

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549**

**FORM S-8
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933**

Epizyme, Inc.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

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

400 Technology Square, 4th Floor
Cambridge, MA
(Address of Principal Executive Offices)

02139
(Zip Code)

2013 Stock Incentive Plan
2013 Employee Stock Purchase Plan
(Full title of the plan)

Robert B. Bazemore
President and Chief Executive Officer
Epizyme, Inc.
400 Technology Square, 4th Floor
Cambridge, MA 02139
(Name and address of agent for service)

(617) 229-5872
(Telephone number, including area code, of agent for service)

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

Large accelerated filer	<input checked="" type="checkbox"/>		Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input type="checkbox"/> (Do not check if a smaller reporting company)		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 7(a)(2)(B) of the Securities Act.

CALCULATION OF REGISTRATION FEE

Title of Securities to be Registered	Amount to be Registered(1)	Proposed Maximum Offering Price Per Share	Proposed Maximum Aggregate Offering Price	Amount of Registration Fee
Common Stock, \$0.0001 par value per share	2,733,333 shares(2)	\$10.62(3)	\$29,027,996.46(3)	\$3,166.95

- (1) In accordance with Rule 416 under the Securities Act of 1933, as amended, this registration statement shall be deemed to cover any additional securities that may from time to time be offered or issued to prevent dilution resulting from stock splits, stock dividends or similar transactions.
- (2) Consists of (i) 2,500,000 additional shares issuable under the 2013 Stock Incentive Plan and (ii) 233,333 additional shares issuable under the 2013 Employee Stock Purchase Plan.
- (3) Estimated solely for the purpose of calculating the registration fee pursuant to Rules 457(c) and 457(h) of the Securities Act of 1933, as amended. The price per share and aggregate offering price are calculated on the basis of \$10.62, the average of the high and low price of the Registrant's Common Stock as reported on the Nasdaq Global Select Market on February 16, 2021.

Statement of Incorporation by Reference

This Registration Statement on Form S-8 is filed to register the offer and sale of (i) an additional 2,500,000 shares of the Registrant's common stock, \$0.0001 par value per share, to be issued under the Registrant's 2013 Stock Incentive Plan and (ii) an additional 233,333 shares of the Registrant's common stock, \$0.0001 par value per share, to be issued under the Registrant's 2013 Employee Stock Purchase Plan. This Registration Statement incorporates by reference the contents of the registration statement on Form S-8, File No. 333-189629, filed by the Registrant on [June 27, 2013](#), relating to the Registrant's 2008 Stock Incentive Plan, 2013 Stock Incentive Plan and 2013 Employee Stock Purchase Plan; the registration statement on Form S-8, File No. 333-194205, filed by the Registrant on [February 28, 2014](#), relating to the Registrant's 2013 Stock Incentive Plan and 2013 Employee Stock Purchase Plan, except for Item 8, Exhibits; the registration statement on Form S-8, File No. 333-202681, filed by the Registrant on [March 12, 2015](#), relating to the Registrant's 2013 Stock Incentive Plan; the registration statement on Form S-8, File No. 333-210028, filed by the Registrant on [March 9, 2016](#), relating to the Registrant's 2013 Stock Incentive Plan; the registration statement on Form S-8, File No. 333-216638, filed by the Registrant on [March 13, 2017](#), relating to the Registrant's 2013 Stock Incentive Plan; the registration statement on Form S-8, File No. 333-223612, filed by the Registrant on [March 13, 2018](#), relating to the Registrant's 2013 Stock Incentive Plan; the registration statement on Form S-8, File No. 333-229878, filed by the Registrant on [February 26, 2019](#), relating to the Registrant's 2013 Stock Incentive Plan; and the registration statement on Form S-8, File No. 333-236707, filed by the Registrant on [February 27, 2020](#), relating to the Registrant's 2013 Stock Incentive Plan and 2013 Employee Stock Purchase Plan.

PART II

INFORMATION REQUIRED IN THE REGISTRATION STATEMENT

Item 8. Exhibits.

Number	Description
--------	-------------

- | | |
|-----|--|
| 4.1 | Restated Certificate of Incorporation of the Registrant (Previously filed with the Securities and Exchange Commission as an Exhibit to the Registrant's Quarterly Report on Form 10-Q (File No. 001-35945) on August 4, 2020 and incorporated herein by reference) |
| 4.2 | Amended and Restated By-Laws of the Registrant (Previously filed with the Securities and Exchange Commission as an Exhibit to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-187982), and incorporated herein by reference) |

-
- 5.1 [Opinion of Wilmer Cutler Pickering Hale and Dorr LLP, counsel to the Registrant](#)
 - 23.1 [Consent of Wilmer Cutler Pickering Hale and Dorr LLP \(included in Exhibit 5.1\)](#)
 - 23.2 [Consent of Ernst & Young LLP](#)
 - 24.1 [Power of attorney \(included on the signature pages of this registration statement\)](#)
 - 99.1 [2013 Stock Incentive Plan, as amended on March 24, 2020 \(Previously filed with the Securities and Exchange Commission as an Exhibit to the Registrant's Quarterly Report on Form 10-Q \(File No. 001-35945\) on May 4, 2020 and incorporated herein by reference\)](#)
 - 99.2 [2013 Employee Stock Purchase Plan \(Previously filed with the Securities and Exchange Commission as an Exhibit to the Registrant's Registration Statement on Form S-1, as amended \(File No. 333-187982\), and incorporated herein by reference\)](#)

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-8 and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Cambridge, Commonwealth of Massachusetts, on this 23rd day of February, 2021.

EPIZYME, INC.

By: /s/ Robert B. Bazemore

Robert B. Bazemore

President and Chief Executive Officer

POWER OF ATTORNEY AND SIGNATURES

We, the undersigned officers and directors of Epizyme, Inc., hereby severally constitute and appoint Robert B. Bazemore and Paolo Tombesi, and each of them singly, our true and lawful attorneys with full power to them, and each of them singly, to sign for us and in our names in the capacities indicated below, the registration statement on Form S-8 filed herewith and any and all subsequent amendments to said registration statement, and generally to do all such things in our names and on our behalf in our capacities as officers and directors to enable Epizyme, Inc. to comply with the provisions of the Securities Act of 1933, as amended, and all requirements of the Securities and Exchange Commission, hereby ratifying and confirming our signatures as they may be signed by our said attorneys, or any of them, to said registration statement and any and all amendments thereto.

Pursuant to the requirements of the Securities Act of 1933, this registration statement has been signed by the following persons in the capacities and on the dates indicated.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Robert B. Bazemore</u> Robert B. Bazemore	President, Chief Executive Officer, Director (Principal Executive Officer)	February 23, 2021
<u>/s/ Paolo Tombesi</u> Paolo Tombesi	Chief Financial Officer (Principal Financial Officer)	February 23, 2021
<u>/s/ Joseph Beaulieu</u> Joseph Beaulieu	Corporate Controller and Treasurer (Principal Accounting Officer)	February 23, 2021
<u>/s/ Andrew R. Allen</u> Andrew R. Allen, M.D., Ph.D.	Director	February 23, 2021
<u>/s/ Kenneth Bate</u> Kenneth Bate	Director	February 23, 2021
<u>/s/ Grant Bogle</u> Grant Bogle	Director	February 23, 2021
<u>/s/ Kevin T. Conroy</u> Kevin T. Conroy	Director	February 23, 2021
<u>/s/ Michael F. Giordano</u> Michael F. Giordano, M.D.	Director	February 23, 2021
<u>/s/ Carl Goldfischer</u> Carl Goldfischer, M.D.	Director	February 23, 2021

<u>/s/ Pablo Legorreta</u> Pablo Legorreta	Director	February 23, 2021
<u>/s/ David M. Mott</u> David M. Mott	Director	February 23, 2021
<u>/s/ Victoria Richon</u> Victoria Richon	Director	February 23, 2021

February 23, 2021

Epizyme, Inc.
400 Technology Square
Cambridge, MA 02139

Re: 2013 Stock Incentive Plan and 2013 Employee Stock Purchase Plan

Ladies and Gentlemen:

We have assisted in the preparation of a Registration Statement on Form S-8 (the "Registration Statement") to be filed with the Securities and Exchange Commission (the "Commission") under the Securities Act of 1933, as amended (the "Securities Act"), relating to an aggregate of 2,733,333 additional shares of common stock, \$0.0001 par value per share (the "Shares"), of Epizyme, Inc., a Delaware corporation (the "Company"), issuable under the Company's 2013 Stock Incentive Plan and 2013 Employee Stock Purchase Plan (collectively, the "Plans").

We have examined the Certificate of Incorporation and By-Laws of the Company, each as amended and restated to date, and originals, or copies certified to our satisfaction, of all pertinent records of the meetings of the directors and stockholders of the Company, the Registration Statement and such other documents relating to the Company as we have deemed material for the purposes of this opinion.

In our examination of the foregoing documents, we have assumed the genuineness of all signatures, the authenticity of all documents submitted to us as originals, the conformity to original documents of all documents submitted to us as certified, photostatic or other copies, the authenticity of the originals of any such documents and the legal competence of all signatories to such documents.

We assume that the appropriate action will be taken, prior to the offer and sale of the Shares in accordance with the Plans, to register and qualify the Shares for sale under all applicable state securities or "blue sky" laws.

We express no opinion herein as to the laws of any state or jurisdiction other than the state laws of The Commonwealth of Massachusetts, the General Corporation Law of the State of Delaware and the federal laws of the United States of America.

It is understood that this opinion is to be used only in connection with the offer and sale of the Shares while the Registration Statement is in effect.

Please note that we are opining only as to the matters expressly set forth herein, and no opinion should be inferred as to any other matters.

Based on the foregoing, we are of the opinion that the Shares have been duly authorized for issuance and, when the Shares are issued and paid for in accordance with the terms and conditions of the Plans, the Shares will be validly issued, fully paid and nonassessable.

We hereby consent to the filing of this opinion with the Commission in connection with the Registration Statement in accordance with the requirements of Item 601(b)(5) of Regulation S-K under the Securities Act. In giving such consent, we do not hereby admit that we are in the category of persons whose consent is required under Section 7 of the Securities Act or the rules and regulations of the Commission.

Very truly yours,

WILMER CUTLER PICKERING HALE AND DORR LLP

By: /s/ Stuart Falber

Stuart M. Falber, Partner

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the Registration Statement (Form S-8) pertaining to the 2013 Stock Incentive Plan and 2013 Employee Stock Purchase Plan of Epizyme, Inc. of our reports dated February 23, 2021, with respect to the consolidated financial statements of Epizyme, Inc. and the effectiveness of internal control over financial reporting of Epizyme, Inc., included in its Annual Report (Form 10-K) for the year ended December 31, 2020, filed with the Securities and Exchange Commission.

/s/ Ernst & Young LLP

Boston, Massachusetts
February 23, 2021