



EPIZYME, INC.
400 Technology Square
Cambridge, Massachusetts 02139

NOTICE OF 2015 ANNUAL MEETING OF STOCKHOLDERS

To be held May 19, 2015

You are cordially invited to attend the 2015 Annual Meeting of Stockholders (the "Annual Meeting") of Epizyme, Inc., which is scheduled to be held on Tuesday, May 19, 2015 at 10:00 a.m. Eastern time, at the offices of Wilmer Cutler Pickering Hale and Dorr, 60 State Street, Boston, Massachusetts 02109.

Only stockholders who owned common stock at the close of business on April 1, 2015 can vote at the Annual Meeting or any adjournment that may take place. At the Annual Meeting, the stockholders will consider and vote on the following matters:

1. Election of two class II directors to our board of directors, each to serve until the 2018 annual meeting of stockholders;
2. Ratification of the appointment of Ernst & Young LLP as our independent registered public accounting firm for the fiscal year ending December 31, 2015; and
3. Transaction of any other business properly brought before the Annual Meeting or any adjournment or postponement of the Annual Meeting.

You can find more information, including the nominees for directors, in the attached Proxy Statement. The board of directors recommends that you vote in favor of each of proposals one and two as outlined in the attached Proxy Statement.

We cordially invite all stockholders to attend the Annual Meeting in person. Stockholders of record at the close of business on April 1, 2015, the record date for the Annual Meeting, are entitled to notice of, and to vote at, the Annual Meeting or any adjournment or postponement of the Annual Meeting. You may obtain directions to the location of the Annual Meeting by calling our offices at 617-229-5872. Whether or not you expect to attend the Annual Meeting in person, please complete, sign, date and return the enclosed proxy card as promptly as possible in the postage-prepaid envelope provided to ensure your representation and the presence of a quorum at the Annual Meeting. Alternatively, you may vote your shares on the Internet by visiting <http://www.investorvote.com/epzm> or by telephone by calling 1-800-652-VOTE (8683) and following the recorded instructions. Your vote is important regardless of the number of shares you own. If you send in your proxy card or vote by telephone or the Internet and then decide to attend the Annual Meeting to vote your shares in person, you may still do so. Your proxy is revocable in accordance with the procedures set forth in the Proxy Statement.

If your shares are held in "street name," that is, held for your account by a broker or other nominee, you will receive instructions from the holder of record that you must follow for your shares to be voted.

By order of the Board of Directors,

/s/ Robert J. Gould

Robert J. Gould, Ph.D.

President, Chief Executive Officer and Secretary

Cambridge, Massachusetts
April 15, 2015

Epizyme, Inc.

Proxy Statement

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**EPIZYME, INC.
400 Technology Square
Cambridge, Massachusetts 02139
617-229-5872**

**PROXY STATEMENT
FOR THE 2015 ANNUAL MEETING OF STOCKHOLDERS
to be held May 19, 2015**

This proxy statement and the enclosed proxy card contain information about the 2015 Annual Meeting of Stockholders of Epizyme, Inc. (the "Annual Meeting") to be held on Tuesday, May 19, 2015 at 10:00 a.m. Eastern time, at the offices of Wilmer Cutler Pickering Hale and Dorr LLP, 60 State Street, Boston, Massachusetts, 02109. The board of directors of Epizyme, Inc. is using this proxy statement to solicit proxies for use at the Annual Meeting. In this proxy statement, unless expressly stated otherwise or the context otherwise requires, the use of "Epizyme," "our," "we" or "us" refers to Epizyme, Inc. and its subsidiary.

All properly submitted proxies will be voted in accordance with the instructions contained in those proxies. If no instructions are specified, the proxies will be voted in accordance with the recommendation of our board of directors with respect to each of the matters set forth in the accompanying Notice of Meeting. You may revoke your proxy at any time before it is exercised at the meeting by giving our Secretary written notice to that effect.

Our Annual Report to Stockholders for the fiscal year ended December 31, 2014 and this proxy statement and proxy card are first being mailed to stockholders on or about April 22, 2015.

**Important Notice Regarding the Availability of Proxy Materials for
the Annual Meeting of Stockholders to be Held on May 19, 2015:**

**This proxy statement and our 2014 Annual Report to Stockholders are
available for viewing, printing and downloading at <http://www.edocumentview.com/EPZM>.**

A copy of our Annual Report on Form 10-K for the fiscal year ended December 31, 2014, as filed with the Securities and Exchange Commission, or SEC, except for exhibits, will be furnished without charge to any stockholder upon written request to Epizyme, Inc. 400 Technology Square, Cambridge, Massachusetts 02139. This proxy statement and our Annual Report on Form 10-K for the fiscal year ended December 31, 2014 are also available on the SEC's website at <http://www.sec.gov>.

IMPORTANT INFORMATION ABOUT THE ANNUAL MEETING AND VOTING

Purpose of the Annual Meeting

At the Annual Meeting, our stockholders will consider and vote on the following matters:

1. Election of two class II directors to our board of directors, each to serve until the 2018 annual meeting of stockholders;
2. Ratification of the appointment of Ernst & Young LLP as our independent registered public accounting firm for the fiscal year ending December 31, 2015; and
3. Transaction of any other business properly brought before the 2015 Annual Meeting or any adjournment or postponement thereof.

As of the date of this proxy statement, we are not aware of any business to come before the meeting other than the first two items noted above.

Board of Directors Recommendation

Our board of directors unanimously recommends that you vote:

FOR the election of the two nominees to serve as class II directors on our board of directors for a three-year term; and

FOR the ratification of the appointment of Ernst & Young LLP as our independent registered public accounting firm for the fiscal year ending December 31, 2015.

Availability of Proxy Materials

The proxy materials, including this proxy statement, a proxy card or voting instruction card and Epizyme's 2014 Annual Report, are being mailed to stockholders on or about April 22, 2015. These materials are also available for viewing, printing and downloading on the Internet at <http://www.edocumentview.com/EPZM>.

Who Can Vote at the Annual Meeting

Only stockholders of record at the close of business on the record date of April 1, 2015, are entitled to receive notice of the Annual Meeting and to vote the shares of Epizyme common stock that they held on that date. As of April 1, 2015, there were 40,483,223 shares of common stock issued and outstanding. Each share of common stock is entitled to one vote on each matter properly brought before the Annual Meeting.

Difference between a "stockholder of record" and a beneficial owner of shares held in "street name"

Stockholder of Record. If your shares are registered directly in your name with our transfer agent, Computershare, then you are considered a "stockholder of record" of those shares. In this case, your set of proxy materials has been sent to you directly by us. You may vote your shares by proxy prior to the Annual Meeting by following the instructions contained on the enclosed proxy card.

Beneficial Owners of Shares Held in Street Name. If your shares are held in a brokerage account or by a bank, trust or other nominee or custodian, then you are considered the beneficial owner of those shares, which are held in "street name." In this case, your set of proxy materials has been forwarded to you by that organization. The organization holding your account is considered the stockholder of record for purposes of voting at the Annual Meeting. As the beneficial owner, you have the right to instruct that organization as to how to vote the shares held in your account by following the instructions contained on the voting instruction card provided to you by that organization.

How to Vote

If you are a stockholder of record, you can vote your shares in one of two ways: either by proxy or in person at the Annual Meeting. If you choose to vote by proxy, you may do so by telephone, via the Internet or by mail. Each of these methods is explained below. **If you hold your shares of Epizyme common stock in multiple accounts, you should vote your shares as described in each set of proxy materials you receive.**

- *By Telephone.* You may transmit your proxy voting instructions by calling the telephone number specified on the enclosed proxy card. You will need to have the proxy card in hand when you call. If you choose to vote by telephone, you do not have to return the proxy card.
- *Via the Internet.* You may transmit your proxy voting instructions via the Internet by accessing the website specified on the enclosed proxy card. You will need to have the proxy card in hand when you access the website. If you choose to vote via the Internet, you do not have to return the proxy card.
- *By Mail.* You may vote by proxy by completing, signing and dating the enclosed proxy card and returning it in the enclosed prepaid envelope.
- *In Person at the Annual Meeting.* You may vote in person at the Annual Meeting. We will give you a ballot when you arrive. If you are the beneficial owner of shares held in “street name” and you wish to vote in person at the Annual Meeting, you must obtain a legal proxy from the organization that holds your shares and present it with your ballot to the inspector of election at the Annual Meeting. Even if you plan to attend the Annual Meeting, we urge you to vote your shares by proxy in advance of the Annual Meeting so that if you should become unable to attend the Annual Meeting your shares will be voted as directed by you.

Telephone and Internet voting for stockholders of record will be available up until 1:00 a.m. Eastern time on May 19, 2015, and mailed proxy cards must be received by May 18, 2015 in order to be counted at the Annual Meeting. If the Annual Meeting is adjourned or postponed, these deadlines may be extended.

The voting deadlines and availability of telephone and Internet voting for beneficial owners of shares held in “street name” will depend on the voting processes of the organization that holds your shares. Therefore, we urge you to carefully review and follow the voting instruction card and any other materials that you receive from that organization.

Quorum

A quorum of stockholders is necessary to hold a valid meeting. Our amended and restated by-laws provide that a quorum will exist if stockholders holding a majority of the shares of stock issued and outstanding and entitled to vote are present at the meeting in person or by proxy. Abstentions and broker non-votes count as present for establishing a quorum but will not be counted as votes cast. Broker non-votes occur when your broker or other nominee submits a proxy for your shares (because the broker or other nominee has received instructions from you on one or more proposals, but not all, or has not received instructions from you but is entitled to vote on a particular “discretionary” matter) but does not indicate a vote for a particular proposal because the broker or other nominee either does not have the authority to vote on that proposal and has not received voting instructions from you or has discretionary authority but chooses not to exercise it. If a quorum is not present, the meeting may be adjourned until a quorum is obtained.

Ballot Measures Considered “Routine” and “Non-Routine”

The election of directors (Proposal No. 1) is a matter considered non-routine under applicable rules. A broker or other nominee cannot vote without instructions on non-routine matters, and therefore there may be broker non-votes on Proposal No. 1.

The ratification of the appointment of Ernst & Young LLP as Epizyme’s independent registered public accounting firm for 2015 (Proposal No. 2) is a matter considered routine under applicable rules. A broker or

other nominee may generally exercise discretionary authority and vote on routine matters. If they exercise this discretionary authority, no broker non-votes are expected to exist in connection with Proposal No. 2.

Votes Required to Elect a Director and Ratify Appointment of Ernst & Young LLP

To be elected, a director must receive a plurality of the votes cast by stockholders entitled to vote at the meeting (Proposal No. 1).

The ratification of the appointment of Ernst & Young LLP as Epizyme's independent registered public accounting firm requires the affirmative vote of the majority of the shares of common stock present or represented by proxy and voted "for" or "against" such matter (Proposal No. 2).

Abstentions and broker non-votes will not be counted as votes cast on any of the proposals. Accordingly, abstentions and broker non-votes will have no effect on the voting on any of the proposals.

Method of Counting Votes

Each holder of common stock is entitled to one vote at the Annual Meeting on each matter to come before the Annual Meeting, including the election of a director, for each share held by such stockholder as of the record date. Votes cast in person at the Annual Meeting or by proxy by mail, via the Internet or by telephone will be tabulated by the inspector of election appointed for the Annual Meeting, who will also determine whether a quorum is present.

Revoking a Proxy; Changing Your Vote

If you are a stockholder of record, you may revoke your proxy before the vote is taken at the meeting:

- by submitting a new proxy with a later date before the applicable deadline either signed and returned by mail or transmitted using the telephone or Internet voting procedures described in the "How to Vote" section above;
- by voting in person at the meeting; or
- by filing a written revocation with our corporate Secretary.

If your shares are held in "street name," you may submit new voting instructions by contacting your broker or other organization holding your account. You may also vote in person at the Annual Meeting, which will have the effect of revoking any previously submitted voting instructions, if you obtain a legal proxy from the organization that holds your shares as described in the "How to Vote" section above.

Your attendance at the Annual Meeting will not automatically revoke your proxy.

Costs of Proxy Solicitation

We will bear the costs of soliciting proxies. In addition to solicitations by mail, our directors, officers and regular employees, without additional remuneration, may solicit proxies by telephone, facsimile, email, personal interviews and other means.

Voting Results

We plan to announce preliminary voting results at the Annual Meeting and will publish final results in a Current Report on Form 8-K to be filed with the SEC within four business days following the Annual Meeting.

PROPOSAL NO. 1—ELECTION OF TWO CLASS II DIRECTORS

Our board of directors currently consists of seven members. In accordance with the terms of our certificate of incorporation and by-laws, our board of directors is divided into three classes, class I, class II and class III, with members of each class serving staggered three-year terms. The members of the classes are divided as follows:

- the class I directors are Andrew R. Allen, M.D., Ph.D. and Kenneth Bate, and their term will expire at the annual meeting of stockholders to be held in 2017;
- the class II directors are Carl Goldfischer, M.D. and Beth Seidenberg, M.D., and their term expires at the 2015 Annual Meeting; and
- the class III directors are Robert J. Gould, Ph.D., David M. Mott and Richard F. Pops, and their term will expire at the annual meeting of stockholders to be held in 2016.

The current class II and class III directors were initially elected as directors pursuant to a voting agreement to which we were a party with the former holders of our preferred stock prior to our initial public offering. The voting agreement terminated upon the closing of our initial public offering, and we have no further contractual obligations regarding the election of our directors.

Upon the expiration of the term of a class of directors, directors in that class will be eligible to be elected for a new three-year term at the annual meeting of stockholders in the year in which their term expires.

Our certificate of incorporation and by-laws provide that the authorized number of directors may be changed only by resolution of our board of directors. Our certificate of incorporation and by-laws also provide that our directors may be removed only for cause by the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in an annual election of directors, and that any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in office.

Our board of directors has nominated Carl Goldfischer, M.D. and Beth Seidenberg, M.D. for election as class II directors at the Annual Meeting. Each of the nominees is presently a director, and each has indicated a willingness to continue to serve as director, if elected. If a nominee becomes unable or unwilling to serve, however, the proxies may be voted for substitute nominees selected by our board of directors.

We have no formal policy regarding board diversity. Our priority in selection of board members is identification of members who will further the interests of our stockholders through their established record of professional accomplishment, the ability to contribute positively to the collaborative culture among board members, knowledge of our business and understanding of the competitive landscape.

Nominees for Election as Class II Directors

Biographical information as of February 28, 2015, including principal occupation and business experience during the last five years, for our nominees for election as class II directors at our 2015 Annual Meeting is set forth below.

	<u>Age</u>	<u>Director Since</u>
<p><i>Carl Goldfischer, M.D.</i> has served as a director since September 2009. Dr. Goldfischer has served as an Investment Partner and Managing Director of Bay City Capital LLC, or Bay City Capital, a life sciences investment firm and a holder of more than 5% of our voting securities, serving as a member of the board of directors and executive committee, and has been with the firm since January 2000. Prior to joining Bay City Capital, Dr. Goldfischer was Chief Financial Officer of ImClone Systems Incorporated, a biopharmaceutical company. Since 2004, Dr. Goldfischer has served on the board of directors of EnteroMedics Inc., a publicly traded medical device company. He has previously served on the board of directors of two other publicly traded companies, MAP Pharmaceuticals, Inc. from 2004 to 2011 and Poniard Pharmaceuticals, Inc. from 2000 to 2012. Dr. Goldfischer received a B.A. from Sarah Lawrence College and an M.D. with honors in Scientific Research from Albert Einstein College of Medicine. We believe that Dr. Goldfischer’s extensive finance and investment experience, his experience as an executive and his service on the board of directors of numerous public and privately held companies allow him to be a key contributor to our board of directors.</p>	55	September 2009
<p><i>Beth Seidenberg, M.D.</i> has served as a director since February 2008. Dr. Seidenberg has been a partner at Kleiner Perkins Caufield & Byers, a venture capital firm and a holder of more than 5% of our voting securities, since May 2005, where she has primarily focused on life sciences investing. Dr. Seidenberg was previously the Senior Vice President, Head of Global Development and Chief Medical Officer at Amgen, Inc., a biotechnology company. In addition, Dr. Seidenberg was a senior executive in research and development at Bristol Myers Squibb Company, a biopharmaceutical company, and Merck. Dr. Seidenberg received a B.S. from Barnard College and an M.D. from the University of Miami School of Medicine and completed her post-graduate training at The Johns Hopkins University, George Washington University and the National Institutes of Health. Dr. Seidenberg serves on the boards of directors of TESARO, Inc., or TESARO, and Atara Biotherapeutics. We believe that Dr. Seidenberg’s extensive experience in the life sciences industry as a senior executive and venture capitalist, as well as her training as a physician, provide her with the qualifications and skills to serve as a director of our company.</p>	57	February 2008

The proxies will be voted in favor of the nominees unless a contrary specification is made in the proxy. The nominees have consented to serve as our directors if elected. However, if either nominee is unable to serve or for good cause will not serve as a director, the persons named in the proxy intend to vote in their discretion for one or more substitutes who will be designated by our board of directors.

The board of directors recommends voting “FOR” the election of Carl Goldfischer and Beth Seidenberg as class II directors, for a three-year term ending at the annual meeting of stockholders to be held in 2018.

Directors Continuing in Office

Biographical information as of February 28, 2015, including principal occupation and business experience during the last five years, for our directors continuing in office is set forth below.

	<u>Age</u>	<u>Director Since</u>
<i>Class III Directors (Term Expires at 2016 Annual Meeting)</i>		
<p><i>Robert J. Gould, Ph.D.</i> has served as a director since March 2008, our Chief Executive Officer since March 2010 and our President since September 2014. Prior to joining us, from November 2006 to March 2010, Dr. Gould served as Director of Novel Therapeutics at The Broad Institute of MIT and Harvard, or Broad, a research institute. Prior to that, Dr. Gould was Vice President, Licensing and External Research, Merck Research Laboratories, at Merck & Co., Inc., or Merck, a healthcare company, where he held a variety of leadership positions during his tenure of over 20 years. Dr. Gould received a B.A. from Spring Arbor College and a Ph.D. from The University of Iowa and undertook post-doctoral studies at The Johns Hopkins University. We believe that Dr. Gould’s detailed knowledge of our company and his over 30 years in the pharmaceutical and biotechnology industries, including his roles at Broad and at Merck, provide a valuable contribution to our board of directors.</p>	60	March 2008
<p><i>David M. Mott</i> has served as a director since December 2009. Mr. Mott has served as a general partner of New Enterprise Associates, Inc., an investment firm focused on venture capital and growth equity investments and a holder of more than 5% of our voting securities, since September 2008, where he leads the healthcare investing practice. From 1992 until 2008, Mr. Mott worked at MedImmune, Inc., or MedImmune, a biotechnology company and subsidiary of AstraZeneca Plc, or AstraZeneca, and served in numerous roles during his tenure, including Chief Financial Officer, President and Chief Operating Officer, and most recently as Chief Executive Officer from October 2000 to July 2008. During that time, Mr. Mott also served as Executive Vice President of AstraZeneca from June 2007 to July 2008 following AstraZeneca’s acquisition of MedImmune in June 2007. Prior to joining MedImmune, Mr. Mott was a Vice President in the healthcare investment banking group at Smith Barney, Harris Upham & Co. Inc. Mr. Mott received a B.A. from Dartmouth College. Mr. Mott also serves as the Chairman of the Board of Directors of both TESARO and Ardelyx, Inc. We believe that Mr. Mott’s extensive experience in the life sciences industry as a senior executive and venture capitalist, as well as his service on the boards of directors of other life sciences companies, provide him with the qualifications and skills to serve as a director of our company.</p>	49	December 2009
<p><i>Richard F. Pops</i> has served as a director since September 2008. Mr. Pops has served as Chief Executive Officer of Alkermes plc, or Alkermes, a publicly traded biopharmaceutical company since 1991. Mr. Pops has been a director of Alkermes since February 1991 and has been Chairman of the Board of Directors since April 2007. Mr. Pops also serves on the board of directors of Neurocrine Biosciences, Inc. and Acceleron Pharma, Inc. Mr. Pops received a B.A. in economics from Stanford University. We believe that Mr. Pops’ leadership experience, including as chief executive officer of a public pharmaceutical company, his business judgment and his industry knowledge provide him with the qualifications to serve as a director of our company.</p>	52	September 2008

	<u>Age</u>	<u>Director Since</u>
<i>Class I Directors (Term Expires at 2017 Annual Meeting)</i>		
<p>Andrew R. Allen, M.D., Ph.D. has served as a director since June 2014. Dr. Allen is a co-founder of Clovis Oncology, Inc., or Clovis, a biopharmaceutical company, and has served as Executive Vice President of Clinical and Pre-Clinical Development and Chief Medical Officer of Clovis since its inception in April 2009. Prior to co-founding Clovis, he served in the same role at Pharmion Corporation, a pharmaceutical company, beginning in 2006. From 2004 to 2006, Dr. Allen served as Vice President of BioPharma Development and Head of the Oncology Therapeutic Unit for Chiron Corporation, a biotechnology company. Prior to that, Dr. Allen served as global project head in Abbott Laboratories' oncology franchise, and he progressed through positions of increasing responsibility at the management consulting firm McKinsey & Company, with a focus on oncology strategy. Dr. Allen qualified in medicine at Oxford University and earned his Ph.D. from the Imperial College of Science, Technology and Medicine in London. Dr. Allen also obtained post-graduate internal medicine qualification as a Member of Royal College of Physicians. We believe that Dr. Allen's extensive experience in the pharmaceutical industry and his expertise in oncology clinical development and oncology strategy make him a valuable member of our board of directors.</p>	47	June 2014
<p>Kenneth Bate has served as a director since December 2014. Mr. Bate is currently an independent consultant in the biotechnology field. From 2009 to 2012, Mr. Bate served as President and Chief Executive Officer of Archemix, Inc., or Archemix, a privately-held biotechnology company. Prior to Archemix, from 2006 to 2009, Mr. Bate served in various positions at NitroMed, Inc., a pharmaceutical company, most recently as President and Chief Executive Officer. From 2002 to 2005, Mr. Bate served as Chief Financial Officer of Millennium Pharmaceuticals, where he headed the commercial organization. Prior to joining Millennium Pharmaceuticals, Mr. Bate co-founded JSB Partners, LLC, a banking and advisory services firm for biopharmaceutical and life sciences companies. From 1990 to 1996, he was with Biogen Inc., a biotechnology company, first as their Chief Financial Officer, and then as head of the commercial organization responsible for launching the multiple sclerosis business. Mr. Bate serves on the board of directors of AVEO Pharmaceuticals, Inc., BioMarin Pharmaceuticals, Inc. and Genocera Biosciences, Inc. and, through December 2014, served on the board of directors of Cubist Pharmaceuticals, Inc, where he was the chairman of the board of directors. He is also a member of the board of directors of Catabasis Pharmaceuticals, Inc., a privately-held biotherapeutics company, and TransMedics, Inc. a privately-held medical device company. Mr. Bate received his B.A. in chemistry from Williams College and his M.B.A. from the Wharton School of the University of Pennsylvania. We believe that Mr. Bate's extensive finance and leadership experience, his experience as an executive and his service on the board of directors of numerous public and privately held companies allow him to be a key contributor to our board of directors.</p>	64	December 2014

There are no family relationships between or among any of our directors or executive officers. The principal occupation and employment during the past five years of each of our directors was carried on, in each case except as specifically identified above, with a corporation or organization that is not a parent, subsidiary or other affiliate of us. There is no arrangement or understanding between any of our directors and any other person or persons pursuant to which he or she is to be selected as a director.

There are no material legal proceedings to which any of our directors is a party adverse to us or any of our subsidiaries or in which any such person has a material interest adverse to us or any of our subsidiaries.

Executive Officers Who Are Not Directors

Biographical information as of February 28, 2015 for our executive officers who are not directors is listed below.

	<u>Age</u>	<u>Officer Since</u>
<p>Andrew E. Singer has served as our Executive Vice President, Finance and Administration, Chief Financial Officer and Treasurer since February 2015. Prior to joining us, from 2004 to January 2015, Mr. Singer served in increasing levels of responsibility in the Health Care Investment Banking Group at RBC Capital Markets Corporation, or RBC, an investment bank, serving as a Managing Director from 2007 to 2015. Prior to joining RBC, Mr. Singer worked at Petkevitch & Company, co-founded MVC Capital, and worked at Robertson, Stephens & Co., The Shansby Group and The Blackstone Group. Mr. Singer serves on the board of directors of the J.F. Kapnek Trust. Mr. Singer received a B.A. from Yale University and an M.B.A. from Harvard University Graduate School of Business.</p>	44	February 2015
<p>Robert A. Copeland, Ph.D. has served as our President of Research and Chief Scientific Officer since January 2015 and previously served as our Executive Vice President and Chief Scientific Officer from September 2008 to January 2015. Prior to joining us, from January 2003 to September 2008, Dr. Copeland was Vice President, Cancer Biology, Oncology Center of Excellence in Drug Discovery, at Glaxosmithkiline, or GSK, a pharmaceutical company. Before joining GSK, Dr. Copeland held scientific staff positions at Merck Research Laboratories of Merck and Bristol-Myers Squibb Company, a biopharmaceutical company, and a faculty position at the University of Chicago Pritzker School of Medicine. Dr. Copeland received a B.S. in chemistry from Seton Hall University, a Ph.D. in chemistry from Princeton University and did postdoctoral studies as the Chaim Weizmann Fellow at the California Institute of Technology.</p>	58	September 2008
<p>Peter T.C. Ho, M.D., Ph.D. has served as our Chief Development Officer since September 2014. Prior to joining us, from February 2013 to September 2014, Dr. Ho served as Chief Executive Officer of Metastagen Inc., a pharmaceutical preparation company that he co-founded. Prior to that, Dr. Ho served as President of BeiGene Ltd., a biopharmaceutical company that he co-founded, from October 2010 to December 2012, as Vice President of Oncology Development at Johnson & Johnson from September 2008 to September 2010 and, prior to that, as Senior Vice President of the Oncology Center of Excellence for Drug Development at GSK. Dr. Ho is a board-certified pediatric hematologist/oncologist and was formerly a fellow at the Dana-Farber Cancer Institute, the National Cancer Center Institute, or NCI, and the FDA. He received a B.A. in biology from the Johns Hopkins University and an M.D. and Ph.D. (pharmacology) from the Yale University School of Medicine.</p>	53	September 2014

The principal occupation and employment during the past five years of each of our executive officers was carried on, in each case except as specifically identified above, with a corporation or organization that is not a parent, subsidiary or other affiliate of us. There is no arrangement or understanding between any of our executive officers and any other person or persons pursuant to which he was or is to be selected as an executive officer.

There are no material legal proceedings to which any of our executive officers is a party adverse to us or any of our subsidiaries or in which any such person has a material interest adverse to us or any of our subsidiaries.

**PROPOSAL NO. 2—RATIFICATION OF THE APPOINTMENT OF ERNST & YOUNG LLP
AS EPIZYME’S INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM FOR THE
FISCAL YEAR ENDING DECEMBER 31, 2015**

Epizyme’s stockholders are being asked to ratify the appointment by the audit committee of the board of directors of Ernst & Young LLP as Epizyme’s independent registered public accounting firm. Ernst & Young LLP has served as Epizyme’s independent registered public accounting firm since 2008.

The audit committee is solely responsible for selecting Epizyme’s independent registered public accounting firm for the fiscal year ending December 31, 2015. Stockholder approval is not required to appoint Ernst & Young LLP as Epizyme’s independent registered public accounting firm. However, the board of directors believes that submitting the appointment of Ernst & Young LLP to the stockholders for ratification is good corporate governance. If the stockholders do not ratify this appointment, the audit committee will reconsider whether to retain Ernst & Young LLP. If the selection of Ernst & Young LLP is ratified, the audit committee, in its discretion, may direct the appointment of a different independent registered public accounting firm at any time it decides that such a change would be in the best interest of Epizyme and its stockholders.

A representative of Ernst & Young LLP is expected to be present at the Annual Meeting and will have an opportunity to make a statement if he or she desires to do so and to respond to appropriate questions from our stockholders.

Epizyme incurred the following fees from Ernst & Young LLP for the audit of the consolidated financial statements and for other services provided during the years ended December 31, 2014 and 2013.

	2014	2013
Audit fees (1)	\$424,280	\$1,175,843
Audit-related fees	—	—
Tax fees (2)	111,847	68,000
All other fees (3)	—	1,995
Total fees	\$536,127	\$1,245,838

- (1) Audit fees consist of fees for the audit of our financial statements, the review of the interim financial statements included in our quarterly reports on Form 10-Q, and other professional services provided in connection with registration statements including our initial public offering.
- (2) Tax fees consist of fees for tax compliance, tax advice and tax planning services.
- (3) All other fees represent payment for access to the Ernst & Young LLP online accounting research database.

Audit Committee Pre-approval Policy and Procedures

Our audit committee has adopted policies and procedures relating to the approval of all audit and non-audit services that are to be performed by our independent registered public accounting firm. This policy provides that we will not engage our independent registered public accounting firm to render audit or non-audit services unless the service is specifically approved in advance by our audit committee or the engagement is entered into pursuant to the pre-approval procedure described below.

From time to time, our audit committee may pre-approve specified types of services that are expected to be provided to us by our independent registered public accounting firm during the next 12 months. Any such pre-approval is detailed as to the particular service or type of services to be provided and is also generally subject to a maximum dollar amount.

During our 2014 and 2013 fiscal years, no services were provided to us by Ernst & Young LLP other than in accordance with the pre-approval policies and procedures described above.

The board of directors recommends voting “FOR” Proposal No. 2 to ratify the appointment of Ernst & Young LLP as Epizyme’s independent registered public accounting firm.

CORPORATE GOVERNANCE

Director Nomination Process

Our nominating and corporate governance committee is responsible for identifying individuals qualified to serve as directors, consistent with criteria approved by our board, and recommending the persons to be nominated for election as directors, except where we are legally required by contract, law or otherwise to provide third parties with the right to nominate.

The process followed by our nominating and corporate governance committee to identify and evaluate director candidates includes requests to board members and others for recommendations, meetings from time to time to evaluate biographical information and background material relating to potential candidates and interviews of selected candidates by members of the committee and our board. The qualifications, qualities and skills that our nominating and corporate governance committee believes must be met by a committee-recommended nominee for a position on our board of directors are as follows:

- Nominees should have a reputation for integrity, honesty and adherence to high ethical standards.
- Nominees should have demonstrated business acumen, experience and ability to exercise sound judgments in matters that relate to Epizyme's current and long-term objectives and should be willing and able to contribute positively to Epizyme's decision-making process.
- Nominees should have a commitment to understand Epizyme and its industry and to regularly attend and participate in meetings of the board of directors and its committees.
- Nominees should have the interest and ability to understand the sometimes conflicting interests of our various constituencies, which include stockholders, employees, customers, governmental units, creditors and the general public, and to act in the interests of all stockholders.
- Nominees should not have, nor appear to have, a conflict of interest that would impair the nominee's ability to represent the interests of all of our stockholders and to fulfill the responsibilities of a director.
- Nominees shall not be discriminated against on the basis of race, religion, national origin, sex, sexual orientation, disability or any other basis proscribed by law. The value of diversity on our board of directors is considered.
- Nominees should normally be able to serve for at least three years before reaching the age of 75.

Stockholders may recommend individuals to the nominating and corporate governance committee for consideration as potential director candidates. Any such proposals should be submitted to our corporate secretary at our principal executive offices and should include appropriate biographical and background material to allow the nominating and corporate governance committee to properly evaluate the potential director candidate and the number of shares of our stock beneficially owned by the stockholder proposing the candidate. Assuming that biographical and background material has been provided on a timely basis, any recommendations received from stockholders will be evaluated in the same manner as potential nominees proposed by the nominating and corporate governance committee. If our board of directors determines to nominate a stockholder-recommended candidate and recommends his or her election, then his or her name will be included on our proxy card for the next annual meeting.

Director Independence

Applicable NASDAQ rules require a majority of a listed company's board of directors to be comprised of independent directors within one year of listing. In addition, the NASDAQ rules require that, subject to specified exceptions, each member of a listed company's audit, compensation and nominating and corporate governance committees be independent and that audit committee members also satisfy independence criteria set forth in Rule 10A-3 under the Securities Exchange Act of 1934, as amended, or the Exchange Act and that compensation

committee members satisfy independence criteria set forth in Rule 10C-1 under the Exchange Act. Under applicable NASDAQ rules, a director will only qualify as an “independent director” if, in the opinion of the listed company’s board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. In order to be considered independent for purposes of Rule 10A-3, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors, or any other board committee, accept, directly or indirectly, any consulting, advisory, or other compensatory fee from the listed company or any of its subsidiaries or otherwise be an affiliated person of the listed company or any of its subsidiaries. In addition, in affirmatively determining the independence of any director who will serve on a company’s compensation committee, Rule 10C-1 under the Exchange Act requires that a company’s board of directors must consider all factors specifically relevant to determining whether a director has a relationship to such company which is material to that director’s ability to be independent from management in connection with the duties of a compensation committee member, including: the source of compensation to the director, including any consulting, advisory or other compensatory fee paid by such company to the director, and whether the director is affiliated with the company or any of its subsidiaries or affiliates.

In March 2015, our board of directors undertook a review of the composition of our board of directors and the independence of each director. Based upon information requested from and provided by each director concerning his or her background, employment and affiliations, including family relationships, our board of directors determined that each of our directors, with the exception of Dr. Gould, is an “independent director” as defined under applicable NASDAQ rules. In making such determination, our board of directors considered the relationships that each such non-employee director has with our company and all other facts and circumstances that our board of directors deemed relevant in determining his or her independence, including the beneficial ownership of our capital stock by each non-employee director. Dr. Gould is not an independent director under these rules because he is our chief executive officer.

Board Committees

Our board of directors has established an audit committee, a compensation committee and a nominating and corporate governance committee. Each of the audit committee, compensation committee and nominating and corporate governance committee operates under a charter, and each such committee reviews its respective charter at least annually. A current copy of the charter for each of the audit committee, compensation committee and the nominating and corporate governance committee is posted on the corporate governance section of the “Investor Center” on our website, <http://www.epizyme.com>.

Audit Committee

The members of our audit committee are Dr. Goldfischer, Mr. Bate and Mr. Pops. Kazumi Shiosaki, Ph.D. was a member of our board of directors and our audit committee until our 2014 Annual Meeting, and Dr. Allen was a member of the audit committee from his election to the board of directors in June 2014 until the election of Mr. Bate to the board of directors in December 2014. Dr. Goldfischer is chair of the audit committee. Our audit committee met five times during 2014. Our audit committee’s responsibilities include:

- appointing, approving the compensation of, and assessing the independence of our registered public accounting firm;
- overseeing the work of our independent registered public accounting firm, including through the receipt and consideration of reports from that firm;
- reviewing and discussing with management and our independent registered public accounting firm our annual and quarterly financial statements and related disclosures;
- monitoring our internal control over financial reporting, disclosure controls and procedures and code of conduct;

- overseeing our internal audit function, if any;
- discussing our risk management policies;
- establishing policies regarding hiring employees from our independent registered public accounting firm and procedures for the receipt and retention of accounting related complaints and concerns;
- meeting independently with our internal audit staff, if any, our independent registered public accounting firm and management;
- reviewing and approving or ratifying any related person transactions; and
- preparing the audit committee report required by Securities and Exchange Commission, or SEC, rules.

All audit and non-audit services, other than *de minimis* non-audit services, to be provided to us by our independent registered public accounting firm must be approved in advance by our audit committee.

Our board of directors has determined that Dr. Goldfischer is an “audit committee financial expert” as defined in applicable SEC rules. We believe that the composition of our audit committee meets the requirements for independence under current NASDAQ and SEC rules and regulations.

Compensation Committee

The members of our compensation committee are Dr. Seidenberg, Mr. Mott and Dr. Allen. Thomas O. Daniel, M.D. was a member of our board of directors until our 2014 Annual Meeting and a member of our compensation committee until his resignation from our compensation committee in April 2014. Mr. Mott is chair of the compensation committee. Our compensation committee met twice during 2014. Our compensation committee’s responsibilities include:

- reviewing and making recommendations to our board of directors with respect to our chief executive officer’s compensation;
- reviewing and approving, or making recommendations to our board of directors with respect to, the compensation of our other executive officers;
- overseeing an evaluation of our senior executives;
- reviewing and making recommendations to our board of directors with respect to management succession planning;
- overseeing and administering our cash and equity incentive plans;
- reviewing and making recommendations to our board of directors with respect to director compensation;
- reviewing and discussing annually with management our “Compensation Discussion and Analysis” disclosure if and to the extent then required by SEC rules; and
- preparing the compensation committee report if and to the extent then required by SEC rules.

We believe that the composition of our compensation committee meets the requirements for independence under current NASDAQ and SEC rules and regulations. Our board of directors has determined that Dr. Seidenberg and Mr. Mott are independent as currently defined in applicable NASDAQ listing standards.

Compensation Committee Interlocks and Insider Participation

During 2014, the members of our compensation committee were Dr. Seidenberg and Mr. Mott. Dr. Daniel was a member of our compensation committee until his resignation from our compensation committee in April 2014.

Dr. Daniel is an executive vice president and president of research and early development of Celgene Corporation, and we have entered into certain transactions with an affiliate of Celgene Corporation, as further described in “Transactions with Related Persons” section below.

None of our executive officers has served as a director or member of the compensation committee (or other committee serving an equivalent function) of any other entity whose executive officers served as one of our directors or a member of the compensation committee.

Nominating and Corporate Governance Committee

The members of our nominating and corporate governance committee are Drs. Goldfischer and Seidenberg. Dr. Shiosaki was a member of our nominating and corporate governance committee until our 2014 Annual Meeting. Dr. Goldfischer is chair of the nominating and corporate governance committee. Our nominating and corporate governance committee met once during 2014. Our nominating and corporate governance committee’s responsibilities include:

- identifying individuals qualified to become members of our board of directors;
- recommending to our board of directors the persons to be nominated for election as directors and to each of our board’s committees;
- developing and recommending to our board of directors corporate governance principles; and
- overseeing an annual evaluation of our board of directors.

We believe that the composition of our nominating and corporate governance committee meets the requirements for independence under current NASDAQ and SEC rules and regulations.

Board and Committee Meetings Attendance

The full board of directors met seven times during 2014. During 2014, each member of the board of directors attended in person or participated in 75% or more of the aggregate of (i) the total number of meetings of the board of directors (held during the period for which such person has been a director) and (ii) the total number of meetings held by all committees of the board of directors on which such person served (during the periods that such person served).

Director Attendance at Annual Meeting of Stockholders

Directors are responsible for attending the annual meeting of stockholders. Three members of our board of directors attended the 2014 Annual Meeting of Stockholders.

Code of Business Conduct and Ethics

We have adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. A current copy of the code is posted on the corporate governance section of the “Investor Center” on our website, which is located at <http://www.epizyme.com>. If we make any substantive amendments to, or grant any waivers from, the code of business conduct and ethics for any officer or director, we will disclose the nature of such amendment or waiver on our website or in a current report on Form 8-K.

Board Leadership Structure and Board’s Role in Risk Oversight

Our board of directors has not established a chairman of the board, but our board of directors has appointed a lead independent director who fulfills a similar role. The lead independent director is nominated annually by the

nominating and corporate governance committee and voted on by the board of directors. Separating the duties of the lead independent director from the duties of the chief executive officer allows our chief executive officer to focus on our day-to-day business, while allowing the lead independent director to lead the board of directors in its fundamental role of providing advice to and independent oversight of management. Specifically, our lead independent director runs meetings of our independent directors, facilitates communications between management and the board of directors and assists with other corporate governance matters. Our board of directors believes that this structure ensures a greater role for the independent directors in the oversight of our company and active participation of the independent directors in setting agendas and establishing priorities and procedures for the work of our board of directors. Our board of directors believes its administration of its risk oversight function has not affected its leadership structure. Our board of directors believes that we have an appropriate leadership structure for us at this time which demonstrates our commitment to good corporate governance. David M. Mott serves as the lead independent director of the board of directors.

Risk is inherent with every business and how well a business manages risk can ultimately determine its success. We face a number of risks, including those described under “Risk Factors” in our Annual Report on Form 10-K for the year ended December 31, 2014. Our board of directors is actively involved in oversight of risks that could affect us. This oversight is conducted primarily by our full board of directors, which has responsibility for general oversight of risks.

Our board of directors satisfies this responsibility through full reports by each committee chair regarding the committee’s considerations and actions, as well as through regular reports directly from officers responsible for oversight of particular risks within our company. Our audit committee oversees risk management activities related to financial controls and legal and compliance risks. Our compensation committee oversees risk management activities relating to our compensation policies and practices. Our nominating and corporate governance committee oversees risk management activities relating to board composition and management succession planning. In addition, members of our senior management team attend our quarterly board meetings and are available to address any questions or concerns raised by the board on risk management and any other matters. Our board of directors believes that full and open communication between management and the board of directors is essential for effective risk management and oversight.

Communication with the Directors of Epizyme

Any interested party with concerns about our company may report such concerns to the board of directors, or the lead independent director of our board of directors, or otherwise the chairman of the nominating and corporate governance committee, by submitting a written communication to the attention of such director at the following address:

c/o Epizyme, Inc.
400 Technology Square
Cambridge, Massachusetts 02139
United States

You may submit your concern anonymously or confidentially by postal mail. You may also indicate whether you are a stockholder, customer, supplier, or other interested party.

A copy of any such written communication may also be forwarded to Epizyme’s legal counsel and a copy of such communication may be retained for a reasonable period of time. The director may discuss the matter with Epizyme’s legal counsel, with independent advisors, with non-management directors, or with Epizyme’s management, or may take other action or no action as the director determines in good faith, using reasonable judgment, and discretion.

Communications may be forwarded to all directors if they relate to important substantive matters and include suggestions or comments that may be important for the directors to know. In general, communications relating to

corporate governance and long-term corporate strategy are more likely to be forwarded than communications relating to ordinary business affairs, personal grievances, and matters as to which we tend to receive repetitive or duplicative communications.

The audit committee oversees the procedures for the receipt, retention, and treatment of complaints received by Epizyme regarding accounting, internal accounting controls, or audit matters, and the confidential, anonymous submission by employees of concerns regarding questionable accounting, internal accounting controls or auditing matters. Epizyme has also established a toll-free telephone number for the reporting of such activity, which is 866-858-6315.

Director Compensation

The table below shows all compensation paid to our non-employee directors during 2014.

Name	Fees Paid In Cash \$(1)	Option Awards \$(2)(3)	Total (\$)
Andrew R. Allen, M.D., Ph.D. (4)	13,079	322,924	336,003
Kenneth Bate (5)	—	266,702	266,702
Thomas O. Daniel, M.D. (6)	—	—	—
Carl Goldfischer, M.D.	58,477	165,053	223,530
David M. Mott	45,887	165,053	210,940
Richard F. Pops	42,721	165,053	207,774
Beth Seidenberg, M.D.	42,579	165,053	207,632
Kazumi Shiosaki, Ph.D. (7)	30,806	—	30,806

- (1) Amounts represent cash compensation for services rendered by each member of the board of directors.
- (2) In 2014, following the annual meeting of stockholders, each of Dr. Goldfischer, Mr. Mott, Mr. Pops and Dr. Seidenberg was granted an option to purchase 7,333 shares of common stock. Each of Dr. Allen and Mr. Bate was granted an option to purchase 17,666 shares of common stock upon his initial election to the board of directors.
- (3) Amounts shown reflect the grant date fair value of option awards granted during 2014. The grant date fair value was computed in accordance with Accounting Standards Codification Topic 718, *Compensation—Stock Compensation*. See note 10 to the financial statements in our annual report on Form 10-K for the year ended December 31, 2014 regarding assumptions we made in determining the fair value of option awards.
- (4) Dr. Allen was elected to the board of directors in June 2014.
- (5) Mr. Bate was elected to the board of directors in December 2014.
- (6) Dr. Daniel ceased serving as a member of our board of directors at the 2014 Annual Meeting. We did not provide any compensation to Dr. Daniel for his service as a director.
- (7) Dr. Shiosaki ceased serving as a member of our board of directors at the 2014 Annual Meeting.

During 2014, we did not provide any cash compensation to Dr. Gould, our president and chief executive officer, for his service as a director. Dr. Gould’s compensation as an executive officer is set forth under “Executive Compensation—Summary Compensation Table.”

Under our director compensation program, we pay our non-employee directors a cash retainer for service on the board of directors and for service on each committee on which the director is a member. The chairman of each committee receives higher retainers for such service. These fees are payable in arrears in four equal quarterly installments on the last day of each quarter, provided that the amount of such payment is prorated for any portion of such quarter that the director is not serving on our board of directors. The fees paid to non-employee directors for service on the board of directors and for service on each committee of the board of directors on which the director is a member are as follows:

	<u>Member Annual Fee</u>	<u>Chairman Additional Annual Fee</u>
Board of Directors	\$35,000	\$ —
Audit Committee	7,000	8,000
Compensation Committee	5,000	5,000
Nominating and Corporate Governance Committee	2,500	2,500

We also reimburse our non-employee directors for reasonable travel and out-of-pocket expenses incurred in connection with attending our board of director and committee meetings.

In addition, under our director compensation program, each non-employee director upon his or her initial election to our board of directors will receive an option to purchase 17,666 shares of our common stock. Each of these options will vest as to 25% of the shares of our common stock underlying such option on the one-year anniversary of the grant date and as to an additional 2.0833% of the shares of our common stock underlying such option at the end of each successive month following the first anniversary of the grant date until the fourth anniversary of the grant date, subject to the non-employee director's continued service as a director. Further, on the date of the first board meeting held after each annual meeting of stockholders, each non-employee director that has served on our board of directors for at least six months will receive an option to purchase 7,333 shares of our common stock. Each of these options will vest in full on the one-year anniversary of the grant date, subject to the non-employee director's continued service as a director. All options issued to our non-employee directors under our director compensation program will become exercisable in full upon a change in control of our company. The exercise price of these options will equal the fair market value of our common stock on the date of grant.

This program is intended to provide a total compensation package that enables us to attract and retain qualified and experienced individuals to serve as directors and to align our directors' interests with those of our stockholders.

Executive Compensation

Our named executive officers for the year ended December 31, 2014 include our principal executive officer and our two other most highly compensated executive officers:

- Robert J. Gould, Ph.D., our president and chief executive officer;
- Robert A. Copeland, Ph.D., our president of research and chief scientific officer; and
- Peter T.C. Ho, M.D., Ph.D., our chief development officer.

Andrew E. Singer, our executive vice president, finance and administration, and chief financial officer joined us in February 2015.

Summary Compensation Table

The following table presents the compensation awarded to, earned by or paid to each of our named executive officers for the years ended December 31, 2014 and 2013.

<u>Name and Principal Position</u>	<u>Year</u>	<u>Salary (\$)</u>	<u>Bonus \$(1)</u>	<u>Option Awards \$(2)</u>	<u>All Other Compensation (\$)</u>	<u>Total (\$)</u>
Robert J. Gould, Ph.D. President and Chief Executive Officer	2014	472,782	180,000	1,299,907	5,692	1,958,381
	2013	387,668	177,022	1,699,821	1,995	2,266,506
Robert A. Copeland, Ph.D. President of Research and Chief Scientific Officer	2014	395,684	136,000	649,942	6,390	1,188,016
	2013	348,201	139,280	473,666	4,598	965,745
Peter T.C. Ho, M.D., Ph.D. Chief Development Officer	2014	122,500	41,192	3,165,510	136,370	3,465,572
	2013	N/A	N/A	N/A	N/A	N/A

- (1) The 2014 amounts reflect the discretionary bonus paid in 2015 for performance during 2014, as discussed under “—Narrative to Summary Compensation Table—Annual Bonus.” The bonus paid to Dr. Ho was prorated based on his September 2014 employment commencement date.
- (2) The amounts reflect the grant date fair value for awards granted during the applicable year. The grant date fair value was computed in accordance with Financial Accounting Standards Board Accounting Standards Codification Topic 718, *Compensation—Stock Compensation*. See note 10 to the financial statements in our annual report on Form 10-K for the year ended December 31, 2014 regarding assumptions we made in determining the fair value of option awards.

Narrative to Summary Compensation Table

We review compensation annually for all employees, including our executives. In setting executive base salaries and bonuses and granting equity incentive awards, we consider compensation for comparable positions in the market, the historical compensation levels of our executives, individual performance as compared to our expectations and objectives, our desire to motivate our employees to achieve short- and long-term results that are in the best interests of our stockholders, and a long-term commitment to our company. We do not target a specific competitive position or a specific mix of compensation among base salary, bonus or long-term incentives.

Our board of directors has historically determined our executives’ compensation. Our compensation committee typically reviews and discusses management’s proposed compensation with the chief executive officer for all executives other than the chief executive officer. Based on those discussions and its discretion, the compensation committee then recommends the compensation for each executive officer. Our board of directors, without members of management present, discusses the compensation committee’s recommendations and ultimately approves the compensation of our executive officers. Our compensation committee engaged Pearl Meyer & Partners, LLC, or PM&P, as its independent compensation consultant to review our executive compensation peer group and program design and assess our executives’ compensation relative to comparable companies. PM&P provides our compensation committee with information regarding market compensation practices and trends. Our compensation committee considered the relationship that PM&P has with us, the members of our board of directors and our executive officers. Based on the committee’s evaluation, the compensation committee has determined that PM&P is serving as an independent and conflict-free advisor to the committee.

Annual Base Salary. The following table presents the base salaries for each of our named executive officers for the years 2014 and 2015. The 2014 base salaries became effective on January 1, 2014 for all of the named

executive officers other than Dr. Ho, whose 2014 base salary became effective upon his September 11, 2014 employment commencement. The 2015 base salaries became effective on January 1, 2015.

Name	2014 Base Salary (\$)	2015 Base Salary (\$)
Robert J. Gould, Ph.D.	480,000	500,000
Robert A. Copeland, Ph.D.	400,000	425,000
Peter T.C. Ho, M.D., Ph.D.	420,000	420,000

Annual Bonus. Our bonus plan motivates and rewards our executives for achievements relative to our goals and expectations for each fiscal year. Each named executive officer has a target bonus opportunity, defined as a percentage of his annual salary. Following the end of each year, our board of directors determines bonuses. Material considerations in determining bonuses include our financial performance relative to our plan and achievement of corporate objectives for the year; the individual executive’s handling of unplanned events and opportunities; and the chief executive officer’s input with respect to the performance of our company and of our executives. Based on these factors and in the sole discretion of our board of directors, we approved the following bonuses in 2015 for our named executive officers for 2014.

Name	Target Bonus (% of salary)	Actual Bonus (\$)	Actual Bonus (% of salary)
Robert J. Gould, Ph.D.	50	180,000	38
Robert A. Copeland, Ph.D.	40	136,000	34
Peter T.C. Ho, M.D., Ph.D.	40	41,192	34

Target bonuses as a percentage of annual salary for 2015 remain the same as those target bonuses as a percentage of annual salary for each executive in 2014.

Specific achievements and performance considered by our board of directors in determining bonuses for 2014 included:

- the achievement of clinical proof-of-concept in both of our clinical stage programs, EPZ-6438 and EPZ-5676;
- our maintaining budgetary alignment with major research and development milestones and ending the year with significant cash and cash equivalents; and
- progress achieved in expanding the clinical opportunity of EPZ-6438 and our goal to strengthen our participation in the future of EPZ-6438.

Long-Term Incentives. We typically grant equity incentive awards at the start of employment to each executive and our other employees, grant annual stock option awards thereafter, and may periodically grant additional equity incentive awards during employment based on individual role, performance and contribution. Equity incentive awards to our executive officers are typically granted annually in connection with the annual performance review.

The option exercise price equals the fair market value of our common stock on the date of grant, which is typically equal to the closing price of our common stock on the NASDAQ Global Market on the date of grant. Vesting begins on the date of grant. Time vested stock option grants to our executives typically vest 25% on the first anniversary of grant or, if earlier, the initial employment date, and 1/48th per month thereafter, are fully vested at the end of four years and have a term of 10 years from the grant date.

In January 2014, we awarded time-vested stock options to Drs. Gould and Copeland in recognition of achievements and performance during 2013. In September 2014, we awarded a time-vested stock option to Dr. Ho in connection with his commencing employment with us. All of these awards were on our standard terms.

Other Compensation. In 2014, we paid \$100,000 to Dr. Ho for relocation and \$31,170 for commercial airfare and other travel-related expenses and lodging in connection with his pre-relocation commuting from his residence in Delaware to our headquarters in Massachusetts on a regular basis. In 2015, we expect to pay Dr. Ho an additional \$100,000 for relocation as well as commercial airfare and other travel-related expenses and lodging in connection with his pre-relocation commuting. Other amounts shown in the “All Other Compensation” column in the Summary Compensation Table for each named executive officer relate to premiums paid by us for long-term disability and term life insurance policies and for our fitness benefits and 401(k) matching contributions, consistent with those provided to all Epizyme employees.

We do not provide additional perquisites or personal benefits to our named executive officers. We do, however, pay the premiums for term life insurance and long-term disability for all of our employees, including our named executive officers. In 2014, we paid premiums for term life insurance of \$3,564, \$5,330 and \$414 for Drs. Gould, Copeland and Ho, respectively. The term life insurance premium paid for Dr. Copeland includes \$3,008 for a supplemental life insurance policy. We do not sponsor any qualified or non-qualified defined benefit plans for any of our employees or executives.

Employment Arrangements. Please see “—Amended and Restated Employment, Severance and Change of Control Arrangements” for information regarding the employment and severance agreements for each of our named executive officers.

Outstanding Equity Awards at 2014 Fiscal Year End Table

The following table presents information regarding all outstanding stock options held by each of our named executive officers on December 31, 2014.

Name	Grant Date	Notes	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Option Exercise Price (\$)	Option Expiration Date
Robert J. Gould, Ph.D.	3/18/2010		567,223	—	0.51	3/17/2020
	10/3/2012		54,410	—	2.19	10/2/2022
	1/25/2013	(1)	161,639	175,694	3.54	1/24/2023
	1/28/2014	(2)	—	54,813	31.20	1/27/2024
Robert A. Copeland, Ph.D. . .	3/18/2010		1,250	—	0.51	3/17/2020
	3/11/2011	(3)	22,867	6,861	0.60	3/10/2021
	10/3/2012		16,396	—	2.19	10/2/2022
	1/25/2013	(1)	45,041	48,959	3.54	1/24/2023
	1/28/2014	(2)	—	27,406	31.20	1/27/2024
Peter T.C. Ho, M.D., Ph.D. . .	9/11/2014	(4)	—	150,000	28.20	9/10/2024

- (1) The unvested shares under these options are scheduled to vest in approximately equal monthly installments through January 25, 2017.
- (2) The shares under this option are scheduled to vest as to 25% of the unvested shares on January 28, 2015, with the remainder vesting in approximately equal monthly installments through January 28, 2018.
- (3) The unvested shares under this option are scheduled to vest in approximately equal monthly installments through March 11, 2015.
- (4) The shares under this option are scheduled to vest as to 25% of the unvested shares on September 11, 2015, with the remainder vesting in approximately equal monthly installments through September 11, 2018.

February 2015 Equity Awards to Named Executive Officers

In February 2015, our compensation committee approved a grant of stock options under our 2013 Stock Incentive Plan, or 2013 Plan, to our named executive officers. Each of these equity awards has an exercise price of \$21.58 per share and vests with respect to 25% of the shares on February 13, 2016 and with respect to the remaining shares in approximately equal monthly installments over the following three years. The following table sets forth the number of shares of common stock issuable upon exercise of the stock options granted to our named executive officers in February 2015:

Name	Number of Securities Underlying Options (#) Granted
Robert J. Gould, Ph.D.	97,579
Robert A. Copeland, Ph.D.	65,052
Peter T.C. Ho, M.D., Ph.D.	35,778

Employment, Severance and Change in Control Arrangements

In April 2013, we entered into amended and restated employment offer letters with each of Drs. Gould and Copeland. In September 2014, we entered into an employment offer letter with Dr. Ho in connection with his commencing employment with us, and in February 2015, we entered into an employment offer letter with Andrew E. Singer in connection with his commencing employment with us. Each of our executive officers is employed at will.

Andrew E. Singer. Mr. Singer’s employment offer letter establishes his title and base salary; his eligibility for an annual bonus of up to 40% of his base salary; his eligibility for benefits made available to employees generally; and provides for a one-time payment of \$200,000 to assist in his relocation to the greater Boston area.

Pursuant to Mr. Singer’s employment agreement, on February 9, 2015, we granted Mr. Singer a stock option to purchase 104,169 shares of our common stock and an award of 37,313 restricted stock units. These awards are subject to time-based vesting. Additionally, in accordance with the terms of his employment offer letter and subject to his continued employment with us, Mr. Singer will be granted a second restricted stock unit award upon the first anniversary of the commencement of his employment with us. The number of restricted stock units to be issued under the second restricted stock unit award will be determined by dividing \$750,000 by the closing price of our common stock on the first anniversary of the commencement of his employment. This award will also be subject to time-based vesting.

Mr. Singer is also eligible for severance benefits under our Executive Severance and Change in Control Plan.

Each executive officer has entered into a non-competition and non-solicitation agreement, which will prohibit him from competing with us and soliciting or hiring our employees for a period of one year following the end of his employment with us.

Each executive officer is also eligible for severance benefits in specified circumstances, as set forth in our Executive Severance and Change in Control Plan. Under the terms of this plan, upon execution and effectiveness of a severance agreement and release of claims, each executive officer will be entitled to severance payments if we:

- terminate his employment without cause, prior to or more than 12 months following a change in control; or
- terminate his employment without cause or he terminates employment with us for good reason within 12 months following a change in control.

Additionally, Dr. Gould is entitled to severance payments if he terminates his employment with us for good reason prior to or more than 12 months following a change in control.

The following definitions have been adopted in our Executive Severance and Change in Control Plan under which our executive officers participate:

- “cause” means any of: (a) the executive’s conviction of, or plea of guilty or nolo contendere to, any crime involving dishonesty or moral turpitude or any felony; or (b) a good faith finding by us that the executive has (i) engaged in dishonesty, willful misconduct or gross negligence, (ii) breached or threatened to breach the terms of any restrictive covenants or confidentiality agreement or any similar agreement with us, (iii) violated company policies or procedures, or (iv) failed to perform his assigned duties to our satisfaction, following notice of such failure by us and a period of 15 days to cure.
- “good reason” means the occurrence, without the executive’s prior written consent, of any of the following events: (i) a material reduction in the executive’s authority, duties, or responsibilities; (ii) the relocation of the principal place at which the executive provides services to us by at least 30 miles and to a location such that his daily commuting distance is increased; or (iii) a material reduction of the executive’s base salary, other than in connection with, and in an amount substantially proportionate to, reductions made by us to the base salaries of other similarly-situated employees. No resignation will be treated as a resignation for good reason unless (x) the executive has given written notice to us of his intention to terminate his or her employment for good reason, describing the grounds for such action, no later than 90 days after the first occurrence of such circumstances, (y) the executive has provided us with at least 30 days in which to cure the circumstances, and (z) if we are not successful in curing the circumstances, the executive ends his employment within 30 days following the cure period in (y).
- “change in control” means any of the following:
 - (i) the acquisition by an individual, entity or group within the meaning of Section 13(d)(3) or 14(d)(2) of the Exchange Act, referred to as a “Person” of beneficial ownership of any of our capital stock if, after such acquisition, such Person beneficially owns more than 50% of either (x) our then-outstanding shares of common stock or (y) the combined voting power of our then-outstanding securities entitled to vote generally in the election of directors; provided, however, that any acquisition directly from us will not be a change in control, nor will any acquisition by any individual, entity, or group pursuant to specified business combinations;
 - (ii) the consummation of a merger, consolidation, reorganization, recapitalization or share exchange involving us or a sale or other disposition of in excess of 85% of our assets subject to specified exceptions; or
 - (iii) the liquidation or dissolution of our company;

provided that, where required to avoid additional taxation under Section 409A, the event that occurs must also be a “change in the ownership or effective control of a corporation, or a change in the ownership of a substantial portion of the assets of a corporation” as defined under applicable regulations.

The following table summarizes the schedule of severance payments our executive officers would receive in the event of a qualifying termination.

Scenario and Executive Level	Salary Continuation	Bonus	Continuation of Employer Portion of Medical, Dental and Vision Benefit Premiums	Acceleration of Unvested Equity
Prior to a Change in Control				
Robert J. Gould	12 months	None	12 months	None
Andrew E. Singer, Robert A. Copeland and Peter T. C. Ho	6 months	None	6 months	None
Following a Change in Control				
Robert J. Gould	18 months	150% of target	18 months	100%
Andrew E. Singer, Robert A. Copeland and Peter T. C. Ho	12 months	100% of target	12 months	100%

Additional Narrative Disclosure

401(k) Savings Plan. We maintain a defined contribution employee retirement plan for our employees. Our 401(k) plan is intended to qualify as a tax-qualified plan under Section 401 of the Internal Revenue Code so that contributions to our 401(k) plan, and income earned on such contributions, are not taxable to participants until withdrawn or distributed from the 401(k) plan. Our 401(k) plan provides that each participant may contribute up to 90% of his or her pre-tax compensation, up to a statutory limit, which was \$17,500 for 2014. Participants who are at least 50 years old can also make “catch-up” contributions, which in 2014 could be up to an additional \$5,500 above the statutory limit. Under our 401(k) plan, each employee is fully vested in his or her deferred salary contributions. Employee contributions are held and invested by the plan’s trustee, subject to participants’ ability to give investment directions by following certain procedures. During the year ended December 31, 2014, we implemented a matching contribution to the 401(k) Plan, matching 50% of an employee’s contribution up to a maximum of 3% of the participant’s compensation. Matching contributions made to each of our named executive officers are included in the “Summary Compensation Table—All Other Compensation.”

Health and Welfare Benefits. All of our full-time employees, including our executive officers are eligible to participate in certain medical, disability and life insurance benefit programs offered by us. We pay the premiums for term life insurance and long-term disability for all of our employees, including our executive officers. We do not sponsor any qualified or non-qualified defined benefit plans for any of our employees or executives.

Securities Authorized for Issuance Under Equity Compensation Plans

Plan Category	Equity Compensation Plan Information As of December 31, 2014		
	(a) Number of Securities to be Issued Upon Exercise of Outstanding Options	(b) Weighted-Average Exercise Price of Outstanding Options	(c) Number of Securities Remaining Available for Future Issuance Under Equity Compensation Plans (Excluding Securities Reflected in Column (a))
Equity compensation plans approved by security holders (1) (2)	2,959,506	\$10.66	1,738,970
Equity compensation plans not approved by security holders	—	—	—
Total	2,959,506	\$10.66	1,738,970

(1) As of December 31, 2014, 2,215,042 shares were authorized for issuance under our 2013 Plan, which became effective on June 5, 2013, the effective date of our initial public offering,

including 332,708 remaining shares available for future issuance under our 2008 Stock Incentive Plan, or 2008 Plan, which were transferred to the 2013 Plan. The number of shares of our common stock reserved for issuance under the 2013 Plan will be increased (i) from time to time by the number of shares of our common stock forfeited upon the expiration, cancellation, forfeiture, cash settlement or other termination of awards under the 2008 Plan, and (ii) annually on the first day of each year, by up to the lesser of (x) 2,500,000 shares of our common stock, (y) 5.0% of the number of shares of our common stock outstanding on the first day of the applicable year and (z) an amount determined by our board of directors. The number of shares authorized for issuance as of December 31, 2014 does not reflect the annual increase on January 1, 2015.

- (2) As of December 31, 2014, 481,978 shares were reserved for issuance under our 2013 Employee Stock Purchase Plan, or 2013 ESPP, which became effective on June 5, 2013, the effective date of our initial public offering. The number of shares of our common stock reserved for issuance under the 2013 ESPP will be increased annually on the first day of each year, by up to the lesser of (x) 233,333 shares of our common stock, (y) 1% of the number of shares of our common stock outstanding on the first day of the applicable year and (z) an amount determined by our board of directors. The board of directors determined not to increase the shares available for issuance under the 2013 ESPP in January 2015.

TRANSACTIONS WITH RELATED PERSONS

The following is a description of transactions entered into after January 1, 2014 to which we have been a party, in which the amount involved in the transaction exceeds \$120,000 and in which any of our directors or executive officers or their immediate family members or beneficial owners of more than 5% of our voting securities had or will have a direct or indirect material interest. We believe that all of these transactions were on terms as favorable as could have been obtained from unrelated third parties.

Participation in February 2014 Public Offering

In February 2014, we sold 3,673,901 shares of our common stock at a price of \$29.25 per share pursuant to an underwritten public offering, which we refer to as our February 2014 offering. In our February 2014 offering, Celgene European Investment Company LLC, or CEIC, which is affiliated with one of our collaborators, Celgene Corporation, and was an existing investor, purchased 340,000 shares of our common stock for approximately \$9.9 million through the underwriters at the public offering price. Dr. Daniel, who was a member of our board of directors at the time of the offering, is an executive vice president and president of research and early development of Celgene Corporation.

Participation in March 2015 Public Offering

In March 2015, we sold 6,000,000 shares of our common stock at a price of \$20.75 per share pursuant to an underwritten public offering, which we refer to as our March 2015 offering. In our March 2015 offering, PRIMECAP Management Company and FMR LLC, which were existing beneficial owners of more than 5% of our voting securities, purchased an additional 900,000 shares and 873,432 shares, for approximately \$18.7 million and \$18.1 million, respectively, of our common stock through the underwriters at the public offering price.

2014 Transactions under Our Collaboration Agreement with Celgene Corporation

In April 2012, we entered into a collaboration and license agreement with Celgene to discover, develop and commercialize, in all countries other than the United States, small molecule HMT inhibitors targeting DOT1L, including our inhibitor EPZ-5676, and any other HMT targets from our product platform, excluding the EZH2 HMT and targets covered by our GSK collaboration, which we refer to as the available targets. Under this agreement, we are eligible to receive payments from Celgene for option fees or extensions, milestones earned under the agreement and global development co-funding for certain phases of development for selected targets. In 2014, we collected \$28.9 million from Celgene, comprising \$25.0 million for a clinical development milestone earned in the fourth quarter of 2013 and \$3.9 million in global development co-funding related to EPZ-5676.

Policies and Procedures for Related Person Transactions

Our board of directors has adopted a written related person transaction policy to set forth policies and procedures for the review and approval or ratification of related person transactions. This policy covers any transaction, arrangement or relationship, or any series of similar transactions, arrangements or relationships, in which we were or are to be a participant, the amount involved exceeds \$120,000, and one of our executive officers, directors, director nominees or 5% stockholders, or their immediate family members, each of whom we refer to as a "related person," had or will have a direct or indirect material interest, including, without limitation, purchases of goods or services by or from the related person or entities in which the related person has a material interest, indebtedness, guarantees of indebtedness and employment by us of a related person.

If a related person proposes to enter into such a transaction, arrangement or relationship, which we refer to as a "related person transaction," the related person must report the proposed related person transaction to our general

counsel, or if we do not have a general counsel, our chief financial officer. The policy calls for the proposed related person transaction to be reviewed and, if deemed appropriate, approved by our audit committee. Whenever practicable, the reporting, review and approval will occur prior to entry into the transaction. If advance review and approval is not practicable, the audit committee will review, and, in its discretion, may ratify the related person transaction. The policy also permits the chairman of the audit committee to review and, if deemed appropriate, approve proposed related person transactions that arise between audit committee meetings, subject to ratification by the audit committee at its next meeting. Any related person transactions that are ongoing in nature will be reviewed annually.

A related person transaction reviewed under the policy will be considered approved or ratified if it is authorized by the audit committee after full disclosure of the related person's interest in the transaction. As appropriate for the circumstances, the audit committee will review and consider:

- the related person's interest in the related person transaction;
- the approximate dollar value of the amount involved in the related person transaction;
- the approximate dollar value of the amount of the related person's interest in the transaction without regard to the amount of any profit or loss;
- whether the transaction was undertaken in the ordinary course of our business;
- whether the terms of the transaction are no less favorable to us than terms that could have been reached with an unrelated third party;
- the purpose of, and the potential benefits to us of, the transaction; and
- any other information regarding the related person transaction or the related person in the context of the proposed transaction that would be material to investors in light of the circumstances of the particular transaction.

Our audit committee may approve or ratify the transaction only if it determines that, under all of the circumstances, the transaction is in, or is not inconsistent with, our best interests. Our audit committee may impose any conditions on the related person transaction that it deems appropriate.

In addition to the transactions that are excluded by the instructions to the SEC's related person transaction disclosure rule, our board of directors has determined that the following transactions do not create a material direct or indirect interest on behalf of related persons and, therefore, are not related person transactions for purposes of this policy:

- interests arising solely from the related person's position as an executive officer of another entity whether or not the person is also a director of the entity, that is a participant in the transaction, where the related person and all other related persons own in the aggregate less than a 10% equity interest in such entity, the related person and his or her immediate family members are not involved in the negotiation of the terms of the transaction and do not receive any special benefits as a result of the transaction and the amount involved in the transaction is less than the greater of \$200,000 or 5% of the annual gross revenues of the company receiving payment under the transaction; and
- a transaction that is specifically contemplated by provisions of our certificate of incorporation or by-laws.

The policy provides that transactions involving compensation of executive officers shall be reviewed and approved by our compensation committee in the manner specified in the compensation committee's charter.

PRINCIPAL STOCKHOLDERS

The following table sets forth information, to the extent known by us or ascertainable from public filings, with respect to the beneficial ownership of our common stock as of February 28, 2015 by:

- each of our directors;
- each of our named executive officers;
- all of our directors and executive officers as a group; and
- each person, or group of affiliated persons, who is known by us to beneficially own more than 5% of our common stock.

The column entitled “Percentage Beneficially Owned” is based on a total of 34,459,968 shares of our common stock outstanding as of February 28, 2015.

Beneficial ownership is determined in accordance with the rules and regulations of the SEC and includes voting or investment power with respect to our common stock. Shares of our common stock subject to options that are currently exercisable or exercisable within 60 days of February 28, 2015 are considered outstanding and beneficially owned by the person holding the options for the purpose of calculating the percentage ownership of that person but not for the purpose of calculating the percentage ownership of any other person. Except as otherwise noted, the persons and entities in this table have sole voting and investing power with respect to all of the shares of our common stock beneficially owned by them, subject to community property laws, where applicable. Except as otherwise indicated in the table below, addresses of named beneficial owners are in care of Epizyme, Inc., 400 Technology Square, Cambridge, Massachusetts 02139.

Name of Beneficial Owner	Number of Shares Beneficially Owned	Percentage Beneficially Owned
5% Stockholders:		
Entities affiliated with New Enterprise Associates (1) . . .	5,156,089	15.0%
FMR LLC (2)	4,391,746	12.7%
Entities affiliated with Kleiner, Perkins, Caufield & Byers (3)	4,115,555	11.9%
PRIMECAP Management Company (4)	4,114,008	11.9%
Celgene European Investment Company LLC (5)	3,674,640	10.7%
Entities affiliated with Bay City Capital (6)	2,825,396	8.2%
Entities affiliated with MPM Capital (7)	2,413,819	7.0%
Directors and Executive Officers:		
David M. Mott (8)	5,156,089	15.0%
Beth Seidenberg, M.D. (9)	4,115,555	11.9%
Carl Goldfischer, M.D. (10)	2,825,396	8.2%
Andrew R. Allen, M.D., Ph.D.	—	—
Kenneth Bate	—	—
Richard F. Pops	60,000	*
Robert J. Gould, Ph.D. (11)	828,511	2.3%
Andrew E. Singer	—	—
Robert A. Copeland, Ph.D. (11)	108,812	*
Peter T.C. Ho, M.D., Ph.D. (12)	1,400	*
All current executive officers and directors as a group (10 persons) (13)	13,095,763	37.0%

* Represents beneficial ownership of less than one percent of our outstanding common stock.

- (1) Consists of 5,149,740 shares of common stock held of record by New Enterprise Associates 13, L.P. (“NEA13”) and 6,349 shares of common stock held of record by NEA Ventures 2009, L.P. (“Ven 2009”). NEA Partners 13, L.P. (“NEA Partners 13”) is the sole general partner of NEA 13 and NEA 13 GP, LTD (“NEA 13 LTD”) is the sole general partner of NEA Partners 13. The individual directors (collectively, the “NEA 13 Directors”) of NEA 13 LTD are M. James Barrett, Peter J. Barris, Forest Baskett, Ryan D. Drant, Patrick J. Kerins, Krishna “Kittu” Kolluri, David M. Mott, a member of our board of directors, Scott D. Sandell, Ravi Viswanathan and Harry R. Weller. The NEA 13 directors share voting and dispositive power with regard to the shares directly held by NEA 13. Karen P. Welsh, the general partner of Ven 2009, shares voting and dispositive power with regard to the shares directly held by Ven 2009. The principal business address of New Enterprise Associates, Inc. is 1954 Greenspring Drive, Suite 600, Timonium, MD 21093.
- (2) The information reported is based on a Schedule 13G/A, as filed with the SEC on February 13, 2015, in which FMR LLC and certain of its affiliates reported that FMR LLC, a parent holding company, Edward C. Johnson, 3d, the chairman of FMR LLC, and Abigail P. Johnson, the Vice Chairman, Chief Executive Officer and President of FMR LLC have sole dispositive power over all of the shares but share voting control over the shares with certain affiliates of FMR LLC. The principal business address of FMR LLC is 245 Summer Street, Boston, MA 02210.
- (3) Consists of 3,838,167 shares of common stock held by Kleiner Perkins Caufield & Byers XIII, LLC (“KPCB XIII”), 55,356 shares of common stock held by Raymond J. Lane and 222,032 shares of common stock beneficially owned by individuals and entities associated with Kleiner Perkins Caufield & Byers (collectively, “KPCB Direct”). All shares are held for convenience in the name of “KPCB Holdings, Inc. as nominee,” for the accounts of such individuals and entities who each exercise their own voting and dispositive control over such shares. The managing member of KPCB XIII is KPCB XIII Associates, LLC (“KPCB XIII Associates”). Brook H. Byers, L. John Doerr, Joseph Lacob, Raymond J. Lane and Theodore E. Schlein, the managing directors of KPCB XIII Associates, LLC, and Dr. Seidenberg, a member of our board of directors and of KPCB XIII Associates, exercise shared voting and dispositive control over the shares directly held by KPCB XIII. Dr. Seidenberg disclaims beneficial ownership of all shares held by KPCB XIII except to the extent of her pecuniary interest therein. The principal business address for all entities and individuals affiliated with Kleiner Perkins Caufield & Byers is 2750 Sand Hill Road, Menlo Park, CA 94025.
- (4) The information reported is based on a Schedule 13G/A, as filed with the SEC on January 6, 2015. The principal business address of PRIMECAP Management Company is 225 South Lake Avenue, #400, Pasadena, CA 91101.
- (5) The principal business address of Celgene European Investment Company LLC is 86 Morris Avenue, Summit, NJ 07901.
- (6) Consists of 2,772,562 shares of common stock held by Bay City Capital Fund V, L.P. and 52,834 shares of common stock held by Bay City Capital Fund V Co-Investment Fund, L.P. Bay City Capital Management V LLC (“GP V”) is the general partner of Bay City Capital Fund V, L.P. and Bay City Capital Fund V Co-Investment Fund, L.P. (collectively, “BCC V”). Bay City Capital LLC (“BCC LLC”) is the manager of GP V. BCC V has shared voting and dispositive power with respect to the shares held by BCC V. GP V has sole voting and dispositive power with respect to the shares held by BCC V. GP V disclaims beneficial ownership of these shares, except to the extent of its pecuniary interest therein. BCC LLC has sole voting and dispositive power with respect to the shares held by BCC V. BCC LLC disclaims beneficial ownership of these shares, except to the extent of its pecuniary interest therein. Dr. Carl Goldfischer, a member of our board of directors, is a managing director of Bay City Capital LLC and shares voting and dispositive power with respect to shares held by BCC V. Dr. Goldfischer disclaims beneficial ownership of these shares, except to the extent of its pecuniary interest therein. The principal business address of Bay City Capital Management V LLC is 750 Battery Street Suite 400, San Francisco, CA 94111.
- (7) Consists of (i) 1,951,645 shares of common stock held by MPM BioVentures IV-QP, L.P., (ii) 75,188 shares of common stock held by MPM BioVentures IV GmbH & Co. Beteiligungs KG, (iii) 55,495 shares of common stock held by MPM Asset Management Investors BV4 LLC and (iv) 331,491 shares of common stock held by MPM BioVentures IV Strategic Fund, L.P. MPM Asset Management LLC is the management

company of MPM BioVentures IV LLC. MPM BioVentures IV LLC is the managing member of MPM BioVentures IV GP LLC, which is the general partner of MPM BioVentures IV-QP, L.P. and MPM BioVentures IV Strategic Fund, L.P. and the managing limited partner of MPM BioVentures IV GmbH & Co. Beteiligungs KG. MPM BioVentures IV LLC is the manager of MPM Asset Management Investors BV4 LLC. Ansbert Gadicke, Luke Evin, Todd Foley, John Vander Vort, James P. Scopa and Vaughn M. Kailian are the members of MPM BioVentures IV LLC. All members share all power to vote, acquire, hold and dispose of all shares. Each member disclaims beneficial ownership of the securities except to the extent of his or her pecuniary interest therein. The address for the funds managed by MPM Capital is 450 Kendall Street, Cambridge, MA 02142.

- (8) Consists of the shares described in note (1) above. Mr. Mott is a general partner of New Enterprise Associates a member of the board of directors of NEA Management Company, LLC and a director of both NEA 13 LTD, the general partner of NEA Partners 13, the general partner of NEA 13, and as such Mr. Mott may be deemed to share voting and dispositive power with respect to all shares held by these entities. Mr. Mott disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein. Mr. Mott's business address is 5425 Wisconsin Avenue, Suite 800, Chevy Chase, MD 20815.
- (9) Consists of the shares described in note (3) above. Dr. Seidenberg is a partner at Kleiner Perkins Caufield & Byers, and as such Dr. Seidenberg may be deemed to share voting and dispositive power with respect to all shares held by these entities. Dr. Seidenberg disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein. Dr. Seidenberg's business address is 2750 Sand Hill Road, Menlo Park, California 94025.
- (10) Consists of the shares described in note (6) above. Dr. Goldfischer is an investment partner and managing director of BCC LLC and shares voting and dispositive power with respect to shares held by BCC V. Dr. Goldfischer disclaims beneficial ownership of these shares, except to the extent of any pecuniary interest therein. Dr. Goldfischer's business address is 750 Battery Street Suite 400, San Francisco, CA 94111.
- (11) Consists of shares of common stock issuable upon the exercise of options exercisable within 60 days after February 28, 2015.
- (12) Consists of 200 shares of common stock held by Dr. Ho and 1,200 shares of common stock held in trust for the benefit of Dr. Ho's children.
- (13) Consists of 12,158,440 shares of common stock and 937,323 shares of common stock issuable upon the exercise of options exercisable within 60 days after February 28, 2015.

SECTION 16(a) BENEFICIAL OWNERSHIP REPORTING COMPLIANCE

Section 16(a) of the Exchange Act requires our directors, executive officers, and persons holding more than 10% of our common stock to report their initial ownership of the common stock and other equity securities and any changes in that ownership in reports that must be filed with the SEC. The SEC has designated specific deadlines for these reports, and we must identify in this proxy statement those persons who did not file these reports when due.

Based solely on a review of reports furnished to us, or written representations from reporting persons, we believe all directors, executive officers, and 10% owners timely filed all reports regarding transactions in our securities required to be filed for 2014 by Section 16(a) under the Exchange Act, except that Mr. Mott, one of our directors, filed one late Form 4 on July 28, 2014 to report the acquisition of a stock option on July 23, 2014.

REPORT OF THE AUDIT COMMITTEE

The audit committee is appointed by the board of directors to assist the board of directors in fulfilling its oversight responsibilities with respect to (1) the integrity of Epizyme's financial statements and financial reporting process and systems of internal controls regarding finance, accounting, and compliance with legal and regulatory requirements, (2) the qualifications, independence, and performance of Epizyme's independent registered public accounting firm, (3) the performance of Epizyme's internal audit function, if any, and (4) other matters as set forth in the charter of the audit committee approved by the board of directors.

Management is responsible for the preparation of Epizyme's financial statements and the financial reporting process, including its system of internal control over financial reporting and its disclosure controls and procedures. The independent registered public accounting firm is responsible for performing an audit of Epizyme's financial statements in accordance with the standards of the Public Company Accounting Oversight Board, or PCAOB, and issuing a report thereon. The audit committee's responsibility is to monitor and oversee these processes.

In connection with these responsibilities, the audit committee reviewed and discussed with management and the independent registered public accounting firm the audited consolidated financial statements of Epizyme for the fiscal year ended December 31, 2014. The audit committee also discussed with the independent registered public accounting firm the matters required to be discussed by the PCAOB's Auditing Standard No. 16, *Communication with Audit Committees*. In addition, the audit committee received written communications from the independent registered public accounting firm confirming their independence as required by the applicable requirements of the PCAOB and has discussed with the independent registered public accounting firm their independence.

Based on the reviews and discussions referred to above, the audit committee recommended to the board of directors that the audited consolidated financial statements of Epizyme be included in Epizyme's Annual Report on Form 10-K for the fiscal year ended December 31, 2014, that was filed with the SEC.

THE AUDIT COMMITTEE OF THE BOARD OF
DIRECTORS OF EPIZYME, INC.

Carl Goldfischer, M.D., Chairman
Kenneth Bate
Richard F. Pops

April 15, 2015

HOUSEHOLDING

Some banks, brokers and other nominee record holders may be participating in the practice of “householding” proxy statements and annual reports. This means that only one copy of our documents, including the annual report to stockholders and proxy statement, may have been sent to multiple stockholders in your household. We will promptly deliver a separate copy of either document to you upon written or oral request to Epizyme, Inc., 400 Technology Square, Cambridge, Massachusetts 02139, Attention: IR, telephone: 617-229-5872. If you want to receive separate copies of the proxy statement or annual report to stockholders in the future, or if you are receiving multiple copies and would like to receive only one copy per household, you should contact your bank, broker or other nominee record holder, or you may contact us at the above address and phone number.

STOCKHOLDER PROPOSALS

A stockholder who would like to have a proposal considered for inclusion in our 2016 proxy statement must submit the proposal in accordance with the procedures outlined in Rule 14a-8 of the Exchange Act so that it is received by us no later than December 17, 2015. However, if the date of the 2016 Annual Meeting of Stockholders is changed by more than 30 days from the date of the previous year’s meeting, then the deadline is a reasonable time before we begin to print and send our proxy statement for the 2015 Annual Meeting of Stockholders. SEC rules set standards for eligibility and specify the types of stockholder proposals that may be excluded from a proxy statement. Stockholder proposals should be addressed to Epizyme, Inc., 400 Technology Square, Cambridge, Massachusetts 02139, Attention: IR.

If a stockholder wishes to propose a nomination of persons for election to our board of directors or present a proposal at an annual meeting but does not wish to have the proposal considered for inclusion in our proxy statement and proxy card, our amended and restated by-laws establish an advance notice procedure for such nominations and proposals. Stockholders at an annual meeting may only consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of the board of directors or by a stockholder of record on the record date for the meeting, who is entitled to vote at the meeting and who has delivered timely notice in proper form to our corporate secretary of the stockholder’s intention to bring such business before the meeting.

The required notice must be in writing and received by our corporate secretary at our principal executive offices not less than 90 days nor more than 120 days prior to the first anniversary of the preceding year’s annual meeting. However, in the event that the date of the annual meeting is advanced by more than 20 days, or delayed by more than 60 days, from the first anniversary of the preceding year’s annual meeting, a stockholder’s notice must be so received no earlier than the 120th day prior to such annual meeting and not later than the close of business on the later of (A) the 90th day prior to such annual meeting and (B) the tenth day following the day on which notice of the date of such annual meeting was mailed or public disclosure of the date of such annual meeting was made, whichever first occurs. For stockholder proposals to be brought before the 2016 Annual Meeting of Stockholders, the required notice must be received by our corporate secretary at our principal executive offices no earlier than January 20, 2016 and no later than February 19, 2016.

OTHER MATTERS

Our board of directors does not know of any other matters to be brought before the Annual Meeting. If any other matters not mentioned in this proxy statement are properly brought before the meeting, the individuals named in the enclosed proxy intend to use their discretionary voting authority under the proxy to vote the proxy in accordance with their best judgment on those matters.

By Order of the Board of Directors

/s/ Robert J. Gould

Robert J. Gould, Ph.D.

President, Chief Executive Officer and Secretary

