of origin for preferential trade with the E.U. Epizyme shall undertake to provide legal authorizations for the issue of preference certificates, in particular the status of the authorized exporter under E.U. free trade agreements or a comparable status in other E.U. preferential agreements (for example, the status as a registered exporter in the general preferential system) and ensure the correct exercise of the obligations resulting from the granting of the respective status. Following the expiration or termination of this Agreement, Epizyme shall continue to support BII in matters related to taxes and customs with respect to the Materials shipped to BII pursuant to this Section 4.3.1 (Provision of Materials) for a period of [**] following such expiration or termination.

4.3.2 Provision of Protocols. In order to enable BII to perform Compound synthesis or production as provided under this Agreement, Epizyme agrees to transfer, and shall use reasonable efforts to cause its Third Party manufacturers to transfer (including by using reasonable efforts to negotiate contractual obligations for such Third Party manufacturers to do so under agreements entered into following the Effective Date) the synthesis or production protocols of all Compounds and relevant assay protocols to BII and to provide reasonable assistance requested by BII to enable BII (or its Affiliate or designated Third Party manufacturer, as applicable) to understand and implement such synthesis or production protocols at the facilities designated by BII. Such transfer shall be conducted at (a) BII's expense, if related to the BII Compound and (b) at BII's and Epizyme's expense, if related to the Joint Compound, which shall be split in accordance with the Development Cost allocation principles found in Section 5.2.1(b)(iv) (Allocation).

4.3.3 Limitations. All Materials shall be used (a) only for the specific purpose provided for in the applicable Research Plan and (b) solely under the control of the receiving Party. Unless set forth in the Research Plan, the Materials may not be used or delivered to or for the benefit of any Third Party without the prior written consent of the supplying Party, and shall not be used in research or testing involving human subjects, except as expressly contemplated in the applicable Research Plan or in accordance with this Agreement. All Materials shall be destroyed after completion of the permitted use. For clarity, Materials provided by one Party to the other Party may continue to be used by the other Party after the Research Period expires; *provided that* such receiving Party continues to use such Materials for further research and Development efforts covered under this Agreement and in accordance with any licenses granted under ARTICLE 6 (Grant of Rights).

4.3.4 DISCLAIMER. ANY MATERIALS ARE PROVIDED "AS IS" AND WITHOUT ANY REPRESENTATION OR WARRANTY, EXPRESS OR IMPLIED, INCLUDING ANY IMPLIED WARRANTY OF MERCHANTABILITY OR OF FITNESS FOR ANY PARTICULAR PURPOSE OR ANY WARRANTY THAT THE USE OF THE MATERIALS WILL NOT INFRINGE OR VIOLATE ANY PATENT OR OTHER PROPRIETARY RIGHT OF ANY THIRD PARTY.

4.3.5 Research Compounds. In order for Epizyme to fully exercise the research license granted to it by BII pursuant to Section 6.1.2 (Grant to Epizyme), BII will transfer to Epizyme [**].

4.4. Exclusivity.

4.4.1 [].**

(a) During the Term (other than in connection with a Party's activities under this Agreement), neither Party nor its Affiliates may, directly or indirectly, (i) conduct research with the intent to identify or synthesize any [**] Competing Product or (ii) Develop, Manufacture or Commercialize any [**] Competing Product, in either case, until [**] for a Compound arising from a Target Project directed to a [**] target under this Agreement; *provided that* [**].

(b) Notwithstanding anything to the contrary in this Agreement, the restrictions on BII and its Affiliates or Epizyme and its Affiliates in Section 4.4.1(a) (Exclusivity – [**]) will not extend to any Third Party developing or commercializing a product where such Third Party becomes an Affiliate of either BII or Epizyme after the Effective Date as a result of a Change in Control of BII or Epizyme or by any Affiliates of such Third Party that existed prior to such Change in Control if (i) such product is being clinically developed or commercialized by such Third Party or any of such Affiliates of such Third Party prior to the date of such a Change in Control of BII or Epizyme or after such a Change in Control of BII or Epizyme without any access to any BII Know-How or Epizyme Know-How or Joint Know-How and any unpublished BII Patents or Epizyme Patents or Joint Patents, (ii) a “firewall” of reasonable safeguards (including physical separation, where appropriate) is put in place by BII or Epizyme and such Third Party or any of such Affiliates of such Third Party between individuals with access to Confidential Information of BII or Epizyme, BII Know-How or Epizyme Know-How or Joint Know-How, and any unpublished BII Patents or Epizyme Patents and Joint Patents, on the one hand, and the personnel responsible for the development or commercialization of any such product, on the other hand and (c) such development or commercialization of such product continues or is undertaken without the use of any BII Know-How or Epizyme Know-How or Joint Know-How and any unpublished BII Patents or Epizyme Patents or Joint Patents after such Third Party becomes an Affiliate of BII or Epizyme.

4.4.2 [].**

(a) During the Term (other than in connection with a Party's activities under this Agreement), neither Party nor its Affiliates may, directly or indirectly, (i) conduct research with the intent to identify or synthesize any [**] Competing Product or (ii) Develop, Manufacture or Commercialize any [**] Competing Product, in either case, until [**] for a Compound arising from a Target Project directed to a [**] target under this Agreement.

(b) Notwithstanding anything to the contrary in this Agreement, the restrictions on BII and its Affiliates or Epizyme and its Affiliates in Section 4.4.2(a) (Exclusivity – [**]) will not extend to any Third Party developing or commercializing a product where such Third Party becomes an Affiliate of either BII or Epizyme after the Effective

Date as a result of a Change in Control of BII or Epizyme or by any Affiliates of such Third Party that existed prior to such Change in Control if (i) such product is being clinically developed or commercialized by such Third Party or any of such Affiliates of such Third Party prior to the date of such a Change in Control of BII or Epizyme or after such a Change in Control of BII or Epizyme without any access to any BII Know-How or Epizyme Know-How or Joint Know-How, and any unpublished BII Patents or Epizyme Patents or Joint Patents, (ii) a “firewall” of reasonable safeguards (including physical separation, where appropriate) is put in place by BII or Epizyme and such Third Party or any of such Affiliates of such Third Party between individuals with access to Confidential Information of BII or Epizyme, BII Know-How or Epizyme Know-How or Joint Know-How, and any unpublished BII Patents or Epizyme Patents and Joint Patents, on the one hand, and the personnel responsible for the development or commercialization of any such product, on the other hand and (c) such development or commercialization of such product continues or is undertaken without the use of any BII Know-How or Epizyme Know-How or Joint Know-How and any unpublished BII Patents or Epizyme Patents or Joint Patents after such Third Party becomes an Affiliate of BII or Epizyme.

ARTICLE 5 POST-RESEARCH RESPONSIBILITIES

5.1. BII Controlled Project.

5.1.1 BII Products Report. Following [**] with respect to the BII Controlled Project, BII (and its Affiliates), at its sole cost, shall have sole decision-making authority and control over the BII Controlled Project, including with respect to Developing, Manufacturing, pursuing Regulatory Approval for, Commercializing and otherwise Exploiting (a) Compounds arising from the BII Controlled Project (“**BII Compounds**”), (b) Products containing the BII Compounds (“**BII Products**”) and (c) Diagnostic Products for the BII Compound and BII Products. Prior to the [**] of BII Product, BII will provide Epizyme through its Alliance Manager, within [**], with a written report summarizing BII’s, its Affiliates’ and Sublicensees’ activities and results with respect to the previous [**] period and the then-current expected activities for the next [**] period for Development of the BII Compounds, the BII Product and Diagnostic Products for the BII Compound and BII Product in the Field in the Territory (such report, the “**BII Products Report**”).

5.1.2 BII Diligence. BII, itself or through its Affiliates or Sublicensees, shall use Commercially Reasonable Efforts to (a) Develop and pursue Regulatory Approval for at least one BII Product and (b) Commercialize one BII Product in the Territory where Regulatory Approval is received for such Product. With respect to certain countries, the Parties understand that due to pricing or reimbursement limitations, parallel trade and importation issues or other market related considerations that may arise, it may become impractical, unprofitable, undesirable or unreasonable to launch and sell BII Product in such countries alone or when considering potential impacts on other countries where BII Product shall be Commercialized and, in all such like instances, BII shall be entitled to decide to not Commercialize BII Product in such countries and not be in breach of its Commercially Reasonable Efforts and other obligations under this Section 5.1.2 (BII Diligence).

5.2. Jointly Controlled Project.

5.2.1 Development Responsibilities and Expenses.

(a) **General.** Unless otherwise agreed to by the JSC in the Joint Development Plan and Budget pursuant to Section 5.2.1(b) (Joint Development Plan and Budget), upon [**] with respect to the Jointly Controlled Project, whichever occurs first, BII shall have operational responsibility for the Jointly Controlled Project.

(b) Joint Development Plan and Budget.

(i) **Initial Development Plan and Budget.** Subject to Section 5.2.1(a) (Jointly Controlled Project – General), with respect to Developing, Manufacturing and seeking Regulatory Approval for (A) Compounds arising from the Jointly Controlled Project (“**Joint Compounds**”), (B) Products containing Joint Compounds (“**Joint Products**”) and (C) Diagnostic Products for the Joint Compound or Joint Product, the JSC shall allocate such responsibilities between the Parties pursuant to a [**] rolling Development plan and budget approved by the JSC (such plan and budget, together with all revisions and amendments thereto, the “**Joint Development Plan and Budget**”); *provided that* BII shall be solely responsible for pursuing Regulatory Approval for Joint Products and Diagnostic Products for Joint Compounds or Joint Products if such Regulatory Approvals relate solely to an ROW country or countries. Without limitation, the Joint Development Plan and Budget shall set forth, among other things, (1) the specific Clinical Trials to be Conducted, including those that are committed and those that are conditioned upon the results of ongoing Clinical Trials, (2) the anticipated timelines for such Clinical Trials and (3) the Clinical Trial activities to be assigned to each Party, with respect to (1)-(3), for the Joint Product in the Territory. The Parties shall not conduct any Development, Manufacturing or Regulatory Activities with respect to the Joint Compounds, Joint Products or Diagnostic Products for Joint Compounds or Joint Products that are inconsistent with the Joint Development Plan and Budget. In the event the JSC has been disbanded pursuant to Section 2.1.4 (Disbandment), the Joint Development Plan and Budget will terminate (except as provided for under any transition related plans), and BII will be responsible for preparing and providing Epizyme with [**] reports with respect to the Joint Product that correspond with the reporting provisions found in Section 5.1.1 (BII Products Report) of this Agreement, *mutatis mutandis*.

(ii) **Revisions.** The JSC shall revise the Joint Development Plan and Budget [**] so that immediately following such revision the Joint Development Plan and Budget always sets forth a [**] rolling Development plan and budget for the Joint Compound and Joint Product in the Territory. The budget for the [**] period (the “[**]”) of the Joint Development Plan and Budget shall be firm. In connection with making [**] revisions to the Joint Development Plan and Budget pursuant to this Section 5.2.1(b)(ii) (Revisions), unless the Parties otherwise mutually agree, the JSC may not increase the budget for such activities (A) with respect to the [**] (which had previously been [**] (the “[**]”) in the previous Joint Development Plan and Budget), by more than [**] percent ([**]%) of the budget set forth in the previous Joint Development Plan and Budget for such months and (B) with respect to the [**] period (which had previously been [**] (the “[**]”) in the previous Joint Development Plan and Budget), by more than [**] percent ([**]%) of the budget set forth in the

previous Joint Development Plan and Budget for such [**]. The JSC shall act in good faith when establishing the budget for the Joint Development Plan and Budget. In the event the JSC decides to revise the Joint Development Plan and Budget prior to the expiration of the then-current [**] period (i.e., before [**] revision is required) (each such revision, an “**Off-Cycle Amendment**”), then the [**] rolling period for the Joint Development Plan and Budget shall commence anew as of the effective date of the Off-Cycle Amendment, but such Off-Cycle Amendment shall otherwise remain subject to the terms of this Section 5.2.1(b)(ii) (Revisions), including that: (1) the Joint Development Plan and Budget shall be revised [**] from the effective date of the Off-Cycle Amendment so that it always sets forth a [**] rolling Development plan and budget for the Joint Compound and Joint Product in the Territory; (2) the JSC may not increase the budget for any [**] that were previously included in the [**], unless the Parties, acting through their JSC members, otherwise mutually agree (without reference to the tie-breaking provisions of Section 2.2.3 (Disagreement Resolution)); (3) the JSC may not increase the budget by more than [**] percent ([**]%) for any [**] that were previously included in the [**] and (4) the JSC may not increase the budget by more than [**] percent ([**]%) for any [**] that were previously included in the [**].

(iii) **Other Amendments.** Subject to the budgeting restrictions set forth in Section 5.2.1(b)(ii) (Revisions), the JSC shall review the Joint Development Plan and Budget [**] to determine if any non-budgetary amendments are necessary to the Joint Development Plan and Budget, and shall approve any such amendments to the Joint Development Plan and Budget.

(iv) **Allocation.** Sixty-five percent (65%) of the Development Costs associated with Developing, Manufacturing and seeking Regulatory Approval for Joint Compounds and Joint Products shall be allocated to BII and thirty-five percent (35%) of such Development Costs shall be allocated to Epizyme; *provided that* (1) to the extent any such Development Costs relate to activities undertaken solely to obtain Regulatory Approval in the U.S., the Parties shall equally share such costs (50:50) and (2) to the extent any such Development Costs relate to activities undertaken solely to obtain Regulatory Approval in a ROW country or countries, BII shall be solely responsible for all such costs.

(c) **JSC Development Responsibility.**

(i) **United States.** The JSC will monitor the Development of Joint Products for the United States and will serve as the primary decision-making forum with respect to significant decisions affecting the Development of the Joint Product for the United States; *provided that* each Party undertaking such Development activities will have control over the day-to-day conduct of such activities. Each Party will submit to the JSC for its review, within [**], a report with respect to its Development activities for the Joint Product for the United States undertaken by such Party during [**].

(ii) **ROW.** The JSC will monitor the Development of the Joint Product for the ROW and will serve as a forum for the Parties with respect to discussing matters affecting the Development of the Joint Product for the ROW and U.S. and Information sharing with respect thereto. In connection with the foregoing, BII will submit to the JSC for its review, within [**], a report with respect to its Development activities for the Joint Product for the ROW during [**].

(d) **Reporting and Reconciliation Payments; Overruns.**

(i) **Reporting; Audit.** Each Party shall report to the other, within [**], the actual Development Costs incurred by such Party with respect to the Joint Compound and Joint Product [**]. Such report shall specify, in reasonable detail, such Development Costs. Within [**], BII shall reconcile all Development Costs incurred [**] by the Parties and provide Epizyme with written notice of the results of such reconciliation. Based on the results of such reconciliation, a payment shall be made by one Party to the other as may be necessary to effect the division of Development Costs set forth in Section 5.2.1(b)(iv) (Allocation), which payment shall be made within [**] following Epizyme's receipt of the reconciliation notice. If either Party believes, in good faith, that the Development Costs reported by the other Party [**] are not accurate, then the Parties shall meet and discuss the alleged inaccuracy and attempt to come to resolution with respect thereto. In the event the Parties are unable to resolve the alleged inaccuracy, the Party alleging the inaccuracy will have the right to perform an audit of the other Party's Development Costs pursuant to the provisions of Section 7.10 (Audit; Audit Dispute), *mutatis mutandis*.

(ii) **FTE Records and Calculations.** Each Party shall record and account for its FTE effort with respect to Joint Products in the Territory to the extent that such FTE efforts are included in Development Costs that are shared under this Agreement. Each Party shall calculate and maintain records relating to FTE efforts incurred by it in a manner consistent with the provisions found within this Agreement and generally as used for other products developed by such Party.

(iii) **Development Overruns.** If the Development Costs incurred by a Party for Development activities exceed the amounts set forth in the Joint Development Plan and Budget by more than [**] percent ([**]%) (calculated for all costs incurred over the [**] (as such may be adjusted pursuant to Section 5.2.1(b)(ii)) for all budgeted activities), such excess Development Costs (each, a "**Development Overrun**") shall be borne by the Party responsible for performing or causing to be performed such activities and such Development Overrun shall be excluded from the division of Development Costs set forth in Section 5.2.1(b)(iv) (Allocation); *provided that*, if such Development Overrun was outside the reasonable control of, and not attributable to a failure to use Commercially Reasonable Efforts by, the Party responsible for such Development Overrun, or did not result from the failure of such Party to adequately supervise a Third Party performing such activities, then the Party incurring such Development Overrun may petition the JSC to have such Development Overrun included in the division of Development Costs and shared by the Parties pursuant to Section 5.2.1(b)(iv) (Allocation) and, only if the Parties, acting through their JSC representatives, mutually agree (without reference to the tie-breaking provisions of Section 2.2.3 (Disagreement Resolution)) that such Development Overrun should be included in the division of Development Cost (without BII exercising its tie-breaking authority pursuant to Section 2.2.3 (Disagreement Resolution)), will such Development Overrun be shared by the Parties pursuant to Section 5.2.1(b)(iv) (Allocation).

(e) **Development Diligence.** Each Party, itself or through its Affiliates or permitted Contractors or Sublicensees, shall use Commercially Reasonable Efforts to perform the activities allocated to it under the Joint Development Plan and Budget, including by Developing and pursuing Regulatory Approval for Joint Products as set forth in the Joint Development Plan and Budget. For the avoidance of doubt, BII shall be solely responsible for submitting all Drug Approval Applications to Regulatory Authorities for Regulatory Approvals, and any and all such Drug Approval Applications that have received Regulatory Approval shall be solely owned by and held in BII's name.

5.2.2 Commercialization Responsibilities and Expenses.

(a) **Joint Commercialization Plan and Budget.**

(i) **Initial Commercialization Plan and Budget.** With respect to the Commercialization of Joint Products throughout the U.S., the JSC shall allocate such responsibilities between the Parties pursuant to a [**] rolling Commercialization plan and budget approved by the JSC (such plan and budget, together with all revisions and amendments thereto, the “**Joint Commercialization Plan and Budget**”), which shall be agreed to [**] of a Joint Product in the United States. Without limitation, the Joint Commercialization Plan and Budget shall set forth, among other things, [**]. Notwithstanding the foregoing, if the JSC determines to adopt a Joint Commercialization Plan and Budget [**] of the Joint Product, then the JSC may determine to include in such Joint Commercialization Plan and Budget, [**] budget (rather than a [**] rolling budget) and such Joint Commercialization Plan and Budget need not include all of the items set forth in ensuing subclauses (A)-(N), as the JSC deems appropriate. The JSC shall, at all times, except as provided elsewhere in this Agreement, endeavor to split Commercialization responsibilities with respect to the Joint Compound and Joint Product in the United States equally between the Parties, including 50:50 participation in co-promotion, Detailing and medical science liaison activities. [**] of Joint Product in the U.S., Epizyme shall have established a commercial team composed of qualified marketing and other commercial-oriented employees, knowledgeable and experienced in the sale of oncology pharmaceutical products, and [**] of Joint Product in the U.S., Epizyme shall have established a sales force organization, sales representatives and a medical science liaison organization of suitable size, composition and with relevant oncology product experience to perform the anticipated Detailing, medical education and other responsibilities required in the then current Joint Commercialization Plan and Budget. Unless otherwise agreed to by the JCC, at least [**] percent ([**]%) of all such sales force representatives and medical science liaisons performing Epizyme's delegated activities shall be Epizyme employees (or any such lesser percentage if BII or its Affiliate(s) employs such lesser percentage of its sales force representatives and medical science liaisons in performing BII's delegated activities), and all such representatives shall be fully trained and qualified, based on the same criteria applicable by BII to the qualification and training of its sales representatives generally, [**] of Product in the U.S., unless the JSC provides otherwise through the Joint Commercialization Plan and Budget. The Parties shall not conduct any Commercialization activities for the Joint Compound and Joint Product inconsistent with the Joint Commercialization Plan and Budget. BII shall be solely responsible for Commercializing the Joint Product in the ROW.

(ii) **Revisions.** The JSC shall revise the Joint Commercialization Plan and Budget [**] so that immediately following such revision the Joint Commercialization Plan and Budget always sets forth a [**] rolling Commercialization plan and budget for the Joint Compound and Joint Product in the Territory. The budget for the [**] of the Joint Commercialization Plan and Budget shall be firm. In connection with making [**] revisions to the Joint Commercialization Plan and Budget pursuant to this Section 5.2.2(a)(ii) (Revisions), unless the Parties otherwise mutually agree, the JSC may not increase the budget for such activities (A) with respect to the [**], by more than [**] percent ([**]%) of the budget set forth in the previous Joint Commercialization Plan and Budget for such [**] and (B) with respect to the [**], by more than [**] percent ([**]%) of the budget set forth in the previous Joint Commercialization Plan and Budget for such months. The JSC shall act in good faith when establishing the budget for the Joint Commercialization Plan and Budget. In the event the JSC decides to make an Off-Cycle Amendment to the Joint Commercialization Plan and Budget prior to the expiration of then then-current [**] period (i.e., before [**] revision is required), then the [**] rolling period for the Joint Commercialization Plan and Budget shall commence anew as of the effective date of the Off-Cycle Amendment, but such Off-Cycle Amendment shall otherwise remain subject to the terms of this Section 5.2.2(a)(ii) (Revisions), including that: (1) the Joint Commercialization Plan and Budget shall be revised [**] from the effective date of the Off-Cycle Amendment so that it always sets forth a [**] rolling Commercialization plan and budget for the Joint Compound and Joint Product in the United States; (2) the JSC may not increase the budget for any [**] that were previously included in the [**] unless the Parties, acting through their JSC members, otherwise mutually agree (without reference to the tie-breaking provisions of Section 2.2.3 (Disagreement Resolution)); (3) the JSC may not increase the budget by more than [**] percent ([**]%) for any [**] that were previously included in the [**]; and (4) the JSC may not increase the budget by more than [**] percent ([**]%) for any [**] that were previously included in the [**].

(iii) **Other Amendments.** Subject to the budgeting restrictions set forth in Section 5.2.2(a)(ii) (Revisions), the JSC shall review the Joint Commercialization Plan and Budget [**] to determine if any non-budgetary amendments are necessary to the Joint Commercialization Plan and Budget and shall approve any such amendments to the Joint Commercialization Plan and Budget.

(iv) **Allocation.** Epizyme shall receive fifty percent (50%) of all Net Sales and bear fifty percent (50%) of all Allowable Expenses resulting from Commercialization of Joint Products in the United States and BII shall receive fifty percent (50%) of all Net Sales and bear fifty percent (50%) of all Allowable Expenses resulting from Commercialization of Joint Products in the United States.

(b) **JSC Commercialization Responsibility.**

(i) **United States.** The JSC will monitor the Commercialization of Joint Products for the United States and will serve as the primary decision-making forum with respect to significant decisions affecting the Commercialization of the Joint Product for the United States; *provided that*, each Party undertaking such Commercialization activities will have control over the day-to-day conduct of such activities. Each Party will submit to the JSC for its review, within [**], a report with respect to its Commercialization activities for the Joint Product for the United States during the previous [**].

(ii) **ROW.** The JSC will monitor the Commercialization of the Joint Product for the ROW and will serve as a forum for the Parties with respect to discussing matters affecting the Commercialization of the Joint Product for the ROW and U.S. and Information sharing with respect thereto. In connection with the foregoing, BII will submit to the JSC for its review, within [**], a report with respect to its Commercialization activities for the Joint Product for the ROW during the previous [**].

(c) **Profit Share.** In furtherance of the 50:50 allocation of Net Sales and Allowable Expenses as set forth in Section 5.2.2(a) (Joint Commercialization Plan and Budget):

(i) **Reports and Payments in General.** Each Party shall report to the other Party, within [**] after the end of each Calendar Quarter, the actual Net Sales and Allowable Expenses incurred by such Party with respect to Joint Products in the U.S. during such Calendar Quarter. Such report shall specify in reasonable detail all deductions allowed in the calculation of such Net Sales and all expenses included in Allowable Expenses. Within [**] after the end of each Calendar Quarter, BII shall reconcile all Net Sales and Allowable Expenses to ascertain whether there is a Net Profit or Net Loss and provide Epizyme with written notice of the results of such reconciliation. Based on the results of such reconciliation, payments shall, subject to Section 5.2.2(c)(iv) (Overruns), be made as follows: (A) if there is a Net Profit for such Calendar Quarter, then BII shall pay to Epizyme an amount equal to fifty percent (50%) of the Net Profit for such Calendar Quarter; or (B) if there is a Net Loss for such Calendar Quarter, then the Party that has borne less than fifty percent (50%) of the aggregate Allowable Expenses incurred by the Parties during such Calendar Quarter shall make a reconciling payment to the other Party so that each Party bears fifty percent (50%) of the aggregate Allowable Expenses during such Calendar Quarter. Such payments shall be made within [**] following Epizyme's receipt of the reconciliation notice. If either Party believes, in good faith, that the Net Sales or Allowable Expenses reported by the other Party for a Calendar Quarter are not accurate, then the Parties shall meet and discuss the alleged inaccuracy and attempt to come to resolution with respect thereto. In the event the Parties are unable to resolve the alleged inaccuracy, the Party alleging the inaccuracy will have the right to perform an audit of the other Party's Net Sales and Allowable Expenses pursuant to the provisions of Section 7.10 (Audit; Audit Dispute), *mutatis mutandis*.

(ii) **FTE Records and Calculations.** Each Party shall record and account for its FTE effort with respect to Joint Products in the U.S. to the extent that such FTE efforts are included in Allowable Expenses that are shared under this Agreement. Each Party shall calculate and maintain records relating to FTE efforts incurred by it in a manner consistent with the provisions found within this Agreement and generally as used for other products developed by such Party. Each Party shall charge the FTE Rate for all FTEs who perform Commercialization activities encompassed within the definition of Allowable Expenses, except with respect to those activities encompassed within the definition of Sales and Marketing Costs. The FTE Rate(s) for activities encompassed within the definition of Sales and Marketing Costs shall be discussed by the JSC and the representatives of the Parties shall use good faith efforts to mutually agree on such FTE Rate(s) to be applied; *provided that*, in the event that the representatives of the Parties are unable to mutually agree on an FTE Rate(s), or the JSC has been disbanded under Section 2.1.4 (Disbandment) due to a Change in Control of Epizyme, then

the Parties shall use the FTE Rate set forth in Schedule 1.81. Notwithstanding the foregoing, the Allowable Expenses for sales representatives co-promoting the Joint Product in the U.S. shall be based on a fixed cost for Details in the primary or secondary position for similar prescriber specialties, and established by the JSC (or by BII in the event the JSC has been disbanded under Section 2.1.4 (Disbandment) due to a Change in Control of Epizyme) based on industry standard comparable benchmarks.

(iii) **Last Calendar Quarter.** No separate payment shall be made for the last Calendar Quarter in any Calendar Year. Instead, at the end of each such Calendar Year, a final reconciliation shall be conducted by comparing the share of Net Profit or Net Loss to which a Party is otherwise entitled for such Calendar Year against the sum of all amounts (if any) previously paid or retained by such Party for prior Calendar Quarters during such Calendar Year, and the Parties shall make reconciling payments to one another no later than **[**]** after the end of such Calendar Quarter, if and as necessary to ensure that each Party receives for such Calendar Year its share of Net Profits and bears its share of Net Losses in accordance with Section 5.2.2(a)(iv) (Allocation).

(iv) **Commercialization Overruns.** If the Allowable Expenses incurred by a Party for Commercialization activities exceed the amounts set forth in the Joint Commercialization Plan and Budget by more than **[**]** percent (**[**]**%) (calculated for all costs incurred over the **[**]** (as such may be adjusted on account of an Off-Cycle Amendment pursuant to Section 5.2.2(a)(ii) (Revisions)) for all budgeted activities), such excess Allowable Expenses (each, a “**Commercialization Overrun**”) shall be borne by the Party responsible for performing or causing to be performed such activities and shall be excluded from “Allowable Expenses” hereunder; *provided that*, if such Commercialization Overrun was outside the reasonable control of, and not attributable to a failure to use Commercially Reasonable Efforts by, the Party responsible for such Commercialization Overrun, or did not result from the failure of such Party to adequately supervise a Third Party performing such activities, then the Party incurring such Commercialization Overrun may petition the JSC to have such Commercialization Overrun included in the division of Allowable Expenses and shared by the Parties pursuant to Section 5.2.2(a)(iv) (Allocation) and, only if the Parties, acting through their JSC representatives, mutually agree (without reference to the tie-breaking provisions of Section 2.2.3 (Disagreement Resolution)) that such Commercialization Overrun should be included in the division of Allowable Expenses (without BII exercising its tie-breaking authority pursuant to Section 2.2.3 (Disagreement Resolution)), will such Commercialization Overrun be shared by the Parties pursuant to Section 5.2.2(a)(iv) (Allocation).

(d) **Commercialization Diligence.** BII, with respect to the ROW, and each Party, with respect to the United States, itself or through its Affiliates or permitted Contractors or Sublicensees, shall use Commercially Reasonable Efforts to Commercialize Joint Products in the Territory where Regulatory Approval is received for such Product. Each Party will use Commercially Reasonable Efforts to perform the activities allocated to it under the Joint Commercialization Plan and Budget. With respect to certain countries, the Parties understand that due to pricing or reimbursement limitations, parallel trade and importation issues or other market related considerations that may arise, it may become impractical, unprofitable, undesirable or unreasonable to launch and sell Joint Product(s) in such countries alone or when considering potential impacts on other countries where Joint Product(s)

shall be Commercialized and, in all such like instances, BII shall be entitled to decide to not Commercialize Joint Product(s) in such countries and not be in breach of its Commercially Reasonable Efforts and other obligations under this Section 5.2.2(d) (Commercialization Diligence).

(e) **Delegation to JCC.** For clarity, the JSC may delegate any or all of its responsibilities under Section 5.2.2 (Commercialization Responsibilities and Expenses) to the JCC pursuant to Section 2.4 (Working Groups), but, in such event, the JSC will remain responsible for approving the Joint Commercialization Plan and Budget established by the JCC, including all revisions and any other amendments thereto.

5.2.3 Adverse Actions. In the event that Epizyme reasonably believes, in good faith, that any proposed activity by BII with respect to a Joint Product in an ROW country could adversely affect the Development or Commercialization of a Joint Product in the U.S., then Epizyme shall inform the JSC in writing of its concerns and the JSC shall promptly meet and no later than at the next regularly scheduled JSC meeting, and consult on such matters to determine whether BII should make any changes to its proposed activities. Notwithstanding the foregoing, in all instances, BII shall have final decision-making authority with respect to such ROW Development or Commercialization activities and whether to implement or not implement any potential changes pursuant to Section 2.2.3 (Disagreement Resolution).

5.2.4 Booking of Sales; Distribution. BII and its Affiliates will have the sole right in setting prices, determining discounts, contracting with Third Parties, invoicing and booking sales (in relation to gross sales and Net Sales), warehousing and distributing Joint Products in the Territory, and to perform or cause to be performed all related services, subject to the JSC's role in determining the terms thereof with respect to the Joint Product in the United States pursuant to Section 5.2.2(b)(i) (JSC Commercialization Responsibility – United States), but always subject to Section 2.2.3 (Disagreement Resolution) where BII has final decision making powers. BII and its Affiliates will handle all returns, recalls or withdrawals, order processing, invoicing, collection, distribution and inventory management with respect to Joint Products in the Territory.

5.2.5 Epizyme Opt-Out. With respect to the Joint Product, Epizyme may, [**] included in such Joint Product, upon prior written notice to BII (such notice, the “**Opt-Out Notice**”), elect to cease its participation in the Development and Commercialization of such Joint Product (for clarity, if elected [**], Epizyme shall continue to perform its obligations with respect to the Research Activities under the Research Plan and those obligations contained in ARTICLE 2 (Collaboration Management), ARTICLE 3 (Research Plan; Research Period) and ARTICLE 4 (Research Program) of this Agreement that relate to Joint Product). The Epizyme Opt-Out Notice shall become effective (a) upon [**] prior written notice, if given [**], (b) upon [**] prior written notice, if given [**] or (c) upon [**] prior written notice, if given [**]; *provided, however, that* Epizyme may only cease its participation in the Development and Commercialization of the Joint Product during the [**] period [**] if BII agrees and provides its prior written consent that Epizyme may opt-out as aforesaid. Epizyme may always provide an Opt-Out Notice to BII at any time after [**]. In the event Epizyme does provide BII with an Opt-Out Notice as aforesaid, once effective: (i) Epizyme shall have no further obligation to, and shall cease to, perform Development activities (other than any Research Activities to be performed

under the Research Plan if such Opt-Out Notice is provided [**] as set forth in the first sentence of this Section 5.2.5 (Epizyme Opt-Out)) and Commercialization activities with respect to such Joint Compound or Joint Product in the United States, which cessation will occur pursuant to a mutually agreed to transition plan that will wind-down Epizyme’s performance of (A) Development activities as soon as reasonably practicable following the effective date of the opt-out (subject to the requirement that Epizyme continue to perform its obligations with respect to the Research Activities under the Research Plan if the Opt-Out Notice is provided prior to [**] as set forth in the first sentence of this Section 5.2.5 (Epizyme Opt-Out)) and using reasonable efforts to avoid unnecessary Development disruptions and (B) Commercialization activities over a period of not more than [**] following the effective date of the opt-out and using reasonable efforts to avoid unnecessary Commercialization disruptions, and for the avoidance of doubt, upon the completion of the Epizyme activities described in (A)-(B) and reflected in the transition plan, the license grants under Section 6.1.1 shall expire and terminate; (ii) Epizyme shall remain responsible for one hundred percent (100%) of its share of Allowable Expenses that were (A) actually incurred prior to the effective date of the Opt-Out Notice or (B) if not actually incurred prior to the effective date of the Opt-Out Notice, are nevertheless Committed Costs; (iii) Epizyme shall remain responsible for one hundred percent (100%) of its share of Development Costs that were (A) actually incurred prior to the effective date of the Opt-Out Notice or (B) if not actually incurred prior to the effective date of the Opt-Out Notice, are nevertheless Committed Costs; and (iv) the 50:50 profit and cost share set forth in Section 5.2.2 (Commercialization Responsibilities and Expenses) with respect to Net Sales of Joint Products in the U.S. shall cease and, instead, BII shall pay Epizyme a royalty based on future Net Sales of such Joint Product in the U.S. as follows (the “**Opt-Out Royalties**”):

<u>Timing of Opt-Out Notice</u>	<u>Royalty Rate</u>
If the Opt-Out Notice is given [**] with respect to such Joint Product	BII Controlled Project royalty rates (as set forth in <u>Section 7.4.1</u>) shall apply.
If the Opt-Out Notice is [**] with respect to such Joint Product	BII Controlled Project royalty rates (as set forth in <u>Section 7.4.1</u>) shall apply, plus [**] percent ([**]%)
If the Opt-Out Notice is [**], with respect to such Joint Product	BII Controlled Project royalty rates (as set forth in <u>Section 7.4.1</u>) shall apply, plus [**] percent ([**]%)
If the Opt-Out Notice is [**]	BII Controlled Project royalty rates (as set forth in <u>Section 7.4.1</u>) shall apply, plus [**] percent ([**]%)

For the avoidance of doubt, BII's payment of Opt-Out Royalties shall be governed by Sections 7.4.2 (Royalty Term), 7.4.3 (Reductions), 7.5 (Royalty Payments and Reports), 7.6 (Mode of Payment; Offsets), 7.7 (Taxes; Withhold Taxes), 7.8 (Interest on Late Payments), 7.9 (Financial and Other Records), 7.10 (Audit; Audit Dispute) and 7.11 (Confidentiality).

5.3. Manufacturing; Technology Transfer.

5.3.1 Supply Plans. The JSC shall establish the pre-clinical, clinical and commercial supply strategy for Joint Compounds, Joint Products and Diagnostic Products for Joint Compounds or Joint Products in the United States, including Manufacturing plans with respect thereto. BII or its Affiliates, or its or their Contractors or Sublicensees, shall Manufacture (a) all pre-clinical and clinical requirements of Joint Compounds, Joint Products (including placebo or other comparators) and Diagnostic Products for Joint Compounds or Joint Products, with respect to each, for use by the Parties in connection with Development activities as contemplated in the Joint Development Plan and Budget and (b) all commercial requirements of Joint Compounds, Joint Products and Diagnostic Products for Joint Compounds or Joint Products, with respect to each, for use by the Parties in connection with Commercialization activities as contemplated in the Joint Commercialization Plan and Budget, with respect to (a)-(b), in accordance with the JSC-approved supply strategy and Manufacturing plans. If, pursuant to the Joint Development Plan and Budget, the JSC appoints Epizyme to Conduct a Clinical Trial for a Joint Product, then BII and Epizyme shall promptly enter into a (i) supply agreement for the supply and Manufacture of the Joint Compounds, Joint Products or Diagnostic Products for Joint Compounds or Joint Products that are the subject of such Clinical Trial and (ii) a quality agreement related to such Manufacture and supply, which will set forth the applicable quality, release and approval procedures.

5.3.2 Manufacture. All Compounds and Products (and any applicable placebos or other comparators) Manufactured and delivered by BII or its Affiliates, or its or their Contractors or Sublicensees, pursuant to Section 5.3.1 (Supply Plans) shall be Manufactured, transported, stored and handled in accordance with GMP and all other Applicable Laws.

5.4. Recalls. BII or its Affiliates shall use reasonable efforts to notify Epizyme promptly following its determination that any event, incident, or circumstance has occurred that may result in the need for a recall, market suspension, or market withdrawal of a Joint Product in the Territory and shall include in such notice the reasoning behind such determination, and any supporting facts. BII (or its Affiliates or Sublicensee) shall have the right to make the final determination whether to voluntarily implement any such recall, market suspension or market withdrawal in the Territory. If a recall, market suspension, or market withdrawal is mandated by a Regulatory Authority in the Territory, then BII (or its Affiliates or its Sublicensee) shall initiate such a recall, market suspension, or market withdrawal in compliance with Applicable Law. For all recalls, market suspensions or market withdrawals undertaken pursuant to this Section 5.4 (Recalls), BII (or its Affiliates or Sublicensee) responsible for the recall, market suspension, or market withdrawal shall be solely responsible for the execution thereof and Epizyme shall reasonably cooperate in all such recall efforts. Subject to ARTICLE 12 (Indemnity), (a) in the event that a recall, market suspension or market withdrawal resulted from a Party's or its Affiliate's breach of its obligations hereunder, or from such Party's or its Affiliate's negligence

or willful misconduct, such Party shall bear the expense of such recall, market suspension or market withdrawal, (b) with respect to any other recall, market suspension or market withdrawal of the Joint Product in the U.S., the expenses incurred by the Parties as a result of such recall, market suspension or market withdrawal shall be included in Allowable Expenses hereunder and resolved pursuant to Section 5.2.2(a)(iv) (Allocation) and (c) with respect to any recall, market suspension or market withdrawal not covered by clause (a) or (b), BII shall be responsible for all costs of such recall, market suspension or market withdrawal.

ARTICLE 6 GRANT OF RIGHTS

6.1. Grant to Epizyme. Subject in the first instance to Section 6.2 (Grant to BII), and subject to Section 6.4 (Sublicenses), BII (on behalf of itself and its Affiliates) hereby grants back to Epizyme and solely to those Epizyme Affiliates whereby, consistent with the definitional guidance provided under Section 1.2 (Definition of “Affiliate”), Epizyme controls such Person that is an Affiliate of Epizyme, but no licenses are granted to any Epizyme Affiliates whereby the Person that is an Affiliate of Epizyme either controls Epizyme or is under common control with Epizyme:

6.1.1 a non-exclusive, royalty-free and non-transferable (except in accordance with Section 14.4 (Assignment)) license under the Collaboration Technology to (a) conduct the Research Activities assigned to it under the Research Plan and (b) Develop, Manufacture, Commercialize and otherwise Exploit the Joint Compound and Joint Product in accordance with the Joint Development Plan and Budget and Joint Commercialization Plan and Budget in the United States; and

6.1.2 a limited, non-exclusive, royalty-free, non-transferable (except pursuant to Section 14.4 (Assignment)), research license to use BII Research Compounds solely in Counter Screens for the sole purpose to identify inhibitors of other helicase targets and histone acetyl transferase targets other than a [**] target or [**] target.

6.2. Grant to BII. In the first instance and prior to any of the license grants in Section 6.1 (Grant to Epizyme), and subject to Section 6.4 (Sublicenses), Epizyme (on behalf of itself and its Affiliates) hereby grants to BII and its Affiliates:

6.2.1 an exclusive, royalty-free and non-transferable (except in accordance with Section 14.4 (Assignment)) license under the Epizyme Technology and Epizyme’s interest in Joint Technology for the purpose of conducting the Research Activities assigned to it under the Research Plan and with respect to Compounds and Products in the Field and in the Territory; and

6.2.2 an exclusive (even with respect to Epizyme and its Affiliates), royalty-bearing and non-transferable (except in accordance with Section 14.4 (Assignment)) license under the Epizyme Technology and Epizyme’s interest in Joint Technology to Develop, Manufacture, Commercialize and otherwise Exploit in the Field and in the Territory Compounds and Products, including (i) the BII Compound and BII Product and (ii) the Joint Compound and Joint Product.

6.3. Negative Covenant. With respect to the licenses granted to Epizyme under Section 6.1.1(b), BII hereby covenants that it shall not grant any similar licenses to Third Parties other than to those who are considered Contractors pursuant to Section 6.5 (Contractors) of this Agreement.

6.4. Sublicenses. Either Party may sublicense the rights granted to it in Section 6.1 (Grant to Epizyme) or Section 6.2 (Grant to BII) as follows:

6.4.1 (a) with respect to the rights granted to Epizyme in Section 6.1.1 or Section 6.1.2 and (b) with respect to the rights granted to BII in Section 6.2.1, to Third Parties engaged by a Party pursuant to Section 6.5 (Subcontracting);

6.4.2 with respect to the rights granted BII in Section 6.2.2, through multiple tiers, to Third Parties (each, a “Sublicensee”);

6.4.3 any sublicense granted by a Party to a Contractor or Sublicensee pursuant to this Section 6.4 (Sublicenses) shall be granted pursuant to a written agreement that is consistent with the terms and conditions of this Agreement, a copy of which shall be provided to the non-granting Party within [**] of execution. The Party granting the sublicense shall remain liable for any breach by a Contractor or Sublicensee that would constitute a breach of this Agreement.

6.5. Subcontracting. BII shall have the right to subcontract any of its activities to a Contractor; provided that BII will remain responsible and liable for the actions of its Contractors, including with respect to the achievement of Milestone Events and breaches of this Agreement. Epizyme shall have the right to subcontract any of its activities: (i) under the Research Plan to a Contractor without BII’s consent, unless such activities relate to (A) Compound synthesis directed toward in vivo safety studies, (B) the performance of in vivo safety studies (including histology analysis and CV assessment) or (C) assay development using human tissue, each of which ((A)-(C)) require BII’s prior written consent (not to be unreasonably withheld or delayed) or (ii) under the Joint Development Plan and Budget or Joint Commercialization Plan and Budget, provided Epizyme first obtains BII’s prior written consent (not to be unreasonably withheld or delayed), unless such subcontracting and Contractor are specifically contemplated under the Joint Development Plan and Budget or Joint Commercialization Plan and Budget. Epizyme will remain responsible and liable for the actions of its Contractors, including with respect to breaches of this Agreement.

6.6. Retention of Rights. Except as expressly provided herein, Epizyme grants no additional rights or licenses to BII or its Affiliates in, to or under any intellectual property rights Controlled by Epizyme. Except as expressly provided herein, BII grants no additional rights or licenses to Epizyme or its Affiliates in, to or under any intellectual property rights Controlled by BII.

6.7. Recordation. Following the Effective Date or at any time during the Term, either Party at the request and expense of the other Party, shall promptly register or record the licenses (including by registering a short-form license) granted to such other Party under this Agreement with the appropriate patent offices in all applicable countries of the Territory;

provided that such registration or recordation specifies the applicable limitations of such license; and provided further that such registration shall have no effect on the allocation of Prosecution and Maintenance rights and obligations set forth in ARTICLE 8 (Intellectual Property). In the event any of the licenses granted by a Party to the other Party under this Agreement are terminated, such other Party shall promptly take such actions and execute such documents as are reasonably requested by the granting Party, to cancel such registration(s) or recordation(s) in the applicable countries with respect to the terminated license grants, at the expense of the Party that had requested such registration(s) or recordation(s).

ARTICLE 7 PAYMENTS AND RECORDS

7.1. Upfront Payment. No later than [**] following the Effective Date (provided BII has received both an originally signed version of this Agreement and an Invoice from Epizyme), BII will pay Epizyme an upfront amount equal to Fifteen Million Dollars (\$15,000,000). Such payment will be non-creditable against any other payments due hereunder.

7.2. Research Funding.

7.2.1 Calendar Year 2019. As partial consideration (“**Research Funding**”) for the costs to be incurred by Epizyme in connection with its Research Activities pursuant to the Research Plan or any Remedial Plan for Calendar Year 2019 (with the Parties acknowledgment that a portion of the amounts payable for achieving preclinical research Milestone Events include partial consideration for the costs to be incurred by Epizyme in connection with its Research Activities pursuant to the Research Plan), BII will pay Epizyme Five Million Dollars (\$5,000,000), divided into [**] payments of [**] Dollars (\$[**]), and payable by BII in [**] installments due within [**] for Calendar Year 2019, as long as BII has received an Invoice from Epizyme with respect to the payment of such amounts.

7.2.2 Calendar Year 2020. In the event BII elects to extend the Research Period pursuant to Section 3.2.2 (Extension), any additional Research Funding from BII to Epizyme as consideration for the costs to be incurred by Epizyme in connection with: (i) performing Research Activities not completed by Epizyme under the prior Research Plan that BII desires for Epizyme to continue during Calendar Year 2020; and (ii) any additional Research Activities not already covered under the existing Research Plan (if any) undertaken pursuant to any revisions made to the Research Plan for Calendar Year 2020, with respect to (i)-(ii), and the timing of such payments, shall be agreed to by the Parties pursuant to Section 3.2.2 (Extension; *provided that*, with respect to (i)-(ii), BII shall be allowed to credit against any such additional Research Funding an amount equal to the total budget of [**] Dollars (\$[**]) that Epizyme has allocated for its performance of Research Activities under the Research Plan in Calendar Year 2019, minus the expenses Epizyme actually incurred in connection with the performance of such activities, and BII shall make such payments in accordance with such payment schedule.

subsequent Milestone Event before achieving a prior Milestone Event (“subsequent” being read to mean a Milestone Event (other than any of the described [**] Milestone Events) that appears lower in the above table when compared to another Milestone Event), then the Milestone Payments for both the subsequent Milestone Event and for any previously unpaid and unachieved Milestone Events for such Compound or Product shall be due and payable to Epizyme upon achievement of the subsequent Milestone Event. For example, (i) if a Product were to achieve the Milestone Event associated with [**] and subsequently achieve [**] without achieving [**], then, upon [**], both the Milestone Payment associated with [**] and the Milestone Payment associated with [**] would become due and payable to Epizyme with respect to such Product, (ii) if a Product were to achieve the Milestone Event associated with [**] prior to achieving [**], then, upon [**], both the Milestone Payment associated with [**] and the Milestone Payment associated with [**] would become due and payable to Epizyme with respect to such Product and (iii) for clarity, if a Product were to achieve a Milestone Event associated with [**] Milestone Events not yet achieved with respect to such Product shall not become due and payable to Epizyme until such [**] Milestone Event is achieved by such Product.

7.4. Royalties.

7.4.1 Royalty Rates. Commencing upon the First Commercial Sale of a Product in a country in the Territory, on a Product-by-Product basis, BII will pay to Epizyme tiered royalties on Net Sales of each Product in the Territory or ROW as applicable during each Calendar Year at the following rates:

<u>Calendar Year Net Sales of a Product in a Country in the Territory or ROW as Applicable</u>	<u>Royalty Rate</u>
<u>BII Controlled Project (i.e., Achieved by BII Product)</u>	
For that portion of aggregate Net Sales of a Product in the Territory during a Calendar Year that are less than \$[**]	[**]%
For that portion of aggregate Net Sales of a Product in the Territory during a Calendar Year that are more than or equal to \$[**] and less than or equal to \$[**]	[**]%
For that portion of aggregate Net Sales of a Product in the Territory during a Calendar Year that are greater than \$[**] and less than or equal to \$[**]	[**]%
For that portion of aggregate Net Sales of a Product in the Territory during a Calendar Year that are greater than \$[**]	[**]%
<u>Jointly Controlled Project (i.e., Achieved by Joint Product)</u>	
For that portion of aggregate Net Sales of a Product in the ROW during a Calendar Year that are less than \$[**]	[**]%
For that portion of aggregate Net Sales of a Product in the ROW during a Calendar Year that are more than or equal to \$[**] and less than or equal to \$[**]	[**]%
For that portion of aggregate Net Sales of a Product in the ROW during a Calendar Year that are greater than \$[**] and less than or equal to \$[**]	[**]%
For that portion of aggregate Net Sales of a Product the ROW during a Calendar Year that are greater than \$[**]	[**]%

7.4.2 Royalty Term. With respect to each Product in each country in the Territory, from and after the expiration of the Royalty Term for such Product in such country, Net Sales of such Product in such country will be excluded for purposes of calculating the Net Sales thresholds and ceilings set forth in Section 7.4.1 (Royalty Rates), and BII will have no obligation to pay any royalty on Net Sales of any Product in any country in the Territory after the Royalty Term for such Product in such country has expired. Upon expiration of the Royalty Term for a Product in a country, the license granted to BII pursuant to Section 6.2 (Grant to BII) will be fully paid-up, royalty-free, perpetual and irrevocable with respect to such Product in such country.

7.4.3 Reductions. Notwithstanding the foregoing:

(a) in the event that, and in such case from and after the date on which, a Product is sold in a country and is not covered by a Valid Claim of a Patent in such country claiming the composition of matter of the underlying Compound for such Product, the royalty rate set forth in Section 7.4.1 (Royalty Rates) with respect to such country will be reduced by [**] percent ([**]%);

(b) in the event that BII enters into an agreement with a Third Party in order to obtain a license under a Patent or other intellectual property right controlled by such Third Party that is necessary to make, have made, use, offer to sell, sell, import or export a BII Product in any country in the Territory or a Joint Product in any country in ROW, BII will be entitled to deduct [**] percent ([**]%) of all Third Party Payments paid to such Third Party in respect of such agreement from any payments due to Epizyme hereunder with respect to such Product;

(c) in the event that in any country in the Territory during the Royalty Term for a Product there is Generic Competition in such country, then, for each such country, the royalties payable to Epizyme for the Net Sales of such Product in such country will be reduced by [**] percent ([**]%) of the applicable royalty rate(s) set forth in Section 7.4.1 (Royalty Rates); and

(d) notwithstanding the foregoing clauses (a)-(c), in no event will the royalties due to Epizyme for any given Calendar Year in any country in the Territory for any Product during the applicable Royalty Term be reduced by more than [**] percent ([**]%), in the aggregate, of the amount otherwise due and payable to Epizyme in such Calendar Year in such country for such Product pursuant to the reductions set forth in this Section 7.4.3 (Reductions). BII shall have the right to carry forward and offset against future royalties payable to Epizyme with respect to the applicable Product, any amounts that, but for this Section 7.4.3(d), BII would have been entitled to deduct from any royalty payments to Epizyme.

7.5. Royalty Payments and Reports. Royalties will be payable within [**] after the end of the Calendar Quarter during which the applicable Net Sales of Product occurred. In connection with the payment of royalties to Epizyme, BII shall also provide Epizyme with a written report with respect to the Net Sales of Product sold by or on behalf of BII, its Affiliates and Sublicensees during such Calendar Quarter in each country of the Territory or ROW, as applicable, in sufficient detail to permit confirmation of the accuracy of the royalty payments

made to Epizyme. Each payment of royalties due to Epizyme will be accompanied by (a) a statement of the amount of Net Sales of each Product during such Calendar Quarter, (b) an itemized calculation of Net Sales for the Territory as a whole and on a country-by-country basis, showing for both the deductions provided for in the definition of "Net Sales" and (c) a calculation of the royalty payment due on such Net Sales for such Calendar Quarter.

7.6. Mode of Payment; Offsets. All payments to either Party under this Agreement will be made by deposit of Dollars in the requisite amount to such bank account as the receiving Party may from time to time designate by notice to the paying Party. In converting any amount expressed in a foreign currency into Dollars, BII shall use the monthly average exchange rates used by BII throughout its regular accounting system for the Calendar Quarter in which Product is sold.

7.7. Taxes; Withholding Taxes. All payments under or in connection with this Agreement shall be inclusive of any Taxes and each Party shall be responsible for and shall bear, pay or set-off its own Taxes assessed by a tax or other authority except as otherwise set forth in this Agreement (as used in this sentence, "Taxes" shall mean all forms of preliminary or finally imposed taxation, domestic and foreign taxes, fees, levies, duties and other assessments or charges of whatever kind (including but not limited to sales, use, excise, stamp, transfer, property, value added, goods and services, withholding and franchise taxes) together with any interest, penalties or additions payable in connection with such taxes, fees, levies duties and other assessments or charges). For purposes of value added tax ("VAT"), or similar indirect taxes (e.g. goods and service tax), VAT/indirect taxes shall be added to the payments due to the terms if legally applicable. The VAT amounts of invoices received by one Party are not billable to the other Party as far as the first Party has an input VAT deduction, i.e. is able to receive a refund by the competent authority. If VAT is not refundable because of legal restrictions, which are not caused by the first Party, the VAT amounts are billable to the other Party. Prior to the invoicing of the aforementioned billable amounts written approval by the other Party is mandatory. Legal restrictions which are caused by the first Party and lead to a non-billable amount shall be the following but not limited to (a) missing of a limitation period or (b) inaccurate documents in order to receive the input VAT deduction. If Applicable Laws require withholding by BII or its Affiliates of any taxes imposed upon Epizyme on account of any royalties and other payments paid under this Agreement to the benefit of Epizyme, such taxes have to be retained by BII or its Affiliates as required by local law from such remittable royalty and other payment and shall be paid by BII or its Affiliates to the proper tax authorities on account of Epizyme. Official receipts of payment of any retained local withholding tax shall be secured and sent by BII or its Affiliates to Epizyme as evidence of such payment only on Epizyme's request. The Parties shall cooperate and exercise their best efforts to ensure that any withholding taxes imposed on Epizyme are reduced as far as possible under the provisions of any relevant double tax treaty. Withholding taxes retained by BII or its Affiliates and paid to the proper German/local tax authorities as well as a possible refund of retained and paid local withholding taxes from the German/local tax authorities in favor of Epizyme are paid in local/German currency (Local currency/EUR). Any effect by currency conversion is to the benefit or burden of Epizyme as tax-payer and are not refundable or taken by BII and/or its Affiliates.

7.8. Interest on Late Payments. Any undisputed amounts owed by a Party under this Agreement that is not paid on or before the date such payment is due shall bear interest, to the extent permitted by Applicable Law, at an annual rate of [**] percent ([**]%) above the one (1) month EUR LIBOR rate that applied on the first date on which payment was delinquent and calculated for the exact number of days in the interest period based on a year of three hundred sixty (360) days (actual/360). If the LIBOR is no longer published, the Parties will agree upon another internationally recognized rate which has historically been substantially equivalent to the one (1) month EUR LIBOR rate and utilize such rate retroactively to such time as the rate was no longer available. Interest shall not accrue on undisputed amounts that were paid after the due date as a result of mistaken actions by the receiving Party (e.g., if a payment is late as a result of the receiving Party providing an incorrect account for receipt of payment).

7.9. Financial and Other Records. Each Party shall, and shall cause its Affiliates to, keep complete and accurate books and records pertaining to Net Sales of Products and Net Profits and Net Losses with respect to Joint Products in sufficient detail to calculate all amounts payable hereunder and to verify compliance with its obligations under this Agreement. Such books and records shall be retained by such Party and its Affiliates until [**] after the end of the period to which such books and records pertain or for such longer period as may be required by Applicable Law.

7.10. Audit; Audit Dispute. At the request of the other Party, each Party will, and will cause its Affiliates to, permit an independent public accounting firm of nationally recognized standing designated by the other Party and reasonably acceptable to the audited Party, at reasonable times during normal business hours and upon reasonable notice, to audit the books and records maintained pursuant to Section 7.9 (Financial and Other Records) solely to confirm the accuracy of all Net Sales, royalty payments, Milestone Payments and financial reports and payments made hereunder. Such examinations may not (a) be conducted for any Calendar Quarter more than [**] after the end of such Calendar Quarter, (b) be conducted more than [**] period (unless a previous audit during such [**] period revealed an underpayment of at least [**] percent ([**]%) of the amount actually due with respect to such period) or (c) be repeated for any Calendar Quarter. The accounting firm will execute a reasonable written confidentiality agreement with the audited Party and will disclose to the auditing Party only such Information as is reasonably necessary to provide the auditing Party with information regarding any actual or potential discrepancies between amounts reported and actually paid and amounts payable under this Agreement. The accounting firm's report will include the methodology and calculations used to determine the results, will be delivered to each Party at the same time and, unless such report is disputed by a Party as set forth below, will be deemed final [**] after it is received by both Parties. Each Party will have the right during such [**] period to discuss the report with the accounting firm. In the event a Party disputes any portion of the accounting firm's report following such [**] period, then, no later than [**] following the end of such [**] period, such Party may refer such dispute for resolution in accordance with Section 14.7 (Dispute Resolution). The auditing Party shall bear the full cost of any such audit, unless the accounting firm's report discloses an underpayment by the audited Party of more than [**] percent ([**]%) of the amount due for any Calendar Quarter, in which case the audited Party shall bear the full cost of such audit. The audited Party shall pay the amount of any undisputed underpayment disclosed in the accounting firm's report, together with interest thereon from the date such payment was originally due, within [**] after delivery to the Parties of the accounting firm's

report. If the accounting firm's report discloses an undisputed overpayment by the audited Party, the auditing Party will reimburse the audited Party for such excess amount within [**] after delivery to the Parties of the accounting firm's report (or credit such overpayment against any royalties subsequently owed to Epizyme in the event the audited Party is BII, unless, for clarity, there are insufficient subsequent royalties due to Epizyme, in which case, upon the expiration of BII's obligations to pay royalties hereunder, Epizyme will reimburse BII for the amount of such overpayment not previously credited). Upon the expiration of [**] following the end of any Calendar Quarter, the calculation of royalty payments with respect to such Calendar Quarter shall be binding on the Parties and each Party shall be released from any liability and obligation with respect to payments for such year, except in the case of fraud or willful deceit.

7.11. Confidentiality. The receiving Party will treat all Information subject to review under this ARTICLE 7 (Payments and Records) in accordance with the confidentiality provisions of ARTICLE 10 (Confidentiality and Non-Disclosure).

ARTICLE 8 INTELLECTUAL PROPERTY

8.1. Ownership of Intellectual Property.

8.1.1 Ownership of Technology. Subject to Section 8.1.2 (Ownership of Joint Technology), as between the Parties, each Party shall own and retain all right, title and interest in and to any and all: (a) Information and inventions that are conceived, discovered, developed or otherwise made by or on behalf of such Party (or its Affiliates or Sublicensees) under or in connection with this Agreement, whether or not patented or patentable, and any and all Patents and other intellectual property rights with respect thereto, except to the extent that any such Information or invention or any Patent or intellectual property rights with respect thereto, is Joint Know-How or Joint Patents; *provided that* any Information or inventions conceived, discovered, developed or otherwise made by or on behalf of such Party (or its Affiliates or Sublicensees) while exercising its rights under Section 8.2.2 (Epizyme Patents) or Section 8.2.3 (BII Patents) to review and comment on any material communications to and from any Patent authority or drafts of any material filings or responses to be made to Patent authorities in connection with the preparation, filing, prosecution or maintenance of a specific Patent shall inure to the benefit of and be owned by the Party who owns such Patent and (b) other Information, inventions, Patents and other intellectual property rights that are owned or otherwise Controlled (other than pursuant to the licenses granted under Sections 6.1 (Grant to Epizyme) and 6.2 (Grant to BII)) by such Party, its Affiliates or its Sublicensees.

8.1.2 Ownership of Joint Technology. As between the Parties, the Parties shall each own an equal, undivided interest in any and all (a) Information and inventions that are conceived, discovered, developed or otherwise made jointly by or on behalf of Epizyme or its Affiliates or Sublicensees, on the one hand, and BII or its Affiliates and Sublicensees, on the other hand, in connection with the work conducted under or in connection with this Agreement, in each case, whether or not patented or patentable (the “**Joint Know-How**”) and (b) Patents (the “**Joint Patents**”) and other intellectual property rights with respect to the Information and inventions described in clause (a) (together with Joint Know-How and Joint Patents, the “**Joint Technology**”). Each Party shall promptly disclose to the other Party in writing, and shall cause its Affiliates and Sublicensees to so disclose, the development, making, conception or reduction to practice of any Joint Technology. Subject to the licenses granted under Section 6.1 (Grant to Epizyme) and Section 6.2 (Grant to BII), the exclusivity obligations under Section 4.4 (Exclusivity) and any other conditions, requirements or limitations under this Agreement, each Party shall have the right to Exploit the Joint Technology without a duty of seeking consent or accounting to the other Party.

8.1.3 United States Law. The determination of whether Information and inventions are conceived, discovered, developed, or otherwise made by a Party for the purpose of allocating proprietary rights (including Patent, copyright or other intellectual property rights) therein, shall, for purposes of this Agreement, be made in accordance with Applicable Law in the United States irrespective of where such conception, discovery, development or making occurs.

8.1.4 Assignment Obligation. Each Party shall cause all Persons who perform Research Activities or who conduct Development, Manufacturing and Commercialization activities for such Party under this Agreement with respect to Compounds or Products to be under an obligation to assign their rights in any Information and inventions resulting therefrom to such Party, except where Applicable Law requires otherwise.

8.1.5 Ownership of Product Marks. BII shall own all Trademarks, together with all goodwill related thereto, used on or in connection with Products in the Territory (collectively, “**Product Marks**”), and shall, at its sole cost and acting in its sole discretion, be responsible for the procurement, maintenance, enforcement and defense of all Product Marks in the Territory. BII shall have the right to obtain from the World Health Organization International Nonproprietary Name Committee and the US Adopted Names Council a generic name for the Products.

8.1.6 German Statute. With respect to “Employee Inventions” as defined by and subject to the German Employee Inventions Act (Gesetz über Arbeitnehmererfindungen “**ArbnErfG**”) that are conceived, discovered, developed, or otherwise made by employees of a Party (or its Affiliates) under or in connection with this Agreement, such Party shall claim rights in and to such Employee Inventions in accordance with Section 6 et seq. of the ArbnErfG, unless and to the extent the JSC has resolved that it would not be commercially reasonable to do so. The Party subject to the ArbnErfG shall be solely responsible for any payments to its employees and such Party will take all actions necessary to obtain the rights to use any such inventions for the other Party. This section shall also apply to “Technical Improvements” as defined in Section 3 of the ArbnErfG.

8.2. Maintenance and Prosecution of Patents.

8.2.1 Patent Liaisons. Promptly (but in no event more than [**]) following the Effective Date, the Parties shall each designate a representative to consult with the other Party's representative with respect to preparing, filing, prosecuting, maintaining, enforcing and defending the Epizyme Patents, BII Patents and Joint Patents (such representatives, the "**Patent Liaisons**"). The Patent Liaisons shall discuss and provide input to each other, at such times, places and frequencies as mutually agreed, all material issues with respect to preparing, filing, prosecuting, maintaining, enforcing and defending the Epizyme Patents, BII Patents and Joint Patents; *provided that* all final decisions related to preparing, filing, prosecuting, maintaining, enforcing and defending any Epizyme Patents, BII Patents or Joint Patents shall be made by the Party with the right to control such preparation, file, prosecution, maintenance, enforcement or defense, as applicable, as set forth in this ARTICLE 8 (Intellectual Property).

8.2.2 Epizyme Patents. Epizyme shall be responsible for the Prosecution and Maintenance of the Epizyme Patents (other than Epizyme Product Patents, which are subject to Section 8.2.4 (Joint Patents and Epizyme Product Patents)) and Epizyme Carve-Out Patents, which are subject to Section 8.2.5 (Epizyme Carve-Out Patents), at its sole expense. Epizyme will reasonably inform BII (or its designee) regarding the filing, prosecution, defense and maintenance of the Epizyme Patents (including in any case, an update at least [**]), and Epizyme shall give BII (or its designee) an opportunity to review the text of each application, office action response or other substantive document for such Epizyme Patent before filing with any patent office in the Territory, and shall reasonably consider BII's (or its designee's) reasonable comments with respect thereto, and shall supply BII (or its designee) with a copy of each such application, office action response or other substantive document as filed, together with notice of its filing date and serial number. Epizyme shall notify BII (or its designee) at least [**] in advance of the next deadline if (i) Epizyme decides that it does not wish to continue paying for the Prosecution and Maintenance of an Epizyme Patent in any country and for which no substitute has been filed or (ii) Epizyme decides to irrevocably abandon a claim scope in an Epizyme Patent and BII determines that such claim scope proposed to be abandoned can be separately filed in a divisional or other filing separate from such Epizyme Patent without having a detrimental effect on the patentability of such claim scope, Epizyme shall allow BII (or its designee) to assume sole responsibility and control for Prosecution and Maintenance of such Epizyme Patent or divisional or other filing, as applicable, including payments incurred, after [**] after receipt of Epizyme's notice. If BII determines that the proposed abandoned claim scope cannot be separately filed without having a detrimental effect on the patentability of such claim scope, then Epizyme shall maintain and continue to prosecute such claim scope in the Epizyme Patent and the Parties will thereafter equally share all fees and costs related to Prosecution and Maintenance of such Epizyme Patent. If BII (or its designee) assumes such responsibility and control, then BII (or its designee) may designate any counsel of its choice to handle the Prosecution and Maintenance of such Epizyme Patent or of such divisional or other filings, as applicable, and (A) it shall no longer be considered an Epizyme Patent, (B) such Patent or such divisional or other filing, as applicable, shall cease to be considered an Epizyme Patent and (C) Epizyme hereby assigns and transfers all its right, title and interest in such Patent or such divisional or other filing, as applicable, to BII as the sole owner and shall execute any documents necessary to reflect such ownership. For clarity, BII's step-in rights to Prosecute and Maintain an Epizyme Patent or such divisional or other filing under this Section 8.2.2 shall only apply to the Epizyme Patents that are not also Epizyme Product Patents (which step-in rights are governed by Section 8.2.4(e)).

8.2.3 BII Patents. For clarity, BII shall always be responsible for the Prosecution and Maintenance of any BII Patents, at its sole expense and in its sole discretion; *provided that*, with respect to any BII Patents that Cover a Compound or Product or method of use of a Compound or Product (the “**BII Product Patents**”), BII shall give Epizyme (or its designee) an opportunity to review the text of each application, office action response or other substantive document for such BII Product Patent before filing with any patent office in the Territory, and shall reasonably consider Epizyme’s (or its designee’s) reasonable comments with respect thereto, and shall supply Epizyme (or its designee) with a copy of each such application, office action response or other substantive document as filed, together with notice of its filing date and serial number. BII shall notify Epizyme (or its designee) at least [**] in advance of the next deadline if (i) BII decides that it does not wish to continue paying for the Prosecution and Maintenance of such BII Product Patent in any country and for which no substitute has been filed or (ii) BII decides to irrevocably abandon a claim scope in a BII Product Patent and Epizyme determines that such claim scope proposed to be abandoned can be separately filed in a divisional or other filing separate from such BII Product Patent without having a detrimental effect on the patentability of such claim scope, BII shall allow Epizyme (or its designee) to assume sole responsibility and control for Prosecution and Maintenance of such BII Product Patent or divisional or other filing, as applicable, including payments incurred, after [**] after receipt of BII’s notice. If Epizyme determines that the proposed abandoned claim scope cannot be separately filed without having a detrimental effect on the patentability of such claim scope, then BII shall maintain and continue to prosecute such claim scope in the BII Patent and the Parties will thereafter equally share all fees and costs related to Prosecution and Maintenance of such BII Patent. If Epizyme (or its designee) assumes such responsibility and control, then Epizyme (or its designee) may designate any counsel of its choice to handle the Prosecution and Maintenance of such BII Product Patent or of such divisional or other filings, as applicable, and (A) it shall no longer be considered a BII Product Patent, (B) such Patent or such divisional or other filing, as applicable, shall cease to be considered a BII Product Patent and (C) BII hereby assigns and transfers all its right, title and interest in such Patent or such divisional or other filing, as applicable, to Epizyme as the sole owner and shall execute any documents necessary to reflect such ownership.

8.2.4 Joint Patents and Epizyme Product Patents. The Prosecution and Maintenance of the Epizyme Product Patents and Joint Patents (collectively, the “**Joint Counsel Patent Rights**”) shall be through mutually selected patent counsel. Within a reasonable period of time following the Effective Date, the Parties shall mutually agree on a patent counsel (“**Joint Counsel**”) who shall be engaged by both Parties for the Prosecution and Maintenance of all Joint Counsel Patent Rights. Subject to Section 8.5.2 (Invalidity or Unenforceability Defenses or Actions – Epizyme Product Patents and Joint Patents), the following terms shall apply to each Joint Counsel Patent Right:

(a) The Joint Counsel shall give BII and Epizyme (or each Party’s designee) an opportunity to review the text of each application, office action response or other substantive document for a Joint Counsel Patent Right before filing with any patent office in the Territory, shall incorporate BII’s and Epizyme’s (or each Party’s designee) reasonable comments with respect thereto and shall supply BII and Epizyme (or each Party’s designee) with a copy of each such application, office action response or other substantive document as filed, together with notice of its filing date and serial number; *provided that* Epizyme, through counsel

of its choosing, will have the right to draft each initial application for an Epizyme Product Patent or Joint Patent and will provide BII with such draft application for review, comment and proposed edits, and the Parties will discuss and agree on the final text of such application and, in the event of a disagreement among the Parties, the Joint Counsel will decide on the final text of the application with a clear prioritization, in all instances, to protecting the worldwide patentability of the Compounds covered by such application, even if such prioritization results in any detrimental effects to compounds (which are not Compounds) that may be covered under such application. Once the final text of any patent application under this Section 8.2.4(a) is available, such patent application will then be Prosecuted and Maintained in accordance with this Section 8.2.4 (Joint Patents and Epizyme Product Patents). In addition to the foregoing, BII and Epizyme (or each Party's designee) may also provide the Joint Counsel with proactive suggestions with respect to the Prosecution and Maintenance of the Joint Counsel Patent Rights at times when no filing is otherwise requested or contemplated, and the Joint Counsel shall reasonably consider any such suggestions. In the event that Epizyme and BII provide Joint Counsel with conflicting instructions regarding the Prosecution and Maintenance of a Joint Counsel Patent Right, Joint Counsel shall make the Parties aware of such conflicting instructions and, if the Parties are not able to resolve such conflict within a reasonable time prior to the applicable filing deadline, then the Joint Counsel shall take such action as would reasonably be expected to maximize the scope, extent and coverage of such Joint Counsel Patent Right with a clear prioritization, in all instances, to protecting the worldwide patentability of Compounds covered by such Joint Counsel Patent Right, even if such prioritization results in any detrimental effects to compounds (which are not Compounds) that may be covered under such Joint Counsel Patent Right. Notwithstanding the foregoing, BII shall have final decision-making authority with respect to the subject matter to be filed on (subject to Section 8.2.5(b)), the timing of filing and country scope for any Joint Counsel Patent Right; *provided that* BII shall not, and shall direct the Joint Counsel to not, without first obtaining Epizyme's prior written consent, allow the Epizyme Product Patent directed to [**] to lapse or expire without having filed at least a PCT application by the [**] of the filing date of the application for such Epizyme Product Patent. Notwithstanding the foregoing, in the event that: (i) no Compound included in the PCT application has received [**] and (ii) BII, in good faith, determines that publication of such PCT application may have a detrimental effect on the patentability of any Compound that may receive [**], then BII may direct the Joint Counsel to withdraw the aforementioned Epizyme Product Patent prior to its publication in order to prevent its publication. Joint Counsel shall be given the directive that, in the Prosecution and Maintenance of the Joint Counsel Patent Rights, Joint Counsel shall take all actions with a clear prioritization, in all instances, to protecting the worldwide patentability of the Compounds and Products covered by such Joint Counsel Patent Right, even if such prioritization results in any detrimental effects to compounds (which are not Compounds) that may be covered under such Joint Counsel Patent Right. Once any Joint Counsel Patent Right is granted, issued or indicated as allowable by any patent authority, under no circumstances shall any reissue, reexamination or other reopening of the prosecution be allowed for the purposes of protecting (1) a product that is not a Product, (2) a compound that is not a Compound or (3) the manufacture or use of any of the foregoing (1)-(2), absent BII's prior written consent, which may be withheld in BII's sole discretion.

(b) Both Parties shall reasonably cooperate with Joint Counsel in Prosecution and Maintenance of patent applications for Joint Counsel Patent Rights, including providing Joint Counsel with data and other Information as appropriate with respect thereto.

(c) Joint Counsel shall keep BII and Epizyme advised of the status of the Prosecution and Maintenance of Joint Counsel Patent Rights, including actual and prospective patent filings for Joint Counsel Patent Rights, and shall provide each Party with advance copies of any and all papers related thereto. Joint Counsel shall promptly give notice to BII and Epizyme of the grant, lapse, revocation, surrender, invalidation or abandonment of any Joint Counsel Patent Right.

(d) BII shall bear all fees and costs charged by Joint Counsel with respect to the Prosecution and Maintenance of Joint Counsel Patent Rights and all other mutually agreed and approved out-of-pocket costs and expenses incurred by either Party in connection with such Prosecution and Maintenance of Joint Counsel Patent Rights.

(e) BII shall notify Epizyme and Joint Counsel at least [**] in advance of the next deadline if (i) BII decides that it does not wish to continue paying for the Prosecution and Maintenance of any Joint Counsel Patent Right and for which no substitute has been filed or (ii) BII decides that it intends to irrevocably abandon claim scope in any Joint Counsel Patent Right, in which case, with respect to this clause (ii), Epizyme may assume responsibility for such claim scope. In such cases (i) or (ii), BII shall allow Epizyme to assume responsibility and control for Prosecution and Maintenance of the respective Patent, including payments incurred after [**] after receipt of BII's notice. If Epizyme assumes such responsibility and control, then: (1) Epizyme may designate any counsel of its choice to handle the Prosecution and Maintenance of such Joint Counsel Patent Right or of such claim scope, as applicable, and such Patent shall no longer be considered a Joint Counsel Patent Right but, rather, shall be considered an Epizyme Patent and (2) in case of a Joint Patent or claim scope therein, BII shall and hereby does assign and transfer all right, title and interest in such Joint Patent or such claim scope therein, as applicable, to Epizyme as the sole owner. If Epizyme decides not to assume such responsibility, then it shall instruct Joint Counsel to abandon the Prosecution and Maintenance of such Joint Counsel Patent Right or claim scope, as applicable.

(f) At least every [**] during the Term, the Parties through their respective Patent Liaison's will work together to generate appropriate lists clearly designating Epizyme Patents (and of those which are Epizyme Product Patents), BII Patents and any Joint Patents.

8.2.5 Epizyme Carve-Out Patents.

(a) With respect to any Epizyme Product Patent that is not yet the subject of a PCT application or U.S. non-provisional application and that has a specification that Epizyme believes, in good faith, sets forth one or more claims that Cover (i) a product that is not a Product, (ii) a compound that is not a Compound or (iii) the manufacture or use of any of the foregoing (i)-(ii) and, wherein (i)-(iii) are based upon a compound which has a core structure that is different and considered by the Parties to be patentably distinct from any Compound set forth in such Epizyme Product Patent, Epizyme may request, in writing to BII, that BII consider the feasibility of filing one or more separate patent applications for such claims. In the event that Epizyme makes such a request, the Parties shall work together to determine the feasibility of filing such separate patent applications. If the Parties: (1) agree on the feasibility of filing such separate patent applications, they shall direct Joint Counsel to prepare the text of such

applications, subject to the Parties review and input as described further below or (2) do not agree on the feasibility of filing such separate patent applications, then the Joint Counsel shall promptly consider Epizyme's request and, if the Joint Counsel determines, acting in good faith, that making one or more separate patent applications is feasible and will not have any detrimental effect on the Patents Covering Compounds or Products, then the Joint Counsel shall file, in Epizyme's name, one or more separate patent applications requested by Epizyme (such applications and issued Patents under either clause (1) or (2), the "**Epizyme Carve-Out Patents**"). The Joint Counsel shall give Epizyme (or its designee) and BII (or its designee) an opportunity to review the text of each such application prior to filing, shall incorporate Epizyme's and BII's (or each Party's designee) comments with respect thereto and shall supply BII and Epizyme (or each Party's designee) with a copy of each such application, together with notice of its filing date and serial number. Upon such filing, Epizyme shall assume responsibility for Prosecuting and Maintaining such Epizyme Carve-Out Patent pursuant to Section 8.2.5(c). With respect to any Epizyme Product Patent that is already the subject of a filed PCT application or U.S. non-provisional application, then an Epizyme Carve-Out Patent filing shall only be authorized upon BII's prior written consent and in BII's sole discretion.

(b) In the event that the Joint Counsel determines that making one or more separate patent applications as set forth in Section 8.2.5(a) is not feasible or may have a detrimental effect on the Compounds or Products such that no Epizyme Carve-Out Patent is filed, then, with respect to the claims of the Epizyme Product Patent Covering such products, compounds or manufacturing or use rights, the Joint Counsel shall nevertheless incorporate Epizyme's (or its designee) reasonable comments, statements or amendments with respect thereto in the text of each application, office action response or other substantive document for such Epizyme Product Patent, unless BII believes, acting in good faith, that such comments, statements or amendments, if incorporated, may have a detrimental effect on Patents Covering the Compounds or Products.

(c) With respect to the Epizyme Carve-Out Patents, once the Joint Counsel files a patent application for an Epizyme Carve-Out Patent pursuant to Section 8.2.5(a), Epizyme shall be responsible for the Prosecution and Maintenance of such Epizyme Carve-Out Patent, at its sole expense and in its sole discretion. For clarity, in no event will an Epizyme Carve-Out Patent be deemed to be an Epizyme Patent or a Joint Counsel Patent Right. Notwithstanding the foregoing, Epizyme shall not take any action or fail to take any action in connection with the Prosecution and Maintenance of any Epizyme Carve-Out Patent that may have, or actually results in, any detrimental effect upon the patentability, validity or enforceability of any Patent Right Covering Compounds or Products and Epizyme shall keep BII fully advised of any references, other evidence and any other actions taken in connection with the Prosecution and Maintenance of Epizyme Carve-Out Patents that may be relevant to the patentability, validity or enforceability of any Patent Right Covering Compounds or Products. Without limiting the foregoing, Epizyme shall not introduce any disclosure or claims in any Epizyme Carve-Out Patent covering Compounds.

(d) Epizyme shall ensure that all obligations of Epizyme under this Agreement with respect to the Epizyme Carve-Out Patents will be placed upon any Third Party who secures rights with respect to the Prosecution and Maintenance of the Epizyme Carve-Out Patents.

8.2.6 Patent Term Extensions. Notwithstanding anything to the contrary in this ARTICLE 8 (Intellectual Property), the Parties shall discuss in good faith and seek to reach mutual agreement for which, if any, of the Patents within the Epizyme Product Patents, BII Product Patents and Joint Product Patents they shall apply to obtain patent term extensions, adjustments, restorations or supplementary protection certificates under Applicable Laws, based on the best commercial interests of the Compounds or Products Covered by such Patents. If the Parties are unable to reach mutual agreement on which Patent to apply to obtain patent term extensions, adjustments, restorations or supplementary protection certificates, then BII shall have the right to make the final decision. If, with respect to a Product, the Patents for which the Parties (or BII, in the event the Parties are unable to mutually agree) determine to apply to obtain patent term extensions, adjustments, restorations or supplementary protection certificates do not claim the composition of matter of the Compound in such Product, then, notwithstanding the decision to extend a non-composition of matter Patent, in determining the Royalty Term for such Product, the period referred to in clause (a) of the definition of Royalty Term shall refer to expiration of the last Epizyme Patent, BII Patent or Joint Patent that includes a Valid Claim claiming the composition of matter of the Compound in such Product as if such Epizyme Patent, BII Patent or Joint Patent had been extended.

8.2.7 Patent Listings. BII, in consultation with the Patent Liaisons, shall have the sole right to make all filings with Regulatory Authorities throughout the Territory with respect to BII Patents, Joint Patents and Epizyme Product Patents, including as required or allowed in the United States, in the FDA's Orange Book or other international equivalents. Epizyme shall (i) provide to BII all Information necessary or reasonably useful to enable BII to make such filings with Regulatory Authorities in the Territory with respect to such Patents and (ii) cooperate with BII's reasonable requests in connection therewith, including meeting any submission deadlines, in each case ((i) and (ii)), to the extent required or permitted by Applicable Law.

8.3. Enforcement of Patents.

8.3.1 Enforcement of Epizyme Product Patents and Joint Patents. Each Party (or its Patent Liaison) shall promptly notify the other Party in writing of any alleged or threatened infringement of the Epizyme Product Patents or Joint Patents, with respect to each, by a Third Party in the Territory of which it becomes aware (including alleged or threatened infringement based on the development, commercialization or an application to market a product containing a Compound or any Product in the Territory (a "**Joint Product Infringement**")). BII, in consultation with the Patent Liaisons, shall have the first right, but not the obligation, to prosecute any Joint Product Infringement in the Territory (the "**Joint Product Prosecuted Infringements**") at its sole expense and BII shall retain control of the prosecution of such claim, suit or proceeding. In the event BII prosecutes any Joint Product Prosecuted Infringement, Epizyme shall join as a party if requested by BII, at BII's cost, and will otherwise have the right, but not the obligation to join as a party to such claim, suit or proceeding in the Territory and participate with its own counsel at its own expense; *provided that* BII shall retain control of the prosecution of such claim, suit or proceeding. If Epizyme agrees, after good faith discussion with BII, to bring other Epizyme Patents into such claim, suit or proceeding, the Epizyme Patent Liaison shall work with the BII Patent Liaison to identify such other Epizyme Patents and assist and cooperate with BII to assert such Epizyme Patents in such claim, suit or proceeding;

provided that BII shall retain control of the prosecution of such claim, suit or proceeding. During any such claim, suit or proceeding, BII shall not settle any such claim, suit or proceeding except in a manner that BII believes, in good faith, is in the best interests of the Compounds or Products. If BII does not take commercially reasonable steps to prosecute a Joint Product Prosecuted Infringement (i) within [**] following the first notice provided above with respect to the Joint Product Prosecuted Infringement or (ii) provided such date occurs after the first such notice of the Joint Product Prosecuted Infringement is provided, [**] before the time limit, if any, set forth in Applicable Law for filing of such actions, whichever comes first, then Epizyme, in consultation with the Patent Liaisons, may prosecute the Joint Product Prosecuted Infringement at its own expense; *provided, however, that* Epizyme must consider, in good faith, any reasons provided by BII for not prosecuting such Joint Product Infringement. Epizyme shall not, and agrees not to, prosecute any alleged, threatened or actual infringement of any Epizyme Product Patents or Joint Patents that is not a Joint Product Infringement absent prior written consent from BII, which may be withheld in BII's sole discretion. In the event BII provides such consent, Epizyme shall not prosecute such action or settle any such claim, suit or proceeding except in a manner that Epizyme believes, in good faith, is in the best interests of the Compounds or Products covered by such Patent.

8.3.2 Enforcement of Other Epizyme Patents. Each Party (or its Patent Liaison) shall promptly notify the other Party in writing of any alleged or threatened infringement of the Epizyme Patents (other than Epizyme Product Patents, which are handled pursuant to Section 8.3.1 (Enforcement of Epizyme Product Patents and Joint Patents)) or Epizyme Carve-Out Patents by a Third Party in the Territory of which such Party becomes aware. Epizyme shall have the sole right, but not the obligation, in consultation with the Patent Liaisons, to prosecute any such infringement in the Territory at its sole expense and Epizyme shall retain control of the prosecution of such claim, suit or proceeding; *provided that* Epizyme will not be required to consult with the Patent Liaisons in connection with prosecuting an infringement claim concerning the Epizyme Carve-Out Patents.

8.3.3 Enforcement of BII Product Patents. Each Party (or its Patent Liaison) shall promptly notify the other Party in writing of any alleged or threatened infringement of the BII Product Patents by a Third Party in the Territory of which it becomes aware (including alleged or threatened infringement based on the development, commercialization or an application to market a product containing a Compound or any Product in the Territory (a "**BII Product Infringement**")). BII, in consultation with the Patent Liaisons, shall have the first right, but not the obligation, to prosecute any BII Product Infringement in the Territory (the "**BII Product Prosecuted Infringements**") at its sole expense and BII shall retain control of the prosecution of such claim, suit or proceeding. In the event BII prosecutes any BII Product Prosecuted Infringement, Epizyme shall join as a party if requested by BII, at BII's cost, and will otherwise have the right, but not the obligation to join as a party to such claim, suit or proceeding in the Territory and participate with its own counsel at its own expense; *provided that* BII shall retain control of the prosecution of such claim, suit or proceeding. During any such claim, suit or proceeding, BII shall not settle any such claim, suit or proceeding except in a manner that BII believes, in good faith, is in the best interests of the Compounds or Products. If BII does not take commercially reasonable steps to prosecute a BII Product Prosecuted Infringement (i) within [**] following the first notice provided above with respect to the BII Product Prosecuted Infringement or (ii) provided such date occurs after the first such notice of

the BII Product Prosecuted Infringement is provided, [**] before the time limit, if any, set forth in Applicable Law for filing of such actions, whichever comes first, then Epizyme, in consultation with the Patent Liaisons, may prosecute the BII Product Prosecuted Infringement at its own expense; *provided, however, that* Epizyme must consider, in good faith, any reasons provided by BII for not prosecuting such BII Product Infringement. Epizyme shall not, and agrees not to, prosecute any alleged, threatened or actual infringement of any BII Product Patent that is not a BII Product Infringement absent prior written consent from BII, which may be withheld in BII's sole discretion. In the event BII provides such consent, Epizyme shall not prosecute such action or settle any such claim, suit or proceeding except in a manner that Epizyme believes, in good faith, is in the best interests of the Compounds or Products covered by such Patent.

8.3.4 Enforcement of Other BII Patents. Each Party (or its Patent Liaisons) shall promptly notify the other Party in writing of any alleged or threatened infringement of the BII Patents (other than the BII Product Patents, which is handled pursuant to Section 8.3.3 (Enforcement of BII Product Patents)) by a Third Party in the Territory of which such Party becomes aware. BII shall, in consultation with the Patent Liaisons, have the sole right, but not the obligation, to prosecute any such infringement in the Territory at its sole expense and BII shall retain control of the prosecution of such claim, suit or proceeding.

8.3.5 Generic Competition. Notwithstanding the foregoing, if either Party or its Patent Liaison (a) reasonably believes that a Third Party may be filing or preparing or seeking to file a generic or abridged Drug Approval Application that refers or relies on regulatory documentation submitted by either Party to any Regulatory Authority, (b) receives any notice of certification regarding the Epizyme Patents, BII Patents or the Joint Patents pursuant to the U.S. "Drug Price Competition and Patent Term Restoration Act" of 1984 (21 United States Code §355(b)(2)(A)(iv) or (j)(2)(A)(vii)(IV)) ("**ANDA Act**") claiming that any such Patents are invalid or unenforceable or claiming that any such Patents will not be infringed by the Manufacture, use, marketing or sale of a product for which an application under the ANDA Act is filed or (c) receives any equivalent or similar certification or notice in any other jurisdiction, it shall (i) notify the other Party (or its Patent Liaison) in writing identifying the alleged applicant or potential applicant and furnishing the information upon which determination is based and (ii) provide the other Party (or its Patent Liaison) with a copy of any such notice of certification within [**] of the date of receipt and the Parties' rights and obligations with respect to any legal action as a result of such certification shall be as set forth in Sections 8.3.1, 8.3.2, 8.3.3 or 8.3.5, as applicable; *provided that*, if the Party entitled to first enforce the Patents pursuant to the foregoing Sections elects not to bring suit against the Third Party providing notice of such certification within [**] of receipt of such notice, the other Party shall have the right, but shall not be obligated, to bring suit against such Third Party. Notwithstanding the foregoing, Epizyme shall not, and agrees not to, bring such suit against the Third Party if it is not in connection with a Generic Product (as defined in Section 1.84 (Definition of "Generic Product")) absent prior written consent from BII, which may be withheld in BII's sole discretion.

8.3.6 Cooperation. The Parties and their Patent Liaisons agree to cooperate fully in any infringement action pursuant to Section 8.3 (Enforcement of Patents). Where a Party brings such an action, the other Party will, where necessary, furnish a power of attorney solely for such purpose or will join in, or be named as a necessary party to, such action.

Unless otherwise set forth herein, the Party entitled to bring any Patent infringement litigation in accordance with Section 8.3 (Enforcement of Patents) will have the right to settle such claim; *provided that* neither Party will have the right to settle any Patent infringement litigation under Section 8.3 (Enforcement of Patents) in a manner that diminishes or has a material adverse effect on the rights or interest of the other Party, or in a manner that imposes any costs or liability on, or involves any admission by, the other Party, without the express written consent of such other Party. The Party commencing the litigation will provide the other Party's Patent Liaison with copies of all pleadings and other documents filed with the court and will consider reasonable input from the other Party's Patent Liaison during the course of the proceedings.

8.3.7 Recovery. Any recovery realized as a result of such litigation described in Section 8.3 (Enforcement of Patents) (whether by way of settlement or otherwise) will be first, allocated to reimburse the Parties for their costs and expenses in making such recovery (which amounts will be allocated pro rata if insufficient to cover the totality of such expenses). Any remainder after such reimbursement is made will be retained by the Party that has exercised its right to bring the enforcement action; *provided that* (i) to the extent that any award or settlement (whether by judgment or otherwise) is attributable to loss of sales with respect to a BII Product, the Parties will treat such amount as Net Sales for such BII Product, (ii) to the extent that any award or settlement (whether by judgment or otherwise) is attributable to loss of sales with respect to a Joint Product in the ROW, the Parties will treat such amount as Net Sales for such Joint Product in the ROW and (iii) in the event of an infringement that is competitive with a Joint Product in the United States, all recoveries will be treated as Net Sales and allocated in accordance with Section 5.2.2(a)(iv) (Allocation).

8.4. Infringement Claims by Third Parties. If the Development, Manufacture, Commercialization or other Exploitation of a Compound, Product or Diagnostic Product in the Territory pursuant to this Agreement results in, or may result in, any claim, suit or proceeding by a Third Party alleging Patent infringement by a Party (or its Affiliates or Sublicensees), the Party (or its Patent Liaison) first having knowledge of such claim, suit or proceeding shall promptly notify the other Party thereof in writing. BII, in consultation with the Patent Liaisons, shall have the first right, but not the obligation, to defend and control the defense of any such claim, suit or proceeding at its own expense, using counsel of its own choice. Epizyme may participate in any such claim, suit or proceeding with counsel of its choice at its own expense. Without limitation of the foregoing, if BII finds it necessary or desirable to join Epizyme as a party to any such action, Epizyme shall execute all papers and perform such acts as shall be reasonably required at BII's expense. If BII elects (in a written communication submitted to Epizyme within a reasonable amount of time after notice of the alleged Patent infringement) not to defend or control the defense of, or otherwise fails to initiate and maintain the defense of, any such claim, suit or proceeding, within such time periods so that Epizyme is not prejudiced by any delays, Epizyme, in consultation with the Patent Liaisons, may conduct and control the defense of any such claim, suit or proceeding at its own expense. Each Party's Patent Liaison shall keep the other Party's Patent Liaison reasonably informed of all material developments in connection with any such claim, suit or proceeding. Each Party's Patent Liaison shall provide the other Party's Patent Liaison with copies of all pleadings filed in such action and to allow the other Party's Patent Liaison a reasonable opportunity to participate in the defense of the claims. In case either Party desires to submit a counterclaim in such defensive action, Section 8.3 (Enforcement of Patents) applies in case such counterclaim concerns the enforcement of an Epizyme Patent, Joint Patent or BII Patent, including with respect to any recoveries realized as a result of such counterclaim.

8.5. Invalidation or Unenforceability Defenses or Actions.

8.5.1 Notice. Each Party shall promptly notify the other Party in writing of any alleged or threatened assertion of invalidity or unenforceability of any of the Epizyme Patents, BII Patents or Joint Patents by a Third Party, in each case in the Territory and of which such Party becomes aware, which assertion arises outside of the context of an enforcement proceeding under Section 8.3 (Enforcement of Patents).

8.5.2 Epizyme Product Patents and Joint Patents. BII, in consultation with the Patent Liaisons, shall have the first right, but not the obligation, to defend and control the defense of the validity and enforceability of the Epizyme Product Patents or Joint Patents at its own expense in the Territory. Epizyme may participate in any such claim, suit or proceeding in the Territory with counsel of its choice at its own expense; *provided that* BII shall retain control of the defense in such claim, suit or proceeding. If BII elects not to defend or control the defense of the Epizyme Product Patents or Joint Patents in a suit brought in the Territory, or otherwise fails to initiate and maintain the defense of any such claim, suit or proceeding, then Epizyme, in consultation with the Patent Liaisons, may conduct and control the defense of any such claim, suit, or proceeding at its own.

8.5.3 Other Epizyme Patents. Epizyme, in consultation with the Patent Liaisons, shall have the sole right to defend and control the defense of the validity and enforceability of the Epizyme Patents (other than the Epizyme Product Patents, which are handled pursuant to Section 8.5.2 (Epizyme Product Patents and Joint Patents)) and, without consulting the Patent Liaisons, the Epizyme Carve-Out Patents, with respect to each, at its own expense in the Territory. Notwithstanding the foregoing, Epizyme shall not take any action or fail to take any action, in connection with the defense of any Epizyme Carve-Out Patent that may have, or actually results in, any detrimental effect upon the patentability, validity or enforceability of any Patent Right Covering Compounds or Products. Epizyme shall ensure that all obligations of Epizyme under this Agreement with respect to the Epizyme Carve-Out Patents will be placed upon any Third Party who secures rights with respect to the defense of the Epizyme Carve-Out Patents.

8.5.4 BII Product Patents. BII, in consultation with the Patent Liaisons, shall have the first right, but not the obligation, to defend and control the defense of the validity and enforceability of the BII Product Patents at its own expense in the Territory. Epizyme may participate in any such claim, suit or proceeding in the Territory with counsel of its choice at its own expense; *provided that* BII shall retain control of the defense in such claim, suit or proceeding. If BII elects not to defend or control the defense of the BII Product Patents in a suit brought in the Territory, or otherwise fails to initiate and maintain the defense of any such claim, suit or proceeding, then Epizyme, in consultation with the Patent Liaisons, may conduct and control the defense of any such claim, suit, or proceeding at its own expense.

8.5.5 Other BII Patents. BII, in consultation with the Patent Liaisons, shall have the sole right to defend and control the defense of the validity and enforceability of the BII Patents (other than the BII Product Patents, which are handled pursuant to Section 8.5.4 (BII Product Patents)) at its own expense in the Territory.

8.5.6 Cooperation. Each Party shall assist and cooperate with the other Party, including through its Patent Liaison, as such other Party may reasonably request from time to time in connection with its activities set forth in this Section 8.5 (Invalidity or Unenforceability Defenses or Actions), including by being joined as a party plaintiff in such action or proceeding, providing access to relevant documents and other evidence and making its employees available at reasonable business hours. In connection with any such defense or claim or counterclaim, the controlling Party shall consider in good faith any comments from the other Party's Patent Liaison and shall keep the other Party's Patent Liaison reasonably informed of any steps taken, including by providing the other Party's Patent Liaison with copies of all documents filed in connection with such defense, claim or counterclaim. In connection with the activities set forth in this Section 8.5 (Invalidity or Unenforceability Defenses or Actions), each Party's Patent Liaison shall consult with the other Party's Patent Liaison as to the strategy for the defense of the Epizyme Patents, BII Patents and Joint Patents, but the Party having control of such proceeding as specified in this Section 8.5 (Invalidity or Unenforceability Defenses or Actions) shall have final decision making authority with respect thereto.

8.6. Third Party Licenses. If, in the reasonable opinion of a Party, the Development, Manufacture or Commercialization of any Compound or Product by the Parties or any of its Affiliates or any of its or their Sublicensees infringes or misappropriates any Patent, trade secret or other intellectual property right of a Third Party in any country in the Territory, then (i) with respect to the BII Compound and BII Product in the Territory, BII has the sole right to negotiate and obtain a license from such Third Party for BII or its Affiliates, or its and their Sublicensees, to Develop, Manufacture and Commercialize BII Compounds and BII Products in the Territory; *provided that*, BII shall be solely responsible for any Third Party Payments owed in connection with such license pursuant to Section 5.1 (BII Controlled Project), subject to Section 7.4.3(b) (Reductions), (ii) with respect to the Joint Compound or Joint Product in the ROW, BII has the sole right to negotiate and obtain a license from such Third Party for BII or its Affiliates, or its and their Sublicensees, to Develop, Manufacture and Commercialize Joint Compounds and Joint Product in the ROW, subject to Section 7.4.3(b) (Reductions) and (iii) with respect to the Joint Compound and Joint Product in the U.S., BII will have the right to negotiate and obtain a license from such Third Party for either Party or its Affiliates, and its and their Sublicensees, to Develop, Manufacture and Commercialize Joint Compounds and Joint Products in the United States; *provided that* (i) BII will keep Epizyme reasonably informed as to the status of such negotiations, including by providing Epizyme with copies thereof, and will reasonably consider any comments offered by Epizyme with respect thereto and (ii) any Third Party Payments owed in connection with such license shall be included in Allowable Expenses and the Parties shall share such Third Party Payments consistent with Section 5.2.2(a)(iv) (Allocation).

8.7. Product Marks.

8.7.1 Ownership and Prosecution of Product Marks. BII will own all right, title, and interest to the Product Marks in the Territory, and will be responsible for the preparation, filing, prosecution and maintenance thereof. All costs and expenses of registering, prosecuting and maintaining the Product Marks will be borne solely by BII. Epizyme will provide all assistance and documents reasonably requested by BII in support of its prosecution, registration and maintenance of the Product Marks.

8.7.2 Enforcement of Product Marks. BII will have the sole right and responsibility for taking such action as BII deems necessary against a Third Party based on any alleged, threatened or actual infringement, dilution, misappropriation or other violation of, or unfair trade practices or any other like offense relating to, the Product Marks by a Third Party in the Territory. BII will bear the costs and expenses relating to any enforcement action commenced pursuant to this Section 8.7.2 (Enforcement of Product Marks) and any settlements and judgments with respect thereto, and will retain any damages or other amounts collected in connection therewith.

8.7.3 Third Party Claims. BII will have the sole right and responsibility for defending against any alleged, threatened or actual claim by a Third Party that the use or registration of the Product Marks in the Territory infringes, dilutes, misappropriates or otherwise violates any Trademark or other right of that Third Party or constitutes unfair trade practices or any other like offense, or any other claims as may be brought by a Third Party against a Party in connection with the use of the Product Marks with respect to a Product in the Territory. BII will bear the costs and expenses relating to any defense commenced pursuant to this Section 8.7.3 (Third Party Claims) and any settlements and judgments with respect thereto, and will retain any damages or other amounts collected in connection therewith.

8.7.4 Notice and Cooperation. Each Party will provide to the other Party prompt written notice of any actual or threatened infringement of the Product Marks in the Territory and of any actual or threatened claim that the use of the Product Marks in the Territory violates the rights of any Third Party. Each Party agrees to cooperate fully with the other Party with respect to any enforcement action or defense commenced pursuant to this Section 8.7 (Product Marks).

8.8. Inventor's Remuneration. Each Party will be solely responsible for any remuneration that may be due to such Party's inventors under any applicable inventor remuneration laws.

ARTICLE 9 PHARMACOVIGILANCE AND SAFETY

9.1. Pharmacovigilance. Within [**] after JSC approval of a Joint Development Plan and Budget that includes a Clinical Trial to be sponsored by Epizyme, the Parties shall enter into an agreement to initiate a process for the exchange of safety data (including post-marketing spontaneous reports received by each Party and its Affiliates) in a mutually agreed format in order to monitor the safety of the Compounds, Products and Diagnostic Products and to meet reporting requirements with any applicable Regulatory Authority.

9.2. Global Safety Database. BII shall be responsible for setting up, holding and maintaining (at BII's sole cost and expense) the global safety database for Compounds, Products and Diagnostic Products; *provided that* Epizyme shall have the right to hold and maintain a parallel safety database for the Joint Compound, Joint Product and Diagnostic Products for the Joint Compound only if required by Applicable Laws. Each Party shall provide the other Party with all Information necessary or desirable for the other Party to comply with its pharmacovigilance responsibilities in the Territory, including, as applicable, any adverse drug

experiences, from pre-clinical or clinical laboratory, animal toxicology and pharmacology studies, Clinical Trials and commercial experiences with a Compound, Product or Diagnostic Product, in each case, in the form reasonably requested by the other Party. Each Party's and its Affiliates' and Sublicensees' costs incurred in connection with receiving, recording, reviewing, communicating, reporting and responding to adverse events for Joint Products in the United States shall be included in Allowable Expenses so long as such actions are consistent with the Joint Commercialization Plan and Budget.

ARTICLE 10 CONFIDENTIALITY AND NON-DISCLOSURE

10.1. Confidentiality Obligations. At all times during the Term and for a period of [**] following termination or expiration hereof in its entirety, each Party will, and will cause its Affiliates and its and their respective officers, directors, employees and agents to, keep confidential and not publish or otherwise disclose to a Third Party and not use, directly or indirectly, for any purpose, any Confidential Information furnished or otherwise made known to it, directly or indirectly, by the other Party, except to the extent such disclosure or use is expressly permitted by the terms of this Agreement or is necessary for the performance of, or the exercise of such Party's rights under, this Agreement. Notwithstanding the foregoing, to the extent the receiving Party can demonstrate by documentation or other competent proof, the confidentiality and non-use obligations under this Section 10.1 (Confidentiality Obligations) with respect to any Confidential Information will not include any Information that:

10.1.1 has been published by a Third Party or otherwise is or hereafter becomes part of the public domain by public use, publication, general knowledge or the like through no wrongful act, fault or negligence on the part of the receiving Party;

10.1.2 have been in the receiving Party's possession prior to disclosure by the disclosing Party without any obligation of confidentiality with respect to such Information;

10.1.3 is subsequently received by the receiving Party from a Third Party without restriction and without breach of any agreement between such Third Party and the disclosing Party;

10.1.4 that is generally made available to Third Parties by the disclosing Party without restriction on disclosure; or

10.1.5 have been independently developed by or for the receiving Party without reference to, or use or disclosure of, the disclosing Party's Confidential Information.

Specific aspects or details of Confidential Information will not be deemed to be within the public domain or in the possession of the receiving Party merely because the Confidential Information is embraced by more general Information in the public domain or in the possession of the receiving Party. Further, any combination of Confidential Information will not be considered in the public domain or in the possession of the receiving Party merely because individual elements of such Confidential Information are in the public domain or in the possession of the receiving Party unless the combination and its principles are in the public domain or in the possession of the receiving Party.

10.2. Permitted Disclosures. Each Party may disclose the Confidential Information of the other Party that is received in connection with this Agreement to the extent that such disclosure is:

10.2.1 in the reasonable opinion of the receiving Party's legal counsel, required to be disclosed pursuant to Applicable Law or a valid order of a court of competent jurisdiction or other supra-national, federal, national, regional, state, provincial and local governmental body of competent jurisdiction, (including by reason of filing with securities regulators, but subject to Section 10.5 (Agreement Redactions)); *provided that* the receiving Party will first have given prompt written notice (and to the extent possible, at least [**] notice) to the disclosing Party and given the disclosing Party a reasonable opportunity to take whatever action it deems necessary to protect its Confidential Information (for example, quash such order or to obtain a protective order or confidential treatment requiring that the Confidential Information and documents that are the subject of such order be held in confidence by such court or governmental body or, if disclosed, be used only for the purposes for which the order was issued). In the event that no protective order or other remedy is obtained, or the disclosing Party waives compliance with the terms of this Agreement, the receiving Party will furnish only that portion of Confidential Information which the receiving Party is advised by counsel is legally required to be disclosed;

10.2.2 made by or on behalf of the receiving Party to the Regulatory Authorities as required in connection with any filing, application or request for Regulatory Approval in accordance with the terms of this Agreement; *provided that* reasonable measures will be taken to assure confidential treatment of such Confidential Information to the extent practicable and consistent with Applicable Law;

10.2.3 made by or on behalf of the receiving Party to a Patent authority as may be reasonably necessary or useful for purposes of obtaining, defending or enforcing a Patent in accordance with the terms of this Agreement; *provided that* reasonable measures will be taken to assure confidential treatment of such Confidential Information, to the extent practicable and consistent with Applicable Law;

10.2.4 made by the receiving Party to: (a) its Board of Directors, accountants and legal advisors who have a need to know the disclosing Party's Confidential Information, (b) its Affiliates who have a need to know the disclosing Party's Confidential Information, however never to any Affiliates who control a [**] Competing Product or [**] Competing Product and always conforming with the exclusivity obligations under Section 4.4 (Exclusivity) of this Agreement or (c) its or their consultants, advisors, Sublicensees or Contractors who have a need to know the disclosing Party's Confidential Information in connection with the research, Development, Manufacture, Commercialization, use or other Exploitation of Compounds, Products or Diagnostic Products; *provided that* such Persons will be subject to obligations of confidentiality and non-use with respect to such Confidential Information at least as protective to the disclosing Party as the obligations of confidentiality and non-use of the receiving Party pursuant to this Agreement;

10.2.5 made by the receiving Party to its actual investors, bankers, financial advisors, lenders or financing sources (and their respective attorneys and professional advisors) on a need to know basis, each of whom prior to disclosure must be subject to appropriate obligations of confidentiality and non-use equivalent in scope and time to those set forth in this Agreement; *provided that* a disclosure pursuant to this Section 10.2.5 is limited to (a) a high-level status overview of and projections for the research, Development, Manufacturing or Commercialization of Compounds and Products, and the actual and projected financial payments to and from Epizyme with respect thereto, and, for clarity, does not include chemical structures, chemical names and molecular weights of Compounds and (b) the terms of this Agreement, but excluding the terms of the Research Plan, Joint Development Plan and Budget, Joint Commercialization Plan and Budget, the SoLO Criteria or SoD Criteria, unless such investors, bankers, financial advisors, lenders or financing sources (or their respective attorneys and professional advisors) request disclosure of such terms, in which case, such terms shall be disclosed only after suitable redactions have been made and have been agreed to by BII, such agreement not to be unreasonably withheld;

10.2.6 made by the receiving Party to its bona fide prospective investors, acquirers, lenders or financing sources on a need to know basis in connection with any transaction, each of whom prior to disclosure must be subject to appropriate obligations of confidentiality and non-use equivalent in scope and time to those set forth in this Agreement; *provided that* a disclosure pursuant to this Section 10.2.6 is limited to (a) a high-level status overview of and projections for the research, Development, Manufacturing or Commercialization of Compounds and Products, and the actual and projected financial payments to and from Epizyme with respect thereto, and, for clarity, does not include chemical structures, chemical names and molecular weights of Compounds and (b) to the extent necessary for the relevant transaction, the terms of this Agreement, but excluding the terms of the Research Plan, Joint Development Plan and Budget, Joint Commercialization Plan and Budget, the SoLO Criteria or SoD Criteria, unless such prospective investors, acquirers, lenders or financing sources request disclosure of such terms, in which case, such terms shall be disclosed only after suitable redactions have been made and have been agreed to by BII, such agreement not to be unreasonably withheld; and

10.2.7 made by the receiving Party to the extent mutually agreed to in writing by the Parties.

10.3. Use of Name. Except as expressly provided herein, neither Party will mention or otherwise use the name, logo or Trademark of the other Party or any of its Affiliates (or any abbreviation or adaptation thereof) in any publication, press release, marketing and promotional material, or other form of publicity without the prior written approval of such other Party. The restrictions imposed by this Section 10.3 (Use of Name) will not prohibit either Party from making any disclosure identifying the other Party that, in the opinion of the disclosing Party's counsel, is required by Applicable Law; *provided that* such Party will submit the proposed disclosure identifying the other Party in writing to the other Party as far in advance as reasonably practicable (and in no event less than [**] prior to the anticipated date of disclosure) so as to provide a reasonable opportunity to comment thereon.

10.4. Press Releases. The Parties have agreed upon the content of a joint press release, which shall be issued substantially in the form attached hereto as Schedule 10.4, the release of which the Parties shall coordinate to issue such release as soon as practicable after execution of this Agreement. Subject to the other provisions of this Agreement, no other press release, public statement or public disclosure concerning the existence or terms of this Agreement shall be made, either directly or indirectly, by either Party, without first obtaining the written approval of the other Party, such written approval not to be unreasonably withheld (for clarity, either Party may disclose in any subsequent press release the contents of Schedule 10.4 without having to obtain the other Party's consent, provided such press release is limited to disclosing only the Information contained in Schedule 10.4); *provided that*, in connection with issuing subsequent press releases, Epizyme may disclose its achievement of any Milestone Event and receipt of any Milestone Payment, including the amount thereof without obtaining BII's prior written consent. Epizyme may only disclose in a press release (i) material developments with respect to the Joint Product in the United States or (ii) information required to be disclosed as described in Section 10.2.1, with respect to (i)-(ii), provided it first obtains BII's prior written consent, not to be unreasonably withheld. Subject to Section 10.2.1, in no event shall any such subsequent press release, public statement or public disclosure by a Party disclose, if previously undisclosed, the identity of any Compound or Product, the stage of development of any Product or the financial terms of this Agreement. Once any public statement or public disclosure has been approved in accordance with this Section 10.4 (Press Release), then either Party may appropriately communicate information contained in such permitted statement or disclosure.

10.5. Agreement Redactions. Notwithstanding any of the provisions of this ARTICLE 10 (Confidentiality and Non-Disclosure), a Party may disclose the existence and terms of this Agreement (however, excluding, as far as legally possible, any and all information and terms contained within the Agreement) or the Parties' activities under this Agreement, where required, as reasonably determined by the legal counsel of the disclosing Party, by Applicable Law, by applicable stock exchange regulation or by order or other ruling of a competent court; *provided that*, to the extent practicable, the other Party shall be given [**] advance notice of any such legally required disclosure, so such other Party may provide comments to the disclosing Party, and the disclosing Party shall use their commercially reasonable efforts to reasonably consider such comments provided by such other Party on the proposed disclosure, and the disclosing Party shall use reasonable efforts to redact the information contained within the Agreement in a consistent manner and consistent with the intentions of this Agreement that information shall not be disclosed unless absolutely required by Applicable Law or regulations or if the other Party provides its prior written consent. In case either Party is obliged to publish the Agreement as a "material agreement" in accordance with the U.S. stock exchange regulations ("**SEC Filing**") or any other similar stock exchange regulations throughout the Territory, the Agreement shall be redacted by the filing Party as far as legally possible, and the filing Party shall cooperate with the other Party reasonably in advance to such SEC Filing to enable the other Party to review and comment on the scope of such redaction, all in accordance with the requirements found in the immediately preceding sentence.

10.6. Publications. Within [**] of the Effective Date, the Parties, through the JSC, shall develop policies and procedures ("**Publication Policies**") for any publication with respect to Development of Compounds (including any research results arising from the conduct of Research Activities under the Research Plan), Products and Diagnostic Products, including the

results of Clinical Trials and disclosure in applicable clinical trial registries, which policies and procedures shall be consistent with the Parties' respective policies and procedures for publication and disclosure of the results of Clinical Trials, with disputes to be resolved in favor of the policy that provides for the narrowest disclosure of such results. All abstracts, manuscripts and presentations (including Information to be presented verbally) that disclose results of the Development of Compounds (including any research results arising from the conduct of Research Activities under the Research Plan), Products and Diagnostic Products, shall be reviewed and approved by the JSC in accordance with the Publication Policies. Notwithstanding the foregoing, each Party shall provide to the other Party (through the JSC) the opportunity to review each of the submitting Party's proposed abstracts, manuscripts or presentations (including Information to be presented verbally) that relate to any activities under the Research Plan or otherwise with respect to a Compound, Product or Diagnostic Product at least [**] prior to its intended presentation or submission for publication and such submitting Party agrees, upon written request from the other Party given within such [**] period, as applicable, not to submit such abstract or manuscript for publication or to make such presentation until the other Party is given up to [**] from the date of such written request to seek appropriate Patent protection for any material in such publication or presentation that it reasonably believes, in good faith, may be patentable. Both Parties understand that a reasonable commercial strategy may require the delay of publications of information or the filings of patent applications with respect to activities performed or results obtained pursuant to this Agreement, and in such instances, such information shall not be published until a patent application is filed or it is otherwise deemed suitable for publication by both Parties, and always subject to BII's rights to determine the timing of filings of Joint Counsel Patent Rights as specified in Section 8.2.4(a) (Joint Patents and Epizyme Product Patents). For clarity and notwithstanding anything to the contrary contained in this Section 10.6 (Publications), BII and its Affiliates may publish or present results, data or scientific findings of any of their activities performed with respect to the BII Compound or BII Product [**] has been achieved with respect to such BII Compound or BII Product without the prior review or consent of Epizyme, unless Epizyme is required to be or is otherwise acknowledged in or listed as an author of such publication or presentation, in which event BII may not make such presentation or publication without Epizyme's prior written consent, such consent not to be unreasonably withheld. Each Party also shall have the right to require that any of its Confidential Information (but not the results of Clinical Trials that have been approved for disclosure pursuant to the Publication Policies) that is disclosed in any such proposed publication or presentation be deleted prior to such publication or presentation. Any publication shall include recognition of the contributions of the other Party according to standard practice for assigning scientific credit, either through authorship or acknowledgement, as may be appropriate.

10.7. Confidentiality Redaction. Each Party also shall have the right to require that any of its Confidential Information (but not the results of Clinical Trials that have been approved for disclosure pursuant to the Publication Policies) that is disclosed in any such proposed publication or presentation be deleted prior to such publication or presentation. Any publication or presentation shall include recognition of the contributions of the other Party according to standard practice for assigning scientific credit, either through authorship or acknowledgement, as may be appropriate.

10.8. Survival. All Confidential Information will continue to be subject to the terms of this Agreement for the period set forth in Section 10.1 (Confidentiality Obligations).

ARTICLE 11
REPRESENTATIONS AND WARRANTIES

11.1. Mutual Representations and Warranties. Each Party hereby represents and warrants to the other, as of the Effective Date, that:

11.1.1 it is a corporation duly organized, validly existing, and in good standing under the laws of the jurisdiction of its organization, and has all requisite power and authority, corporate or otherwise, to execute, deliver and perform this Agreement;

11.1.2 the execution and delivery of this Agreement and the performance by it of the transactions contemplated hereby have been duly authorized by all necessary corporate action, and do not violate (a) such Party's charter documents, bylaws, or other organizational documents, (b) any agreement, instrument, or contractual obligation to which such Party is bound, (c) any requirement of any Applicable Law or (d) any order, writ, judgment, injunction, decree, determination, or award of any court or governmental agency presently in effect applicable to such Party;

11.1.3 this Agreement is a legal, valid and binding obligation of such Party enforceable against it in accordance with its terms and conditions, subject to the effects of bankruptcy, insolvency, or other laws of general application affecting the enforcement of creditor rights, judicial principles affecting the availability of specific performance, and general principles of equity (whether enforceability is considered a proceeding at law or equity);

11.1.4 it is not under any obligation, contractual or otherwise, to a Person that conflicts with or is inconsistent with the terms of this Agreement, or that would impede the diligent and complete fulfillment of its obligations hereunder;

11.1.5 to its knowledge, it has not (i) employed and has not used a Contractor or consultant that has employed, any Person debarred by the FDA (or subject to similar sanctions of the EMA or other Regulatory Authority) or (ii) employed any Person that is the subject of an FDA debarment investigation or proceeding (or similar proceeding of the EMA or other Regulatory Authority), with respect to (i)-(ii), in the conduct of any pre-clinical activities with respect to Compounds;

11.1.6 no consent of any Third Party is required for such Party to grant the licenses and rights granted to the other Party under this Agreement or to perform its obligations hereunder; and

11.1.7 all of such Party's personnel and employees and Third Parties, including Contractors, hired by such Party and involved in activities under this Agreement are, or when hired will be, under a written agreement whereby they have presently assigned to such Party any right that they may have in any invention first invented, discovered, made, conceived or reduced to practice while employed by or working on behalf of such Party in the conduct of activities pursuant to the Research Plan, or in the Development, Manufacture or Commercialization of any of such Compounds or Products, and all intellectual property rights therein.

11.2. Additional Representations and Warranties of Epizyme. Epizyme further represents and warrants to BII, as of the Effective Date, that:

11.2.1 Epizyme has the right to grant all rights and license it purports to grant to BII with respect to the Epizyme Technology under this Agreement;

11.2.2 Epizyme has not granted any right or license to any Third Party relating to any Epizyme Technology that would conflict with or interfere with or limit the scope of any rights or licenses granted to BII hereunder;

11.2.3 Epizyme has not granted any liens or security interest on the Epizyme Technology that would limit the scope of any rights or licenses granted to BII hereunder;

11.2.4 Neither Epizyme nor its Affiliates have knowledge of or have received any written notice of any claim that any Patent or trade secret right Controlled by a Third Party would be infringed or misappropriated by the Manufacture, use, sale, offer for sale or importation of the Compounds or Products, as contemplated by this Agreement;

11.2.5 To Epizyme's knowledge, the Epizyme Technology is not being infringed or misappropriated by a Third Party; and

11.2.6 The inventions claimed or covered by the Epizyme Patents existing as of the Effective Date (a) were not conceived, discovered, developed, or otherwise made in connection with any research activities funded, in whole or in part, by the federal government of the United States or any agency thereof, (b) are not a "subject invention" as that term is described in 35 U.S.C. Section 201(f) and (c) are not otherwise subject to the provisions of the Bayh-Dole Act.

11.3. Mutual Covenants. Each Party hereby covenants to the other Party, as of the Effective Date, that:

11.3.1 all of its and its Affiliates' employees who are working under this Agreement will presently assign all right, title and interest in and to their inventions and discoveries, whether or not patentable, to such Party as the sole owner thereof;

11.3.2 to the best of its knowledge, without further duty of inquiry, such Party will not (a) employ or use any Contractor or consultant that employs any Person debarred by the FDA (or subject to similar sanction of the EMA or other Regulatory Authority) or (b) employ any Person that is the subject of an FDA debarment investigation or proceeding (or similar proceeding of the EMA or other Regulatory Authority), in each of (i)-(ii), in the conduct of its activities under this Agreement;

11.3.3 it will perform or cause to be performed, its Research Activities and any activities assigned to it under the Joint Development Plan and Budget and Joint Commercialization Plan and Budget, in good scientific manner and in compliance with all Applicable Laws; and

11.3.4 neither Party shall, during the Term, enter into an agreement with a Third Party, or grant any right or license to any Third Party relating to any of the intellectual property rights it Controls, or otherwise encumber such intellectual property rights it Controls, that would conflict with any of the rights, obligations or licenses granted to the other Party hereunder.

11.4. DISCLAIMER OF WARRANTIES. EXCEPT FOR THE EXPRESS WARRANTIES SET FORTH HEREIN, NEITHER PARTY MAKES ANY REPRESENTATIONS OR GRANTS ANY WARRANTIES, EXPRESS OR IMPLIED, EITHER IN FACT OR BY OPERATION OF LAW, BY STATUTE OR OTHERWISE, AND EACH PARTY SPECIFICALLY DISCLAIMS ANY OTHER WARRANTIES, WHETHER WRITTEN OR ORAL, OR EXPRESS OR IMPLIED, INCLUDING ANY WARRANTY OF QUALITY, MERCHANTABILITY, OR FITNESS FOR A PARTICULAR USE OR PURPOSE OR ANY WARRANTY AS TO THE VALIDITY OF ANY PATENTS OR THE NON-INFRINGEMENT OF ANY INTELLECTUAL PROPERTY RIGHTS OF THIRD PARTIES.

ARTICLE 12 INDEMNITY

12.1. Indemnification of Epizyme. BII will indemnify Epizyme, its Affiliates and its and their respective directors, officers, employees and agents (the “**Epizyme Indemnitees**”) and defend and save each of them harmless, from and against any and all losses, damages, liabilities, penalties, costs and expenses (including reasonable attorneys’ fees and expenses) (collectively, “**Losses**”) in connection with any and all suits, investigations, claims or demands of Third Parties (collectively, “**Third Party Claims**”) incurred by or rendered against the Epizyme Indemnitees arising from or occurring as a result of: (a) the breach by BII or its Affiliates of this Agreement; (b) the fraud, gross negligence or willful misconduct on the part of BII or its Affiliates or their respective directors, officers, employees and agents in performing its or their obligations under this Agreement; (c) the use of Product Marks in connection with the Exploitation of Products in the Territory; (d) the Exploitation of BII Products in the Territory by BII or its Affiliates; and (e) the Exploitation of Joint Products in the Territory by BII or its Affiliates; *provided that*, in the case of clauses (a)-(e), for those Losses for which Epizyme, in whole or in part, has an obligation to indemnify BII pursuant to Section 12.2 (Indemnification of BII) hereof, as to which Losses each Party will indemnify the other to the extent of their respective liability for such Losses.

12.2. Indemnification of BII. Epizyme will indemnify BII, its Affiliates and its and their respective directors, officers, employees and agents (the “**BII Indemnitees**”), and defend and save each of them harmless, from and against any and all Losses in connection with any and all Third Party Claims incurred by or rendered against the BII Indemnitees arising from or occurring as a result of: (a) the breach by Epizyme or its Affiliates of this Agreement; (b) the fraud, gross negligence or willful misconduct on the part of Epizyme or its Affiliates or its or their respective directors, officers, employees and agents in performing its obligations under this Agreement; and (c) the Exploitation of Joint Products in the Territory by Epizyme or its Affiliates; *provided that*, in the case of clauses (a)-(c), for those Losses for which BII, in whole or in part, has an obligation to indemnify Epizyme pursuant to Section 12.1 (Indemnification of Epizyme) hereof, as to which Losses each Party will indemnify the other to the extent of their respective liability for the Losses.

12.3. Procedure. In the event of a claim by a Third Party against a Person entitled to indemnification under this Agreement (“**Indemnified Party**”), the Indemnified Party shall promptly notify the other Party (“**Indemnifying Party**”) in writing of the claim and the Indemnifying Party shall undertake and solely manage and control, at its sole expense, the defense of the claim, including any settlement thereof. The Indemnified Party shall, at the Indemnifying Party’s expense, reasonably cooperate with the Indemnifying Party in connection with the defense of such claim and may, at its option and expense, be represented in any such action or proceeding by counsel of its choice. The Indemnifying Party shall not be liable for any litigation costs or expenses incurred by the Indemnified Party without the Indemnifying Party’s written consent. The Indemnifying Party shall not settle any such claim unless such settlement fully and unconditionally releases the Indemnified Party from all liability relating thereto, unless the Indemnified Party agrees in writing otherwise.

12.4. No Consequential Damages. EXCEPT (A) FOR THE FRAUD OR WILLFUL MISCONDUCT OR GROSS NEGLIGENCE OF A PARTY, (B) FOR A PARTY’S BREACH OF ITS OBLIGATIONS UNDER ARTICLE 10 (CONFIDENTIALITY AND NON-DISCLOSURE), (C) TO THE EXTENT ANY SUCH DAMAGES ARE REQUIRED TO BE PAID TO A THIRD PARTY AS PART OF A CLAIM FOR WHICH A PARTY PROVIDES INDEMNIFICATION UNDER THIS ARTICLE 12 (INDEMNITY) OR (D) A PARTY’S BREACH OF SECTION 4.4 (EXCLUSIVITY), NEITHER PARTY NOR ANY OF ITS AFFILIATES OR ITS OR THEIR SUBLICENSEES WILL BE LIABLE FOR INDIRECT, INCIDENTAL, SPECIAL, EXEMPLARY, PUNITIVE OR CONSEQUENTIAL DAMAGES, INCLUDING LOSS OF PROFITS OR BUSINESS INTERRUPTION, HOWEVER CAUSED AND ON ANY THEORY OF LIABILITY, WHETHER IN CONTRACT, TORT, NEGLIGENCE, BREACH OF STATUTORY DUTY OR OTHERWISE IN CONNECTION WITH OR ARISING IN ANY WAY OUT OF THE TERMS OF THIS AGREEMENT OR THE TRANSACTIONS CONTEMPLATED HEREBY OR THE USE OF THE LICENSED CONSTRUCTS OR LICENSED PRODUCT, EVEN IF ADVISED OF THE POSSIBILITY OF SUCH DAMAGE.

12.5. Insurance. Each Party will obtain and carry in full force and effect the minimum insurance requirements set forth below, except that BII may alternatively decide to self-insure itself in its sole discretion. Such insurance (a) will be primary insurance with respect to each Party’s own participation under this Agreement, (b) will be issued by a recognized insurer rated by A.M. Best “A-VII” (or its equivalent) or better, or an insurer pre-approved in writing by the other Party and (c) will list the other Party as an additional named insured thereunder, as applicable.

12.5.1 Types and Minimum Limits. The types of insurance, and minimum limits will be:

(a) Any insurance policy that is required by any Applicable Law, including workers compensation and employer’s liability policies where applicable.

(b) General liability insurance with a minimum limit of [**] Dollars (\$[**]) per occurrence and [**] Dollars (\$[**]) in the aggregate; *provided that* beginning at least [**] prior to the Initiation of any Clinical Trial Conducted by a Party, such Party’s

general liability insurance will also include (i) Clinical Trial insurance with a minimum limit of [**] Dollars (\$[**]) in the aggregate and (ii) cyber/network liability insurance with a minimum limit of [**] Dollars (\$[**]) in the aggregate, in each case, to be maintained throughout the Conduct of any such Clinical Trials.

12.5.2 Certificates of Insurance. Upon request by a Party, the other Party will provide Certificates of Insurance evidencing compliance with this Section 12.5 (Insurance), except to the extent BII decides to self-insure itself. The insurance policies will be under an occurrence form, but if only a claims-made form is available to a Party, then such Party will continue to maintain such insurance after the expiration or termination of this Agreement for the longer of (a) a period of [**] following termination or expiration of this Agreement in its entirety, or (b) with respect to a particular Party, last sale of a Product (or but for expiration or termination, would be considered a Product) sold under this Agreement by a Party.

ARTICLE 13 TERM AND TERMINATION

13.1. Term.

13.1.1 Term. This Agreement shall commence on the Effective Date and continue, unless terminated earlier pursuant to Section 13.2 (Termination), on a Product-by-Product basis, until the last to expire Royalty Term for such Product; *provided that*, with respect to the Joint Product in the U.S., this Agreement shall continue until both Parties mutually agree to cease Commercialization of the Joint Product in the U.S. (such period until this Agreement has expired pursuant to this Section with respect to all Products, the “**Term**”).

13.2. Termination.

13.2.1 Termination of Agreement for Cause. This Agreement may be terminated at any time during the Term, on a Target Project-by-Target Project basis, or in its entirety should the alleged material breach concern both Target Projects, upon written notice by either Party (the “**Non-Defaulting Party**”) upon the material breach of the other Party (the “**Defaulting Party**”), which material breach remains uncured for [**] (or [**] in the event of non-payment) after written notice requesting cure of such material breach. The Non-Defaulting Party shall provide written notice to the Defaulting Party, which notice shall identify the material breach, the intent to so terminate and the actions or conduct that it considers would be an acceptable cure of such material breach. If the Defaulting Party disputes that a material breach has occurred or the actions that would constitute an acceptable cure, then such dispute shall be resolved in accordance with Section 14.7 (Dispute Resolution) and the cure period will be tolled during the pendency of such dispute. If, as a result of such dispute resolution process, it is determined that the alleged Defaulting Party committed a material breach and the Defaulting Party does not cure such material breach within [**] (or [**] in the event of a non-payment) after the date of such dispute resolution award (but in no event less than the [**] or [**] cure periods described above) (the “**Additional Cure Period**”), then such termination shall be effective as of the expiration of the Additional Cure Period. If the Parties dispute whether such material breach was so cured, either Party alone may request the same tribunal to determine whether it was so cured, and the Parties shall cooperate to allow such determination to be made within [**] after

such request by either Party. Any such dispute resolution proceeding does not suspend any obligation of either Party hereunder, and each Party shall use reasonable efforts to mitigate any damage. If, as a result of any such dispute resolution proceeding, it is determined that the alleged Defaulting Party did not commit such material breach (or such material breach was cured in accordance with this Section), then no termination shall be effective, and this Agreement shall continue in full force and effect.

13.2.2 Termination if BII Challenges Epizyme Patents. If BII or any of its Affiliates or Sublicensees, (a) initiates or requests an interference, post-grant review, derivation proceeding or opposition proceeding against any Epizyme Patent, (b) makes, files or maintains any claim, demand, lawsuit or cause of action to challenge the validity, enforceability, patentability or scope of any claim within any Epizyme Patent in a tribunal or forum or (c) opposes any extension of, or the grant of a supplementary protection certificate with respect to, any Epizyme Patent, with respect to (a)-(c), Epizyme shall have the right to terminate this Agreement (i) on a Target Project-by-Target Project basis, as it concerns the subject matter covered under the challenged Epizyme Patent or (ii) in its entirety, if the challenged Epizyme Patent concerns both Target Projects, with respect to each, and upon [**] written notice to BII. Any such termination shall only become effective if BII or its Affiliates or Sublicensees, as applicable, (1) have not withdrawn such action before the end of the above notice period, (2) withdrew the action before the end of the above notice period but the action was not terminated as a result of such withdrawal or (3) with respect to any BII Sublicensee, BII has not terminated its agreement with such Sublicensee before the end of the above notice period. The Parties acknowledge and agree that it shall not be grounds for terminating this Agreement if BII or any of its Affiliates or Sublicensees challenges the validity, enforceability, patentability or scope of any claim within an Epizyme Patent in defense of an action for infringement of such Epizyme Patent brought by Epizyme or any of its Affiliates solely with respect to BII's or its Affiliates' or Sublicensees' activities outside the scope of this Agreement.

13.2.3 Termination if Epizyme Challenges Patents Controlled by BII. If Epizyme or any of its Affiliates (a) initiates or requests an interference, post-grant review, derivation proceeding or opposition proceeding against any BII Patent, (b) makes, files or maintains any claim, demand, lawsuit or cause of action to challenge the validity, enforceability, patentability or scope of any claim within any BII Patent in a tribunal or forum or (c) opposes any extension of, or the grant of a supplementary protection certificate with respect to, any BII Patent, with respect to (a)-(c), BII shall have the right to terminate this Agreement (i) on a Target Project-by-Target Project basis, as it concerns the subject matter covered under the challenged BII Patent or (ii) in its entirety, if the challenged BII Patent concerns both Target Projects, with respect to each, and upon [**] written notice to Epizyme. Any such termination shall only become effective if Epizyme or its Affiliates, as applicable, (1) have not withdrawn such action before the end of the above notice period or (2) withdrew the action before the end of the above notice period but the action was not terminated as a result of such withdrawal. The Parties acknowledge and agree that it shall not be grounds for terminating this Agreement if Epizyme or any of its Affiliates challenges the validity, enforceability, patentability or scope of any claim within an BII Patent in defense of an action for infringement of such BII Patent brought by BII or any of its Affiliates or Sublicensees solely with respect to Epizyme's or its Affiliates' activities outside the scope of this Agreement.

13.2.4 Termination by BII Without Cause. BII shall have the right to terminate the Agreement, at any time, in its entirety or on a Target Project-by-Target Project basis, (a) if terminating with respect to a Target Project during the Research Period for such Target Project, upon [**] notice to Epizyme, (b) if terminating with respect to a Target Project after the Research Period but prior to [**] for such Target Project, upon [**] notice to Epizyme, (c) if terminating with respect to a Target Project following [**] for such Target Project, [**] notice to Epizyme and (d) if terminating in its entirety and neither Target Project was the subject of a previous termination, then the corresponding notice periods for each of the two Target Projects in subclauses (a) through (c) shall separately apply, as applicable.

13.2.5 Termination for Insolvency. In the event that either Party: (a) files for protection under bankruptcy or insolvency laws; (b) makes an assignment for the benefit of creditors; (c) appoints or suffers appointment of a receiver or trustee over substantially all of its property that is not discharged within [**] after such filing; (d) proposes a written agreement of composition or extension of its debts; (e) proposes or is a party to any dissolution or liquidation; (f) files a petition under any bankruptcy or insolvency act or has any such petition filed against that is not discharged within [**] of the filing thereof; or (g) admits in writing its inability generally to meet its obligations as they fall due in the general course, then the other Party may terminate this Agreement in its entirety effective immediately upon written notice to such Party. All rights and licenses (collectively, the “**Intellectual Property**”) granted under or pursuant to this Agreement are intended to be, and will otherwise be deemed to be, for purposes of Section 365(n) of the United States Bankruptcy Code (the “**Bankruptcy Code**”) or any analogous provisions in any other country or jurisdiction, licenses of rights to “intellectual property” as defined under Section 101(35A) of the Bankruptcy Code. The Parties agree that the licensee of such intellectual property under this Agreement will retain and may fully exercise all of its rights and elections under the Bankruptcy Code, including Section 365(n) of the Bankruptcy Code, or any analogous provisions in any other country or jurisdiction. All of the rights granted to either Party under this Agreement will be deemed to exist immediately before the occurrence of any bankruptcy case in which the other Party is the debtor. If a bankruptcy proceeding is commenced by or against either Party under the Bankruptcy Code or any analogous provisions in any other country or jurisdiction, the non-debtor Party will be entitled to a complete duplicate of (or complete access to, as appropriate) any intellectual property and all embodiments of such intellectual property, which, if not already in the non-debtor Party’s possession, will be delivered to the non-debtor Party within [**] of such request; *provided that* the debtor Party is excused from its obligation to deliver the intellectual property to the extent the debtor Party continues to perform all of its obligations under this Agreement and the Agreement has not been rejected pursuant to the Bankruptcy Code or any analogous provision in any other country or jurisdiction.

13.3. Effects of Termination.

13.3.1 Termination by BII for Cause, Epizyme Patent Challenge or Epizyme Insolvency. If BII has the right to terminate this Agreement with respect to a specific Target Project or in its entirety pursuant to Sections 13.2.1 (Termination of Agreement for Cause), Section 13.2.3 (Termination if Epizyme Challenges Patents Controlled by BII) or Section 13.2.5 (Termination for Insolvency), then BII may, in its sole discretion, elect either of the following options, which will be applied on a Target Project-by-Target Project basis (if BII

has the right to terminate this Agreement with respect to a specific Target Project) or with respect to both Target Projects (if BII has the right to terminate this Agreement in its entirety)), and if BII has not provided written notice of its election within [**] from the end of the relevant cure periods under Sections 13.2.1 (Termination of Agreement for Cause) or Section 13.2.3 (Termination if Epizyme Challenges Patents Controlled by BII), as applicable, then BII shall be deemed to have elected clause (a):

(a) BII may terminate this Agreement; *provided that*, in such event, (i) Sections 13.3.2(a)-13.3.2(d) shall apply and (ii) BII may solely determine whether or not the Parties will, within [**] following BII's written notice of its decision to terminate, enter into a Transition Agreement that adheres to the requirements of Sections 13.3.2(f) and, in connection with entering into such Transition Agreement, the Parties shall negotiate with each other in good faith and set forth in such Transition Agreement commercially reasonable consideration to be paid by Epizyme to BII in connection with the assignments and licenses granted to Epizyme in such Transition Agreement; *provided, however, that* if the Parties are unable to reach agreement with respect to commercially reasonable consideration to be paid to BII within [**] following BII's written notice of its decision to terminate, then the matter shall, at the request of either Party, be submitted to arbitration using the process set forth in Schedule 13.3 to determine industry standard, commercially reasonable consideration, the results of which shall be binding on the Parties, but in all instances, the Parties agree that any such awarded consideration shall not be less than [**] percent ([**]%) of any Milestone Payments and royalties that would otherwise have been due and payable by BII to Epizyme; or

(b) (i) BII may elect not to terminate this Agreement and instead have this Agreement, including BII's licenses pursuant to this Agreement, continue in accordance with its terms; *provided that*, in such event, BII shall continue to fulfill its Milestone Payment and royalty obligations as specified herein, except that BII may reduce its Milestone Payments or royalty payments under ARTICLE 7 (Payments and Records) by [**] percent ([**]%), which shall be BII's sole remedy with respect to such breach, (ii) Epizyme shall, within [**] after the effective date of such termination, return or cause to be returned to BII, copies of all BII's Confidential Information provided by BII in connection with this Agreement, except that Epizyme may retain one copy of BII's Confidential Information solely for legal archive purposes and to exercise the licenses granted to Epizyme which survive termination of this Agreement, (iii) BII shall be released of its ongoing disclosure and information exchange obligations under this Agreement, except for information sharing that relates to (A) disclosure of Joint Technology pursuant to Section 8.1.2 (Ownership of Joint Technology), (B) the Prosecution and Maintenance of Epizyme Patents, BII Patents or Joint Patents pursuant to Section 8.2 (Maintenance and Prosecution of Patents), (C) enforcement of the Epizyme Patents, BII Patents or Joint Patents pursuant to Section 8.3 (Enforcement of Patents), (D) infringement claims brought by Third Parties pursuant to Section 8.4 (Infringement Claims by Third Parties), (E) invalidity or unenforceability actions pursuant to Section 8.5 (Invalidity or Unenforceability Defenses or Actions) or (F) a Party's indemnification obligation pursuant to ARTICLE 12 (Indemnification), (iv) the JSC and its working groups shall be disbanded and (v) if the breach relates to the Joint Product, then Epizyme shall be deemed to have provided an Opt-Out Notice to BII with respect to the Joint Product and its Development and Commercialization interests with respect to the United States pursuant to Section 5.2.5 (Epizyme Opt-Out).

13.3.2 Termination by BII Without Cause or by Epizyme for Cause, BII Patent Challenge or BII Insolvency. Upon termination of this Agreement by BII under Section 13.2.4 (Termination by BII Without Cause) or by Epizyme under Section 13.2.1 (Termination of Agreement for Cause), Section 13.2.2 (Termination if BII Challenges Epizyme Patents) or Section 13.2.5 (Termination for Insolvency), then with respect to the terminated Target Project (if this Agreement is terminated on a Target Project-by-Target Project basis) or with respect to both Target Projects (if this Agreement is terminated in its entirety), as applicable:

(a) BII's licenses pursuant to Section 6.2 (Grant to BII) shall terminate as of the effective date of termination;

(b) Epizyme's licenses pursuant to Section 6.1 (Grant to Epizyme) shall terminate as of the effective date of termination;

(c) the Parties' exclusivity obligations pursuant to Section 4.4 (Exclusivity) shall terminate;

(d) each Party shall, within [**] after the effective date of termination, destroy all copies of the other Party's Confidential Information in its possession and confirm such destruction in writing to the other Party; *provided that* the destroying Party will be permitted to retain one copy of such Confidential Information for the sole purpose of performing any continuing obligations or exercising any continuing rights hereunder (and may make additional copies of such Confidential Information for such purposes), as required by Applicable Law or for bona fide archival purposes;

(e) BII shall have no obligation to Initiate any Clinical Trial that has not already been Initiated as of the earlier of (i) the date notice was provided regarding the termination or (ii) the Effective Date of termination, with respect to each, but otherwise may have been planned (whether under the Joint Development Plan and Budget or otherwise); and

(f) Upon Epizyme's written request, such request to be made as soon as reasonably practicable and no later than: (i) [**] after the effective date of termination should Epizyme have terminated under Sections 13.2.1 (Termination of Agreement for Cause), 13.2.2 (Termination if BII Challenges Epizyme Patents) or 13.2.5 (Termination for Insolvency) or (ii) thirty (30) days following Epizyme's receipt of BII's termination notice if BII is terminating under Section 13.2.4 (Termination by BII Without Cause), the Parties shall negotiate and conclude, in good faith, within [**], a written transition agreement (the "**Transition Agreement**") pursuant to which BII and Epizyme will effect and coordinate a transition of relevant obligations and rights. The Transition Agreement shall provide (unless, in the case of clauses (1), (2) and (3) below, BII agrees to assign, rather than provide, the items described in such clauses):

(1) that BII shall provide to Epizyme with the right to use and to permit Third Parties to use, to the extent allowed by Applicable Law, the following materials within [**] following termination or as soon as reasonably possible

thereafter: (i) a list of all terminated Compounds, Products or Diagnostic Products (ii) the key samples of such Compounds, Products and Diagnostic Products, (iii) data supporting Compound Development work on potential drug substance and drug product, (iv) assay results and reports, including structural biology reports and data from biochemical and biology (in vitro and in vivo), pharmacology, toxicology, ADME/DMPK, safety, and Clinical Trial studies and (v) notebook records or reports (or copies thereof) for Clinical Trials required to support Regulatory Approvals;

- (2) that BII shall provide to Epizyme with the right to use and to permit Third Parties to use, within [**] following termination or as soon as reasonably possible thereafter, reports or data files and other results and reports Controlled by BII as of the effective date of termination and generated in and reasonably necessary for the continued Development, Manufacture or Commercialization of Compounds, Products or Diagnostic Products for Compounds or Products from terminated Target Projects, including pharmacology, toxicology, biology, ADME/DMPK, safety, and Clinical Trial data and results, batch records, formulation Information, and other Manufacturing-related Information as well as any Patent-related documents that concern such Compounds, Products or Diagnostic Products that have not already been disclosed to the Epizyme Patent Liaison pursuant to the terms of this Agreement, and all of the above always subject to any limitations as provided under Applicable Laws;
- (3) where permitted by Applicable Law, that (i) BII shall transfer to Epizyme with the right to use and to permit Third Parties to use all of its right, title and interest in all regulatory documentation then owned by BII and in its name that are solely applicable to the terminated Target Project (if terminating on a Target Project-by-Target Project basis) or both Target Projects (if terminating in its entirety), including all INDs, Drug Approval Applications, reimbursement approvals, pricing approvals, drug dossiers, master files and other regulatory filings and regulatory correspondence with Regulatory Authorities related thereto and (ii) BII shall, and does hereby, grant Epizyme a right of reference to all regulatory documentation then owned by BII and in BII's name that is necessary or reasonably useful for Epizyme, its Affiliates or its Sublicensees to Develop, Manufacture or Commercialize any Compounds, Products

or Diagnostic Products arising from the terminated Target Project (if terminating on a Target Project-by-Target Project basis) or both Target Project (if terminating in its entirety) that is not transferred to Epizyme pursuant to clause (i), as such regulatory documentation exists as of the effective date of such termination;

- (4) that BII shall notify the applicable Regulatory Authorities and take any other action reasonably necessary to effect the transfers and the right of reference set forth in clauses (2) and (3) above;
- (5) that (i) if Epizyme elects, upon written notice to BII, not to continue a Clinical Trial being Conducted by BII with respect to a terminated Target Project as of the effective date of termination, then BII shall wind-down and closeout such Clinical Trial at BII's cost and expense, unless BII is prohibited from doing so based on Applicable Law or by any Regulatory Authority and (ii) if Epizyme elects, upon written notice to BII, to continue a Clinical Trial being Conducted by BII with respect to a terminated Target Project as of the effective date of termination, then, unless BII is prohibited from doing so based on Applicable Law or by any Regulatory Authority, BII shall continue to Conduct such Clinical Trial on behalf of Epizyme (A) if such Clinical Trial is for a BII Product, then at Epizyme's cost and (B) if such Clinical Trial is for a Joint Product in the Territory, then BII will remain responsible for its share of Committed Costs with respect to such Clinical Trial as set forth in Section 5.2.1(b)(iv) (Allocation). BII will Conduct such Clinical Trial on behalf of Epizyme until such time as BII is able to transfer control of such Clinical Trial to Epizyme without interruption, pursuant to the Transition Agreement;
- (6) that, at Epizyme's written election, BII shall assign (or cause its Affiliates to assign) to Epizyme all agreements with any Third Party that solely relate to Compounds, Products or Diagnostic Products for Compounds or Products from terminated Target Projects, including any agreement with respect to the Manufacture of such Compounds, such Products or Diagnostic Products for such Compounds or Products and any conduct of pre-clinical Development activities or Clinical Trials for such Compounds, such Products or Diagnostic Products for such Compounds or Products, such as agreements with contract research organizations, clinical sites, investigators and

manufacturing providers, unless, with respect to any such agreement, such agreement (i) expressly prohibits such assignment or (ii) covers Clinical Trials for Combination Products in which any active ingredient that is not a BII Compound or Joint Compound is covered by Patents Controlled by BII or any of its Affiliates. For the avoidance of doubt, to the extent that Epizyme does not request such assignments be made by the earlier of (A) the effective date of the Transition Agreement or (B) within [**] following the effective date of termination, BII shall be entitled to terminate or take any other action with respect to such Third Party agreements, as solely determined by BII;

- (7) that, at Epizyme's written election, BII or its permitted Affiliates or Contractors, as applicable, shall Manufacture and supply Compounds, Products or Diagnostic Products for Compounds or Products from terminated Target Projects to Epizyme (and only to the extent BII currently performs such activities for its own account as of the effective date of termination) until the earlier of (i) [**] following termination, (ii) the assignment to Epizyme of all Third Party agreements that provide for the Manufacture of such Compounds, such Products or Diagnostic Products for such Compounds or Products in accordance with clause (6) or (iii) Epizyme qualifying a Third Party to Manufacture such Compounds, such Products or Diagnostic Products for such Compounds or Products. The manufacture and supply of any such Compounds, Products or Diagnostic Products for such Compounds or Products directly by BII or its Affiliates shall be sold to Epizyme at a negotiated price reflected in the Transition Agreement, not to exceed BII's costs plus [**] percent ([**]%) or, if supplied under a Third Party agreement assigned under subclause (6) hereof, in accordance with the terms of such agreement. If Epizyme requests that BII transfer to Epizyme processes, documents, materials or Information, to the extent Controlled by BII as of the effective date of termination, that are necessary for and used in the Manufacture of Compounds, Products or Diagnostic Products for Compounds or Products, this technology transfer shall be completed at Epizyme's expense;
- (8) that, at Epizyme's written election, BII shall sell to Epizyme, at cost, all or any specified portion of any Compounds, Products and Diagnostic Products for Compounds or Products from terminated Target Projects that are in inventory or in-process as of the effective date of

termination; *provided, however, that*, should any terminated Products be commercialized by BII within any country in the Territory, BII shall have the first right, if BII so elects, to sell such remaining inventory of such Product within [**] following the effective date of termination, so long as BII continues to sell such Product in accordance with the then-existing Joint Commercialization Plan and Budget (including with respect to price) and pays the royalties or share of profits to Epizyme in connection with such sales pursuant to Section 5.2.2(c) (Profit Share) or Section 7.4 (Royalties), as applicable;

- (9) that BII shall assign to Epizyme all right, title, and interest of BII in each Product Trademark;
- (10) (A) BII shall either, as solely determined by BII:
 - (i) grant to Epizyme, exercisable from and after such termination, an exclusive, worldwide, license, with the right to grant sublicenses (through multiple tiers), under BII's and its Affiliates' interest in the Joint Know-How and Joint Patents, solely to the extent that such licenses are necessary to research, Develop, make, have made, use, offer for sale, sell, export and import Compounds, Products and Diagnostic Products for Compounds and Products in the Field in the Territory; or
 - (ii) assign its rights and interest in the Joint Patents, and grant to Epizyme an exclusive, worldwide, license, with the right to grant sublicenses (through multiple tiers), under BII's and its Affiliates' interest in all other Joint Know-How, solely to the extent that such assignment and license is necessary to research, Develop, make, have made, use, offer for sale, sell, export and import such Compounds, Products and Diagnostic Products for Compounds and Products in the Field in the Territory.
- (B) BII shall grant to Epizyme a worldwide, perpetual, irrevocable, exclusive, sublicensable (through multiple tiers) license, under BII Know-How and BII Patents, solely to the limited extent to continue to research,

Develop, make, have made, use, offer for sale, sell, export and import such Compounds, Products and Diagnostic Products for Compounds and Products in the Field in the Territory.

- (C) The Parties shall negotiate with each other, in good faith, commercially reasonable consideration to be paid to BII concerning the rights, assignments and licenses granted in clauses (A) and (B) above; *provided, however, that*, if the Parties are unable to reach agreement within the allotted timeframe with respect to the commercially reasonable consideration to be paid to BII, the matter shall, at the request of either Party, be submitted to arbitration using the process set forth in Schedule 13.3 to determine industry standard, commercially reasonable consideration to be paid to BII, the results of which shall be binding on the Parties, but in all instances, the Parties agree that should BII have **[**]** for any Product, any such awarded consideration shall not be less than **[**]** percent (**[**]**%) of any Milestone Payments and Royalties that would otherwise have been due and payable by BII to Epizyme for such Product.
- (D) In the event that BII grants to Epizyme an exclusive license or assigns Joint Patents to Epizyme under Section 13.3.2(f)(10)(A), Epizyme shall be solely responsible for the Prosecution and Maintenance of such Joint Patents and with respect to any such Joint Patent, Epizyme shall have the first right to enforce such Joint Patent with respect to an infringement by a Third Party infringing the relevant Joint Patent by making, using or selling a product that competes with the relevant Product. In the event that BII grants to Epizyme an exclusive license under Section 13.3.2(f)(10)(B) with respect to any BII Patents or BII Know-How, BII shall determine whether BII or Epizyme shall have the first right to (i) Prosecute and Maintain and enforce such BII Patents with respect to an infringement by a Third Party infringing the relevant BII Patent by making, using or selling a product that competes with the relevant Product and (ii) enforce a legal claim with respect to the misappropriation or unauthorized use of the BII Know-How by a Third Party in the context of making, using or selling a product that competes with the relevant Product.

- (11) The Transition Agreement shall make clear that Epizyme shall be responsible for (i) making any payments (including royalties, milestones and other amounts) arising out of Epizyme's exercise of the rights assigned or granted in Section 13.3.2(f)(10) and payable by BII to Third Parties under any Third Party agreements that may be licensed or assigned to Epizyme by BII by making such payments directly to BII (in case of a license) or such Third Party (in case of an assignment) and, in each instance, Epizyme shall make the requisite payments to BII or the Third Party as applicable and provide the necessary reporting information to BII in sufficient time to enable BII to comply with its obligations under such Third Party agreements and (ii) complying with any other obligations included in any such Third Party agreements that are applicable to the grant to Epizyme of such license or to the exercise of such license by Epizyme or any of its Affiliates or Sublicensees.

13.4. Effects of Expiration and Termination. Upon any expiration or termination of this Agreement with respect to a given Product or in its entirety, (a) all amounts due or payable to a Party that were accrued, or that arise out of acts or events occurring prior to the effective date of expiration or termination, shall remain due and payable and (b) neither Party shall be relieved of any obligation that accrued prior to the effective date of such expiration or termination.

13.5. Remedies. Termination of this Agreement (either in its entirety or with respect to one or more Target Projects) in accordance with the provisions hereof will not limit remedies that may otherwise be available in law or equity.

13.6. Survival. Termination or expiration of this Agreement (either in its entirety or with respect to one or more Target Projects) for any reason will be without prejudice to any rights that will have accrued to the benefit of a Party prior to such termination or expiration. Such termination or expiration will not relieve a Party from obligations that are expressly indicated to survive the termination or expiration of this Agreement. Without limiting the foregoing (i) Sections 4.3.1(b) (Provision of Materials) (with respect to Epizyme continuing to support BII in matters related to taxes and customs for Materials shipped to BII prior to expiration or termination of this Agreement), 4.3.3 (Limitations), 4.3.4 (Disclaimer), 5.2.1(b)(iv) (Allocation) (solely with respect to costs incurred prior to expiration or termination), 5.2.1(d) (Reporting and Reconciliation Payments; Overruns), 5.2.2(a)(iv) (Allocation) (solely with respect to amounts incurred prior to expiration or termination), 5.2.2(c) (Profit Share), 5.4 (Recalls), 6.1.2 (Research Grant), 6.6 (Retention of Rights), 6.7 (Recordation), 7.4.2 (Royalty Term), 7.10 (Audit; Audit Dispute), 8.1 (Ownership of Intellectual Property), 8.7.1 (Ownership and Prosecution of Product Marks), 9.2 (Global Safety Database), 11.4 (Disclaimer), 13.3 (Effects of Termination), 13.4 (Effects of Expiration), 13.5 (Remedies) and 13.6 (Survival) and (ii) ARTICLE 1 (Definitions), ARTICLE 7 (Payments and Records) (solely with respect to amounts incurred prior to expiration or termination), ARTICLE 10 (Confidentiality and Non-Disclosure), ARTICLE 12 (Indemnity) and ARTICLE 14 (Miscellaneous), with respect to each, of this Agreement will survive the termination or expiration of this Agreement for any reason.

ARTICLE 14
MISCELLANEOUS

14.1. Force Majeure. Neither Party will be held liable or responsible to the other Party or be deemed to have defaulted under or breached this Agreement for failure or delay in fulfilling or performing any term of this Agreement when such failure or delay is caused by or results from events beyond the reasonable control of the non-performing Party, including fires, floods, earthquakes, hurricanes, embargoes, shortages, epidemics, quarantines, war, acts of war (whether war be declared or not), terrorist acts, insurrections, riots, civil commotion, strikes, lockouts, or other labor disturbances (whether involving the workforce of the non-performing Party or of any other Person), acts of God or acts, omissions or delays in acting by any governmental authority (except to the extent such delay results from the breach by the non-performing Party or any of its Affiliates of any term or condition of this Agreement). The non-performing Party will notify the other Party of such force majeure within [**] after such occurrence by giving written notice to the other Party stating the nature of the event, its anticipated duration, and any action being taken to avoid or minimize its effect. The suspension of performance will be of no greater scope and no longer duration than is necessary and the non-performing Party will use commercially reasonable efforts to remedy its inability to perform.

14.2. Change in Control. Epizyme (or its successor) shall provide BII with written notice of its Change in Control promptly and no later than [**] following the closing date of such transaction. Upon a Change in Control of Epizyme, the following shall occur:

14.2.1 U.S. Commercialization Rights. Within [**] following BII's receipt of Epizyme's (or its successor's) notice of Epizyme's Change in Control, BII may elect, upon written notice to Epizyme, to terminate Epizyme's Development rights, responsibilities and obligations (other than any Research Activities with respect to the Joint Compound that are set forth in the Research Plan if such Change in Control occurs [**] of the Joint Compound) and Commercialization rights, responsibilities and obligations with respect to the Joint Compound and Joint Product in the U.S. and vest all such rights, responsibilities and obligations for the Joint Compound and Joint Product in BII. In such event, Epizyme (or its successor) shall have no further obligation to, and shall cease to, perform Development activities (other than any Research Activities to be performed under the Research Plan provided such Change in Control occurs [**]) and Commercialization activities with respect to such Joint Compound or Joint Product in the United States, which cessation will occur pursuant to a mutually agreed to transition plan that will wind-down Epizyme's performance of (a) Development activities as soon as reasonably practicable following the effective date of the opt-out (subject to the requirement that Epizyme continue to perform its obligations with respect to the Research Activities under the Research Plan if the Opt-Out Notice is provided prior to [**] as set forth in the first sentence of this Section 5.2.5 (Epizyme Opt-Out)) and using reasonable efforts to avoid unnecessary Development disruptions and (b) Commercialization activities over a period of not more than [**] following Epizyme's receipt of BII's written notice and using reasonable efforts to avoid unnecessary Commercialization disruptions. For the avoidance of doubt, upon the completion of the Epizyme activities described in (a)-(b) and reflected in the transition plan, the license grants under Section 6.1.1 (Grant to Epizyme) shall expire and terminate. If BII does not provide Epizyme with such written notice within the aforementioned [**] period, then BII shall be deemed to have waived its right to terminate Epizyme's

Development and Commercialization rights, responsibilities and obligations with respect to the Joint Compound and Joint Product in the U.S. and to vest all such rights, responsibilities and obligations for the Joint Compound and Joint Product in BII pursuant to this Section 14.2.1 (U.S. Commercialization Rights).

14.2.2 Financial Ramifications. If BII elects to assume Epizyme's U.S. Development and Commercialization rights, responsibilities and obligations with respect to the Joint Product pursuant to Section 14.2.1 (U.S. Commercialization Rights), then, if such Change in Control of Epizyme: (a) occurs [**] with respect to such Joint Product, then the Development Cost share set forth in Section 5.2.1(b)(iv) (Allocation) and the 50:50 profit and cost share set forth in Section 5.2.2(a)(iv) (Allocation) shall cease with respect to such Joint Product and, instead, BII shall pay Epizyme the Opt-Out Royalties pursuant to Section 5.2.5 (Epizyme Opt-Out) on future Net Sales of such Joint Product in the U.S.; and (b) occurs [**] with respect to such Joint Product, then the Development Cost share set forth in Section 5.2.1(b)(iv) (Allocation) and the 50:50 profit and cost share set forth in Section 5.2.2(a)(iv) (Allocation) shall continue with respect to such Joint Product in the U.S. in accordance with the terms of this Agreement, with the Parties agreeing that from the end of the transition plan, all Development Costs and Allowable Expenses shall be fully incurred by BII since all Development and Commercialization rights shall rest with BII, and any and all types of Development Costs and Allowable Expenses incurred by BII shall no longer be subject to a Joint Development Plan and Budget and a Joint Commercialization Plan and Budget; *provided that* the foregoing shall not preclude Epizyme from electing its opt-out option with respect to such Joint Product pursuant to Section 5.2.5 (Epizyme Opt-Out) at a future date.

14.3. Export Control. This Agreement is made subject to any restrictions concerning the export of products or technical Information from the United States or other countries that may be imposed on the Parties from time to time. Each Party agrees that it will not export, directly or indirectly, any technical Information acquired from the other Party under this Agreement or any products using such technical Information to a location or in a manner that at the time of export requires an export license or other governmental approval, without first obtaining the written consent to do so from the appropriate agency or other governmental entity in accordance with Applicable Law.

14.4. Assignment. Without the prior written consent of the other Party, such consent not to be unreasonably withheld, conditioned or delayed, neither Party will sell, transfer, assign, delegate, pledge or otherwise dispose of, whether voluntarily, involuntarily, by operation of law or otherwise, this Agreement or any of its rights or duties hereunder; *provided that* each Party may make such an assignment without the other Party's consent to its Affiliate or to a successor, whether in a merger, sale of stock or sale of substantially all of its assets that relate to this Agreement. With respect to an assignment to an Affiliate, the assigning Party will remain responsible for the performance by such Affiliate of the rights and obligations hereunder. Any attempted assignment or delegation in violation of this Section 14.4 (Assignment) will be void and of no effect. All validly assigned and delegated rights and obligations of the Parties hereunder will be binding upon and inure to the benefit of and be enforceable by and against the successors and permitted assigns of Epizyme or BII, as the case may be. The permitted assignee or transferee will assume all obligations of its assignor or transferor under this Agreement.

14.5. Severability. If any provision of this Agreement is held to be illegal, invalid or unenforceable under any present or future law, and if the rights or obligations of either Party under this Agreement will not be materially and adversely affected thereby: (a) such provision will be fully severable; (b) this Agreement will be construed and enforced as if such illegal, invalid or unenforceable provision had never comprised a part hereof; (c) the remaining provisions of this Agreement will remain in full force and effect and will not be affected by the illegal, invalid, or unenforceable provision or by its severance herefrom; and (d) in lieu of such illegal, invalid or unenforceable provision, there will be added automatically as a part of this Agreement a legal, valid and enforceable provision as similar in terms to such illegal, invalid, or unenforceable provision as may be possible and reasonably acceptable to the Parties. To the fullest extent permitted by Applicable Law, each Party hereby waives any provision of law that would render any provision hereof illegal, invalid, or unenforceable in any respect.

14.6. Governing Law; Service.

14.6.1 Governing Law. This Agreement or the performance, enforcement, breach or termination hereof will be interpreted, governed by and construed in accordance with the laws of the State of New York, excluding any conflicts or choice of law rule or principle that might otherwise refer construction or interpretation of this Agreement to the substantive law of another jurisdiction. The Parties agree to exclude the application to this Agreement of the United Nations Convention on Contracts for the International Sale of Goods.

14.6.2 Service. Each Party further agrees that service of any process, summons, notice or document by registered mail to its address set forth in Section 14.8.2 (Address for Notices) will be effective service of process for any action, suit, or proceeding brought against it under this Agreement in any such court.

14.7. Dispute Resolution. Except for disagreements resolved by the procedures set forth in Sections 2.2.3 (Disagreement Resolution), 7.10 (Audit; Audit Dispute) or 14.11 (Equitable Relief), if a dispute arises between the Parties in connection with or relating to this Agreement or any document or instrument delivered in connection herewith, it will be resolved pursuant to this Section 14.7 (Dispute Resolution).

14.7.1 General. Any dispute will first be referred to the Senior Officers of the Parties, who will confer in good faith on the resolution of the issue. Any final decision mutually agreed to by the Senior Officers will be conclusive and binding on the Parties. If the Senior Officers are not able to agree on the resolution of any such issue within **[**]** (or such other period of time as mutually agreed by the Senior Officers) after such issue was first referred to them, then either Party may, by written notice to the other Party, elect to initiate an alternative dispute resolution proceeding pursuant to the procedures set forth in Section 14.7.2 (ADR; Arbitration) for purposes of having the matter settled.

14.7.2 ADR; Arbitration. If the Parties do not finally and fully resolve a dispute pursuant to Section 14.7.1 (General) and a Party wishes to pursue the matter further, then each such dispute that is not an Excluded Claim shall be finally resolved by binding arbitration in accordance with the Rules of Arbitration of the ICC and judgment on the arbitration award may be entered in any court having jurisdiction thereof.

(a) Except as provided below in this Section 14.7.2(a), the arbitration shall be conducted by a panel of three (3) Persons. Within [**] after initiation of arbitration, each Party shall select one (1) Person to act as arbitrator and the two (2) Party-selected arbitrators shall select a third (3rd) arbitrator within [**] after their appointment. If the dispute involves claims for damages of less than USD [**] (\$[**]), there shall be only one (1) arbitrator, nominated jointly by the Parties within [**] days of initiation of arbitration. If any arbitrator is not nominated within these time periods, the ICC Court of Arbitration shall appoint such arbitrator. The place of arbitration shall be London, United Kingdom, and all proceedings and communications shall be in English.

(b) Either Party may apply to the arbitrators for interim injunctive relief until the arbitration award is rendered or the dispute is otherwise resolved. Either Party also may also, without waiving any remedy under this Agreement, seek from any court having jurisdiction any injunctive or provisional relief necessary to protect the rights or property of that Party pending the arbitration award. The scope of the authority of the arbitrators shall be limited to the strict application of law. The arbitrators shall have no authority to award punitive or any other type of damages not measured by a Party's compensatory damages, except as permitted by Section 12.4 (No Consequential Damages). Each Party participating in an arbitration pursuant to the terms of this Agreement shall, subject to the award of the arbitrators, pay an equal share of the arbitrators' fees. The arbitrators shall have the power to award recovery of all costs (including reasonable attorney's fees, administrative fees, arbitrators' fees and court costs) to the prevailing Party.

(c) Neither Party shall be required to give general discovery of documents, but may be required to produce documents or testimony that are relevant or considered relevant by the arbitrators to the dispute. It is the objective and intent of the Parties that any arbitration proceeding be conducted in such a manner that a decision will be rendered by the arbitrators within [**] after the third arbitrator is appointed to the panel, and the Parties and the panel selected in the manner provided above will adopt rules and procedures intended to implement such objective and intent.

(d) Except to the extent necessary to confirm or vacate an award or as may be required by Applicable Law (including applicable securities laws or the rules of any stock exchange on which a Party's securities may then be listed), neither a Party nor an arbitrator may disclose the existence, content, or results of arbitration without the prior written consent of both Parties. In no event shall arbitration be initiated after the date when commencement of a legal or equitable proceeding based on the dispute, controversy or claim would be barred by the applicable New York statute of limitations.

(e) The Parties agree that any payment made pursuant to this Agreement pending resolution of the dispute shall be refunded or credited if the arbitrators or court determines that such payments are not due.

(f) As used in this Section, the term "**Excluded Claim**" shall mean a dispute that concerns (i) the validity, enforceability, scope or infringement of a Patent, Trademark or copyright; or (ii) any antitrust, anti-monopoly or competition law or regulation, whether or not statutory.

14.7.3 Adverse Ruling. Any determination pursuant to this Section 14.7 (Dispute Resolution) that a Party is in material breach of its material obligations hereunder will specify a (nonexclusive) set of actions to be taken to cure such material breach, if feasible.

14.8. Notices.

14.8.1 Notice Requirements. Any notice, request, demand, waiver, consent, approval or other communication permitted or required under this Agreement will be in writing, will refer specifically to this Agreement and will be deemed given only if (a) delivered by hand or (b) by internationally recognized overnight delivery service that maintains records of delivery, addressed to the Parties at their respective addresses specified in Section 14.8.2 (Address for Notice) or to such other address as the Party to whom notice is to be given may have provided to the other Party in accordance with this Section 14.8.1 (Notice Requirements). Such notice will be deemed to have been given as of the date delivered by hand or on the second Business Day (at the place of delivery) after deposit with an internationally recognized overnight delivery service. This Section 14.8.1 (Notice Requirements) is not intended to govern the day-to-day business communications necessary between the Parties in performing their obligations under the terms of this Agreement.

14.8.2 Address for Notice.

If to Epizyme, to:

Epizyme, Inc.
400 Technology Square, 4th Floor
Attention: Chief Executive Officer
Email: [**]

with a copy (which will not constitute notice) to:

Ropes & Gray LLP
800 Boylston Street, Prudential Tower
Boston, MA 02199, USA
Attention: Marc Rubenstein
Email: marc.rubenstein@ropesgray.com

If to BII, to:

Boehringer Ingelheim Corporate Center GmbH
Attn: Head of Strategic Transactions & Alliance Management
Binger Strasse 173
55216 Ingelheim am Rhein
Germany

with a copy (which will not constitute notice) to:

Boehringer Ingelheim Corporate Center GmbH
Attn: Head of Corporate Legal IU
(same address as above)

14.9. Entire Agreement; Amendments. This Agreement, together with the Schedules attached hereto, sets forth and constitutes the entire agreement and understanding between the Parties with respect to the subject matter hereof and all prior agreements, understandings, promises and representations, whether written or oral, with respect thereto are superseded hereby. Each Party confirms that it is not relying on any representations or warranties of the other Party except as specifically set forth in this Agreement. No amendment, modification, release, or discharge will be binding upon the Parties unless in writing and duly executed by authorized representatives of both Parties.

14.10. English Language. This Agreement will be written and executed in, and all other communications under or in connection with this Agreement will be in, the English language. Any translation into any other language will not be an official version thereof, and in the event of any conflict in interpretation between the English version and such translation, the English version will control.

14.11. Equitable Relief. Section 14.7 (Dispute Resolution) notwithstanding, each Party acknowledges and agrees that remedies available at law for a breach or threatened breach of any of this Agreement may be inadequate and, in recognition of this fact, each Party agrees that, in addition to any remedies available at law (including, without limitation, damages), equitable relief in the form of specific performance, a temporary restraining order, a temporary or permanent injunction or any other equitable remedy shall be available in the event of a breach or threatened breach of this Agreement, without the need for the Party seeking such remedy to post a bond in connection therewith.

14.12. Waiver and Non-Exclusion of Remedies. Any term or condition of this Agreement may be waived at any time by the Party that is entitled to the benefit thereof, but no such waiver will be effective unless set forth in a written instrument duly executed by or on behalf of the Party waiving such term or condition. The waiver by either Party hereto of any right hereunder or of the failure to perform or of a breach by the other Party will not be deemed a waiver of any other right hereunder or of any other breach or failure by such other Party whether of a similar nature or otherwise. The rights and remedies provided herein are cumulative and do not exclude any other right or remedy provided by Applicable Law or otherwise available except as expressly set forth herein.

14.13. No Benefit to Third Parties. Except as set forth ARTICLE 12 (Indemnity), the covenants and agreements set forth in this Agreement are for the sole benefit of the Parties hereto and their successors and permitted assigns, and they will not be construed as conferring any rights on any other Persons.

14.14. Further Assurance. Each Party will duly execute and deliver, or cause to be duly executed and delivered, such further instruments and do and cause to be done such further acts and things, including the filing of such assignments, agreements, documents, and instruments, as may be necessary or as the other Party may reasonably request in connection with this Agreement or to carry out more effectively the provisions and purposes hereof, or to better assure and confirm unto such other Party its rights and remedies under this Agreement.

14.15. Relationship of the Parties. It is expressly agreed that BII, on the one hand, and Epizyme, on the other hand, will be independent contractors and that the relationship between the Parties will not constitute a partnership, joint venture, or agency, including for all tax purposes. Neither BII, on the one hand, nor Epizyme, on the other hand, will have the authority to make any statements, representations or commitments of any kind, or to take any action, which will be binding on the other, without the prior written consent of the other Party to do so. All Persons employed by a Party will be employees of such Party and not of the other Party and all costs and obligations incurred by reason of any such employment will be for the account and expense of such Party.

14.16. Counterparts; Execution. This Agreement may be executed in two (2) or more counterparts, each of which will be deemed an original, but all of which together will constitute one and the same instrument. This Agreement may be executed by electronically transmitted signatures and such signatures will be deemed to bind each Party hereto as if they were original signatures.

14.17. References. Unless otherwise specified, (a) references in this Agreement to any ARTICLE, Section or Schedule will mean references to such ARTICLE, Section or Schedule of this Agreement, (b) references in any Section to any clause are references to such clause of such Section and (c) references to any agreement, instrument, or other document in this Agreement refer to such agreement, instrument or other document as originally executed or, if subsequently amended, replaced, or supplemented from time to time, as so amended, replaced, or supplemented and in effect at the relevant time of reference thereto.

14.18. Construction. Except where the context otherwise requires, wherever used, the singular will include the plural and the plural the singular, the use of any gender will be applicable to all genders and the word “or” is used in the inclusive sense (and/or). Whenever this Agreement refers to a number of days, unless otherwise specified, such number refers to calendar days. The captions of this Agreement are for convenience of reference only and in no way define, describe, extend, or limit the scope or intent of this Agreement or the intent of any provision contained in this Agreement. The term “including,” “include,” or “includes” as used herein will mean “including, but not limited to,” and will not limit the generality of any description preceding such term. The language of this Agreement will be deemed to be the language mutually chosen by the Parties and no rule of strict construction will be applied against either Party hereto. Each Party represents that it has been represented by legal counsel in connection with this Agreement and acknowledges that it has participated in the drafting hereof. In interpreting and applying the terms and provisions of this Agreement, the Parties agree that no presumption will apply against the Party which drafted such terms and provisions.

[SIGNATURE PAGE FOLLOWS]

IN WITNESS WHEREOF, the Parties, through their duly authorized representatives, have entered into this Agreement as of the Effective Date.

**BOEHRINGER INGELHEIM INTERNATIONAL
GMBH**

ppa.

By: Dr. Jochen Gann

Name: Dr. Jochen Gann

Title: Head of CDept. Finance

ppa.

By: /s/ Dorothee Schwall-Rudolph

Name: Dorothee Schwall-Rudolph

Title: Head of Corp. Legal IU

EPIZYME, INC.

By: /s/ Robert Bazemore Jr.

Name: Robert Bazemore Jr.

Title: President & CEO

Schedule 1.40

Compound Criteria

[]Compound Criteria**

[**]

Schedule 1.48

[] Competing Product Criteria**

[**]

Schedule 1.81

FTE Rate

During Calendar Year 2019, the FTE Rate for all FTEs shall be set at a flat rate of [**] U.S. Dollars (\$[**]) per FTE.

Beginning with Calendar Year 2020 (and for each subsequent Calendar Year) the FTE Rate for all FTEs shall be increased or decreased by the percentage increase or decrease, if any, observed in the Consumer Price Index (“CPI”) based on the ‘Annual’ data for Calendar Year 2019 in relation to Calendar Year 2018, where “Consumer Price Index” means the Consumer Price Index – Urban Wage Earners and Clerical Workers, US City Average, All Items, 1982-84 = 100, published by the US Department of Labor, Bureau of Labor Statistics (or its successor equivalent index) , as further reflected in the relevant ‘Annual’ column of data in the below table, taken from the referenced index. For each subsequent Calendar Year, the similar methodology shall be applied to arrive at the appropriate increase or decrease in the FTE Rate for such Calendar Year.

CPI-Urban Wage Earners and Clerical Workers (Current Series)

Series Id:	CWUR0000SA0														
Not Seasonally Adjusted															
Area:	U.S. city average														
Item:	All items														
Base Period:	1982-84=100														
Top of Form															
Download:	Bottom of Form														
Year	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Annual	Half1	Half2
2007	197.559	198.544	200.612	202.130	203.661	203.906	203.700	203.199	203.889	204.338	205.891	205.777	202.767	201.069	204.466
2008	206.744	207.254	209.147	210.698	212.788	215.223	216.304	215.247	214.935	212.182	207.296	204.813	211.053	210.309	211.796
2009	205.700	206.708	207.218	207.925	208.774	210.972	210.526	211.156	211.322	211.549	212.003	211.703	209.63	207.883	211.377
2010	212.568	212.544	213.525	213.958	214.124	213.839	213.898	214.205	214.306	214.623	214.750	215.262	213.967	213.426	214.507
2011	216.400	217.535	220.024	221.743	222.954	222.522	222.686	223.326	223.688	223.043	222.813	222.166	221.575	220.196	222.954
2012	223.216	224.317	226.304	227.012	226.600	226.036	225.568	227.056	228.184	227.974	226.595	225.889	226.229	225.581	226.878
2013	226.520	228.677	229.323	228.949	229.399	230.002	230.084	230.590	230.537	229.735	229.138	229.174	229.324	228.812	229.837
2014	230.04	230.871	232.56	232.56	234.216	234.702	234.525	234.030	234.170	233.229	231.551	229.909	232.771	232.639	232.902
2015	228.294	229.421	231.065	231.520	232.908	233.804	233.806	233.366	232.661	232.373	231.721	230.791	231.810	231.167	232.453
2016	231.061	230.972	232.209	233.438	234.436	235.289	234.771	234.904	235.495	235.732	235.215	235.39	234.076	232.901	235.251
2017	236.854	237.477	237.656	238.432	238.609	238.813	238.617	239.448	240.939	240.573	240.666	240.526	239.051	237.974	240.128

However, during the Term of this Agreement, in no instance shall the FTE Rate be adjusted below [**] U.S. Dollars (\$[**]) per FTE nor shall it exceed [**] U.S. Dollars (\$[**]) per FTE.

Schedule 1.97

Invoice Requirements

Invoices to be sent to:

Boehringer Ingelheim International GmbH
Accounts Payable
HPZ: [**]
Binger Strasse 173
55216 Ingelheim am Rhein
GERMANY

Quote the BI in-house contact person in a corresponding reference field or anywhere on the invoice/credit note outside of the address field:

Contact: [**]

Invoices to contain the following information:

- Name and address of the providing (contracting) companyas listed in the agreement
- Name and address of the recipient (e.g. Boehringer Ingelheim International GmbH)
- Taxpayer Identification No. of the recipient (e.g. Boehringer Ingelheim International GmbH: DE [**])
- Taxpayer Identification No. of providing party (if applicable)
- Date of invoice
- Invoice Due Date (as reflected in agreement)
- Invoice No.
- Contract No. of invoicing party
- Boehringer Ingelheim Contract No. [**]
 - For milestone payments invoice shall indicate specific Compound or Product, if applicable (please adapt wording to specific contract)
 - Time/period of deliveries or services
 - Description of Services
 - Amount due and currency
 - Reverse Charge Clause (not applicable)
 - Electronic Funds Transfer Instructions to include the below information:
 - Name and address of the invoicing party's bank
 - Routing Number
 - Account Number
 - Swift Code
 - IBAN Number
- Additional details are required for VAT purposes

The invoice must be in accordance to the actual tax law to the extent known to the invoicing Party

Schedule 1.156

Research Plan

Overall Objectives

For the [**] Target Project, the overall research objective is to [**] with respect thereto are outlined below in the Research Plan.

For the [**] Target Project, the overall research objective is [**] are outlined below in the Research Plan.

The Research Plan outlines the resources and research activities that are currently expected to be needed in order to successfully achieve the overall objectives for the [**] Target Project and [**] Target Project, based on the [**]. Pursuant to Section 3.3 of the Agreement, the Research Plan will be periodically reviewed and updated by the Parties as necessary pursuant to the terms of the Agreement and based on the progress and results that are made as the Target Projects advance.

Confidential Materials omitted and filed separately with the Securities and Exchange Commission. A total of 65 pages were omitted.

[**]

Schedule 1.164

[] Competing Product Criteria**

[**]

Schedule 10.4

Press Release

Boehringer Ingelheim and Epizyme Announce Worldwide Collaboration to Develop Novel Epigenetic Oncology Therapies

Boehringer Ingelheim Expands Biomarker-driven Oncology Programs

Alliance Enhances Epizyme's Leadership in Oncology Epigenetics

CAMBRIDGE, Mass. and INGELHEIM, Germany, [Insert Date], 2018 -- Boehringer Ingelheim and Epizyme, Inc. (Nasdaq: EPZM) today announced a new global collaboration focused on the research, development and commercialization of novel small molecule inhibitors directed toward two previously unaddressed epigenetic targets as potential therapies for people with cancer. Specifically, these targets are enzymes within the helicase and histone acetyltransferase (HAT) families that when dysregulated have been linked to the development of cancers that currently lack therapeutic options.

“Boehringer Ingelheim’s collaboration with Epizyme furthers our strategic vision to profoundly impact the oncology treatment landscape by enabling a new generation of precision medicines,” said Clive R. Wood, Ph.D., Senior Corporate Vice President, Discovery Research, Boehringer Ingelheim. “We are excited to launch this partnership with Epizyme and to work together with them to advance epigenetic inhibitors that have the potential to transform the lives of patients and help win the fight against difficult-to-treat cancers.”

Epigenetic modification affects how genes are biologically regulated. More than half of cancers can stem from functional errors in epigenetic modification. In particular cases, epigenetic dysregulation is associated with alterations in specific components of gene regulation, which can be used to identify patients most likely to benefit from the therapy. What makes both targets compelling is not only the clear role they play in cancer but that both targets have patient stratification biomarkers, which will enable a focus on the patients most likely to benefit from these potential treatments. Epizyme is a leader in the discovery of the roles of such enzymes and their development as therapy targets.

“This partnership with Boehringer Ingelheim to develop treatments for two novel epigenetic targets, which have been historically viewed as undruggable, further validates the promise of epigenetics for oncology and our pioneering leadership in this field,” said Robert Bazemore, president and chief executive officer of Epizyme. “By combining our innovative target identification and research capabilities with Boehringer Ingelheim’s world-class drug development and commercialization expertise, we are aiming to realize the full potential of these targets and our platform, while continuing to focus on executing development of our lead program in multiple ongoing and planned clinical trials.”

The collaboration has a strategic goal to focus on lung and other solid tumor cancers in patients with defined mutations, sub-populations that currently lack precision medicine treatments. Under

the terms of the agreement, Boehringer Ingelheim and Epizyme will jointly research and develop a helicase program, with both parties sharing U.S. commercialization responsibilities and Boehringer Ingelheim assuming responsibility for commercialization outside the U.S. Epizyme and Boehringer Ingelheim will share research responsibilities for the HAT program, with Boehringer Ingelheim assuming responsibility for worldwide development and commercialization.

Epizyme will receive an upfront payment of \$15 million and an additional \$5 million in research funding in 2019. Epizyme is eligible to receive more than \$280 million in additional payments for research, development, regulatory and commercial milestones. For the helicase program, Epizyme will fund a portion of the global development costs, retain a share of U.S. profits and receive tiered royalties on ex-U.S. sales. For the HAT program, Epizyme is eligible to receive tiered royalties on worldwide sales.

About Helicases and HATs

Helicases are ATP-dependent enzymes that act as molecular motors to unwind and remodel the nucleic acids that compose DNA and RNA. The human genome has a large helicase gene family of more than 100 members, some of which have been linked to multiple cancers when dysregulated.

The family of HATs includes 18 enzymes that add acetyl groups to proteins including histones. Acetylation, along with such other modifications as methylation and phosphorylation, affects how histones interact with DNA. These changes in the structural support provided to chromosomes in turn influence gene expression. Changes in histones, including dysregulated acetylation, have been associated with diseases including multiple cancers.

About Boehringer Ingelheim

Improving the health and quality of life of patients is the goal of the research-driven pharmaceutical company Boehringer Ingelheim. The focus in doing so is on diseases for which no satisfactory treatment option exists to date. The company therefore concentrates on developing innovative therapies that can extend patients' lives. In animal health, Boehringer Ingelheim stands for advanced prevention.

Family-owned since it was established in 1885, Boehringer Ingelheim is one of the pharmaceutical industry's top 20 companies. Some 50,000 employees create value through innovation daily for the three business areas human pharmaceuticals, animal health and biopharmaceuticals. In 2017, Boehringer Ingelheim achieved net sales of nearly 18.1 billion euros. R&D expenditure, exceeding three billion euros, corresponded to 17.0 per cent of net sales.

As a family-owned company, Boehringer Ingelheim plans in generations and focuses on long-term success, rather than short-term profit. The company therefore aims at organic growth from its own resources with simultaneous openness to partnerships and strategic alliances in research. In everything it does, Boehringer Ingelheim naturally adopts responsibility towards mankind and the environment.

More information about Boehringer Ingelheim can be found on www.boehringer-ingelheim.com or in our annual report: <http://annualreport.boehringer-ingelheim.com>.

About Boehringer Ingelheim in Oncology

Cancer takes away loved ones, time and untapped potential. At Boehringer Ingelheim we are providing new hope for patients by taking cancer on. We are collaborating with the oncology community to deliver scientific breakthroughs to transform the lives of patients. Our primary focus is in lung and gastrointestinal cancers, with the goal of delivering breakthrough, first-in-class treatments that can help win the fight against cancer. Our commitment to innovation has resulted in pioneering treatments for lung cancer and we are advancing a unique pipeline of cancer cell directed agents, immune oncology therapies and intelligent combination approaches to help combat many cancers.

About Epizyme, Inc.

Epizyme, Inc. is a clinical-stage biopharmaceutical company committed to rewriting treatment for cancer and other serious diseases through novel epigenetic medicines. Epizyme is broadly developing its lead product candidate, tazemetostat, a first-in-class EZH2 inhibitor, with studies underway in both solid tumors and hematological malignancies, as a monotherapy and combination therapy in relapsed and front-line disease. The company also is developing a novel G9a program with its next development candidate, EZM8266, which is targeting sickle cell disease. By focusing on the genetic drivers of disease, Epizyme's science seeks to match targeted medicines with the patients who need them. For more information, visit www.epizyme.com.

Cautionary Note on Forward-Looking Statements

Any statements in this press release 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: uncertainties relating to the company's ability to resume enrollment in its tazemetostat trials and the timing of such resumption, and the impact of safety findings on enrollment of patients in ongoing and future trials of tazemetostat following the lifting of the partial clinical hold and the resumption of enrollment; uncertainties inherent in the initiation of future clinical studies and in the availability and timing of data from ongoing clinical studies; whether interim results from a clinical trial will be predictive of the final results of the trial; whether results from preclinical studies or earlier clinical studies will be predictive of the results of future 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 Fast Track Designation and Orphan Drug Designations will provide the benefits for which tazemetostat is eligible; expectations for regulatory approvals to conduct trials or to market products; 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 potential of the company's therapeutic candidates; and other factors discussed in the "Risk Factors" section of the company's most recent Form 10-Q 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 press release 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. 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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Contacts

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Schedule 13.3

SPECIAL ARBITRATION

Location. Disputes referred to arbitration covered under this Schedule 13.3 shall be finally resolved by arbitration conducted by three (3) arbitrators in London, United Kingdom in the English language in accordance with the Rules of Arbitration of the ICC (International Chamber of Commerce). Each Party shall be entitled to appoint one arbitrator. The Parties shall appoint their respective arbitrators within [**] after submission for arbitration. The two (2) arbitrators so appointed shall agree on the appointment of the third arbitrator from the list of arbitrators maintained by the ICC. If the Parties' appointed arbitrators fail to agree, within [**] from the date both Parties' arbitrators have been appointed, on the identity of the third arbitrator, then such arbitrator shall be appointed by the ICC pursuant to its procedures. The ICC shall be the administrator of the arbitration proceedings.

Submission of Proposals. Within [**] after appointment of the full arbitration panel, each Party shall provide to the other Party and the arbitration panel its proposal for the matter to be decided, which shall approximate as closely as possible the proposals of such Party previously made in the negotiations between the Parties with respect thereto, together with a brief or other written memorandum supporting the merits of its proposal. The arbitration panel shall promptly convene a hearing, at which time each Party shall have one hour to argue in support of its proposal. Neither Party may call any witnesses in support of its arguments.

Ruling. The arbitration panel shall, within [**] after such hearing, select one Party's proposal, as applicable, and notify the Parties of such selection in writing. In making their selection, (a) the arbitrators shall not modify the terms or conditions of either Party's proposal; (b) the arbitrators shall not combine provisions from both Party's proposals; and (c) to the extent applicable, the arbitrators shall consider the terms and conditions of this Agreement (and shall always consider the provisions found in Section 13.3.1(a) or Section 13.3.2(f)(10)(C) of this Agreement), the relative merits of the proposals, the then current stage of research, Development or Commercialization of the Compounds or Products, and the written and oral arguments of the Parties. The arbitrators may proceed to an award notwithstanding the failure of the other Party to participate in the proceedings. The arbitrators shall issue a written decision in order to explain the basis of the ruling, unless otherwise agreed by the Parties.

Fees. Each Party shall bear its own costs in preparing for the arbitration. The costs of the arbitrators will be equally divided between the Parties.

Finality. Any decision or award of the arbitrators shall be final, conclusive, and binding on the Parties, and judgment may be entered on any award in any court of competent jurisdiction.

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the following Registration Statements:

1. Registration Statement (Form S-8 No. 333-189629) pertaining to the 2008 Stock Incentive Plan, 2013 Stock Incentive Plan, and 2013 Employee Stock Purchase Plan of Epizyme, Inc.,
2. Registration Statement (Form S-8 No. 333-194205) pertaining to the 2013 Stock Incentive Plan and 2013 Employee Stock Purchase Plan of Epizyme, Inc.,
3. Registration Statement (Form S-8 No. 333-202681) pertaining to the 2013 Stock Incentive Plan of Epizyme, Inc.,
4. Registration Statement (Form S-8 No. 333-210028) pertaining to the 2013 Stock Incentive Plan of Epizyme, Inc.,
5. Registration Statement (Form S-8 No. 333-216638) pertaining to the 2013 Stock Incentive Plan of Epizyme, Inc., and
6. Registration Statement (Form S-3 No. 333-210774) and related Prospectus of Epizyme, Inc.;
7. Registration Statement (Form S-8 No. 333-223612) pertaining to the 2013 Stock Incentive Plan of Epizyme, Inc., and
8. Registration Statement (Form S-3 No. 333-224159) and related Prospectus of Epizyme, Inc.

of our reports dated February 26, 2019, with respect to the consolidated financial statements of Epizyme, Inc. and the effectiveness of internal control over financial reporting of Epizyme, Inc. included in this Annual Report (Form 10-K) of Epizyme, Inc. for the year ended December 31, 2018.

/s/ Ernst & Young LLP

Boston, Massachusetts
February 26, 2019

I, Robert B. Bazemore, certify that:

1. I have reviewed this Annual Report on Form 10-K for the year ended December 31, 2018 of Epizyme, Inc.;

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

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

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

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

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

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

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

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

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

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

Date: February 26, 2019

/s/ Robert B. Bazemore

Robert B. Bazemore
President and Chief Executive Officer

I, Matthew E. Ros, certify that:

1. I have reviewed this Annual Report on Form 10-K for the year ended December 31, 2018 of Epizyme, Inc.;

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

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

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

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

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

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

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

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

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

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

Date: February 26, 2019

/s/ Matthew E. Ros

Matthew E. Ros
Chief Strategy and Business Officer,
Principal Financial Officer

**CERTIFICATIONS OF CEO AND CFO PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with this Annual Report on Form 10-K of Epizyme, Inc. (the "Company") for the year ended December 31, 2018, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), each of the undersigned officers of the Company hereby certifies, pursuant to 18 U.S.C. (section) 1350, as adopted pursuant to (section) 906 of the Sarbanes-Oxley Act of 2002, that to the best of his knowledge:

- (1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- (2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: February 26, 2019

/s/ Robert B. Bazemore

Robert B. Bazemore
President and Chief Executive Officer

/s/ Matthew E. Ros

Matthew E. Ros
Chief Strategy and Business Officer