Epizyme, Inc.
Form 8-K
October 03, 2018

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, DC 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d)

of the Securities Exchange Act of 1934

Date of report (Date of earliest event reported):

October 2, 2018

EPIZYME, INC.

(Exact Name of Registrant as Specified in Charter)

Delaware	**001-35945**	**26-1349956**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

400 Technology Square,

Cambridge, Massachusetts **02139**
(Address of Principal Executive Offices) **(Zip Code)**
Registrant s telephone number, including area code: (617) 229-5872

(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (*see* General Instruction A.2. below):

Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))
Indicate by check mark whether the registrant is an emerging growth company as defined in as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company

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

Item 1.01 Entry Into a Material Definitive Agreement

On October 2, 2018, Epizyme, Inc. (the Company or we) entered into an underwriting agreement (the Underwriting Agreement) with Jefferies LLC relating to an underwritten public offering (the Offering) of 8,333,334 shares (the Shares) of the Company s common stock, par value $0.0001 per share (the Common Stock). All of the Shares are being sold by the Company. The price to the public in the Offering is $9.00 per share, and Jefferies, as the sole underwriter, has agreed to purchase the Shares from the Company pursuant to the Underwriting Agreement at a price of $8.46 per share. Under the terms of the Underwriting Agreement, the Company granted Jefferies LLC an option, exercisable for 30 days, to purchase up to an additional 1,250,000 shares of Common Stock (the Additional Shares) at the same price per share as the Shares.

The Shares, and any Additional Shares, will be issued pursuant to a prospectus supplement dated October 2, 2018 and an accompanying base prospectus dated April 5, 2018 that form a part of the automatic registration statement on Form S-3ASR that the Company filed with the U.S. Securities and Exchange Commission (SEC) (File No. 333-224159). The closing of the Offering is expected to take place on or about October 5, 2018, subject to the satisfaction of customary closing conditions.

The Underwriting Agreement contains customary representations, warranties, covenants and agreements by the Company, customary conditions to closing, indemnification obligations of the Company and the underwriter, including for liabilities under the Securities Act of 1933, as amended, other obligations of the parties and termination provisions. The representations, warranties and covenants contained in the Underwriting Agreement were made only for purposes of such agreement and as of specific dates, were solely for the benefit of the parties to such agreement, and may be subject to limitations agreed upon by the contracting parties. A copy of the Underwriting Agreement is attached as Exhibit 1.1 hereto and is incorporated herein by reference. The foregoing description of the material terms of the Underwriting Agreement does not purport to be complete and is qualified in its entirety by reference to such exhibit.

A copy of the legal opinion and consent of Wilmer Cutler Pickering Hale and Dorr LLP relating to the Shares and Additional Shares is attached as Exhibit 5.1 hereto.

Item 8.01 Other Events.

In connection with the Offering, the Company has provided the following summary description of the Company s business as an update to the information provided in the Company s previous periodic filings with the Securities and Exchange Commission in order to reflect recent business developments. The Company is also providing an update on its cash resources.

Company Overview

We are a clinical-stage biopharmaceutical company that is committed to rewriting treatment for cancer and other serious diseases through discovering, developing, and commercializing 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 inhibitor of the EZH2 histone methyltransferase, or HMT, in a range of cancer types and settings, and developing the lead development candidate in 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 that are evaluating tazemetostat as both a monotherapy and combination treatment in both hematological malignancies and solid tumors. Tazemetostat has shown meaningful clinical activity as a monotherapy in indications in both disease areas and has been well tolerated across clinical trials

to date.

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 follicular lymphoma,

or FL, one with patients with EZH2 activating mutations and one with patients without EZH2 activating mutations, and two cohorts were evaluating tazemetostat as a monotherapy for patients with relapsed or refractory diffuse large B-cell lymphoma, or DLBCL, one with patients with EZH2 activating mutations and one with patients without EZH2 activating mutations. An additional arm was evaluating tazemetostat as a combination agent with prednisone in patients with relapsed or refractory DLBCL.

In June 2018, at the 23rd Congress of the European Hematology Association, we reported interim efficacy, safety and biomarker data from patients with FL with EZH2 mutations or with wild-type EZH2. Interim data as of the May 1, 2018 data cut-off date showed that tazemetostat demonstrated meaningful clinical activity and was generally well tolerated in these heavily pre-treated patients. Interim data as of May 1, 2018 included 82 evaluable patients across the two cohorts, prospectively assigned by EZH2 status, including 28 patients with EZH2 activating mutations and 54 patients with wild-type EZH2. In 2017, we fully enrolled the wild-type EZH2 cohort, and we are continuing to enroll patients in our EZH2 activating mutation cohort.

In the EZH2 activating mutation cohort (n=28), an objective response rate, or ORR, of 71 percent was observed with 11 percent of patients having achieved a complete response, or CR, and 61 percent of patients having achieved a partial response, or PR. An additional twenty-nine percent of the patients in the cohort achieved stable disease, or SD, as best response. Of these patients, 21 percent were still on study as of May 1, 2018 with the potential to respond. All patients in this cohort experienced reduction in tumor burden, and no patients experienced progressive disease, or PD, as best response. In addition, as of May 1, 2018, the interim median progression-free survival, or PFS, was 49 weeks and the interim median duration of response, or DOR, was 32 weeks, with both endpoints continuing to mature. In the fully-enrolled cohort of FL patients with wild-type EZH2 (n=54), an ORR of 33 percent was observed with six percent of patients having achieved a CR, and 28 percent of patients having achieved a PR. An additional 31 percent of patients achieved SD as best response, including one patient who was still on study as of May 1, 2018. In addition, as of May 1, 2018 the interim median PFS was 30 weeks and interim median DOR was 76 weeks, with the median DOR endpoint continuing to mature, with more than half of the responders still on therapy at the time. Interim safety results as of May 1, 2018 showed that only six percent of FL patients discontinued treatment due to treatment-related adverse events, or AEs. AEs of Grade 3 or higher were reported across 17 percent of patients, the most frequent of which included thrombocytopenia, anemia, asthenia and fatigue.

Based on initial discussions with the U.S. Food and Drug Administration, or FDA, we believe we have the opportunity to submit for accelerated approval for tazemetostat as a monotherapy in FL, subject to the results of the FL cohorts of the Phase 2 global study and further dialogue with the FDA. We plan to engage with the FDA to further refine our registration strategy for tazemetostat for patients with FL who have received at least two prior lines of treatment by early 2019. In 2019, we plan to commence a combination study of tazemetostat in FL that may serve as a confirmatory study as part of an accelerated approval strategy.

In our hematological malignancy program, we also have two Phase 1b combination studies ongoing through collaborators in DLBCL, in both relapsed or refractory and first-line treatment settings, which are expected to report preliminary data in 2019. The first is being conducted with the Lymphoma Study Association, or LYSA, and is evaluating tazemetostat in combination with R-CHOP as a front-line treatment regimen for high-risk DLBCL patients. We plan to engage further with LYSA to assess the potential of advancing this combination into Phase 2. The other is a combination study with Genentech, Inc., or Genentech, that is investigating tazemetostat in combination with Genentech s checkpoint inhibitor atezolizumab in relapsed or refractory DLBCL. 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 a monotherapy or in combination with prednisolone.

In our solid tumor program, we are conducting a global Phase 2 trial of tazemetostat in adult patients with INI1- and SMARCA4-negative tumors, which we collectively refer to as INI1-negative tumors, including epithelioid sarcoma,

malignant rhabdoid tumors, or MRT, other INI1-negative tumors, and chordoma. 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 in the 60-patient epithelioid sarcoma cohort in July 2017, and 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.

Interim data from the 62 patients in the epithelioid cohort of the ongoing Phase 2 study, as of the August 21, 2018 data cut-off date, are expected to be presented during the European Society for Medical Oncology, or ESMO, 2018 Congress, being held October 19-22, 2018. Of the 62 patients, as of the data cutoff date, eight patients had confirmed objective responses, for a 13 percent objective response rate, the primary endpoint in the trial. In addition, as of the data cut-off date, tazemetostat treatment resulted in a 24 percent disease control rate, a secondary endpoint, which is comprised of confirmed objective responses measured in accordance with Response Evaluation Criteria in Solid Tumors (RECIST 1.1) guidelines, and disease stabilization of 32 weeks or more. There are patients with stable disease who remain on treatment in this trial. In the overall 62 patient population, although there was a decrease in the median progression free survival, a secondary endpoint, from the 5.7 months reported for the initial 31 patients as of May 2017, we believe that this is likely due to a change in the inclusion criteria for the second 31 patients to require active progression of disease. However, we believe that PFS data that are expected to be presented are clinically meaningful in the context of standard of care, which is commonly combination chemotherapy. More detailed data from these patients, including durability and overall survival data, are expected to be presented at the ESMO 2018 Congress, and we also expect to present additional data from these patients, including updated ORR, duration and overall survival data, in 2019.

Based on positive data from the ongoing study, we plan to submit our first NDA to the FDA for tazemetostat for epithelioid sarcoma in the first half of 2019. In connection with this submission, we plan to commence a clinical trial of tazemetostat for epithelioid sarcoma that could serve as the confirmatory trial required in connection with an accelerated approval.

We are also evaluating tazemetostat in the dose-expansion portion of a Phase 1 study in pediatric patients with INI1-negative tumors and in a Phase 2 clinical trial in pediatric patients with solid tumors and lymphoma, called the Pediatric MATCH trial, under a Cooperative Research and Development Agreement, or CRADA, with the National Cancer Institutes, or NCI.

In September 2018, the FDA lifted the partial clinical hold that it had issued in April 2018 on new patient enrollment in the United States in our ongoing clinical trials of tazemetostat. The comparable partial clinical holds that were subsequently placed on new patient enrollment by regulators in France and Germany remain in effect. The partial clinical holds were issued following a safety report from one patient in the dose-ranging portion of our Phase 1 pediatric solid tumor study who developed a secondary case of T-cell lymphoblastic lymphoma, or T-LBL. This child had metastatic poorly differentiated chordoma and entered our study with a poor prognosis following several prior treatments. The patient was on a high dose of tazemetostat for 15 months and achieved an objective response. Following the T-LBL diagnosis, the patient discontinued tazemetostat and began a standard treatment for T-LBL. This remains the only case of T-LBL that we have seen in more than 750 patients treated with tazemetostat.

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, we reconsented 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. We are re-activating clinical trial sites in the United States to resume enrollment in our tazemetostat clinical trials. We plan to engage with regulators in both France and Germany to work toward similar resolutions in those countries. 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.

Subject to the resolution of the holds on enrollment, Genentech has agreed that, as a part of its MORPHEUS study, it will evaluate tazemetostat in combination with atezolizumab (TECENTRIQ®), a PD-L1 inhibitor, in patients with non-small cell lung cancer. Preliminary data from this study are anticipated to be reported in 2019. We also plan to evaluate tazemetostat in a Phase 2 clinical trial in adult patients with ovarian cancer under a CRADA with the NCI.

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, and holds a limited right of first negotiation for the rest of Asia. We are preparing to commercialize tazemetostat, initially in epithelioid sarcoma, and are developing a go-to-market strategy to support the commercial launch of tazemetostat for epithelioid sarcoma in the United States, if approved. Epithelioid sarcoma patients are primarily treated in Oncology Centers of Excellence, which presents a market that we believe is addressable through an efficiently structured field-based sales organization. We are exploring potential alliances for the commercialization of tazemetostat for epithelioid sarcoma outside the United States.

Tazemetostat is covered by claims of U.S. and European composition of matter patents, which are expected to expire in 2032, without taking into consideration any patent term or other extensions. Tazemetostat has been granted Fast Track designation by the FDA in patients with relapsed or refractory FL patients, with or without activating EZH2 mutations and relapsed or refractory DLBCL with EZH2 activating mutations, and orphan drug designation by the FDA for the treatment of malignant rhabdoid tumors, or MRT, and soft tissue sarcoma, or STS. 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 also own global rights to EZM8266 targeting G9a.

We have collaboration agreements with Celgene Corporation and Celgene RIVOT Ltd., an affiliate of Celgene Corporation, which we collectively refer to as Celgene, Glaxo Group Limited (an affiliate of GlaxoSmithKline), or GSK, and Eisai. We also have a collaboration with Roche Molecular Systems, Inc., or Roche Molecular, to develop a companion diagnostic for use with tazemetostat to identify NHL patients with EZH2 activating mutations. These collaborations provide us with access to considerable scientific, development, regulatory and commercial capabilities. As of June 30, 2018, we had received $217.8 million in non-equity funding under these collaborations.

Cash Resources

Based on our research and development plans and our timing expectations related to the progress of our programs, we expect that the net proceeds from the Offering, together with our existing cash, cash equivalents and marketable securities as of June 30, 2018, will enable us to fund our operating expenses and capital expenditure requirements at least into the first quarter of 2020.

Cautionary Note on Forward-Looking Statements

Any statements in this report about future expectations, plans and prospects for the Company and other statements containing the words anticipate, believe, estimate, expect, intend, may, plan, predict, project, target would, could, should, continue, and similar expressions, constitute forward-looking statements within the meaning 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 related to market conditions and the completion of the Offering on the anticipated terms or at all; 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 such as the interim data referenced in this report 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 or submissions for regulatory approval; whether the Company will be able to satisfy the pathway to regulatory approval that it has identified; whether the Company will obtain regulatory approvals to conduct trials or to market products on a timely basis or at all; 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 report 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.

Item 9.01. Financial Statements and Exhibits.

d) Exhibits

Exhibit No.	Description
1.1	Underwriting Agreement, dated October 2, 2018, by and between the Company and Jefferies, LLC
5.1	Opinion of Wilmer Cutler Pickering Hale and Dorr LLP
23.1	Consent of Wilmer Cutler Pickering Hale and Dorr LLP (contained in Exhibit 5.1 above)

SIGNATURES

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

EPIZYME, INC.

Date: October 3, 2018

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