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

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**SCHEDULE 14A**  
**(Rule 14a-101)**  
**INFORMATION REQUIRED IN PROXY STATEMENT**  
**SCHEDULE 14A INFORMATION**

**Proxy Statement Pursuant to Section 14(a) of the  
Securities Exchange Act of 1934**

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Filed by the Registrant

Filed by a party other than the Registrant

Check the appropriate box:

Preliminary Proxy Statement

**Confidential, for Use of the Commission Only** (as permitted by Rule 14a-6(e)(2))

Definitive Proxy Statement

Definitive Additional Materials

Soliciting Material Pursuant to §240.14a-12

**EPIZYME, INC.**

(Name of Registrant as Specified in its Charter)

**Not applicable.**

(Name of Person(s) Filing Proxy Statement, if other than the Registrant)

Payment of Filing Fee (Check all boxes that apply):

No fee required.

Fee paid previously with preliminary materials.

Fee computed on table in exhibit required by Item 25 (b) per Exchange Act Rules 14a-6 (i) (1) and D-11.

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**Online**

Go to [www.investorvote.com/epzm](http://www.investorvote.com/epzm) or scan the QR code – login details are located in the shaded bar below.

**Annual Meeting Notice**

**Important Notice Regarding the Availability of Proxy Materials for the Epizyme, Inc. Annual Meeting of Stockholders to be Held Virtually on May 17, 2022**

Under Securities and Exchange Commission rules, you are receiving this notice that the proxy materials for the annual meeting of stockholders are available on the Internet. Follow the instructions below to view the materials and vote online or request a copy. The items to be voted on and virtual location of the annual meeting are on the reverse side. Your vote is important!

This communication presents only an overview of the more complete proxy materials that are available to you on the Internet. We encourage you to access and review all of the important information contained in the proxy materials before voting. The proxy statement for our 2022 annual meeting of stockholders and our 2021 annual report to stockholders are available at:

[www.investorvote.com/epzm](http://www.investorvote.com/epzm)



**Easy Online Access – View your proxy materials and vote.**

- Step 1:** Go to [www.investorvote.com/epzm](http://www.investorvote.com/epzm)
- Step 2:** Click on the icon on the right to view meeting materials.
- Step 3:** Return to the [investorvote.com](http://investorvote.com) window and follow the instructions on the screen to log in.
- Step 4:** Make your selections as instructed on each screen for your delivery preferences.
- Step 5:** Vote your shares.

When you go online, you can also help the environment by consenting to receive electronic delivery of future materials.



**Obtaining a Copy of the Proxy Materials –** If you want to receive a copy of the proxy materials, you must request one. There is no charge to you for requesting a copy. Please make your request as instructed on the reverse side on or before May 7, 2022 to facilitate timely delivery.



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## Annual Meeting Notice

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Epizyme, Inc.'s Annual Meeting of Stockholders will be held on Tuesday, May 17, 2022, at 10:00 am Eastern Time exclusively by virtual meeting via the internet at [meetnow.global/MM2596W](https://meetnow.global/MM2596W). To access the virtual meeting, you must have the information that is printed in the shaded bar located on the reverse side of this form.

Proposals to be voted on at the meeting are listed below along with the Board of Directors' recommendations.

The Board of Directors recommend a vote **FOR** all the nominees listed, and **FOR** Proposals 2 - 6:

1. Election of the following four individuals nominated to serve as class III directors, each for a three-year term ending at the 2025 annual meeting of stockholders.  
01 - Michael F. Giordano, M.D.  
02 - Pablo Legorreta  
03 - David M. Mott  
04 - Carol Stuckley
2. Ratification of the appointment of Ernst & Young LLP as our independent registered public accounting firm for the fiscal year ending December 31, 2022.
3. Approval on an advisory (non-binding) basis, of the compensation of our named executive officers.
4. Approval of an amendment to our Restated Certificate of Incorporation to increase the number of authorized shares of common stock from 225,000,000 to 450,000,000.
5. Approval of the Epizyme, Inc. 2022 Equity Incentive Plan.
6. Approval of an amendment to the Epizyme, Inc. 2013 Employee Stock Purchase Plan to eliminate the annual "evergreen" provision and authorize 2,500,000 shares of common stock for issuance under such plan.

Note: We may also transact any other business properly brought before the annual meeting or any adjournment or postponement of the annual meeting.

**PLEASE NOTE - YOU CANNOT VOTE BY RETURNING THIS NOTICE.** To vote your shares you must go online or request a paper copy of the proxy materials to receive a proxy card. If you wish to attend and vote at the virtual meeting, please bring this notice with you.



### Here's how to order a copy of the proxy materials and select delivery preferences:

Current and future delivery requests can be submitted using the options below.

If you request an email copy, you will receive an email with a link to the current meeting materials.

**PLEASE NOTE:** You must use the number in the shaded bar on the reverse side when requesting a copy of the proxy materials.

- **Internet** - Go to [www.investorvote.com/epzm](https://www.investorvote.com/epzm)
- **Phone** - Call us free of charge at 1-866-641-4276.
- **Email** - Send an email to [investorvote@computershare.com](mailto:investorvote@computershare.com) with "Proxy Materials Epizyme, Inc." in the subject line. Include your full name and address, plus the number located in the shaded bar on the reverse side, and state that you want a paper copy of the meeting materials.

To facilitate timely delivery, requests for a paper copy of proxy materials must be received by May 7, 2022.