

| OMB APPROVAL | |
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STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

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 Section 30(h) of the Investment Company Act of 1940

| | | |
|---|--|---|
| 1. Name and Address of Reporting Person* <u>Sphera Global Healthcare Management LP</u> (Last) (First) (Middle) C/O SPHERA FUNDS MANAGEMENT LTD. 21 HA'ARBA'AH STREET (Street) TEL AVIV L3 64739 (City) (State) (Zip) | 2. Issuer Name and Ticker or Trading Symbol <u>Werewolf Therapeutics, Inc. [HOWL]</u> | 5. Relationship of Reporting Person(s) to Issuer (Check all applicable) Director <input checked="" type="checkbox"/> 10% Owner Officer (give title below) Other (specify below) |
| | 3. Date of Earliest Transaction (Month/Day/Year) 05/04/2021 | |
| 4. If Amendment, Date of Original Filed (Month/Day/Year) | | |

Table I - Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned

| 1. Title of Security (Instr. 3) | 2. Transaction Date (Month/Day/Year) | 2A. Deemed Execution Date, if any (Month/Day/Year) | 3. Transaction Code (Instr. 8) | | 4. Securities Acquired (A) or Disposed Of (D) (Instr. 3, 4 and 5) | | | 5. Amount of Securities Beneficially Owned Following Reported Transaction(s) (Instr. 3 and 4) | 6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4) | 7. Nature of Indirect Beneficial Ownership (Instr. 4) |
|---------------------------------|--------------------------------------|--|--------------------------------|---|---|------------|-------|---|--|---|
| | | | Code | V | Amount | (A) or (D) | Price | | | |
| Common Stock | 05/04/2021 | | C | | 312,997 ⁽¹⁾ | A | (2) | 312,997 ⁽¹⁾ | I | See footnote ⁽³⁾ |
| Common Stock | 05/04/2021 | | P | | 475,000 ⁽⁴⁾ | A | \$16 | 787,997 ⁽⁵⁾ | I | See footnote ⁽³⁾ |

Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities)

| 1. Title of Derivative Security (Instr. 3) | 2. Conversion or Exercise Price of Derivative Security | 3. Transaction Date (Month/Day/Year) | 3A. Deemed Execution Date, if any (Month/Day/Year) | 4. Transaction Code (Instr. 8) | | 5. Number of Derivative Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5) | | 6. Date Exercisable and Expiration Date (Month/Day/Year) | | 7. Title and Amount of Securities Underlying Derivative Security (Instr. 3 and 4) | 8. Price of Derivative Security (Instr. 5) | 9. Number of derivative Securities Beneficially Owned Following Reported Transaction(s) (Instr. 4) | 10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4) | 11. Nature of Indirect Beneficial Ownership (Instr. 4) |
|--|--|--------------------------------------|--|--------------------------------|---|--|-----|--|-----------------|---|--|--|---|--|
| | | | | Code | V | (A) | (D) | Date Exercisable | Expiration Date | | | | | |
| Series B Preferred Stock | (2) | 05/04/2021 | | C | | 2,713,410 | (2) | (2) | Common Stock | 312,997 ⁽¹⁾ | \$0 | 0 | I | See footnote ⁽³⁾ |

1. Name and Address of Reporting Person*
Sphera Global Healthcare Management LP
 (Last) (First) (Middle)
 C/O SPHERA FUNDS MANAGEMENT LTD.
 21 HA'ARBA'AH STREET
 (Street)
 TEL AVIV L3 64739
 (City) (State) (Zip)

1. Name and Address of Reporting Person*
Sphera Global Healthcare GP Ltd.
 (Last) (First) (Middle)
 C/O SPHERA FUNDS MANAGEMENT LTD.
 21 HA'ARBA'AH STREET
 (Street)
 TEL AVIV L3 64739
 (City) (State) (Zip)

1. Name and Address of Reporting Person*
SPHERA FUNDS MANAGEMENT LTD.
 (Last) (First) (Middle)
 C/O SPHERA FUNDS MANAGEMENT LTD.
 21 HA'ARBA'AH STREET
 (Street)

| | | |
|----------|---------|-------|
| TEL AVIV | L3 | 64739 |
| (City) | (State) | (Zip) |

Explanation of Responses:

1. Includes (a) 187,798 shares held by Sphera Global Healthcare Master Fund (the "Healthcare Fund") and (b) 125,199 shares held by Sphera Biotech Master Fund, LP (the "Biotech Fund" and, together with the Healthcare Fund, the "Funds").
2. On May 4, 2021, the Series B Preferred Stock automatically converted into Common Stock on a 8.6691-for-one basis without payment of further consideration upon closing of the initial public offering of the Issuer's common stock. The shares had no expiration date.
3. Sphera Global Healthcare Management LP is the investment manager for the Funds (the "Management Company"). The Management Company is managed, controlled and operated by its general partner Sphera Global Healthcare GP Ltd. (the "General Partner"), of which Sphera Funds Management Ltd. ("SFML") is the controlling shareholder. Each of the Management Company, the General Partner and SFML may be deemed the indirect beneficial owner of the reported securities for purposes of Section 13(d) of the Securities Exchange Act of 1934, as amended.
4. Includes (a) 300,000 shares held by the Healthcare Fund and (b) 175,000 shares held by the Biotech Fund.
5. Includes (a) 487,798 shares held by the Healthcare Fund and (b) 300,199 shares held by Biotech Fund.

Remarks:

This Form 4 shall not be construed as an admission by any of the Reporting Persons or any other entity named in this Form 4 that it is the beneficial owner of any of the securities covered by this Form 4, and each such Reporting Person or entity disclaims beneficial ownership of any such securities, except to the extent of its pecuniary interest therein. In addition, the Reporting Persons and other entities named in this Form 4 may be deemed to constitute a "group" for purposes of Section 13(d) of the Securities Exchange Act of 1934, as amended. Neither the filing of this Form 4 nor any of its contents shall be deemed to constitute an admission that a group exists for purposes of Section 13(d) of the Securities Exchange Act of 1934, as amended, or for any other purpose, and each of the Reporting Persons and other entities named in this Form 4 disclaims the existence of any such group.

Sphera Global Healthcare Management LP, By: Its General Partner, Sphera Global Healthcare GP Ltd., By: Its controlling shareholder, Sphera Funds Management Ltd., By: /s/ Ori Goldfarb, attorney-in-fact 05/04/2021

Sphera Global Healthcare GP Ltd., By: Its controlling shareholder, Sphera Funds Management Ltd., By: /s/ Ori Goldfarb, attorney-in-fact 05/04/2021

Sphera Funds Management Ltd., By: /s/ Ori Goldfarb, attorney-in-fact 05/04/2021

** Signature of Reporting Person Date

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

* 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.