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INITIAL STATEMENT OF BENEFICIAL OWNERSHIP OF SECURITIES

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

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|---|--|---|---|
| 1. Name and Address of Reporting Person * <u>5AM Partners VII, LLC</u> <hr/> (Last) (First) (Middle) <u>501 2ND STREET, SUITE 350</u> <hr/> (Street) <u>SAN FRANCISCO CA 94107</u> <hr/> (City) (State) (Zip) | 2. Date of Event Requiring Statement (Month/Day/Year) <u>08/18/2023</u> | 3. Issuer Name and Ticker or Trading Symbol <u>Skye Bioscience, Inc. [SKYE]</u> | |
| | | 4. Relationship of Reporting Person(s) to Issuer (Check all applicable) Director <input checked="" type="checkbox"/> 10% Owner Officer (give title below) Other (specify below) | 5. If Amendment, Date of Original Filed (Month/Day/Year) 6. Individual or Joint/Group Filing (Check Applicable Line) Form filed by One Reporting Person <input checked="" type="checkbox"/> Form filed by More than One Reporting Person |

Table I - Non-Derivative Securities Beneficially Owned

| 1. Title of Security (Instr. 4) | 2. Amount of Securities Beneficially Owned (Instr. 4) | 3. Ownership Form: Direct (D) or Indirect (I) (Instr. 5) | 4. Nature of Indirect Beneficial Ownership (Instr. 5) |
|---------------------------------|---|--|---|
| Common Stock | 684,361,447 | I | By 5AM Ventures VII, L.P. ⁽¹⁾ |
| Common Stock | 429,546,911 | I | By 5AM Ventures II, L.P. ⁽²⁾ |
| Common Stock | 16,948,799 | I | By 5AM Co-Investors II, L.P. ⁽³⁾ |

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

| 1. Title of Derivative Security (Instr. 4) | 2. Date Exercisable and Expiration Date (Month/Day/Year) | | 3. Title and Amount of Securities Underlying Derivative Security (Instr. 4) | | 4. Conversion or Exercise Price of Derivative Security | 5. Ownership Form: Direct (D) or Indirect (I) (Instr. 5) | 6. Nature of Indirect Beneficial Ownership (Instr. 5) |
|--|--|-----------------|---|----------------------------|--|--|---|
| | Date Exercisable | Expiration Date | Title | Amount or Number of Shares | | | |
| Warrant (Right to Buy) | 08/18/2023 | 08/18/2033 | Common Stock | 426,348,120 | 0.0206 | I | By 5AM Ventures VII, L.P. ⁽¹⁾ |

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|---|
| 1. Name and Address of Reporting Person * <u>5AM Partners VII, LLC</u> <hr/> (Last) (First) (Middle) <u>501 2ND STREET, SUITE 350</u> <hr/> (Street) <u>SAN FRANCISCO CA 94107</u> <hr/> (City) (State) (Zip) |
|---|

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|--|
| 1. Name and Address of Reporting Person * <u>5AM Ventures VII, L.P.</u> <hr/> (Last) (First) (Middle) <u>501 2ND STREET, SUITE 350</u> <hr/> (Street) <u>SAN FRANCISCO CA 94107</u> <hr/> (City) (State) (Zip) |
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| | | |
|--|---------|----------|
| 1. Name and Address of Reporting Person * | | |
| 5AM Partners II, LLC | | |
| (Last) | (First) | (Middle) |
| 501 2ND STREET, SUITE 350 | | |
| (Street) | | |
| SAN FRANCISCO | CA | 94107 |
| (City) | (State) | (Zip) |
| 1. Name and Address of Reporting Person * | | |
| 5AM Ventures II LP | | |
| (Last) | (First) | (Middle) |
| 501 2ND STREET, SUITE 350 | | |
| (Street) | | |
| SAN FRANCISCO | CA | 94107 |
| (City) | (State) | (Zip) |
| 1. Name and Address of Reporting Person * | | |
| 5AM CO-INVESTORS II LP | | |
| (Last) | (First) | (Middle) |
| 501 2ND STREET, SUITE 350 | | |
| (Street) | | |
| SAN FRANCISCO | CA | 94107 |
| (City) | (State) | (Zip) |
| 1. Name and Address of Reporting Person * | | |
| DIEKMAN JOHN D | | |
| (Last) | (First) | (Middle) |
| C/O 5AM VENTURE MANAGEMENT, LLC 501 2ND STREET, SUITE 350 | | |
| (Street) | | |
| SAN FRANCISCO | CA | 94107 |
| (City) | (State) | (Zip) |
| 1. Name and Address of Reporting Person * | | |
| PARMAR KUSH | | |
| (Last) | (First) | (Middle) |
| C/O 5AM VENTURE MANAGEMENT, LLC 501 2ND STREET, SUITE 350 | | |
| (Street) | | |
| SAN FRANCISCO | CA | 94107 |
| (City) | (State) | (Zip) |
| 1. Name and Address of Reporting Person * | | |
| ROCKLAGE SCOTT M | | |
| (Last) | (First) | (Middle) |
| C/O 5AM VENTURE MANAGEMENT, LLC 501 2ND STREET, SUITE 350 | | |
| (Street) | | |
| SAN FRANCISCO | CA | 94107 |
| (City) | (State) | (Zip) |

Explanation of Responses:

1. 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. Dr. Kush Parmar and Andrew J. Schwab are the managing members of Partners VII and may be deemed to have shared voting and investment power over the securities beneficially owned by Ventures VII. Each of Partners VII and Dr. Parmar disclaims beneficial ownership of such securities except to the extent of its or his respective pecuniary interest therein. Mr. Schwab is a director of the Issuer and files separate Section 16 reports.
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. Dr. John Diekman, Andrew J. Schwab and Dr. Scott M. Rocklage are the managing members of Partners II and may be deemed to have shared voting and investment power over the securities beneficially owned by Ventures II. Each of Partners II, Dr. Diekman and Dr. Rocklage disclaims beneficial ownership of such securities except to the extent of its or his respective pecuniary interest therein. Mr. Schwab is a director of the Issuer and files separate Section 16 reports.
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. Dr. John Diekman, Andrew J. Schwab and Dr. Scott M. Rocklage are the managing members of Partners II and may be deemed to have shared voting and investment power over the securities beneficially owned by Co-Investors II. Each of Partners II, Dr. Diekman and Dr. Rocklage disclaims beneficial ownership of such shares except to the extent of its or his respective pecuniary interest therein. Mr. Schwab is a director of the Issuer and files separate Section 16 reports.

Remarks:

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|---|-----------------------------------|
| <u>5AM Partners VII, LLC, By /s/ Andrew J. Schwab, Managing Member</u> | <u>08/28/2023</u> |
| <u>5AM Ventures VII, L.P., By: 5AM Partners VII, LLC, its General Partner, By /s/ Andrew J. Schwab, Managing Member</u> | <u>08/28/2023</u> |
| <u>5AM Partners II, LLC, By /s/ Andrew J. Schwab, Managing Member</u> | <u>08/28/2023</u> |
| <u>5AM Ventures II, L.P., By: 5AM Partners II, LLC, its General Partner, By /s/ Andrew J. Schwab, Managing Member</u> | <u>08/28/2023</u> |
| <u>5AM Co-Investors II, L.P., By: 5AM Partners II, LLC, its General Partner, By /s/ Andrew J. Schwab, Managing Member</u> | <u>08/28/2023</u> |
| <u>/s/ John Diekman</u> | <u>08/28/2023</u> |
| <u>/s/ Kush Parmar</u> | <u>08/28/2023</u> |
| <u>/s/ Scott M. Rocklage</u> | <u>08/28/2023</u> |
| ** 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 5 (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.