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

**SCHEDULE 14A**

**Proxy Statement Pursuant to Section 14(a) of the  
Securities Exchange Act of 1934  
(Amendment No. )**

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 Under §240.14a-12

**Spero Therapeutics, Inc.**

(Name of Registrant as Specified in its Charter)

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

Payment of Filing Fee (Check the appropriate box 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 0-1.
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SPERO THERAPEUTICS, INC.  
675 MASSACHUSETTS AVE., 14th FLOOR  
CAMBRIDGE, MA 02139

## Your **Vote** Counts!

**SPERO THERAPEUTICS, INC.**

2022 Annual Meeting  
Vote by September 14, 2022  
11:59 PM ET



### You invested in SPERO THERAPEUTICS, INC. and it's time to vote!

You have the right to vote on proposals being presented at the Annual Meeting. **This is an important notice regarding the availability of proxy material for the stockholder meeting to be held on September 15, 2022.**

### Get informed before you vote

View the Notice & Proxy Statement, Form 10-K online OR you can receive a free paper or email copy of the material(s) by requesting prior to September 01, 2022. If you would like to request a copy of the material(s) for this and/or future stockholder meetings, you may (1) visit [www.ProxyVote.com](http://www.ProxyVote.com), (2) call 1-800-579-1639 or (3) send an email to [sendmaterial@proxyvote.com](mailto:sendmaterial@proxyvote.com). If sending an email, please include your control number (indicated below) in the subject line. Unless requested, you will not otherwise receive a paper or email copy.



For complete information and to vote, visit [www.ProxyVote.com](http://www.ProxyVote.com)

Control #

#### Smartphone users

Point your camera here and  
vote without entering a  
control number



#### Vote Virtually at the Meeting\*

September 15, 2022  
9:00 AM EDT

Virtually at:  
[www.virtualshareholdermeeting.com/SPRO2022](http://www.virtualshareholdermeeting.com/SPRO2022)

\*Please check the meeting materials for any special requirements for meeting attendance.

## THIS IS NOT A VOTABLE BALLOT

This is an overview of the proposals being presented at the upcoming stockholder meeting. Please follow the instructions on the reverse side to vote these important matters.

Voting Items	Board Recommends
1. Election of Directors <b>Nominees:</b>	
1a. Frank E. Thomas	✔ For
1b. Patrick Vink, M.D.	✔ For
2. To ratify the appointment of PricewaterhouseCoopers LLP, an independent registered public accounting firm, as the independent auditors of Spero Therapeutics, Inc. for the fiscal year ending December 31, 2022.	✔ For
3. To approve an amendment to the 2017 Stock Incentive Plan.	✔ For

**NOTE:** To transact such other business as may properly come before the meeting or any adjournment thereof.