Form SC 13G/A February 14, 2019
UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549
SCHEDULE 13G
Under the Securities Exchange Act of 1934 (Amendment No. 4)
Epizyme, Inc.
_
(Name of Issuer)
Common Stock
_
(Title of Class of Securities)
29428V104
_
(CUSIP Number)

(Date of Event Which Requires Filing of this Statement)
Check the appropriate box to designate the rule pursuant to which this Schedule is filed:
[X] Rule 13d-1(b)
[] Rule 13d-1(c)
[] Rule 13d-1(d)
The remainder of this cover page shall be filled out for a reporting person's initial filing on this form with respect to the subject class of securities, and for any subsequent amendment containing information which would alter the disclosures provided in a prior cover page.
The information required in the remainder of this cover page shall not be deemed to be "filed" for the purpose of Section 18 of the Securities Exchange Act of 1934 ("Act") or otherwise subject to the liabilities of that section of the Act but shall be subject to all other provisions of the Act (however, see the Notes).
Potential persons who are to respond to the collection of information contained in this form are not required to respond unless the form displays a currently valid OMB control number.
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CUSIP 29428	V104	
_		
	1.	Names of Reporting Persons.  Patrick Lee, MD
_		
2. Check the	Appropriate Box if a Member of a Group (S	See Instructions)
(a) _		
(b) <u>X</u>		
_		
3. SEC Use C	Only	
4. Citizenship	o or Place of Organization U.S.A.	
Number of	<ul><li>5. Sole Voting Power 0</li><li>6. Shared Voting Power 6,935,074</li></ul>	
Shares	7. Sole Dispositive Power <b>0</b>	
Beneficially		
Owned by	8. Shared Dispositive Power <b>6,935,074</b>	
Each Reportin	ng	
Person With:		

9. Aggregate Amount Beneficially Owned by Each Reporting Person **6,935,074** 

	check if the Aggregate Amount in Row (9) Excludes Certain Shares (See ructions)
_	
11.	Percent of Class Represented by Amount in Row (9) 8.76%
-	
12.	Type of Reporting Person (See Instructions) IN, HC
_	

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CUSI	P 29428V104	
_		
	1.	Names of Reporting Persons.  Anthony Joonkyoo Yun, MD
_		
	eck the Appropriate Box if a Member of a C	Group (See Instructions)
(a) _		
(b) _	<u>X</u>	
_		
3. SE	C Use Only	
_		
4. Ci	izenship or Place of Organization U.S.A.	
Numb	er of 5. Sole Voting Power <b>0</b>	
Share		
Benef	6. Shared Voting Power <b>6,935,0</b> icially 7. Sole Dispositive Power <b>0</b>	774
Owne		
Each l	Reporting 8. Shared Dispositive Power <b>6,9</b>	235,074
	n With:	
9. Ag	gregate Amount Beneficially Owned by Ea	ch Reporting Person 6,935,074

	10.	Check if the Aggregate Amount in Row (9) Excludes Certain Shares (See Instructions)
_		
11.	Percent of Class Repres	ented by Amount in Row (9) <b>8.76</b> %
_		
12.	Type of Reporting Perso	on (See Instructions) IN, HC
3		

CUSIP 29428	V104	
_		
		Names of Reporting Persons.
	1.	Palo Alto Investors LP
_		
2. Check the	Appropriate Box if a Member of a Group (S	See Instructions)
(a) _		
(b) <u>X</u>		
_		
3. SEC Use 0	Only	
_		
4. Citizenship	p or Place of Organization California	
Number of	<ul><li>5. Sole Voting Power 0</li><li>6. Shared Voting Power 6,935,074</li></ul>	
Shares	7. Sole Dispositive Power <b>0</b>	
Beneficially		
Owned by	8. Shared Dispositive Power <b>6,935,074</b>	
Each Reportir	ng	
Person With:		
0. 4	A (D C: 11 C 11 E 1 D	( D (025.054
9. Aggregate	Amount Beneficially Owned by Each Repo	orting Person <b>6,935,074</b>

	Check if the Aggregate Amount in Row (9) Excludes Certain Shares (See
msu	ructions)
_	
11.	Percent of Class Represented by Amount in Row (9) <b>8.76</b> %
_	
12.	Type of Reporting Person (See Instructions) OO, IA
_	
4	

	1.	Names of Reporting Persons.  PAI LLC
_		TATLEC
2. Check the A	Appropriate Box if a Member of a Group (Se	ee Instructions)
(a) _		
(b) <u>X</u>		
_		
3. SEC Use On	nly	
_		
4. Citizenship	or Place of Organization California	
Number of	5. Sole Voting Power <b>0</b>	
Shares	<ul><li>6. Shared Voting Power 6,935,074</li><li>7. Sole Dispositive Power 0</li></ul>	
Beneficially		
Owned by	8. Shared Dispositive Power <b>6,935,074</b>	
Each Reporting		
Person With:		
9. Aggregate A	Amount Beneficially Owned by Each Repor	ting Person <b>6,935,074</b>
_		
10. Check if the Instructions) _	ne Aggregate Amount in Row (9) Excludes	Certain Shares (See

\_

11. Percent of Class Represented by Amount in Row (9) 8.76%

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12. Type of Reporting Person (See Instructions) **OO, IA** 

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CUSIP 189464	100
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_	Names of Reporting Persons.  1.  Palo Alto Healthcare Master Fund II, L.P
	Appropriate Box if a Member of a Group (See Instructions)
(a) _ (b) <u>X</u>	
-	
3. SEC Use On	nly
_	
4. Citizenship	or Place of Organization Cayman Islands
Number of Shares	<ul><li>5. Sole Voting Power 0</li><li>6. Shared Voting Power 3,959,270</li></ul>
Beneficially	7. Sole Dispositive Power <b>0</b>
Owned by	
Each Reporting	8. Shared Dispositive Power <b>3,959,270</b>
Person With:	
9. Aggregate A	Amount Beneficially Owned by Each Reporting Person 3,959,270

Instructions)
_
11. Percent of Class Represented by Amount in Row (9) <b>5.00</b> %
_
12. Type of Reporting Person (See Instructions) <b>PN</b>
_
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CUSIP 29428V104 Item 1.
(a) Name of Issuer
Epizyme, Inc.
<del>-</del>
(b) Address of Issuer's Principal Executive Offices
400 Technology Square, 4th Floor, Cambridge, MA 02139
_
Item 2.
(a) The names of the persons filing this statement are:  Palo Alto Investors LP ("PAI")  PAI LLC ("PAI GP")  Patrick Lee, MD  Anthony Joonkyoo Yun, MD
Palo Alto Healthcare Master Fund II, L.P. ("Healthcare Master II") _ (collectively, the "Filers").
(b) The principal business office of the Filers except Healthcare Master II is located at:
470 University Avenue, Palo Alto, CA 94301
The principal business office of Healthcare Master II is located at:
Cayman Corporate Centre, 27 Hospital Road George Town, Grand Cayman KY1-9008 Cayman Islands
_
(c) For citizenship of Filers, see Item 4 of the cover sheet for each Filer.
(d) This statement relates to shares of Common Stock of the Issuer (the "Stock").

(e) The CUSIP number of the Issuer is: 29428V104

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#### CUSIP 29428V104

Item 3. If this statement is filed pursuant to rule 240.13d-1(b) or 240.13d-2(b) or (c), check whether the person filing is a:

(a) [] Broker or dealer registered under section 15 of the Act (15 U.S.C. 78o).
(b) [] Bank as defined in section 3(a)(6) of the Act (15 U.S.C. 78c).
(c) [] Insurance company as defined in section 3(a)(19) of the Act (15 U.S.C. 78c).
(d) [] Investment company registered under section 8 of the Investment Company Act of 1940 (15 U.S.C. 80a-8).
(e) [x] An investment adviser in accordance with section 240.13d-1(b)(1)(ii)(E) (as to PAI).
(f) [] An employee benefit plan or endowment fund in accordance with section 240.13d-1(b)(1)(ii)(F).
(g) [x] A parent holding company or control person in accordance with 240.13d-1(b)(1)(ii)(G) (as to Dr. Lee and Dr. Yun).
(h) [] A savings association as defined in section 3(b) of the Federal Deposit Insurance Act (12 U.S.C. 1813).
(i) [ ] A church plan that is excluded from the definition of an investment company under section 3(c)(14) of the Investment Company Act of 1940 (15 U.S.C. 80a-3).
(j) [] A non-U.S. institution in accordance with §240.13d-1(b)(ii)(J).
(k) [] Group, in accordance with Rule 13d-1(b)(1)(ii)(K).

If filing as a non-U.S. institution in accordance with §240.13d-1(b)(1)(ii)(J), please specify the type of institution
Item 4. Ownership.
See Items 5-9 and 11 of the cover page for each Filer.
Item 5. Ownership of Five Percent or Less of a Class
If this statement is being filed to report the fact that as of the date hereof the reporting person has ceased to be the beneficial owner of more than five percent of the class of securities, check the following [].
Item 6. Ownership of More than Five Percent on Behalf of Another Person.
PAI is a registered investment adviser and investment adviser of investment limited partnerships, and is the investment adviser to other investment funds. PAI GP is the general partner of investment limited partnerships. PAI's clients have the right to receive or the power to direct the receipt of dividends from, or the proceeds from the sale of, the Stock. No individual client outside of Healthcare Master II separately holds more than five percent of the outstanding Stock.
Item 7. Identification and Classification of the Subsidiary Which Acquired the Security Being Reported on By the Parent Holding Company.
Not applicable.
Item 8. Identification and Classification of Members of the Group.
Dr. Lee and Dr. Yun co-manage PAI. The Filers are filing this Schedule 13G jointly, but not as members of a group, and each of them expressly disclaims membership in a group. Each Filer disclaims beneficial ownership of the Stock except to the extent of that Filer's pecuniary interest therein.

In addition, the filing of this Schedule 13G on behalf of Healthcare Master II should not be construed as an admission that any of them is, and each disclaims that it is, a beneficial owner, as defined in Rule 13d-3 under the Securities Exchange Act of 1934, of any of the Stock covered by this Schedule 13G.
Item 9. Notice of Dissolution of Group.
Not applicable.
Item 10. Certification.
By signing below I certify that, to the best of my knowledge and By signing below I certify that, to the best of my knowledge and belief, the securities referred to above were acquired and are held in the ordinary course of business and were not acquired and are not held for the purpose of or with the effect of changing or influencing the control of the issuer of the securities and were not acquired and are not held in connection with or as a participant in any transaction having that purpose or effect.
Exhibits
Exhibit A Joint Filing Agreement.
SIGNATURE
After reasonable inquiry and to the best of my knowledge and belief, I certify that the information set forth in this statement is true, complete and correct.
Dated: February 14, 2019

PALO ALTO HEALTHCARE MASTER FUND II, L.P. PALO ALTO INVESTORS LP

Bv	:	PAI	LLC	C. (	General	P	artner

By: /s/ Angela Nguyen-Dinh, Chief Compliance Officer

**PAILLC** 

By: /s/ Patrick Lee, MD

/s/ Patrick Lee, MD

/s/ Anthony Joonkyoo Yun, MD

**EXHIBIT A** 

AGREEMENT REGARDING JOINT FILING

OF STATEMENT ON SCHEDULE 13D OR 13G

The undersigned agree to file jointly with the Securities and Exchange Commission (the "SEC") any and all statements on Schedule 13D or Schedule 13G (and any amendments or supplements thereto) required under section 13(d) of the Securities Exchange Act of 1934, as amended, in connection with purchases and sales by the undersigned of the securities of any issuer until such time as the undersigned file with the SEC a statement terminating this Agreement Regarding Joint Filing of Statement on Schedule 13D or 13G. For that purpose, the undersigned hereby constitute and appoint Palo Alto Investors, LP, a California limited partnership, as their true and lawful agent and attorney-in-fact, with full power and authority for and on behalf of the undersigned to prepare or cause to be prepared, sign, file with the SEC and furnish to any other person all certificates, instruments, agreements and documents necessary to comply with section 13(d) and section 16(a) of the Securities Exchange Act of 1934, as amended, in connection with said purchases and sales, and to do and perform every act necessary and proper to be done incident to the exercise of the foregoing power, as fully as the undersigned might or could do if personally present, until such time as the undersigned file with the SEC a statement terminating this Agreement Regarding Joint Filing of Statement on Schedule 13D or 13G.

Dated: February 14, 2019

PALO ALTO INVESTORS LP

PALO ALTO HEALTHCARE MASTER FUND II, L.P.

By: PAI LLC, General Partner

By: /s/ Angela Nguyen-Dinh, Chief Compliance Officer

#### PAI LLC

By: /s/ Patrick Lee, MD

/s/ Patrick Lee, MD

/s/ Anthony Joonkyoo Yun, MD