
**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**
Washington, D.C. 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)

2022 Equity Incentive Plan
(Full Title of the Plan)

Grant Bogle
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, a 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
Non-accelerated filer

Accelerated filer
Smaller reporting company
Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act.

PART I
INFORMATION REQUIRED IN THE SECTION 10(a) PROSPECTUS

Item 1. Plan Information.

The information required by Item 1 is included in documents sent or given to participants in the plans covered by this registration statement pursuant to Rule 428(b)(1) of the Securities Act of 1933, as amended (the "Securities Act").

Item 2. Registrant Information and Employee Plan Annual Information.

The written statement required by Item 2 is included in documents sent or given to participants in the plans covered by this registration statement pursuant to Rule 428(b)(1) of the Securities Act.

PART II
INFORMATION REQUIRED IN THE REGISTRATION STATEMENT

Item 3. Incorporation of Documents by Reference.

The registrant is subject to the informational and reporting requirements of Sections 13(a), 14, and 15(d) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and in accordance therewith files reports, proxy statements and other information with the Securities and Exchange Commission (the "Commission"). The following documents, which are on file with the Commission, are incorporated in this registration statement by reference:

(a) The registrant's latest annual report filed pursuant to Section 13(a) or 15(d) of the Exchange Act or the latest prospectus filed pursuant to Rule 424(b) under the Securities Act that contains audited financial statements for the registrant's latest fiscal year for which such statements have been filed.

(b) All other reports filed pursuant to Section 13(a) or 15(d) of the Exchange Act since the end of the fiscal year covered by the document referred to in (a) above.

(c) The description of the securities contained in the registrant's registration statement on Form 8-A filed under the Exchange Act, as the description therein has been updated and superseded by the description of the registrant's capital stock contained in Exhibit 4.3 to the registrant's Annual Report on [Form 10-K](#) for the fiscal year ended December 31, 2021, as filed with the Commission on March 1, 2022, including any amendments or reports filed for the purpose of updating such description.

All documents subsequently filed by the registrant pursuant to Sections 13(a), 13(c), 14 and 15(d) of the Exchange Act, prior to the filing of a post-effective amendment which indicates that all securities offered hereby have been sold or which deregisters all securities then remaining unsold, shall be deemed to be incorporated by reference in this registration statement and to be part hereof from the date of the filing of such documents. Any statement contained in a document incorporated or deemed to be incorporated by reference herein shall be deemed to be modified or superseded for the purposes of this registration statement to the extent that a statement contained herein or in any other subsequently filed document which also is or is deemed to be incorporated by reference herein modifies or supersedes such statement. Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this registration statement.

Item 4. Description of Securities.

Not applicable.

Item 5. Interests of Named Experts and Counsel.

Wilmer Cutler Pickering Hale and Dorr LLP has opined as to the legality of the securities being offered by this registration statement.

Item 6. Indemnification of Directors and Officers.

Section 102 of the Delaware General Corporation Law permits a corporation to eliminate the personal liability of its directors or its stockholders for monetary damages for a breach of fiduciary duty as a director, except where the director breached his or her duty of loyalty, failed to act in good faith, engaged in intentional misconduct or knowingly violated a law, authorized the payment of a dividend or approved a stock repurchase in violation of Delaware corporate law or obtained an improper personal benefit. The registrant's restated certificate of incorporation, as amended, provides that no director shall be personally liable to the registrant or its stockholders for monetary damages for any breach of fiduciary duty as a director, notwithstanding any provision of law imposing such liability, except to the extent that the Delaware General Corporation Law prohibits the elimination or limitation of liability of directors for breaches of fiduciary duty.

Section 145 of the Delaware General Corporation Law provides that a corporation has the power to indemnify a director, officer, employee or agent of the corporation and certain other persons serving at the request of the corporation in related capacities against expenses (including attorneys' fees), judgments, fines and amounts paid in settlements actually and reasonably incurred by the person in connection with an action, suit or proceeding to which he or she is or is threatened to be made a party by reason of such position, if such person acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of the corporation, and, in any criminal action or proceeding, had no reasonable cause to believe his or her conduct was unlawful, except that, in the case of actions brought by or in the right of the corporation, no indemnification shall be made with respect to any claim, issue or matter as to which such person shall have been adjudged to be liable to the corporation unless and only to the extent that the Court of Chancery or other adjudicating court determines that, despite the adjudication of liability but in view of all of the circumstances of the case, such person is fairly and reasonably entitled to indemnification for such expenses which the Court of Chancery or such other court shall deem proper.

The registrant's restated certificate of incorporation, as amended, provides that it will indemnify each person who was or is a party or threatened to be made a party to any threatened, pending or completed action, suit or proceeding whether civil, criminal, administrative or investigative (other than an action by or in the right of the registrant) by reason of the fact that he or she is or was, or has agreed to become, a director or officer of the registrant, or is or was serving, or has agreed to serve, at the registrant's request as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise (all such persons being referred to as an "Indemnitee"), or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred in connection with such action, suit or proceeding and any appeal therefrom, if such Indemnitee acted in good faith and in a manner he or she reasonably believed to be in, or not opposed to, the registrant's best interests, and, with respect to any criminal action or proceeding, he or she had no reasonable cause to believe his or her conduct was unlawful.

The registrant's restated certificate of incorporation, as amended, also provides that it will indemnify any Indemnitee who was or is a party to an action or suit by or in the right of the registrant to procure a judgment in the registrant's favor by reason of the fact that the Indemnitee is or was, or has agreed to become, a director or officer of the registrant, or is or was serving, or has agreed to serve, at the registrant's request as a director, officer, partner, employee or trustee or, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise, or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys' fees) and, to the extent permitted by law, amounts paid in settlement actually and reasonably incurred in connection with such action, suit or proceeding, and any appeal therefrom, if the Indemnitee acted in good faith and in a manner he or she reasonably believed to be in, or not opposed to, the registrant's best interests, except that no indemnification shall be made with respect to any claim, issue or matter as to which such person shall have been adjudged to be liable to the registrant, unless a court determines that, despite such adjudication but in view of all of the circumstances, he or she is entitled to indemnification of such expenses. Notwithstanding the foregoing, to the extent that any Indemnitee has been successful, on the merits or otherwise, he or she will be indemnified by the registrant against all expenses (including attorneys' fees) actually and reasonably incurred by him or her or on his or her behalf in connection therewith. If the registrant does not assume the defense, expenses must be advanced to an Indemnitee under certain circumstances.

The registrant has entered into indemnification agreements with its directors and executive officers. In general, these agreements provide that the registrant will indemnify the director or executive officer to the fullest extent permitted by law for claims arising in his or her capacity as a director or officer of the registrant or in connection with their service at the registrant's request for another corporation or entity. The indemnification agreements also provide for procedures that will apply in the event that a director or executive officer makes a claim for indemnification and establish certain presumptions that are favorable to the director or executive officer.

The registrant maintains a general liability insurance policy that covers certain liabilities of its directors and officers arising out of claims based on acts or omissions in their capacities as directors or officers.

Pursuant to the Agreement and Plan of Merger (the "Merger Agreement") dated as of June 27, 2022, the registrant's directors and executive officers will be entitled to certain indemnification and advancement rights and coverage under directors' and officers' liability insurance policies for a period of time following the effective time of the merger described therein (the "Merger"). Pursuant to the terms of the Merger Agreement, the surviving corporation in the Merger shall maintain or purchase a six-year "tail" directors' and officers' liability insurance policy, subject to the terms of the Merger Agreement.

Item 7. Exemption from Registration Claimed.

Not applicable.

Item 8. Exhibits.

The following exhibits are incorporated herein by reference:

<u>Number</u>	<u>Description</u>
4.1*	Restated Certificate of Incorporation of the Registrant, as amended
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) on April 26, 2013 and incorporated herein by reference)
4.3	Amendment to Amended and Restated By-laws of the Registrant, dated June 26, 2022 (Previously filed with the Securities and Exchange Commission as an Exhibit to the Registrant's Current Report on Form 8-K (File No. 001-35945) on June 27, 2022 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	Epizyme, Inc. 2022 Equity Incentive Plan (Previously filed with the Securities and Exchange Commission as an Exhibit to the Registrant's Current Report on Form 8-K (File No. 001-35945) on May 19, 2022 and incorporated herein by reference)
107*	Filing Fee Table

* Filed herewith

Item 9. Undertakings.

1. *Item 512(a) of Regulation S-K.* The undersigned registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) To include any prospectus required by Section 10(a)(3) of the Securities Act;

(ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement; and

(iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

provided, however, that paragraphs (1)(i) and (ii) do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Commission by the registrant pursuant to Section 13 or Section 15(d) of the Exchange Act that are incorporated by reference in the registration statement.

(2) That, for the purpose of determining any liability under the Securities Act, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

2. Item 512(b) of Regulation S-K. The undersigned registrant hereby undertakes that, for purposes of determining any liability under the Securities Act, each filing of the registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Exchange Act that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

3. Item 512(h) of Regulation S-K. Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

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 4th day of August, 2022.

EPIZYME, INC.

By: /s/ Grant Bogle

Grant Bogle
President and Chief Executive Officer

POWER OF ATTORNEY AND SIGNATURES

We, the undersigned officers and directors of Epizyme, Inc., hereby severally constitute and appoint Grant Bogle and John Weidenbruch, 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/ Grant Bogle</u> Grant Bogle	President, Chief Executive Officer, Director (Principal Executive Officer and Principal Financial Officer)	August 4, 2022
<u>/s/ Joseph Beaulieu</u> Joseph Beaulieu	Corporate Controller and Treasurer (Principal Accounting Officer)	August 4, 2022
<u>/s/ Roy A. Beveridge</u> Roy A. Beveridge, M.D.	Director	August 4, 2022
<u>/s/ Kenneth Bate</u> Kenneth Bate	Director	August 4, 2022
<u>/s/ Kevin T. Conroy</u> Kevin T. Conroy	Director	August 4, 2022
<u>/s/ Michael F. Giordano</u> Michael F. Giordano, M.D.	Director	August 4, 2022

<u>/s/ Carl Goldfischer</u> Carl Goldfischer, M.D.	Director	August 4, 2022
<u>/s/ Pablo Legorreta</u> Pablo Legorreta	Director	August 4, 2022
<u>/s/ David M. Mott</u> David M. Mott	Director	August 4, 2022
<u>/s/ Victoria Richon</u> Victoria Richon, Ph.D.	Director	August 4, 2022
<u>/s/ Carol Stuckley</u> Carol Stuckley	Director	August 4, 2022

RESTATED CERTIFICATE OF INCORPORATION

OF

EPIZYME, INC.

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

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

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

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

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

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

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

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

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

A COMMON STOCK.

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

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

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

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

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

B PREFERRED STOCK.

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

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

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

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

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

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

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

EIGHTH: The Corporation shall provide indemnification as follows:

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

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

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

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

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

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

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

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

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

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

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

12. Insurance. The Corporation may purchase and maintain insurance, at its expense, to protect itself and any director, officer, employee or agent of the Corporation or another corporation, partnership, joint venture, trust or other enterprise (including any employee benefit plan) against any expense, liability or loss incurred by him or her in any such capacity, or arising out of his or her status as such, whether or not the Corporation would have the power to indemnify such person against such expense, liability or loss under the General Corporation Law of the State of Delaware.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

EPIZYME, INC.

By: /s/ Robert J. Gould

Robert J. Gould

President and Chief Executive Officer

**CERTIFICATE OF AMENDMENT OF
RESTATED CERTIFICATE OF INCORPORATION
OF
EPIZYME, INC.**

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

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

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

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

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

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

EPIZYME, INC.

By: /s/ Robert B. Bazemore

Name: Robert B. Bazemore

Title: Chief Executive Officer

**CERTIFICATE OF AMENDMENT OF
RESTATED CERTIFICATE OF INCORPORATION
OF
EPIZYME, INC.**

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

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

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

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

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

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

EPIZYME, INC.

By: /s/ Robert B. Bazemore

Name: Robert B. Bazemore

Title: Chief Executive Officer

**CERTIFICATE OF AMENDMENT OF
RESTATED CERTIFICATE OF INCORPORATION
OF
EPIZYME, INC.**

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

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

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

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

"FOURTH: The total number of shares of all classes of stock which the Corporation shall have the authority to issue is 455,000,000 shares, consisting of (i) 450,000,000 shares of Common Stock, \$0.0001 par value per share ("Common Stock"), and (ii) 5,000,000 shares of Preferred Stock, \$0.0001 par value per share ("Preferred Stock")."

IN WITNESS WHEREOF, this Certificate of Amendment has been executed by a duly authorized officer of the Corporation on this 17th day of May, 2022.

EPIZYME, INC.

By: /s/ Grant Bogle
Name: Grant Bogle
Title: Chief Executive Officer

August 4, 2022

Epizyme, Inc.
400 Technology Square
Cambridge, MA 02139

Re: 2022 Equity Incentive 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 15,151,463 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 2022 Equity Incentive Plan (collectively, the "Plan").

We have examined the Restated Certificate of Incorporation and Restated 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,

/s/ Wilmer Cutler Pickering Hale and Dorr LLP

WILMER CUTLER PICKERING HALE AND DORR LLP

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the Registration Statement (Form S-8) pertaining to the 2022 Equity Incentive Plan of Epizyme, Inc. of our reports dated March 1, 2022, 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, 2021, filed with the Securities and Exchange Commission.

/s/ Ernst & Young LLP

Boston, Massachusetts
August 4, 2022

Calculation of Filing Fee Tables

Form S-8
(Form Type)

Epizyme, Inc.
(Exact Name of Registrant as Specified in its Charter)

Table 1—Newly Registered Securities

Security Type	Security Class Title	Fee Calculation Rule	Amount Registered (1)	Proposed Maximum Offering Price Per Unit	Maximum Aggregate Offering Price	Fee Rate	Amount of Registration Fee
Equity	Common Stock, \$0.0001 par value per share	Other	15,151,463 shares (2)	\$1.49 (3)	\$22,575,680 (3)	\$92.70 per \$1,000,000	\$2,092.77
Total Offering Amounts							\$2,092.77
Total Fee Offsets							\$0
Net Fee Due							\$2,092.77

- (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 15,151,463 shares issuable under the 2022 Equity Incentive 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, and based upon the average of the high and low prices of the Registrant's Common Stock as reported on the Nasdaq Global Select Market on August 2, 2022.