(City)

(Last)

(Street) SAN

FRANCISCO

(State)

(First)

ONE LETTERMAN DRIVE, SUITE D4900

CA

1. Name and Address of Reporting  $\mathsf{Person}^*$ 

BUILDING D, THE PRESIDIO

Aquilo Capital, L.P.

(Zip)

(Middle)

94129

FORM 4

## UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

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| OMB APP           | OMB APPROVAL |  |  |  |  |  |  |  |  |  |  |
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| OMB Number:       | 3235-0287    |  |  |  |  |  |  |  |  |  |  |
| Estimated average | burden       |  |  |  |  |  |  |  |  |  |  |

0.5

hours per response:

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934

|  |   |   |                            |      |  | or  | Sect  | tion 3   | 80(h) of  | the I | nves                             | stmen        | t Co   | mpany Ac  | t of 194  | 0                                      |                                      |  |              |                   |       |                                 |                        |
|--|---|---|----------------------------|------|--|---|-------|--|---|-------|----------------------------------|--------------|--|---|---|--|--------------------------------------|--|--------------|-------------------|-------|---------------------------------|------------------------|
| 1. Name and Address of Reporting Person* <u>Aquilo Capital Management, LLC</u> |   |   |                            |      | 2. Issuer Name <b>and</b> Ticker or Trading Symbol Spero Therapeutics, Inc. [SPRO] |   |       |  |   |       |                                  |              |  | Relationship of Reporting Person(s) to Issuer (Check all applicable)      Director X 10% Owner      Officer (give title Other (specify) |   |  |                                      |  |              |                   |       |                                 |                        |
| (Last) (First) (Middle) ONE LETTERMAN DRIVE SUITE D4900, BUILDING D            |   |   |                            |      |  | 3. Date of Earliest Transaction (Month/Day/Year) 08/20/2021 |       |  |   |       |                                  |              |  |   |   | belov                                  |                                      | ue   |              | ier (s            | респу |                                 |                        |
| (Street) SAN FRANC   |   | CA.   |                            | 412  | 29   | 4.  | If An | Amendment, Date of Original Filed (Month/Day/Year) |   |       |                                  |              |  | Line  | 6. Individual or Joint/Group Filing (Check Applicable Line)  Form filed by One Reporting Person  X Form filed by More than One Reporting Person |  |                                      |  |              |                   |       |                                 |                        |
| (City)   | ()  | State   | e) (Z                      | Zip) |  |   |       |  |   |       |                                  |              |  |   |   |  |                                      |  |              |                   |       |                                 |                        |
|  |   |   | Table                      | 1 -  | Non-Deriva   | tive  | e Se  | ecur   | rities  | Acc   | uir                              | ed,          | Dis  | posed   | of, or  | Bene                                   | eficia                               | lly Own  | ed           |                   |       |                                 |                        |
| 1. Title of Security (Instr. 3)  2. Transaction Date (Month/Day/Ye             |   |   | 2A. Deemed<br>Execution D  |      |  | n Date, Tra   |       | ransaction<br>Code (Instr.                         |   | 4. :  | Securities a<br>sposed Of (      | Acquire      | d (A) o  | r   | 5. Amour<br>Securitie<br>Beneficia<br>Owned<br>Following  | nt of<br>s<br>ully                     | 6. Owr<br>Form:<br>(D) or<br>Indired | Direct<br>ct (I)                               | Indir<br>Ben | eficial<br>ership |       |                                 |                        |
|  |   |   |                            |      |  |   |       |  |   |       | Code V                           |              | An   | nount   | (A) or<br>(D)   | Price                                  |                                      | Reported<br>Transaction(s)<br>(Instr. 3 and 4) |              |                   |       | _                               |                        |
| Common   | Stock, \$0  | .00   | 1 par value <sup>(1)</sup> |      | 08/20/2021   | L   |       |  |   | ]     | P                                |              | 2  | 21,190  | A   | \$14.                                  | 8601                                 | 4,050,399(2)                                   |              | I                 |       | See<br>Footnotes <sup>(1)</sup> |                        |
| Common   | Stock, \$0  | .00   | 1 par value <sup>(1)</sup> |      | 08/23/2021   | L   |       |  |   | ]     | P                                |              | 1  | 37,835  | A   | \$ <del>16</del> .                     | 3336                                 | 3336 4,188,234 <sup>(3)</sup>                  |              |                   | I     |                                 | otnotes <sup>(1)</sup> |
| Common   | Stock, \$0  | .00   | 1 par value <sup>(1)</sup> |      | 08/24/2021   | L   |       |  |   |       | P                                |              | _  | 40,170  | A   | \$16.2757                              |                                      | 4,228,404 <sup>(4)</sup>                       |              |                   |       | See<br>Foo                      | otnotes <sup>(1)</sup> |
|  |   |   | Tal                        | ole  | II - Derivati<br>(e.g., pu   |   |       |  |   |       |                                  |              |  |   |   |  |                                      | y Owne   | d            |                   |       |                                 |                        |
| 1. Title of<br>Derivative<br>Security<br>(Instr. 3)                            | 2.<br>Conversion<br>or Exercise<br>Price of<br>Derivative<br>Security | Conversion Date Execution Date, if any Code (Instr. 8) Transaction Of Code (Instr. 8) Securities Acquired |                            | Ex   | Date E<br>piratio<br>onth/D  | n D   |       | Ame<br>Sec<br>Und<br>Deri                          | itle and<br>ount of<br>urities<br>erlying<br>vative<br>urity (Ir<br>id 4) |       | Derivative Security (Instr. 5) B |              | per of<br>ve<br>les<br>ially<br>ng<br>ed<br>ction(s) | 10.<br>Ownership<br>Form:<br>Direct (D)<br>or Indirect<br>(I) (Instr. 4   |   | Beneficial<br>Ownershi<br>t (Instr. 4) |                                      |  |              |                   |       |                                 |                        |
|  |   |   |                            |      |  | Cod   | de \  | ,  | (A)   | (D)   | Da:                              | te<br>ercisa | ble  | Expiratio<br>Date   | n Title   | or<br>Nun<br>of                        | nber<br>res                          |  |              |                   |       |                                 |                        |
|  |   |   | eporting Person*           | LI   | <u>.C</u>  |   |       |  |   |       |                                  |              |  |   | ·   |  |                                      |  |              |                   |       |                                 |                        |
|  | TTERMA<br>D4900, BU   | N I   |                            |      | (Middle)   |   |       |  |   |       |                                  |              |  |   |   |  |                                      |  |              |                   |       |                                 |                        |
| (Street) SAN FRANC   | ISCO  | C.  | A                          |      | 94129  |   |       |  |   |       |                                  |              |  |   |   |  |                                      |  |              |                   |       |                                 |                        |

| (City) | (State) | (Zip) |
|--------|---------|-------|
|        |         |       |

## **Explanation of Responses:**

- 1. The reporting persons are Aquilo Capital, L.P. (the "Fund"), Aquilo Capital Management, LLC ("Aquilo") and Marc R. Schneidman. Aquilo is the general partner and investment adviser of the Fund and other funds managed by Aquilo that hold securities directly for the benefit of their investors. Aquilo may be deemed to beneficially own such securities indirectly as the investment adviser and general partner of the Fund and affiliated funds, and Mr. Schneidman may be deemed to beneficially own them indirectly as the control person of Aquilo. Each of, Aquilo, the Fund and Mr. Schneidman disclaims beneficial ownership of such securities except to the extent of his or its pecuniary interest therein.
- 2. Aquilo Capital, LP owns only 3,378,881 of the 4,050,399 shares deemed to be beneficially owned by Aquilo Capital Management, LLC. Aquilo Capital, LP did not purchase any of the 221,190 shares purchased in this transaction on 08/20/2021.
- 3. Aquilo Capital, LP owns only 3,378,881 of the 4,188,234 shares deemed to be beneficially owned by Aquilo Capital Management, LLC. Aquilo Capital, LP did not purchase any of the 137,835 shares purchased in this transaction on 08/23/2021.
- 4. Aquilo Capital, LP owns only 3,378,881 of the 4,228,404 shares deemed to be beneficially owned by Aquilo Capital Management, LLC. Aquilo Capital, LP did not purchase any of the 40,170 shares purchased in this transaction on 08/24/2021.

Aquilo Capital Management,

LLC By: its Managing 08/24/2021

08/24/2021

Member, /s/ Marc Schneidman

Aquilo Capital, L.P., By:

Aquilo Capital Management,

LLC, its General Partner By:

Marc Schneidman, its

Managing Member /s/ Marc

Schneidman

\*\* Signature of Reporting Person Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- $^{\star}$  If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- \*\* Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

Persons who respond to the collection of information contained in this form are not required to respond unless the form displays a currently valid OMB Number.