

Flaherty & Crumrine PREFERRED INCOME OPPORTUNITY FUND INC
Form N-Q
October 24, 2017

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM N-Q

**QUARTERLY SCHEDULE OF PORTFOLIO HOLDINGS OF REGISTERED
MANAGEMENT INVESTMENT COMPANY**

Investment Company Act file number 811-06495

Flaherty & Crumrine Preferred Income Opportunity Fund Incorporated
(Exact name of registrant as specified in charter)

301 E. Colorado Boulevard, Suite 720
Pasadena, CA 91101
(Address of principal executive offices) (Zip code)

R. Eric Chadwick
Flaherty & Crumrine Incorporated
301 E. Colorado Boulevard, Suite 720
Pasadena, CA 91101
(Name and address of agent for service)

Registrant's telephone number, including area code: 626-795-7300

Date of fiscal year end: November 30

Date of reporting period: August 31, 2017

Form N-Q is to be used by management investment companies, other than small business investment companies registered on Form N-5 (§§ 239.24 and 274.5 of this chapter), to file reports with the Commission, not later than 60 days after the close of the first and third fiscal quarters, pursuant to rule 30b1-5 under the Investment Company Act of 1940 (17 CFR 270.30b1-5). The Commission may use the information provided on Form N-Q in its regulatory, disclosure review, inspection, and policymaking roles.

A registrant is required to disclose the information specified by Form N-Q, and the Commission will make this information public. A registrant is not required to respond to the collection of information contained in Form N-Q unless the Form displays a currently valid Office of Management and Budget ("OMB") control number. Please direct comments concerning the accuracy of the information collection burden estimate and any suggestions for reducing the burden to the Secretary, Securities and Exchange Commission, 450 Fifth Street, NW, Washington, DC 20549-0609.

The OMB has reviewed this collection of information under the clearance requirements of 44 U.S.C. § 3507.

Item 1. Schedule of Investments.

The Schedule(s) of Investments is attached herewith.

FLAHERTY & CRUMRINE PREFERRED INCOME OPPORTUNITY FUND

To the Shareholders of Flaherty & Crumrine Preferred Income Opportunity Fund (“PFO”):

Fiscal 2017 has been a very good year for preferred securities, and the third fiscal quarter¹ continued in stride. Total return² on net asset value (“NAV”) was 3.1% for the quarter, bringing total return for the first nine months of fiscal 2017 to 15.7%. Total return on market price over the same periods was -0.9% and 19.4%, respectively.

Credit conditions continue to provide a supportive backdrop for yields and spreads, as most issuers of preferreds maintain strong balance sheets. Bank payout ratios (common stock dividends plus share buybacks) are now averaging at or above 100% of current earnings, which means, as a group, banks are no longer adding to their common equity layer of capital. Normally, this could be cause for concern – but given years of balance-sheet strengthening since the financial crisis, these payout ratios are comfortably supported.

Political headlines of all flavors remain omnipresent, including topics such as healthcare reform, tax reform, immigration, and North Korea. Equity and fixed-income markets, however, have largely ignored a lack of near-term progress on these issues and focused on potential for positive economic developments – notably lower taxes and regulatory reform. There are winners and losers in all policy decisions, but markets are pricing in some upside from lower tax rates and reduced regulatory burdens.

Away from these headlines, we have been living in a low-volatility financial environment for quite some time, which has been positive for spreads of most fixed-income products. Mid- to longer-term interest rates generally fell during the quarter, although rates have remained relatively range-bound in recent years. For example, the constant-maturity 10-year Treasury yield, currently around 2.3%, has been within about 0.75% of today’s rate since mid-2011. The economy continues to expand moderately with few signs of higher inflation. As a result, the Federal Reserve is moving very deliberately in removing accommodative monetary policy. The Fed last hiked the federal funds rate in June and has another 0.25% hike penciled in for December. In October, it will begin scaling back reinvestment of Treasury and mortgage-backed securities acquired in the wake of the financial crisis. Although we expect markets will take unwinding of “quantitative easing” in stride, the Fed will be the first major central bank to shrink its balance sheet, and this is a new source of market uncertainty.

Financial regulators in the United Kingdom announced that London banks will no longer be required to submit quotes for LIBOR (London interbank offered rate) after December 31, 2021. Since LIBOR is a reference rate for trillions of dollars of financial instruments – including many floating and fixed-to-floating rate preferred securities – it will be critical to find an alternative benchmark reference rate for instruments continuing past 2021. The Federal Reserve assigned the Alternative Reference Rate Committee (ARRC) to work on a transition from U.S. Dollar LIBOR to a new benchmark reference rate, and they have already identified viable alternatives. Once an alternative is finalized, transition to a new benchmark reference rate will be complicated by the sheer number of instruments involved and mechanics of a change. This process will take time, but we believe market participants have a large incentive to get it right.

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June 1, 2017—August 31, 2017

² Following the methodology required by the Securities and Exchange Commission, total return assumes dividend reinvestment.

One of the best places to find total return this quarter was in the primary market. New issue supply has been limited all year, and redemptions of higher-coupon preferred securities have continued at a healthy pace. Many offerings were met with strong demand that exceeded deal size, which in turn pushed prices up. This robust primary market also boosted secondary markets, as prices adjusted to reflect new-issue clearing levels.

During the quarter, a modest drop in interest rates helped lower-coupon securities outperform higher-coupon securities at the margin. Like last quarter, it is difficult to identify laggards in the portfolio this year. Performance lag has been relative return – not absolute negative return – in most cases – typically a result of call (redemption) features embedded in most preferreds. As a security moves above its call price, the call option limits further upside potential as rates or spread move lower. Investors continue to earn coupons, many of which are tax-advantaged, but price increases become more limited.

Looking forward, returns should come mostly from the coupons on securities as the pace of price gains tapers off or even reverses. Compared to fixed-income alternatives, however, preferred securities continue to offer value. Market volatility could increase, and economic or credit conditions could change – which may cause spreads to widen – but we believe preferreds' combination of credit quality and yield will be difficult to replace in other fixed-income asset classes.

As always, we encourage you to visit the Fund's website, www.preferredincome.com, for important information.

Sincerely,

The Flaherty & Crumrine Portfolio Management Team

September 30, 2017

Flaherty & Crumrine Preferred Income Opportunity Fund Incorporated

PORTFOLIO OVERVIEW
August 31, 2017 (Unaudited)

Fund Statistics

Net Asset Value	\$12.02	
Market Price	\$12.09	
Premium	0.58	%
Yield on Market Price	6.85	%
Common Stock Shares Outstanding	12,492,090	

Moody's Ratings*	% of Net Assets†
A	1.6%
BBB	58.5%
BB	29.3%
Not Rated**	8.8%
Below Investment Grade***	27.7%
Senior Debt Rating Below Investment Grade****	0.1%

* Ratings are from Moody's Investors Service, Inc. "Not Rated" securities are those with no ratings available from Moody's.

** Does not include net other assets and liabilities of 1.8%.

*** Below investment grade by all of Moody's, S&P, and Fitch.

**** Issuer's senior unsecured debt or issuer rating is below investment grade by all of Moody's, S&P, and Fitch.

Industry Categories % of Net Assets†

Top 10 Holdings by Issuer	% of Net Assets†
JPMorgan Chase & Co	4.7%
MetLife	4.5%
Wells Fargo & Company	4.1%
PNC Financial Services Group	4.0%
Morgan Stanley	3.4%
Fifth Third Bancorp	3.1%
BNP Paribas	3.1%
Enbridge Energy Partners	3.0%
Liberty Mutual Group	2.9%
XL Group Limited	2.6%

% of Net Assets***†**

Holdings Generating Qualified Dividend Income (QDI) for Individuals	59%
Holdings Generating Income Eligible for the Corporate Dividends Received Deduction (DRD)	44%

This does not reflect year-end results or actual tax categorization of Fund distributions. These percentages can, ***** and do, change, perhaps significantly, depending on market conditions. Investors should consult their tax advisor regarding their personal situation.

†Net Assets includes assets attributable to the use of leverage.

Flaherty & Crumrine Preferred Income Opportunity Fund Incorporated
PORTFOLIO OF INVESTMENTS
August 31, 2017 (Unaudited)

Shares/\$ Par		Value
Preferred Securities — 92.5%		
	Banking — 50.6%	
16,773	Astoria Financial Corporation, 6.50%, Series C	\$433,624 *
\$1,817,000	Australia & New Zealand Banking Group Ltd., 6.75% to 06/15/26 then ISDA5 + 5.168%, 144A****	2,035,130**(2)
\$400,000	Banco Bilbao Vizcaya Argentaria SA, 9.00% to 05/09/18 then SW5 + 8.262%, 144A****	416,013 **(2)
\$490,000	Banco Mercantil del Norte SA, 7.625% to 01/06/28 then T10Y + 5.353%, 144A****	528,955 **(2)
	Bank of America Corporation:	
\$300,000	6.30% to 03/10/26 then 3ML + 4.553%, Series DD	338,625 *
\$2,540,000	8.00% to 01/30/18 then 3ML + 3.63%, Series K	2,589,276*(1)
\$1,520,000	8.125% to 05/15/18 then 3ML + 3.64%, Series M	1,573,580*(1)
\$1,819,000	Barclays Bank PLC, 7.875% to 03/15/22 then SW5 + 6.772%, 144A****	1,982,617**(2)
	BNP Paribas:	
\$4,661,000	7.375% to 08/19/25 then SW5 + 5.15%, 144A****	5,266,930**(2)
\$1,500,000	7.625% to 03/30/21 then SW5 + 6.314%, 144A****	1,644,375**(2)
	Capital One Financial Corporation:	
12,400	6.00%, Series H	329,375 *
7,000	6.20%, Series F	187,600 *
24,333	6.70%, Series D	662,162 *
	Citigroup, Inc.:	
81,200	6.875% to 11/15/23 then 3ML + 4.13%, Series K	2,350,131*(1)
74,694	7.125% to 09/30/23 then 3ML + 4.04%, Series J	2,200,665*(1)
\$299,000	8.40% to 04/30/18 then 3ML + 4.0285%, min 7.7575%, Series E	312,829 *
	CoBank ACB:	
15,600	6.125%, Series G, 144A****	1,563,900*
9,000	6.20% to 01/01/25 then 3ML + 3.744%, Series H, 144A****	968,344 *
10,000	6.25% to 10/01/22 then 3ML + 4.557%, Series F, 144A****	1,079,063*(1)
\$415,000	6.25% to 10/01/26 then 3ML + 4.66%, Series I, 144A****	457,884 *
\$4,500,000	Colonial BancGroup, 7.114%, 144A****	6,750 (3)(4)††
232,807	Fifth Third Bancorp, 6.625% to 12/31/23 then 3ML + 3.71%, Series I	6,926,590*(1)
	First Horizon National Corporation:	
750	First Tennessee Bank, 3ML + 0.85%, min 3.75%, 3.75% ⁽⁵⁾ , 144A****	585,000 *(1)
1	FT Real Estate Securities Company, 9.50% 03/31/31, 144A****	1,298,750
	Goldman Sachs Group:	
\$195,000	5.70% to 05/10/19 then 3ML + 3.884%, Series L	202,069 *
50,000	6.375% to 05/10/24 then 3ML + 3.55%, Series K	1,450,500*(1)

Flaherty & Crumrine Preferred Income Opportunity Fund Incorporated
PORTFOLIO OF INVESTMENTS (Continued)
August 31, 2017 (Unaudited)

Shares/\$ Par		Value
Preferred Securities — (Continued)		
	Banking — (Continued)	
	HSBC Holdings PLC:	
\$800,000	HSBC Capital Funding LP, 10.176% to 06/30/30 then 3ML + 4.98%, 144A****	\$ 1,274,496 ⁽¹⁾⁽²⁾
\$325,000	HSBC Holdings PLC, 6.00% to 05/22/27 then ISDA5 + 3.746%	342,550 ^{**} (2)
\$937,000	HSBC Holdings PLC, 6.875% to 06/01/21 then ISDA5 + 5.514%	1,021,798 ^{**} (2)
66,960	HSBC Holdings PLC, 8.00%, Series 2	1,815,453 ^{**} (1)(2)
99,000	Huntington Bancshares, Inc., 6.25%, Series D	2,751,457 [*] (1)
	JPMorgan Chase & Company:	
\$300,000	6.00% to 08/01/23 then 3ML + 3.30%, Series R	325,500 [*]
54,650	6.70%, Series T	1,474,457 [*] (1)
\$4,167,000	6.75% to 02/01/24 then 3ML + 3.78%, Series S	4,766,006 [*] (1)
\$3,750,000	7.90% to 04/30/18 then 3ML + 3.47%, Series I	3,867,187 [*] (1)
84,000	KeyCorp, 6.125% to 12/15/26 then 3ML + 3.892%, Series E	2,468,130 [*]
\$2,240,000	M&T Bank Corporation, 6.45% to 02/15/24 then 3ML + 3.61%, Series E	2,520,000 [*] (1)
\$500,000	Macquarie Bank Ltd., 6.125% to 03/08/27 then SW5 + 3.703%, 144A****	516,250 ^{**} (2)
	Morgan Stanley:	
35,000	5.85% to 04/15/27 then 3ML + 3.491%, Series K	954,187 [*]
148,000	6.875% to 01/15/24 then 3ML + 3.94%, Series F	4,308,650 [*] (1)
77,200	7.125% to 10/15/23 then 3ML + 4.32%, Series E	2,272,189 [*] (1)
162,500	New York Community Bancorp, Inc., 6.375% to 03/17/27 then 3ML + 3.821%, Series A	4,771,000 [*]
	PNC Financial Services Group, Inc.:	
298,606	6.125% to 05/01/22 then 3ML + 4.067%, Series P	8,508,031 [*] (1)
\$395,000	6.75% to 08/01/21 then 3ML + 3.678%, Series O	447,831 [*] (1)
\$1,775,000	RaboBank Nederland, 11.00% to 06/30/19 then 3ML + 10.868%, 144A****	2,043,469 ⁽¹⁾⁽²⁾
35,000	Regions Financial Corporation, 6.375% to 09/15/24 then 3ML + 3.536%, Series B	995,837 [*]
\$3,800,000	Societe Generale SA, 7.375% to 09/13/21 then SW5 + 6.238%, 144A****	4,118,250 ^{**} (1)(2)
	Sovereign Bancorp:	
2,600	Sovereign REIT, 12.00%, Series A, 144A****	3,259,750
	Standard Chartered PLC:	
\$1,370,000	7.50% to 04/02/22 then SW5 + 6.301%, 144A****	1,486,861 ^{**} (2)
\$2,500,000	7.75% to 04/02/23 then SW5 + 5.723%, 144A****	2,731,250 ^{**} (2)
83,700	State Street Corporation, 5.90% to 03/15/24 then 3ML + 3.108%, Series D	2,339,624 [*] (1)
10,000	Texas Capital Bancshares Inc., 6.50%, Series A	253,525 [*]
35,000	US Bancorp, 6.50% to 01/15/22 then 3ML + 4.468%, Series F	1,017,537 [*] (1)
28,000	Valley National Bancorp, 5.50% to 09/30/22 then 3ML + 3.578%, Series B	742,000 [*]

59,300 Webster Financial Corporation, 6.40%, Series E

1,507,554^{*(1)}

Flaherty & Crumrine Preferred Income Opportunity Fund Incorporated
PORTFOLIO OF INVESTMENTS (Continued)
August 31, 2017 (Unaudited)

Shares/\$ Par

Preferred Securities — (Continued)

15,000

56,200

\$2,075,000

34,400

\$1,139,000

104,500

\$The members of our compensation committee are Mr. Mott, Dr. Allen, and Dr. Seidenberg. Mr. Mott is chair of the compensation committee. Our compensation committee met four times during 2018. Our compensation committee's responsibilities include:

reviewing and approving, or 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 the evaluations 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; and

preparing the compensation committee report if and to the extent then required by SEC rules.

Our compensation committee may delegate to one or more executive officers the power to grant options or other stock awards pursuant to our incentive plans to employees of the company who are not executive officers or senior vice presidents.

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 Mr. Mott, Dr. Allen, and Dr. Seidenberg are independent as currently defined in applicable Nasdaq listing standards.

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Compensation Committee Interlocks and Insider Participation

During 2018, the members of our compensation committee were Mr. Mott, Dr. Allen, and Dr. Seidenberg. None of the members of our compensation committee is an officer or employee of our company, nor have they ever been an officer or employee of our company. 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. Except as set forth in the Transactions with Related Persons section with respect to entities affiliated with Mr. Mott, none of the members of the compensation committee (or his or her immediate family members) had a direct or indirect material interest in a transaction with the company involving more than \$120,000.

Nominating and Corporate Governance Committee

The members of our nominating and corporate governance committee are Dr. Goldfischer, Mr. Conroy and Dr. Seidenberg. Dr. Goldfischer is chair of the nominating and corporate governance committee. Our nominating and corporate governance committee met once during 2018 and met periodically on an informal basis to discuss management and Board staffing decisions. 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 director's corporate governance guidelines; 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

Our Board recognizes the importance of director attendance at Board and committee meetings. The full board of directors met eleven times during 2018. During 2018, 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. Four members of our board of directors attended the 2018 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 of business conduct and ethics 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.

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Corporate Governance Guidelines

Our board of directors has adopted corporate governance guidelines to assist in the exercise of its duties and responsibilities and to serve the best interests of our company and our stockholders. The guidelines provide that:

our board's principal responsibility is to oversee the management of our company;

a majority of the members of our board must be independent directors;

the independent directors meet in executive session at least twice a year;

directors have full and free access to management and, as necessary, independent advisors; and

our nominating and corporate governance committee will oversee an annual self-evaluation of the board to determine whether it and its committees are functioning effectively.

A copy of the corporate governance guidelines is posted under the heading "Corporate Governance" on the Investor Relations section of our website, which is located at <http://www.epizyme.com>.

Board Leadership Structure and Board's Role in Risk Oversight

In April 2016, we appointed David M. Mott, an independent director under applicable Nasdaq rules, as chairman of the board. Prior to the appointment of Mr. Mott as chairman of the board, we did not have a chairman of the board. Mr. Mott previously served as our lead independent director and, in that capacity, served in a role similar to that of a chairman of the board. Separating the duties of the chairman of the board from the duties of the chief executive officer allows our chief executive officer to focus on our day-to-day business, while allowing the chairman of the board to lead the board of directors in its fundamental role of providing advice to and independent oversight of management. Specifically, our chairman of the board 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.

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, 2018. 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 oversees our risk management processes directly and through its committees. Our management is responsible for risk management on a day-to-day basis and our board and its committees oversee the risk management activities of management. 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.

Table of Contents**Communication with Our Directors**

Any interested party with concerns about our company may report such concerns to the board of directors, or the chairman 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 our legal counsel and a copy of such communication may be retained for a reasonable period of time. The director may discuss the matter with our legal counsel, with independent advisors, with non-management directors, or with our 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 us 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. We have 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 2018.

Name	Fees Paid In Cash (\$)(1)	All Other Compensation (\$)(2)	Option Awards (\$)(3)	Total (\$)
Andrew R. Allen, M.D., Ph.D.	43,854		138,843	182,697
Kenneth Bate	42,471		138,843	181,314
Carl Goldfischer, M.D.	60,081		138,843	198,924
David M. Mott (4)	103,238		138,843	242,081
Richard F. Pops	42,471		138,843	181,314
Kevin Conroy (5)	51,067		138,843	189,910
Beth Seidenberg, M.D. (6)	55,060		138,843	193,903

Michael Giordano, M.D. (7)	19,849	416,034	284,055	719,938
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- (1) Amounts represent cash compensation for services rendered by each member of the board of directors.
- (2) Amount shown consists of fees paid for consulting and advisory services.
- (3) Amounts shown reflect the grant date fair value of option awards granted during 2018. The grant date fair value was computed in accordance with Financial Accounting Standards Board Accounting Standards, or the FASB, 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, 2018 regarding assumptions we made in determining the fair value of option awards.

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- (4) Includes \$82,500 of fees Mr. Mott elected to receive in common stock in lieu of cash for his 2018 annual board of director fees.
- (5) Includes \$39,000 of fees Mr. Conroy elected to receive in common stock in lieu of cash for his 2018 annual board of director fees.
- (6) Includes \$44,000 of fees Dr. Seidenberg elected to receive in common stock in lieu of cash for her 2018 annual board of director fees.
- (7) Dr. Giordano joined our board of directors in March 2018. Fees paid to Dr. Giordano for his services on our board of directors were pro-rated accordingly.

During 2018, we did not provide any cash compensation to Mr. Bazemore, our President and Chief Executive Officer, for his service as a director. Mr. Bazemore's compensation is set forth under Executive Compensation Summary Compensation

Director Compensation Program

Our director compensation 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. 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 the board and the chairman of each committee receive additional 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.

In 2018, directors received the following cash fees under our director compensation program for service on the board of directors, as chairman of our board of directors and for service on each committee of the board of directors on which the director is a member.

	Member Annual Fee	Chairman Additional Annual Fee
Board of Directors	\$ 35,000	\$ 35,000
Audit Committee	7,500	7,500
Compensation Committee	5,000	7,500
Nominating and Corporate Governance Committee	4,000	4,500

Under the director compensation program, directors have the right to elect to receive 100% of their cash fees payable in a calendar year in the form of unrestricted shares of our common stock in lieu of cash fees. These shares of common stock are issued under our 2013 Stock Incentive Plan, or the 2013 Plan. Shares of our common stock issued in lieu of director fees are issued on the date of the annual meeting, and the number of shares to be issued to participating directors is determined by dividing the expected cash fees to be paid for the full year by the closing price of the Company's common stock on the day of the annual meeting. Each incumbent director may elect to receive stock for fees prior to the beginning of each fiscal year, and each new director has the immediate option to elect to receive stock for fees, beginning with the next full fiscal year during which he or she serves. In 2018, three members of the Board, Beth Seidenberg, David Mott and Kevin Conroy, elected to receive their cash fees in the form of unrestricted shares of our common stock.

In addition, in January 2019 our compensation committee, in consultation with Pearl Meyer, recommended for approval by our board of directors, and our board of directors approved, updates to our director compensation program. Under our updated director compensation program, upon a non-employee director's initial election to our board of directors, such director will receive an option to purchase the number of shares of our common stock that have a Black-Scholes value as of the date of grant equal to \$300,000 (as calculated using the same methodology that we use to calculate the value of stock

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awards for purposes of our financial statements);

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however, the number of shares of common stock issuable upon such option may in no event exceed 50,000 shares. On the date of each annual meeting of stockholders, each non-employee director that has served on our board of directors for at least six months and that continues to serve on our board of directors after such annual meeting, will receive an option to purchase the number of shares of our common stock that have a Black-Scholes value as of the date of grant equal to \$150,000 (as calculated using the same methodology that we use to calculate the value of stock awards for purposes of our financial statements); however, in no year may the number of shares of common stock issuable upon such option exceed 25,000 shares. Subject to the non-employee director's continued service as a director, each option will vest with respect to 25% of the shares on the first anniversary of the grant date and the remaining shares vest in equal monthly installments thereafter until the fourth anniversary of the grant date. Under the updated director compensation plan, we also agreed to pay the following annual cash fees to our non-employee directors as consideration for their service on our board:

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

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EXECUTIVE COMPENSATION

Compensation Discussion and Analysis

Overview

Our compensation committee is responsible for reviewing and approving, or recommending for approval by the board of directors, the compensation of our named executive officers, including salary, cash bonus and equity incentive compensation levels, severance arrangements, change in control benefits and other forms of compensation. This section discusses the philosophy, programs, processes, decisions, and other relevant information with respect to the compensation of our named executive officers, or NEOs.

Our NEOs for the year ended December 31, 2018 were:

Name	Title
Robert Bazemore	President and Chief Executive Officer
Matthew Ros	Chief Strategy and Business Officer
Shefali Agarwal	Chief Medical Officer
Susan Graf	(former) Chief Business Officer
Suzanne Fleming	(former) Senior Vice President of Finance and Treasurer

Ms. Graf served as our Chief Business Officer until September 2018. Ms. Fleming served as our Senior Vice President of Finance and Treasurer until January 2019.

Our Vision & Mission

Our vision is to rewrite therapy for cancer and other serious diseases through targeted epigenetic medicines. We aspire to change the standard of care for patients and physicians by developing medicines with fundamentally new mechanisms of action. We are focused on creating medicines that are targeted at specific causes of diseases, that are orally administered,

tolerable, easy to take, and that are based on a deep understanding of the patients that will benefit from them. Since 2011, we have discovered five novel epigenetic therapies, three of which are in clinical development and two that have begun or will soon begin IND-enabling studies.

Our team is wholly dedicated to bringing epigenetic therapies to the many patients who can potentially benefit from them. We believe that we have the opportunity to change the lives of patients living with cancer and other serious diseases.

Business Environment and Performance

As a late-stage biotechnology company headquartered in Cambridge, Massachusetts, we operate in a highly competitive environment for capital and talent. Achieving our mission requires vision, expertise and execution from our executives. 2018 was a year of tremendous progress towards our long-term goals and mission, highlighted by the following:

Scientific / Pipeline

Identified registration path for tazemetostat clinical trials in EZH2 wild type and mutant follicular lymphoma

Successfully resolved partial clinical hold in our tazemetostat clinical trials with no major changes to any of our clinical programs or trial populations

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Completed enrollment in our Phase 2 trial of tazemetostat in follicular lymphoma

Completed good laboratory practice toxicology work necessary to move EZM8266 into the clinic
Collaborations

Entered a strategic collaboration with Boehringer Ingelheim focused on the research, development and commercialization of novel small molecule inhibitors directed toward two previously unaddressed epigenetic targets as potential therapies for people with cancer

Earned an \$8 million milestone payment from Glaxo Group Limited (an affiliate of GlaxoSmithKline) under our collaboration with Glaxo Group Limited following initiation of patient dosing in a Phase 1 clinical trial of GSK3368715, a first-in-class protein arginine methyltransferase1 (PRMT1) inhibitor discovered by us and the second program to enter the clinic under the collaboration
Organizational

Appointed Dr. Agarwal as our Chief Medical Officer

Mr. Ros commenced a new role as Chief Strategy and Business Officer

Key Compensation Decisions and Actions

Our compensation committee took several actions in 2018 taking into account our compensation philosophy and objectives, the needs and performance of our company, individual performance, and other factors such as market data and industry best practices.

Base Salary Adjustments. The compensation committee reviewed base salaries of our NEOs in January 2018. Mr. Bazemore and Mr. Ros each received an annual merit-based salary adjustment reflecting their performance and contributions and to maintain reasonable positioning relative to our peer companies. No adjustments to base salary were made for Ms. Graf or Ms. Fleming. Ms. Graf did not receive a salary adjustment as her base salary had been increased in December 2017 to reflect her assumption of additional responsibilities. The compensation committee determined that Ms. Fleming's salary, which had been set in September 2017 in connection with her hiring, was market competitive. Dr. Agarwal, who joined us in June 2018, was not an employee at the time of the 2018 salary review and her base salary was set at the time of her hire. Further detail relating to salaries paid to our NEOs and the compensation committee's determination of such salaries is provided in the section Compensation Decisions Annual Base Salary .

Short-term Incentive Plan Goals and Design. In January 2018, the compensation committee approved corporate goals and bonus targets for the NEOs as part of our 2018 bonus program. The corporate goals consisted of five corporate objectives, each with its own weighting to reflect their importance to our business. To the extent goals are

partially met or exceeded, the compensation committee may ascribe a partial achievement or overachievement percentage to each goal, as applicable. The compensation committee also reviews individual performance to determine whether the potential bonus should be increased or decreased. In January 2019, the compensation committee reviewed our achievements against our 2018 corporate objectives and agreed to attribute a corporate funding factor of 101.25%. Further detail relating to the Plan is provided in the section Compensation Decisions Short-term Incentives .

Long-term Incentive Grants. In January 2018, the compensation committee approved grants of stock options under the 2013 Stock Incentive Plan to our NEOs. The compensation committee also granted stock options under the 2013 Stock Incentive Plan to Dr. Agarwal at the time of her hire. Further detail relating to our long-term incentive grants is provided in the section Compensation Decisions Long-term Incentives.

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In January 2019, the compensation committee approved 2019 base salaries, bonus targets for 2019, and new long-term incentive grants. The compensation committee determined that, for 2019, eligible NEOs would receive a 75% of their long-term incentive grant in stock options and 25% in restricted stock units, or RSUs. The compensation committee also approved the grant of performance-based RSUs to our NEOs that contain performance based vesting objectives related largely to our clinical programs for tazemetostat in epithelioid sarcoma and follicular lymphoma. The compensation committee believes that these actions align with our overall compensation philosophy and program objectives.

Compensation Philosophy and Process

The goal of our compensation program is to pay for performance. Within this overarching principle, there are a number of key objectives that the compensation program is designed to achieve.

Overarching Philosophy:

Pay for Performance

Key Objectives:

Attract and retain qualified executive talent to support our mission, vision, and business objectives

Motivate individuals to achieve our mission, vision, and business objectives

Foster a culture of camaraderie, collaboration, discipline, innovation, openness, patient-focus, and resilience

Align the interests of our NEOs with our stockholders

To attract and retain qualified executives, we seek to pay our NEOs compensation that is competitive within our industry. To understand the competitive market for NEO compensation in our industry, we engage our independent compensation consultant, Pearl Meyer, to perform benchmarking exercises. We do not explicitly target a certain percentile from our market benchmarking to compensate our NEOs, but rather review each NEO’s positioning relative to the market within the context of his or her experience, contributions, role, potential, and other factors. Similarly, we do not target a specific mix of compensation, although we deliver a majority of compensation through long-term incentives consistent with our pay for performance philosophy, and to be generally competitive with peers in terms of each element of pay.

Role of the Compensation Committee. The compensation committee is responsible for establishing and overseeing our executive compensation program. Our compensation committee typically reviews and discusses with our chief executive officer proposed compensation for all executives other than the chief executive officer. Following the compensation committee’s discussions with our chief executive officer, and in consideration of the information provided by Pearl Meyer, the compensation committee then consults with the Board about the compensation of each NEO before determining and approving each NEOs compensation for the upcoming fiscal year.

Role of our Chief Executive Officer. Our chief executive officer evaluates and reviews with the compensation committee the individual performance and contributions of each of the other NEOs, and makes recommendations to the compensation committee regarding base salary, non-equity incentive plan compensation and equity awards. The compensation committee reviews and considers such recommendations, but ultimately retains full discretion and authority over the final compensation decisions for the NEOs. Our chief executive officer, in consultation with other members of our management team, also recommends the Company performance objectives that are used to determine bonus amounts.

Role of our Independent Compensation Consultant. Pursuant to its charter, the compensation committee has the sole authority to retain compensation consultants to assist in its evaluation of executive and director compensation. Our compensation committee engaged Pearl Meyer as its independent compensation consultant to

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review our executive compensation peer group and program design and assess our executives' compensation relative to comparable companies. Pearl Meyer provides our compensation committee with information regarding market compensation practices and trends. Our compensation committee considered the relationship that Pearl Meyer has with us, the members of our board of directors and our executive officers, and has determined that Pearl Meyer is serving, and has served, as an independent and conflict-free advisor to the compensation committee.

Factors in Setting Compensation

The compensation committee reviews NEO compensation annually. As part of its annual compensation review, the compensation committee evaluates our compensation program and arrangements for our NEOs based on a number of factors, including:

Internal Factors

External Factors

Compensation philosophy and objectives

Peer group information and data

Company goals and objectives

Broader industry specific information and data

Historical company performance and company outlook

Compensation committee experience

Individual NEO roles and profiles

Market dynamics

Individual performance and contributions

Current and historical pay data for NEOs

An important external factor in making compensation decisions is our compensation peer group. The compensation committee considers a select number of key inputs, summarized below, to determine the companies to be included in the peer group. The compensation data from the peer group provide a benchmark for market-competitive base salaries, short- and long-term incentive targets, and estimated total direct compensation. In certain cases where the peer group data is limited for a particular role, Pearl Meyer provides us with a blend of peer data and survey data where it concludes the peer data is not conclusive. This data provides context for the committee in setting targeted pay levels going forward.

In September 2017, the compensation committee, together with Pearl Meyer, used the following screening criteria to determine a recommended group of companies to be in the peer group to be used in setting 2018 compensation:

Criteria

Description

Industry

U.S. publicly-traded biotechnology or pharmaceutical companies

Development Stage

Companies with a lead asset in phase II or III trials

Size

1/3x to 3x that of Epizyme for market capitalization, headcount, and R&D expenses

Other Companies with an oncology focus

Based on this screening criteria, in September 2017 the compensation committee approved a peer group of 20 companies, listed below.

Acceleron Pharma Inc.
Aduro BioTech, Inc.
Agius Pharmaceuticals, Inc.
Akebia Therapeutics, Inc.
Array BioPharma Inc.
bluebird bio, Inc.
Blueprint Medicines Corp.

Celldex Therapeutics, Inc.
Clovis Oncology, Inc.
Dynavax Technologies Corporation
Five Prime Therapeutics, Inc.
Ignyta, Inc.
Inovio Pharmaceuticals, Inc.
Juno Therapeutics, Inc.

Karyopharm Therapeutics Inc.
MacroGenics, Inc
OncoMed Pharmaceuticals, Inc.
Seres Therapeutics, Inc.
Xencor, Inc.
ZIOPHARM Oncology, Inc.

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The summary statistics below demonstrate how we compared to the companies in the peer group in September 2017.

Statistic	Market Capitalization	Headcount	R&D Expense
	(\$B)		(\$M)
75 th Percentile	\$1.8	258	\$171
50 th Percentile	\$0.9	177	\$100
25 th Percentile	\$0.6	108	\$84
Epizyme	\$1.0	112	\$108

In October 2018, the compensation committee, with the assistance of Pearl Meyer, reviewed the companies included in the 2018 peer group for continued appropriateness in 2019 using the same criteria it used to determine the 2018 peer group. Pearl Meyer recommended the following changes to the peer group, which the compensation committee approved. This group was used to set compensation for fiscal year 2019.

Action	Company	Rationale
Companies recommended for exclusion from the current group	Agios Pharmaceuticals, Inc.	Market capitalization above range
	bluebird bio, Inc.	Market capitalization above range
	Celldex Therapeutics, Inc.	Market capitalization below range
	Ignyta, Inc.	Acquired
	Juno Therapeutics, Inc.	Acquired
	OncoMed Pharmaceuticals, Inc.	Market capitalization below range
Companies recommended for inclusion in the 2019 peer group	Deciphera Pharmaceuticals, Inc.	Met screening criteria
	ImmunoGen, Inc.	Met screening criteria
	Iovance Biotherapeutics, Inc.	Met screening criteria
	Mirati Therapeutics, Inc.	Met screening criteria
	Odonate Therapeutics, Inc.	Met screening criteria
	Syros Pharmaceuticals, Inc.	Met screening criteria

Compensation Elements and Decisions

The primary elements of our executive compensation program are:

Element	Purpose	Timing
Base Salary	Fixed amount to attract and retain top talent.	Initial base salaries are set at the time of hire, and adjustments to base salaries are considered in conjunction with changes in job

responsibility or annually as part
of our merit increase process.

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Element	Purpose	Timing
Short-term Incentives	Performance-contingent compensation to reward company and individual performance against a set of annual goals.	Generally measured and paid out on an annual basis, typically in the first quarter of the following fiscal year.
Long-term Incentives	Variable incentive compensation to promote performance, support retention, and create stockholder alignment.	Generally granted at the time of hire, and annually following the close of the previous fiscal year.
Severance and Change in Control Benefits	Competitive benefits consistent with industry practice	Upon a change of control of our company or an NEOs termination of employment
Benefits	Fixed benefits to promote individual health, welfare and financial security.	The timing of our benefits varies by element.

Annual Base Salary.

Base salaries are used to recognize the experience, skills, knowledge and responsibilities required of our NEOs. Base salaries for our NEOs are established at the time the NEO is hired, taking into account the position for which the NEO is being considered and the NEOs qualifications, prior experience and prior salary. None of our NEOs is currently party to an employment agreement that provides for automatic or scheduled increases in base salary. However, on an annual basis, our compensation committee reviews and evaluates, with input from our chief executive officer (other than with respect to himself), the need for adjustment of the base salaries of our NEOs based on changes and expected changes in the scope of a NEOs responsibilities, including promotions, the individual contributions made by and performance of the NEO during the prior year, overall labor market conditions, the relative ease or difficulty of replacing the executive with a well-qualified person, our overall growth and development as a company and general salary trends in our industry and among our peer group and where the NEOs salary falls in the salary range presented by that data. In making decisions regarding salary increases, our compensation committee may also draw upon the experience of members of the committee with other companies. No formulaic base salary increases are provided to our NEOs.

The following table presents the base salaries for each of our NEOs for the years 2017 and 2018, as approved by our compensation committee. The 2017 base salaries became effective on January 1, 2017. The 2018 base salaries became effective on January 1, 2018.

Named Executive	2017 Annualized Salary	January 2018 Adjustment		2018 Annualized Salary	Nature of Increase
		% of Base Salary	Amount		
Officer	(\$)		(\$)	(\$)	
Robert Bazemore	556,200	3.5%	19,467	575,667	Merit increase
Matthew Ros	391,400	7.3%	28,600	420,000	Merit increase and market adjustment

Shefali Agarwal (1)		450,000	Set at time of hire
Susan Graf (2)	415,000	415,000	
Suzanne Fleming (3)	350,000	350,000	

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- (1) Dr. Agarwal was hired in June 2018 and was not part of the January 2018 merit increase process.
- (2) Ms. Graf’s base salary was adjusted in December 2017 to reflect additional responsibilities taken at that time.
- (3) Ms. Fleming was hired in September 2017 and her base salary for 2018 was fixed at that time.

Short-term Incentives. Our bonus program is designed to motivate and reward our NEOs for achievements relative to our goals and expectations for each fiscal year. Under our bonus program, each NEO has a target bonus opportunity, defined as a percentage of his or her annual base salary. The general design of our bonus program is as follows:

$$\begin{array}{rcccl}
 & & \text{NEO} & & \\
 & & \text{Target} & & \\
 \text{NEO Base} & & \text{X} & & \text{Short-term} \\
 \text{Salary} & & \text{Bonus} & & \text{Incentive} \\
 & & & & \text{Earned} \\
 & & \text{X} & & \\
 & & \text{Corporate} & & \text{Individual} \\
 & & \text{Funding} & & \text{Performance} \\
 & & \text{Factor} & & \text{Modifier} \\
 & & & & =
 \end{array}$$

In January 2018, our compensation committee set the following target bonus opportunities for each NEO:

NEO	2018 Base Salary (\$)	Target Bonus %	Target Bonus Award (\$)
Robert Bazemore	575,667	55%	316,617
Matthew Ros	420,000	40%	168,000
Shefali Agarwal (1)	450,000	40%	180,000
Susan Graf	415,000	40%	166,000
Suzanne Fleming	350,000	35%	122,500

(1) Dr. Agarwal’s 2018 target bonus was established at the time of her hire. Our compensation committee then established the following corporate objectives to assess our corporate performance in 2018. In January 2019, the compensation committee reviewed our achievements against these corporate goals to arrive at a corporate funding factor of 101.25%.

Goal /Assessment	Weighting
1. Goal: Develop and execute against an expeditious follicular lymphoma, or FL, registration path, in consultation with the Food and Drug Administration, or FDA, to support submission of an FL New Drug Application, or NDA, in 2019	40%

Assessment:

Successful end-of-Phase 2 meeting with FDA

FL enrollment completed in 4Q

FL natural history assessment completed supports intended registration strategy

Prepare to initiate FL combo studies in 2019

2. **Goal:** Submit epithelioid sarcoma, or ES, NDA in the US (4Q) 30%

Assessment:

ES NDA intentionally delayed until 2Q 2019

ES natural history study completed plan to explore with FDA seeking approval without Phase 3 requirement

Mock inspections initiated, and on track

Supply chain secured / positive chemistry manufacturing and controls meeting with FDA

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	Goal /Assessment	Weighting
3.	<p>Goal: Develop board of directors-approved go-to-market strategic options for tazemetostat (3Q)</p> <p>Assessment:</p> <p style="padding-left: 40px;">Exploring tazemetostat partnering opportunities to maximize asset value</p> <p style="padding-left: 40px;">Operational launch plan developed for ES, and commercial lead hired</p>	15%
4.	<p>Goal: Complete all US investigational new drug application, or IND, and Canadian clinical trial application enabling work for G9a and file IND by year end (4Q)</p> <p>Assessment:</p> <p style="padding-left: 40px;">IND-enabling good laboratory practice toxicology studies concluded</p> <p style="padding-left: 40px;">First-in-Human clinical program designed</p> <p style="padding-left: 40px;">Pre-IND meeting to be scheduled in 2Q</p>	10%
5.	<p>Goal: Goals related to organizational effectiveness, financial rigor and compliance</p> <p>Assessment:</p> <p style="padding-left: 40px;">Boehringer Ingelheim deal executed;</p> <p style="padding-left: 40px;">Financing in October extends cash runway</p> <p style="padding-left: 40px;">Chief Medical Officer hired, and key clinical roles have been filled</p> <p style="padding-left: 40px;">Satellite site closed, and 10 full time employees eliminated</p>	5%
	Total	100%

Individual Performance Considerations

Our compensation committee also evaluates the individual performance of our NEOs. Consistent with this process, our compensation committee assessed the performance of our chief executive officer in 2018 based on our relative achievement of our corporate goals as well as his leadership in driving the execution of our strategic plans. In assessing the individual performance in 2018 of our NEOs other than our chief executive officer, our compensation committee, with the input of our chief executive officer, considered each such officer's individual contributions to the completion of our goals, and the officer's individual achievements in helping to build the company and execute on our strategy. These achievements include the

following:

Robert Bazemore, President & CEO: Mr. Bazemore's short term incentive payment is based 100% upon the achievement of the Company-wide annual goals. Accordingly, for 2018, Mr. Bazemore earned 101.25% of his total target short term incentive payment.

Matthew Ros, Chief Strategy & Business Officer: Mr. Ros was assigned objectives related to (1) providing leadership and continuing to build the organization, (2) successfully concluding the Boehringer Ingelheim collaboration, (3) achieving financial goals related to capital raising activities, (4) exploring tazemetostat partnering opportunities to maximize asset value, and (5) developing the strategic and operational launch plan for tazemetostat in epithelioid sarcoma, as well as hiring a senior vice president to lead the commercial function. Given his exceptional leadership contributions along with taking on additional scope of responsibilities throughout 2018, the Compensation Committee determined Mr. Ros achieved 110% related to his individual objectives.

Shefali Agarwal, Chief Medical Officer: Dr. Agarwal was assigned objectives related to (1) providing leadership and continuing to build the clinical organization, (2) supporting various regulatory objectives

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including development of a registration path in follicular lymphoma (including a successful EOP2 meeting with the FDA and completion of study enrollment), and progression of the NDA in epithelioid sarcoma, and (3) progressing our clinical programs related to the further development of tazemetostat. Given her exceptional results in these areas in her first year of employment, in addition to her key role in the successful resolution of the partial clinical hold on Tazemetostat, the Compensation Committee determined that Dr. Agarwal achieved 110% related to her individual objectives.

Susan Graf, (former) Chief Business Officer: Ms. Graf was assigned objectives related to (1) progressing the Boehringer Ingelheim collaboration, (2) achieving financial goals related to capital raising activities, and (3) exploring tazemetostat partnering opportunities to maximize asset value. The Compensation Committee determined that prior to her departure from the company in 2018, Ms. Graf achieved 90% related to her individual objectives, which was paid on a prorated basis.

Final Calculations

The final calculations used to arrive at the 2018 bonus awards are as follows:

NEO	2018 Base Salary (\$)		Target Bonus %		Corporate Funding Factor		Individual Performance Modifier	=	Bonus Award (\$)
Robert Bazemore	575,667	X	55%	X	101.25%	X	100%	=	320,575
Matthew Ros	420,000	X	40%	X	101.25%	X	110%	=	187,100
Shefali Agarwal (1)	450,000	X	40%	X	101.25%	X	110%	=	200,500
Susan Graf (2)	311,250	X	40%	X	92.50%	X	90%	=	103,646
Suzanne Fleming (3)	350,000	X	35%	X		X		=	0

- (1) Dr. Agarwal's 2018 bonus award represents the full year bonus per her offer letter.
- (2) Ms. Graf departed Epizyme in September 2018. Her base salary is pro-rated for service time to arrive at her award.
- (3) Ms. Fleming departed Epizyme in January 2019.

In addition to these short-term incentive payouts, the compensation committee may approve cash bonuses to induce individuals to join our company or make up for lost compensation opportunities at previous employers, commonly referred to as sign-on bonuses. In 2017, the compensation committee approved a sign-on bonus for Ms. Fleming. The sign-on bonus was structured to include an initial payment of \$75,000 in 2017 and payments of \$50,000 on each of March 1, 2018 and September 1, 2018. Dr. Agarwal received a \$125,000 sign-on bonus upon joining the company in June 2018.

Long-term incentives.

Long-term incentives represent a key component to our overall compensation program, and in many cases represent the majority of total annual compensation.

We believe that equity grants provide our NEOs with a strong link to our long-term performance, create an ownership culture and help to align the interests of our NEOs and our stockholders. Our NEOs benefit from equity awards as our stock price increases through the creation of shareholder value. Accordingly, we believe equity awards provide meaningful incentives to our NEOs to achieve increases in the value of our stock over time. In addition, the vesting feature of our equity awards contributes to NEO retention by providing an incentive to our NEOs to remain employed by us during the vesting period.

The compensation committee typically approves stock option grants for NEOs at the start of their employment, and annually thereafter in connection with the annual performance review. Additionally, the compensation

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committee may periodically grant additional equity awards based on individual role, performance and contribution, as well as competitive market data and information.

None of our NEOs are currently party to an employment agreement that provides for an automatic award of stock options. We grant equity awards to our NEOs with time-based vesting. The stock options that we grant to our NEOs typically become exercisable as to 25% of the shares underlying the option on the first anniversary of the grant date, and as to an additional 1/36th of the shares underlying the option monthly thereafter. The exercise price of all stock options equals the fair market value of shares of our common stock on the date of grant. Prior to the exercise of an option, the holder has no rights as a stockholder with respect to the shares subject to such option, including no voting rights and no right to receive dividends or dividend equivalents. Vesting and exercise rights for stock options cease shortly after termination of employment except in the case of death or disability. In specified termination and change in control circumstances, equity awards held by our NEOs are subject to accelerated vesting. See Severance and Change in Control Benefits for further information.

In determining long-term incentive grants for new hires, the compensation committee evaluates (where available):

market data for annual and new hire long-term incentive grant values;

potential lost long-term incentive opportunity from candidate's current employer, where available; and

candidate background, experience, and potential.

In determining annual long-term incentive grants for existing NEOs, the committee reviews:

market data for annual long-term incentive grant values;

time the NEO has been employed with us;

NEO performance and contributions in the previous year;

overall corporate performance and outlook; and

NEO current outstanding equity, including the value of outstanding unvested awards.

In February 2018, our compensation committee approved the grant of stock options under our 2013 Plan to each of our NEOs other than Dr. Agarwal. Each of these equity awards had an exercise price equal to the fair market value of our common stock on the date of grant and vests with respect to 25% of the shares on February 9, 2019 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 NEOs in February 2018:

February 2018 Stock Option Grant

NEO	Compensation Committee Approved Fair Value (1)	Number of Shares Underlying Options (#)
Robert Bazemore	\$2,750,000	265,860
Matthew Ros	\$1,100,000	106,344
Shefali Agarwal (2)		
Susan Graf	\$1,100,000	106,344
Suzanne Fleming	\$300,000	29,002

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- (1) These figures may be different than those reported in the Summary Compensation Table and other required tabular disclosures due to the process of converting a fair value to a number of stock options and associated rounding.
- (2) Dr. Agarwal was hired in June 2018 and was not part of the February 2018 long-term incentive award process. In addition to these grants, the compensation committee granted stock options to purchase 170,000 shares of our common stock to Dr. Agarwal at the time of her hire, representing approximately \$1,500,000 in grant date fair value. These stock options have the same vesting schedule as the February 2018 grants to the other NEOs.

Severance and Change of Control Benefits

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

terminate his or her employment without cause, prior to or more than 12 months following a change in control; or

terminate his or her employment without cause or he or she terminates employment with us for good reason within 12 months following a change in control.

Additionally, Mr. Bazemore 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. Please refer to Employment, Severance and Change in Control Arrangements below for a more detailed discussion of severance and change in control benefits for our named executive officers.

Benefits.

We generally pay relocation expenses for newly-hired NEOs whom we require to relocate as a condition to their employment with us. We also have, and may in the future, pay local housing expenses and travel costs for executives who maintain a primary residence outside of a reasonable daily commuting range to our headquarters prior to such executive's relocation. We evaluate the competitiveness of our arrangements periodically and have found that our NEO benefits are competitive with our peers. For more information on our employment arrangements, please see Employment, Severance and Change in Control Arrangements. We believe that these are typical benefits offered by comparable companies to executives who are asked to relocate and that we would be at a competitive disadvantage in trying to attract executives who would need to relocate in order to work for us if we did not offer such assistance.

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 \$18,500 for 2018. Participants who are at least 50 years old can also make catch-up contributions, which in 2018 could be up to an additional \$6,000 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, 2018, we provided 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.

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Our NEOs are eligible to participate in all of our employee benefit plans, including our medical, dental, long-term disability and term life insurance plans, our fitness benefits and 401(k) matching contributions, in each case on the same basis as other employees. We do not provide additional perquisites or personal benefits to our NEOs. We do not sponsor any qualified or non-qualified defined benefit plans for any of our employees, including NEOs.

Other

Anti-Hedging and Pledging Policy

Our insider trading policy expressly prohibits all of our employees, including our NEOs, as well as our directors, from engaging in speculative transactions in our stock, including short sales, puts/calls, hedging transactions and margin accounts or pledges.

No Tax Gross-ups

We do not provide for any tax gross-up payments to our NEOs.

Tax and Accounting Considerations

Under Section 162(m) of the Internal Revenue Code of 1986, as amended, a company will generally not be entitled to a tax deduction for individual compensation over \$1 million that is paid to certain executive officers. As in effect prior to its recent amendment by the Tax Cuts and Jobs Act of 2017, Section 162(m) provided an exception to the deductibility limitations for performance-based compensation that met certain requirements. While considering the impact of Section 162(m) and awarding certain elements of compensation that, at the time, were intended to qualify as performance-based compensation, the compensation committee did not adopt a policy requiring all compensation to be fully deductible under Section 162(m). As Section 162(m) has been amended, effective for taxable years beginning after December 31, 2017, the performance-based compensation exception was eliminated from Section 162(m), except for certain grandfathered arrangements under the transition rules. In light of this amendment, the Committee will continue to consider the potential impact of the application of Section 162(m) on compensation for our executive officers and reserves the right to provide compensation to executive officers that may not be tax-deductible, as well as the right to modify compensation that was initially intended to qualify as performance-based compensation if it believes that taking any such action is in the best interests of our company and stockholders.

Compensation Risk Assessment

Our management and the compensation committee review our compensation practices and policies with regard to risk management. We have reviewed our programs and determined that there are no practices or policies that are likely to lead to excessive risk-taking or have a material adverse effect on the Company. Further, we identified the following practices that serve to mitigate risk:

we provide a balance of fixed and performance-based compensation;

our short-term incentive plan is based on a number of challenging goals;

our long-term incentive grants vest over time, generally four years;

our compensation committee has discretion to reduce bonus awards should the objective formula yield an inappropriate result;

we have an independent compensation committee;

we engage with independent compensation advisors;

we have proper administrative and oversight controls; and

we have an established compensation committee calendar for governance purposes.

Table of Contents**Compensation Committee Report**

The compensation committee has reviewed and discussed the Compensation Discussion and Analysis required by Item 402(b) of Regulation S-K with our management. Based on this review and discussion, the compensation committee recommended to the board of directors that the Compensation Discussion and Analysis be included in this proxy statement.

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

David M. Mott, Chairman

Andrew R. Allen, M.D., Ph.D.

Beth Seidenberg, M.D.

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, 2018, 2017 and 2016.

Name and Principal Position	Year	Salary (\$)	Non-equity Stock Incentive plan			All Other Compensation		Total
			Bonus Award (\$)(1)	Option Award (\$)(2)	Option Award (\$)(3)	Option Award (\$)(2)	(\$)(4)	
Robert B. Bazemore Jr. President and Chief Executive Officer	2018	575,667			320,575	2,748,939	5,690	3,650,871
	2017	556,200			282,967	2,748,879	5,603	3,593,649
	2016	540,000			245,700	2,507,753	5,320	3,298,773
Susan E. Graf (5) Former Chief Business Officer	2018	328,009(7)			103,646	1,099,576	114,654	1,645,885
	2017	388,967			153,550	899,627	11,149	1,453,293
Suzanne Fleming (6) Former Senior Vice President, Finance and Treasurer	2018	350,000	100,000			299,875	13,580	763,455
Matthew E. Ros Chief Strategy and Business Officer	2018	420,000			187,100	1,099,576	12,214	1,718,890
	2017	391,400			159,300	899,627	5,666	1,455,993
	2016	237,500	65,000		86,864	1,128,422	2,837	1,520,623
Dr. Shefali Agarwal Chief Medical Officer	2018	199,615	125,000		200,500	1,472,846	1,648	1,999,609

- (1) The 2017 and 2018 amounts reflect one-time sign-on bonuses paid pursuant to the terms of the named executive officer employment agreement.
- (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 FASB 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, 2018 regarding assumptions we made in determining the fair value of option awards.

- (3) The amounts reflect the annual performance bonuses paid, as discussed under Compensation Discussion and Analysis Annual Base Salary Short-term Incentives.
- (4) All other compensation includes the following for the year ended December 31, 2018:

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Name	Gym (\$)	Post Separation Benefits (\$)	401(K) Employer Match (\$)	Transportation Benefits (\$)	Short-term and Long-term Life Insurance Disability Premiums (\$)
Robert B. Bazemore	360			3,900	1,430
Susan E. Graf		103,750	6,256	3,575	1,073
Suzanne Fleming			8,250	3,900	1,430
Matthew Ros			6,884	3,900	1,430
Shefali Agarwal				1,052	596

- (5) Susan E. Graf departed Epizyme in September 2018.
(6) Suzanne Fleming departed Epizyme in January 2019.
(7) Includes a payment of \$8,379 for accrued and unused vacation time.

Grants of Plan-Based Awards Table

The following table sets forth information concerning each grant of an award made to our named executive officer during the fiscal year ended December 31, 2018 under any plan, contract, authorization or arrangement pursuant to which cash, securities, similar instruments or other property may be received.

Name	Grant Date	All other option awards: Number of securities underlying options (#)	Exercise or base price of option awards (\$)	Grant date fair value of stock and option awards (\$)(1)
Robert B. Bazemore (2)	2/9/2018	265,860	16.00	2,748,939
Susan E. Graf (3)	2/9/2018	106,344	16.00	1,099,576
Suzanne Fleming (4)	2/9/2018	29,002	16.00	299,875
Matthew Ros (2)	2/9/2018	106,344	16.00	1,099,576
Shefali Agarwal (2)	7/23/2018	170,000	13.35	1,472,846

- (1) 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 FASB 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, 2018 regarding assumptions we made in determining the fair value of option awards.
(2) For information on vesting acceleration upon termination of employment, see the Employment, Severance and Change in Control Arrangements section below.
(3) None of the awards granted to Ms. Graf during the fiscal year ended December 31, 2018 had vested as of her departure in September 2018. Ms. Graf forfeited these option awards upon her departure.
(4)

None of the awards granted to Ms. Fleming during the fiscal year ended December 31, 2018 had vested as of her departure in January 2019. Ms. Fleming forfeited these option awards upon her departure.

Table of Contents**Outstanding Equity Awards at 2018 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, 2018.

Name	Grant Date	Notes	Option Awards			
			Number of Securities		Option Exercise Price (\$)	Option Expiration Date
			Unexercised Options (#)	Underlying Unexercisable Options (#)		
Robert B. Bazemore	8/5/2015	(1)	250,000	50,000	22.29	8/4/2025
	2/8/2016	(2)	292,187	120,313	8.98	2/7/2026
	2/8/2017	(3)	153,864	181,840	12.45	2/7/2027
	2/9/2018	(4)		265,860	16.00	2/8/2028
Susan E. Graf(9)	4/25/2016	(5)			12.12	4/24/2026
	2/8/2017	(3)			12.45	2/7/2027
	2/9/2018	(4)			16.00	2/8/2028
Suzanne Fleming	9/20/17	(6)	28,181	61,999	18.70	9/19/2027
	2/9/2018	(4)		29,002	16.00	2/8/2028
Matthew Ros	5/16/2016	(7)	39,748	61,426	9.58	5/15/2026
	2/8/2017	(3)	50,355	59,511	12.45	2/7/2027
	2/9/2018	(4)		106,344	16.00	2/8/2028
Shefali Agarwal	7/23/2018	(8)		170,000	13.35	7/22/2028

- (1) The shares under this option vested as to 25% of the unvested shares on August 5, 2016, with the remainder vesting in approximately equal monthly installments through August 5, 2019.
- (2) The shares under this option vested as to 25% of the unvested shares on February 8, 2017, with the remainder vesting in approximately equal monthly installments through February 8, 2020.
- (3) The shares under this option vested as to 25% of the unvested shares on February 8, 2018, with the remainder vesting in approximately equal monthly installments through February 8, 2021.
- (4) The shares under this option vested as to 25% of the unvested shares on February 9, 2019, with the remainder vesting in approximately equal monthly installments through February 9, 2022.
- (5) The shares under this option vested as to 25% of the unvested shares on April 25, 2017, with the remainder vesting in approximately equal monthly installments through April 25, 2020.
- (6) The shares under this option vested as to 25% of the unvested shares on September 20, 2018, with the remainder vesting in approximately equal monthly installments through September 20, 2021.
- (7) The shares under this option vested as to 25% of the unvested shares on May 16, 2017, with the remainder vesting in approximately equal monthly installments through May 16, 2020.
- (8) The shares under this option vested as to 25% of the unvested shares on July 23, 2019, with the remainder vesting in approximately equal monthly installments through July 23, 2022.
- (9) Susan E. Graf's options expired 90 days following her departure from Epizyme in September 2018.

Option Exercises and Stock Vested

The following table sets forth information concerning option exercises and stock vested for each of our named executive officers during the fiscal year ended December 31, 2018:

	Option Awards	
	Number of Shares	Value Realized
	Acquired on Exercise (#)	on Exercise
		(\$)
Robert B. Bazemore		
Susan E. Graf		
Suzanne Fleming		
Matthew Ros	72,264	1,201,693
Shefali Agarwal		

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Employment, Severance and Change in Control Arrangements

Robert Bazemore. We entered into an employment offer letter with Mr. Bazemore, our president and chief executive officer, on August 5, 2015. The employment offer letter established the terms of his employment with us, including his title, salary, bonus and eligibility for benefits. Pursuant to the employment offer letter, on August 5, 2015, the Company granted to Mr. Bazemore stock options to purchase 300,000 shares of common stock of the Company. This award is subject to time-based vesting. The employment offer letter also provides that Mr. Bazemore may be eligible for additional equity award grants from time to time.

Matthew Ros. We entered into an employment offer letter with Mr. Ros, our chief operating officer, on April 15, 2016. The employment offer letter established the terms of his employment with us, including his title, salary, bonus and eligibility for benefits. Pursuant to the employment offer letter, on April 15, 2016, the Company granted to Mr. Ros stock options to purchase 173,438 shares of common stock of the Company. This award is subject to time-based vesting. The employment offer letter also provides that Mr. Ros may be eligible for additional equity award grants from time to time.

Shefali Agarwal. We entered into an employment offer letter with Dr. Agarwal, our chief medical officer on June 18, 2018. The employment offer letter established the terms of her employment with us, including his title, salary, bonus and eligibility for benefits. Pursuant to the employment offer letter, on June 18, 2018, the Company granted to Dr. Agarwal stock options to purchase 170,000 shares of common stock of the Company. This award was subject to time-based vesting. The employment offer letter also provides that Dr. Agarwal may be eligible for additional equity award grants from time to time.

Each of our named executive officers is employed at-will.

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

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

terminate his or her employment without cause, prior to or more than 12 months following a change in control; or

terminate his or her employment without cause or he terminates employment with us for good reason within 12 months following a change in control.

Additionally, Mr. Bazemore 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 named executive officers participate:

cause means (I) with respect to a termination prior to or more than 12 months following a change in control, any (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 and (II) with respect to a termination upon or during the 12-month period following a change in control,

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(i) the executive's conviction of, or plea of guilty or nolo contendere to, any felony; (ii) the willful and continued failure by the executive (other than any such failure resulting from the executive's incapacity due to physical or mental illness) to perform substantially the duties and responsibilities of the executive position after a written demand for substantial performance (providing a period of 15 days to cure) is delivered to the executive by the Company; (iii) the material breach by the executive of the terms of any restrictive covenants or confidentiality agreement with the Company; or (iv) the willful engaging by the executive in fraud or dishonesty which is demonstrably and materially injurious to the Company or its reputation, monetarily or otherwise. No act, or failure to act, on the executive's part shall be deemed willful unless committed or omitted by the executive in bad faith without reasonable belief that the executive's act or failure to act was in, or not opposed to, the best interest of the Company.

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. 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 all or substantially all 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.

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The following table summarizes the schedule of severance payments our current named 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 Bazemore	12 months	None	12 months	None
Matthew Ros	9 months	None	9 months	None
Shefali Agarwal	9 months	None	9 months	None
Following a Change in Control				
Robert Bazemore	18 months	150% of target	18 months	100%
Matthew Ros	12 months	100% of target	12 months	100%
Shefali Agarwal	12 months	100% of target	12 months	100%

Securities Authorized for Issuance Under Equity Compensation Plans**Equity Compensation Plan Information As of December 31, 2018**

Plan Category	(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	5,152,787(1)	\$ 14.48	5,937,859(2)(3)
Equity compensation plans not approved by security holders			
Total	5,152,787	\$ 14.48	5,937,859

- (1) Consists of stock options and restricted stock units issued under our 2008 Stock Incentive Plan, or 2008 Plan, and the 2013 Plan.
- (2) As of December 31, 2018, 11,090,646 shares were available for future issuance under our 2013 Plan, which became effective on June 5, 2013. 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. On

January 1, 2019, 2,500,000 shares of our common stock were added to the 2013 Plan pursuant to this provision, which shares are not reflected in the number of shares available for issuance under the 2013 Plan.

- (3) As of December 31, 2018, 381,534 shares were available for future issuance under our 2013 Employee Stock Purchase Plan, or 2013 ESPP, which became effective on June 5, 2013. 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 2019.

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Proposal No. 3.

ADVISORY VOTE ON EXECUTIVE COMPENSATION

We are providing our stockholders the opportunity to vote to approve, on an advisory, non-binding basis, the compensation of our named executive officers as disclosed in this proxy statement in accordance with the SEC's rules. This proposal, which is commonly referred to as "say-on-pay," is required by the recently enacted Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010, which added Section 14A to the Exchange Act. Section 14A of the Exchange Act also requires that stockholders have the opportunity to cast an advisory vote with respect to whether future executive compensation advisory votes will be held every one, two or three years, which is the subject of Proposal No. 4.

Our executive compensation programs are designed to attract and retain qualified executive talent to support our mission, vision, and business objectives. These programs embody a pay-for-performance philosophy and reward NEOs for the achievement of our near-term and longer-term financial and strategic goals and for driving corporate financial performance and stability. The programs contain elements of cash and equity-based compensation and are designed to align the interests of our executives with those of our stockholders. We believe our compensation policy strikes an appropriate balance between the implementation of responsible, measured compensation practices and the effective provision of incentives for our NEOs to exert their best efforts for our success. At the same time, we believe our program does not encourage excessive risk-taking by management.

The Executive Compensation section of this proxy statement beginning on page 20, including Compensation Discussion Analysis, describes in detail our executive compensation programs and the decisions made by the Compensation Committee and the Board of Directors with respect to the year ended December 31, 2018.

Our Board of Directors is asking stockholders to approve a non-binding advisory vote on the following resolution:

RESOLVED, that the compensation paid to the Company's named executive officers, as disclosed pursuant to the compensation disclosure rules of the Securities and Exchange Commission, including the compensation discussion and analysis, the compensation tables and any related material disclosed in this proxy statement, is hereby approved.

As an advisory vote, this proposal is not binding. Neither the outcome of this advisory vote nor of the advisory vote included in Proposal No. 4 overrules any decision by the Company or the Board of Directors (or any committee thereof), creates or implies any change to the fiduciary duties of the Company or the Board of Directors (or any committee thereof), or creates or implies any additional fiduciary duties for the Company or the Board of Directors (or any committee thereof). However, our compensation committee and Board of Directors value the opinions expressed by our stockholders in their vote on this proposal and will consider the outcome of the vote when making future compensation decisions for named executive officers.

The Board of Directors recommends that stockholders vote to approve the compensation of our named executive officers by voting FOR Proposal No. 3.

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Proposal No. 4.

ADVISORY VOTE ON THE FREQUENCY OF FUTURE EXECUTIVE COMPENSATION ADVISORY VOTES

In Proposal No. 3, we are providing our stockholders the opportunity to vote to approve, on an advisory, non-binding basis, the compensation of our named executive officers. In this Proposal No. 4, we are asking our stockholders to cast a non-binding advisory vote regarding the frequency of future executive compensation advisory votes. Stockholders may vote for a frequency of every one, two, or three years, or may abstain.

The Board of Directors will take into consideration the outcome of this vote in making a determination about the frequency of future executive compensation advisory votes. However, because this vote is advisory and non-binding, the Board of Directors may decide that it is in the best interests of our stockholders and the Company to hold the advisory vote to approve executive compensation more or less frequently. In the future, we will propose an advisory vote on the frequency of the executive compensation advisory vote at least once every six calendar years.

After careful consideration, the Board of Directors believes that an executive compensation advisory vote should be held every year, and therefore our Board of Directors recommends that you vote for a frequency of every ONE YEAR for future executive compensation advisory votes.

The Board of Directors believes that an annual executive compensation advisory vote will facilitate more direct stockholder input about executive compensation. An annual executive compensation advisory vote is consistent with our policy of reviewing our compensation program annually, as well as seeking frequent input from our stockholders on corporate governance and executive compensation matters. We believe an annual vote would be the best governance practice for our Company at this time.

Therefore, the Board of Directors believes that holding the executive compensation advisory vote every year is in the best interests of the Company and its stockholders and recommends voting for a frequency of every ONE YEAR

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TRANSACTIONS WITH RELATED PERSONS

Since January 1, 2018 we have engaged in the following transactions 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 no less favorable as could have been obtained from unrelated third parties.

Consulting Agreement with Michael Giordano

On December 1, 2017, we entered into a consulting agreement with Michael Giordano, who was subsequently elected to our board of directors in March 2018. Under the agreement, Dr. Giordano agreed to provide consulting and advisory services related to epigenetics and our research, discovery and development portfolio. Under the agreement, Dr. Giordano agreed to work approximately 16 to 20 hours a week, and we agreed to pay him consulting fees of approximately \$12,000 per week. We also agreed to reimburse Dr. Giordano for his travel expenses. The agreement was allowed to be terminated immediately by us in the event of an uncurable breach or at any time with thirty days prior written notice to Dr. Giordano, and by Dr. Giordano with thirty days prior written notice to us in the event we breached the agreement and failed to cure the breach within thirty days of receipt of notice of breach. Dr. Giordano also agreed that, during the term of the agreement and for one year following the expiration or termination of the agreement, he would not work as an employee or consultant for a third party on a project in which we are directly and actively involved or which concerns a therapeutic product or product candidate in our research, discovery and development portfolio, or as a result of which Dr. Giordano's responsibilities to us would be materially limited. Although the initial term of the agreement ended on March 31, 2018, we and Dr. Giordano agreed to extend the term of the agreement until August 31, 2018. We terminated Dr. Giordano's consulting agreement on December 31, 2018.

Participation in October 2018 Public Offering

In October 2018, we sold 9,583,334 shares of our common stock at a price to the public of \$9.00 per share pursuant to an underwritten public offering, which we refer to as our October 2018 offering. In our October 2018 offering, New Enterprise Associates 13 L.P., which was a beneficial owner of more than 5% of our voting securities prior to the October 2018 offering purchased an additional 416,667 shares of our common stock, for approximately \$3.75 million, through the underwriters at the public offering price.

Redmile Group, LLC, which was not a beneficial owner of more than 5% of our voting securities prior to the October 2018 offering, purchased in our October 2018 offering 3,888,889 shares of our common stock, for approximately \$35.0 million, through the underwriters at the public offering price, which purchase resulted in Redmile Group, LLC becoming a beneficial owner of more than 5% of our voting securities following the October 2018 offering.

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.

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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.

Table of Contents**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 March 31, 2019 by:

each of our directors;

each of our named executive officers;

all of our current 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 90,803,078 shares of our common stock outstanding as of March 31, 2019.

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 March 31, 2019 or shares of restricted stock that vest within 60 days of March 31, 2019 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:		
PRIMECAP Management Company (1)	9,556,527	10.5%
Palo Alto Investors, LLC (2)	6,935,074	7.6%
Redmile Group, LLC (3)	6,637,278	7.3%
Entities affiliated with New Enterprise Associates (4)	6,460,851	7.1%
Blackrock, Inc. (5)	5,193,287	5.7%
Directors and Named Executive Officers:		
David M. Mott (6)	6,543,422	7.2%
Beth Seidenberg, M.D. (7)	3,914,446	4.3%
Carl Goldfischer, M.D. (8)	3,450,783	3.8%
Richard F. Pops (9)	69,832	*

Andrew R. Allen, M.D., Ph.D. (10)	62,499	*
Kenneth Bate (11)	62,499	*
Kevin Conroy (12)	29,440	*
Michael F. Giordano, M.D. (13)	7,291	*
Robert B. Bazemore (14)	969,506	1.1%
Matthew Ros (15)	189,676	*
Shefali Agarwal (16)	32,894	*
All current executive officers and directors as a group (11 persons) (17)	15,332,288	16.6%

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

- (1) PRIMECAP Management Company has sole voting power with respect to 9,040,927 shares of common stock and sole dispositive power with respect to 9,556,527 shares of common stock. The information reported is based on a Schedule 13G/A, as filed with the SEC on February 8, 2019. The principal business address of PRIMECAP Management Company is 177 E. Colorado Blvd., 11th Floor, Pasadena, CA 91105.
- (2) Palo Alto Investors, LLC (PAI) has shared voting and dispositive power over all of its shares of common stock. The information reported is based on a Schedule 13G/A, as filed with the SEC on February 14, 2019. The principal business address of PAI is 470 University Avenue, Palo Alto, CA 94301.
- (3) Redmile Group, LLC (Redmile) has shared voting and dispositive power over all of its shares of common stock. The information reported is based on a Schedule 13G/A, as filed with the SEC on February 14, 2019. The principal business address of Redmile is One Letterman Dr, Building D, Suite D3-300, The Presidio of San Francisco, CA 94129.
- (4) Consists of 6,471,018 shares of common stock held of record by New Enterprise Associates 13, L.P. (NEA13) and 406,500 shares of common stock held of record by Growth Equity Opportunities Fund II, LLC (GEO II). 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. NEA 13 is the sole member of GEO II. The individual directors (collectively, the NEA 13 Directors) of NEA 13 LTD are M. James Barrett, Peter J. Barris, Forest Baskett, Patrick J. Kerins, Krishna S. 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. The information reported is based on a Schedule 13D/A filed with the SEC on January 19, 2016 and Form 4 filed by Mr. Mott with the SEC on October 5, 2018. The principal business address of New Enterprise Associates, Inc. is 1954 Greenspring Drive, Suite 600, Timonium, MD 21093.
- (5) BlackRock, Inc. holds sole dispositive power over 5,193,287 of its shares of common stock, and holds sole voting power over 5,066,159 shares of common stock. The information reported is based on a Schedule 13G/A, as filed with the SEC on February 4, 2019. BlackRock Inc.'s principal business address is 55 East 52nd Street, New York, NY 10055.
- (6) Consists of the shares described in note (4) above, 12,088 shares of common stock held by Mr. Mott, 651 shares of common stock held by the David Mott Declaration of Trust dated May 31, 2001 as amended (the Mott Trust) and 69, shares of common stock which may be acquired by Mr. Mott upon the exercise of options that are exercisable within 60 days after March 31, 2019. Mr. Mott disclaims beneficial ownership of the shares in the Mott Trust except to the extent of any pecuniary interest therein. Mr. Mott is a general partner of New Enterprise Associates, and a member of the board of directors of NEA Management Company, LLC and NEA 13 LTD, which is the general partner of NEA Partners 13, and NEA Partners 13 is 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.
- (7) Consists of 6,447 shares of common stock, 69,832 shares of common stock issuable upon the exercise of options exercisable within 60 days after March 31, 2019 and shares held by certain entities associated with Kleiner Perkins Caufield & Byers (KPCB) because, as a partner of KPCB, Dr. Seidenberg may be deemed to share voting and dispositive power with respect to all shares held by entities associated with KPCB. Shares beneficially owned by KPCB consists of 3,838,167 shares of common stock held by Kleiner Perkins Caufield & Byers XIII, LLC (KPCB XIII) and 277,388 shares of common stock beneficially owned by individuals and entities associated with KPCB (collectively, KPCB Direct). All shares are held for convenience in the name of KPCB Holdings, Inc. as nominee, for the account 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), which has the sole voting and dispositive power over the shares held by KPCB XIII. 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

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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. The information reported is based on a Form 4 filed by Dr. Seidenberg with the SEC on July 2, 2018 and Schedule 13/G, as filed with the SEC on February 13, 2019.

- (8) Consists of 3,380,951 shares of common stock held by entities affiliated with Bay City Capital, LLC including Bay City Capital Fund V, L.P. and Bay City Capital Fund V Co-Investment Fund, L.P. and 69,832 shares of common stock which may be acquired by Dr. Goldfischer upon the exercise of options that are exercisable within 60 days after March 31, 2019. 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. 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.
- (9) Consists of 69,832 shares of common stock issuable upon the exercise of options exercisable within 60 days after March 31, 2019.
- (10) Consists of 62,499 shares of common stock issuable upon the exercise of options exercisable within 60 days after March 31, 2019.
- (11) Consists of 62,499 shares of common stock issuable upon the exercise of options exercisable within 60 days after March 31, 2019.
- (12) Consists of 26,562 shares of common stock issuable upon the exercise of options exercisable within 60 days after March 31, 2019.
- (13) Consists of 7,291 shares of common stock issuable upon the exercise of options exercisable within 60 days after March 31, 2019.
- (14) Consists of 888,318 shares of common stock issuable upon the exercise of options exercisable within 60 days after March 31, 2019.
- (15) Consists of 152,845 shares of common stock issuable upon the exercise of options exercisable within 60 days after March 31, 2019.
- (16) Consists of zero shares of common stock issuable upon the exercise of options exercisable within 60 days after March 31, 2019.
- (17) Consists of 1,479,342 shares of common stock issuable upon the exercise of options exercisable within 60 days after March 31, 2019.

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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 2018 by Section 16(a) under the Exchange Act.

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 system 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, 2018. The audit committee also discussed with the independent registered public accounting firm the matters required to be discussed by the AS No. 1301, *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, 2018, which 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

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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 Notice of Internet Availability of Proxy Materials or, if requested, the 2018 Annual Report and proxy statement, may have been sent to multiple stockholders in your household. We will promptly deliver a separate copy of any of the above documents 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 Notice of Internet Availability of Proxy Materials, 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 2020 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 6, 2019. However, if the date of the 2020 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 2020 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 2020 annual meeting of stockholders, the required notice must be received by our corporate Secretary at our principal executive offices no earlier than February 1, 2020 and no later than March 2, 2020.

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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 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 Bazemore

Robert Bazemore

President and Chief Executive Officer

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