FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

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| OMB Number: | 3235-0287 | | | |
|--------------------------|-----------|--|--|--|
| Estimated average burden | | | | |
| hours per response: | 0.5 | | | |

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

Check this box to indicate that a transaction was made pursuant to a contract, instruction or written plan for the purchase or sale of equity securities of the issuer that is intended to satisfy the affirmative defense conditions of Rule

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

| 10b5-1(c). See Ins | struction 10. | | | |
|--|---------------|-------|--|--|
| Name and Address of Reporting Person* Schwab Andrew J. | | | 2. Issuer Name and Ticker or Trading Symbol Skye Bioscience, Inc. [SKYE] | 5. Relationship of Reporting Person(s) to Issuer (Check all applicable) X Director X 10% Owner |
| (Last) (First) (Middle) | | ` , | 3. Date of Earliest Transaction (Month/Day/Year) 08/21/2025 | Officer (give title Other (specify below) |
| C/O 5AM VENTURE MANAGEMENT, LLC 4 EMBARCADERO CENTER, SUITE 3110 | | | If Amendment, Date of Original Filed (Month/Day/Year) | Individual or Joint/Group Filing (Check Applicable Line) X Form filed by One Reporting Person Form filed by More than One Reporting Person |
| (Street) SAN FRANCISCO | CA | 94111 | | |
| (City) | (State) | (Zip) | | |

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

| 1. Title of Security (Instr. 3) | 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 | 6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4) | Beneficial Ownership |
|---------------------------------|--------------------------|---|---|---|--|---------------|-----------|--|---|---|
| | | | Code | v | Amount | (A) or (D) | Price | Transaction(s) (Instr. 3 and 4) | | (Instr. 4) |
| Common Stock | 08/21/2025 | | S | | 58,642 | D | \$3.57(1) | 1,621,043 | I | By 5AM Ventures II, L.P. ⁽²⁾ |
| Common Stock | 08/21/2025 | | S | | 2,314 | D | \$3.57(1) | 63,963 | I | By 5AM Co- Investors II, L.P. ⁽³⁾ |
| Common Stock | 08/22/2025 | | S | | 163,979 | D | \$3.42(4) | 1,457,064 | I | By 5AM Ventures II, L.P. ⁽²⁾ |
| Common Stock | 08/22/2025 | | S | | 6,470 | D | \$3.42(4) | 57,493 | I | By 5AM Co- Investors II, L.P. ⁽³⁾ |
| Common Stock | | | | | | | | 8,167,206 | I | By 5AM Ventures VII, L.P. ⁽⁵⁾ |

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 | 3A. Deemed Execution Date, if any (Month/Day/Year) | Code (Ir | Transaction Derivative Code (Instr. Securities | | Expiration Date (Month/Day/Year) | | 7. Title and Amount of Securities Underlying Derivative Security (Instr. 3 and 4) | | Derivative Security (Instr. 5) | 9. Number of derivative Securities Beneficially Owned Following Reported | Ownership Form: Direct (D) | Beneficial Ownership (Instr. 4) | | | | |
|--|---|---|----------|--|--|-------------------------------------|---|--|-----|--------------------------------------|--|----------------------------------|---------------------------------------|--|------------------------------|--|--|
| | | | | | | Code | v | (A) | (D) | Date Exercisable | Expiration Date | Title | Amount or Number of Shares | | Transaction(s) (Instr. 4) | | |

Explanation of Responses:

- 1. The price reported in Column 4 is a weighted average price. These shares were sold in multiple transactions at prices ranging from \$3.55 to \$3.69 inclusive. The Reporting Persons undertake to provide to the Issuer, any security holder of the Issuer, or the staff of the Securities and Exchange Commission, upon request, full information regarding the number of shares sold at each separate price within the range set forth in this footnote.
- 2. The securities are directly held by 5AM Ventures II, L.P. ("Ventures II"). 5AM Partners II, LLC ("Partners II") is the sole general partner of Ventures II. The Reporting Person is a managing member of Partners II and may be deemed to have shared voting and investment power over the shares beneficially owned by Ventures II. The Reporting Person disclaims beneficial ownership of such securities except to the extent of his pecuniary interest therein.
- 3. The securities are directly held by 5AM Co-Investors II, L.P. ("Co-Investors II"). Partners II is the sole general partner of Co-Investors II. The Reporting Person is a managing member of Partners II and may be deemed to have shared voting and investment power over the shares beneficially owned by Co-Investors II. The Reporting Person disclaims beneficial ownership of such securities except to the extent of his pecuniary interest therein.
- 4. The price reported in Column 4 is a weighted average price. These shares were sold in multiple transactions at prices ranging from \$3.30 to \$3.59 inclusive. The Reporting Persons undertake to provide to the Issuer, any security holder of the Issuer, or the staff of the Securities and Exchange Commission, upon request, full information regarding the number of shares sold at each separate price within the range set forth in this footnote.
- 5. The securities are directly held by 5AM Ventures VII, L.P. ("Ventures VII"). 5AM Partners VII, LLC ("Partners VII") is the sole general partner of Ventures VII. The Reporting Person is a managing member of Partners VII and may be deemed to have shared voting and investment power over the shares beneficially owned by Ventures VII. The Reporting Person disclaims beneficial ownership of such securities except to the extent of his pecuniary interest therein.

** 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.