Epizyme, Inc. Form SC 13G/A February 13, 2015

Item 12:

ΙV

SCHEDULE 13G Amendment No. 2 EPIZYME INC COMMON STOCK Cusip #29428V104 Check the appropriate box to designate the rule pursuant to which this Schedule is filed: Rule 13d-1(b) [x] Rule 13d-1(c) [] Rule 13d-1(d) [] Cusip #29428V104 Item 1: Reporting Person - FMR LLC Item 2: (a) [] [] (b) Item 4: Delaware Item 5: 0 Item 6: 0 Item 7: 4,391,746 Item 8: Item 9: 4,391,746 Item 11: 12.855% Item 12: HC. Cusip #29428V104 Item 1: Reporting Person - Edward C. Johnson 3d Item 2: (a) [] [] (b) United States of America Item 4: Item 5: Item 6: Item 7: 4,391,746 Item 8: Item 9: 4,391,746 Item 11: 12.855% Item 12: ΙN Cusip #29428V104 Item 1: Reporting Person - Abigail P. Johnson Item 2: (a) [] (b) [] Item 4: United States of America Item 5: Item 6: 4,391,746 Item 7: Item 8: 4,391,746 Item 9: Item 11: 12.855% Item 12: Cusip #29428V104 Item 1: Reporting Person - Select Biotechnology Portfolio Item 2: (a) [] [] Item 4: Massachusetts Item 5: 3,358,275 Item 6: 0 Item 7: 0 Item 8: 0 Item 9: 3,358,275 9.830% Item 11:

Item 1(a). Name of Issuer: EPIZYME INC Item 1(b). Address of Issuer's Principal Executive Offices: 400 TECHNOLOGY SQUARE 4th floor Cambridge, MA 02139 USA Item 2(a). Name of Person Filing: FMR LLC Item 2(b). Address or Principal Business Office or, if None, Residence: 245 Summer Street, Boston, Massachusetts 02210 Item 2(c). Citizenship: Not applicable Item 2(d). Title of Class of Securities: COMMON STOCK Item 2(e). CUSIP Number: 29428V104 Item 3. This statement is filed pursuant to Rule 13d-1(b) or 13d-2(b) or (c) and the person filing, FMR LLC, is a parent holding company in accordance with Section 240.13d-1(b)(1)(ii)(G). (Note: See Exhibit A). Item 4. Ownership Amount Beneficially Owned: 4,391,746 (a) Percent of Class: 12.855% (b) Number of shares as to which such person has: (C) (i) sole power to vote or to direct the vote: 0 shared power to vote or to direct the vote: 0 (ii) sole power to dispose or to direct the disposition of: 4,391,746 (iv) shared power to dispose or to direct the disposition of: Item 5. Ownership of Five Percent or Less of a Class. Not applicable. Item 6. Ownership of More than Five Percent on Behalf of Another Person.

Not applicable.

Item 7. Identification and Classification of the Subsidiary Which Acquired the Security Being Reported on By the Parent Holding Company.

See attached Exhibit A.

Item 8. Identification and Classification of Members of the Group.

Not applicable.

Item 9. Notice of Dissolution of Group.

Not applicable.

Item 10. Certifications.

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.

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.

February 13, 2015 Date

/s/ Scott C. Goebel Signature

Scott C. Goebel

Duly authorized under Power of Attorney effective as of June 1, 2008, by and on behalf of FMR LLC and its direct and indirect subsidiaries*

* This power of attorney is incorporated herein by reference to Exhibit B to the Schedule 13G filed by FMR LLC on June 10, 2014, accession number: 0000315066-14-003512.

Exhibit A

Pursuant to the instructions in Item 7 of Schedule 13G, the following table lists the identity and Item 3 classification, if applicable, of each relevant entity that beneficially owns shares of the security class being reported on this Schedule 13G.

Entity ITEM 3 Classification

FMR CO., INC * IA

* Entity beneficially owns 5% or greater of the outstanding shares of the security class being reported on this Schedule 13G.

Edward C. Johnson 3d is a Director and the Chairman of FMR LLC and Abigail P. Johnson is a Director, the Vice Chairman, the Chief Executive Officer and the President of FMR LLC.

Members of the family of Edward C. Johnson 3d, including Abigail P. Johnson, are the predominant owners, directly or through trusts, of Series B voting common shares of FMR LLC, representing 49% of the voting power of FMR LLC. The Johnson family group and all other Series B shareholders have entered into a shareholders' voting agreement under which all Series B voting common shares will be voted in accordance with the majority vote of Series B voting common shares. Accordingly, through their ownership of voting common shares and the execution of the shareholders' voting agreement, members of the Johnson family may be deemed, under the Investment Company Act of 1940, to form a controlling group with respect to FMR LLC.

Neither FMR LLC nor Edward C. Johnson 3d nor Abigail P. Johnson has the sole power to vote or direct the voting of the shares owned directly by the various investment companies registered under the Investment Company Act ("Fidelity Funds") advised by Fidelity Management & Research Company ("FMR Co"), a wholly owned subsidiary of FMR LLC, which power resides with the Fidelity Funds' Boards of Trustees. Fidelity Management & Research Company carries out the voting of the shares under written guidelines established by the Fidelity Funds' Boards of Trustees.

This filing reflects the securities beneficially owned, or that may be deemed to be beneficially owned, by FMR LLC, certain of its subsidiaries and affiliates, and other companies (collectively, the "FMR Reporters"). This filing does not reflect securities, if any, beneficially owned by certain other companies whose beneficial ownership of securities is disaggregated from that of the FMR Reporters in accordance with Securities and Exchange Commission Release No. 34-39538 (January 12, 1998).

RULE 13d-1(k)(1) AGREEMENT

The undersigned persons, on February 13, 2015, agree and consent to the joint filing on their behalf of this Schedule 13G in connection with their beneficial ownership of the COMMON STOCK of EPIZYME INC at December 31, 2014.

FMR LLC

By /s/ Scott C. Goebel Scott C. Goebel Duly authorized under Power of Attorney effective as of June 1, 2008, by

and on behalf of FMR LLC and its direct and indirect subsidiaries*

Edward C. Johnson 3d

By /s/ Scott C. Goebel

Scott C. Goebel

Duly authorized under Power of Attorney effective as of June 1, 2008, by and on behalf of Edward C. Johnson $3d\star$

Abigail P. Johnson

By /s/ Scott C. Goebel

Scott C. Goebel

Duly authorized under Power of Attorney effective as of April 24, 2014, by and on behalf of Abigail P. Johnson*

Select Biotechnology Portfolio

By /s/ Scott C. Goebel Scott C. Goebel Secretary

* This power of attorney is incorporated herein by reference to Exhibit B to the Schedule 13G filed by FMR LLC on June 10, 2014, accession number: 0000315066-14-003512.