

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

Post-Effective Amendment No. 1
to

FORM S-1 on Form S-3

REGISTRATION STATEMENT

Under

THE SECURITIES ACT OF 1933

SKYE BIOSCIENCE, INC.

(Exact Name of Registrant as Specified in its Charter)

Nevada

2834

45-0692882

(State or other jurisdiction of incorporation or organization)

(Primary Standard Industrial Classification Code Number)

(I.R.S. Employer Identification Number)

**11250 El Camino Real, Suite 100
San Diego, CA 92130
(858) 410-0266**

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

**Punit Dhillon
Chief Executive Officer
Skye Bioscience, Inc.
11250 El Camino Real, Suite 100
San Diego, CA 92130
(858) 410-0266**

(Name, address, including zip code, and telephone number, including area code, of agent for service)

With copies to:
**Steven G. Rowles
Scott Lesmes
John Hensley
Morrison & Foerster, LLP
12531 High Bluff Drive, #100
San Diego, CA 92130
Tel: (858) 720-5100**

Approximate date of commencement of proposed sale to the public: From time to time after the effective date. If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933 check the following box.

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	<input type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input checked="" type="checkbox"/>	Smaller reporting company	<input checked="" type="checkbox"/>
		Emerging growth company	<input type="checkbox"/>

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided to Section 7(a)(2)(B) of the Securities Act.

The registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act or until the Registration Statement shall become effective on such date as the SEC, acting pursuant to said Section 8(a), may determine.

EXPLANATORY NOTE

On March 27, 2024, Skye Bioscience, Inc. (the “Company,” “we,” “us,” or “our”) filed a registration statement with the Securities and Exchange Commission (the “SEC”) on Form S-1 (File No. 333-278286) (the “Registration Statement”), which Registration Statement, as amended, was declared effective by the SEC on April 10, 2024. This post-effective amendment No. 1 to Form S-1 on Form S-3 (“Post-Effective Amendment No. 1”) is being filed to convert the Registration Statement into a Registration Statement on Form S-3. No additional securities are being registered under this Post-Effective Amendment No. 1. All applicable filing fees were paid at the time of the initial filing of the Registration Statement.

The information in this prospectus is not complete and may be changed. These securities may not be sold until the Registration Statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any State where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED April 24, 2024

PRELIMINARY PROSPECTUS



SKYE BIOSCIENCE, INC.

Up to 6,100,821 Shares of Common Stock Issuable Pursuant to an Agreement and Plan of Merger and Reorganization

Up to 14,039,201 Shares of Common Stock Issuable Pursuant to Securities Purchase Agreements

Up to 2,665,537 Shares of Common Stock Issuable Upon Exercise of Warrants

Up to 968,973 Shares of Common Stock Issuable Upon Conversion of a Secured Convertible Promissory Note

Up to 9,978,739 Shares of Common Stock Issuable Upon Exercise of Pre-Funded Warrants

This prospectus relates to the possible resale from time to time by the selling securityholders named herein of up to 33,753,271 shares of common stock, \$0.001 par value per share (the "Common Stock"), of which 103,660 shares of Common Stock have been sold by the selling securityholders pursuant to the Registration Statement and which consists of (i) 6,100,821 shares of Common Stock issued pursuant to the Agreement and Plan of Merger and Reorganization, dated August 15, 2023 (the "Merger Agreement") by and among us, Aquila Merger Sub, Inc. and Bird Rock Bio, Inc., (ii) 2,325,537 shares of Common Stock issued pursuant to that certain Securities Purchase Agreement, dated as of August 15, 2023, by and between us and the institutional investors identified therein (the "2023 Purchase Agreement"), (iii) 2,325,537 shares of Common Stock issuable upon the exercise of the warrants issued pursuant to the 2023 Purchase Agreement (the "2023 Warrants"), (iv) 968,973 shares of Common Stock issuable upon conversion of that certain secured convertible promissory note, dated as of August 15, 2023, by and between us and MFDI, LLC, (v) 340,000 shares of Common Stock issuable upon exercise of that certain warrant, dated as of August 15, 2023, by and between us and MFDI, LLC (the "MFDI Warrant"), (vi) 11,713,664 shares of Common Stock issued pursuant to that certain Securities Purchase Agreement, dated as of January 29, 2024, by and between us and the institutional investors identified therein (the "January 2024 Purchase Agreement"), of which 103,660 shares of Common Stock have been sold by the selling securityholders pursuant to the Registration Statement and (vii) 9,978,739 shares of Common Stock issuable upon exercise of the pre-funded warrants (the "Pre-Funded Warrants" together with the 2023 Warrants and the MFDI Warrant, the "Warrants") issued pursuant to the January 2024 Purchase Agreement.

We will not receive any cash proceeds from any sale of the shares of our Common Stock by the selling securityholders. We will, however, receive the net proceeds of any Warrants exercised for cash.

We are registering the securities for resale pursuant to the selling securityholders' registration rights under certain agreements between us and the selling securityholders. We are registering the resale of shares of our Common Stock to permit the selling securityholders to sell such shares without restriction in the open market. However, the registration of the potential resale shares of our Common Stock hereunder does not necessarily mean that the selling securityholders will sell the shares. The selling securityholders or their permitted transferees or other successors-in-interest may, but are not required to, sell the shares of our Common Stock offered by this prospectus from time to time in a number of different ways and at varying prices as determined by the prevailing market price for shares or in negotiated transactions. See "[Plan of Distribution](#)" on page 8 for a description of how the selling securityholders may dispose of the shares covered by this prospectus.

We will pay all expenses incident to the registration of the potential resale of the 33,753,271 shares of our Common Stock offered herein (other than for any discounts or commissions to any underwriter or broker attributable to the sale of shares of our Common Stock or any fees or expenses incurred by a holder of shares of our Common Stock that, according to the written instructions of any regulatory authority, we are not permitted to pay).

Our Common Stock is listed on the Nasdaq Global Market under the symbol "SKYE." On April 19, 2024, the last reported sale price of our Common Stock on the Nasdaq Global Market was \$16.14. Our corporate offices are located at 11250 El Camino Real, Suite 100, San Diego, CA 92130 and our telephone number is (858) 410-0266.

See the section entitled "[Risk Factors](#)" beginning on page 6 of this prospectus and other documents that are incorporated by reference in this prospectus to read about factors you should consider before buying our securities.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

We are a "smaller reporting company" under applicable Securities and Exchange Commission rules and, as such, have elected to comply with certain reduced public company disclosure requirements for this prospectus and future filings. See "Prospectus Summary—Implications of Being a Smaller Reporting Company" for additional information.

The date of this prospectus is _____, 2024

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You should rely only on the information provided in this prospectus, as well as the information incorporated by reference into this prospectus and any applicable prospectus supplement. Neither we nor the Selling Securityholders have authorized anyone to provide you with different information. Neither we nor the Selling Securityholders are making an offer of these securities in any jurisdiction where the offer is not permitted. You should not assume that the information in this prospectus or any applicable prospectus supplement is accurate as of any date other than the date of the applicable document. Since the date of this prospectus and the documents incorporated by reference into this prospectus, our business, financial condition, results of operations and prospects may have changed.

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the SEC under the Securities Act of 1933, as amended (the “Securities Act”). Under this process, the selling securityholders named in this prospectus may sell our common stock, par value \$0.001 per share (the “Common Stock”) from time to time. The prospectus provides you with a general description of our Common Stock that the selling securityholders may offer. Each time the selling securityholders sell shares of our Common Stock, the selling securityholders will provide a prospectus supplement containing specific information about the terms of the applicable offering, as required by law. Such prospectus supplement may add, update or change information contained in this prospectus,

Statements contained in this prospectus about the contents of any document are not necessarily complete. If SEC rules require that a document be filed as an exhibit to the registration statement, please see such document for a complete description of these matters. You should carefully read this prospectus, together with the additional information described under the headings “*Where You Can Find Additional Information*” and “*Incorporation by Reference*” before making an investment decision. You should rely only on the information contained or incorporated by reference in this prospectus, any applicable prospectus supplement and any related free writing prospectus. Neither we, nor the selling securityholders, have authorized anyone to provide you with different information. If anyone provides you with additional, different or inconsistent information, you should not rely on it. You should not assume that the information we have included in this prospectus, any applicable prospectus supplement, any related free writing prospectus is accurate as of any date other than the dates of those documents. Our business, financial condition, results of operations and prospects may have changed since those dates.

The selling securityholders may from time to time offer and sell, transfer or otherwise dispose of any or all of the shares of our Common Stock covered by this prospectus through underwriters or dealers, directly to purchasers or through broker-dealers or agents. A prospectus supplement may describe the terms of the plan of distribution and set forth the names of any underwriters involved in the sale of the securities. See “*Plan of Distribution*” for more information on this topic.

This document may only be used where it is legal to sell these securities. This prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Unless the context indicates otherwise, as used in this prospectus, the terms “Skye Bioscience,” “Skye,” the “Company,” “we,” “us” and “our” refer to Skye Bioscience, Inc., together with its wholly-owned subsidiaries.

Solely for convenience, the trademarks and trade names in this prospectus may be referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. We do not intend our use or display of other companies’ trademarks and trade names to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and any accompanying prospectus supplement, as well as the documents incorporated by reference therein, contain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 and releases issued by the SEC and within the meaning of Section 27A of the Securities Act, and Section 21E of the Exchange Act. Forward-looking statements include, among others, information concerning our strategy, future operations, future financial position, future revenue, projected expenses, business prospects, and plans and objectives of management. Forward-looking statements include all statements that are not historical facts and can be identified by terms such as “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “seek,” “should,” “target,” “will,” “would,” or similar expressions and the negatives of those terms. These statements relate to future events or to our future operating or financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by the forward-looking statements.

Forward-looking statements contained in this prospectus and the documents incorporated by reference herein include, but are not limited to, statements about the following:

- the results of our research and development activities, including uncertainties relating to the discovery of potential product candidates and the preclinical and clinical testing of our product candidates;
- the timing, progress and results of our clinical studies for SBI-100 Ophthalmic Emulsion (SBI-100 OE) and nimacimab and our estimates regarding the market opportunity for SBI-100 OE and nimacimab if approved;
- the early stage of our product candidates presently under development;
- our ability to obtain and, if obtained, maintain regulatory approval of our current product candidates, and any of our other future product candidates, and any related restrictions, limitations, and/or warnings in the label of any approved product candidate;
- our ability to retain or hire key scientific or management personnel;
- our ability to protect our intellectual property rights that are valuable to our business, including patent and other intellectual property rights;
- our dependence on University of Mississippi, third party manufacturers, suppliers, research organizations, testing laboratories and other potential collaborators, including global supply chain disruptions;
- our ability to develop successful sales and marketing capabilities in the future as needed;
- the size and growth of the potential markets for any of our current product candidates, and the rate and degree of market acceptance of any of our current product candidates;
- competition in our industry;
- regulatory developments in the United States and foreign countries; and
- current pending litigation matters, including the Cunning Lawsuit.

Forward-looking statements are subject to a number of risks, uncertainties and assumptions, including those described in “*Risk Factors*” and elsewhere in this prospectus. Moreover, we operate in a very competitive and rapidly changing environment, and new risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed in this prospectus may not occur and actual results could differ materially and adversely

from those anticipated or implied in the forward-looking statements. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Also, forward-looking statements represent our management's beliefs and assumptions only as of the date of this prospectus. You should read this prospectus and the documents that we have filed as exhibits to the registration statement, of which this prospectus is a part, completely and with the understanding that our actual future results may be materially different from what we expect.

Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in these forward-looking statements, even if new information becomes available in the future.

PROSPECTUS SUMMARY

The following summary highlights certain information about us, this offering and selected information contained elsewhere in this prospectus or incorporated by reference in this prospectus. This summary does not contain all of the information you should consider before investing in our common stock, par value \$0.001 per share (the "Common Stock"). Before making an investment decision, you should carefully read the entire prospectus, especially the risks of investing in our Common Stock discussed under the heading "Risk Factors" in this prospectus. You should also carefully read the information in this prospectus and other information we incorporate by reference herein, including our financial statements, and the exhibits to the registration statement of which this prospectus is a part.

The following summary is qualified in its entirety by the more detailed information and financial statements and notes thereto included elsewhere in this prospectus.

Overview

We are a clinical stage biopharmaceutical company with a mission to pioneer the development of new medicines that unlock the pharmaceutical potential of the endocannabinoid system ("ECS"). Our clinical assets focus on the modulation of cannabinoid receptor 1 ("CB1") to provide novel treatments and alternatives for diseases caused by metabolic disorders, inflammation, fibrosis and neurodegeneration, such as obesity and glaucoma. Our Phase 2 clinical candidates include nimacimab, a negative allosteric modulating antibody that inhibits peripheral CB1 receptors, currently being developed for the treatment of obesity and SBI-100 Ophthalmic Emulsion ("SBI-100 OE"), a CB1 agonist (activator), currently being developed for the treatment of glaucoma and ocular hypertension. Both of these differentiated drug candidates are focused on distinct opportunities with large unmet needs: 1) Obesity - where a patients now need additional treatments that have the ability to preserve muscle tissue and improve metabolic dysfunction either as new monotherapies or in combination with existing treatments, and 2) Glaucoma - where novel drugs with distinct mechanisms are needed, especially those that are safe, well-tolerated and have neuroprotective potential. We have filed and successfully opened an Investigational New Drug ("IND") application with the U.S. Food and Drug Administration ("FDA") for nimacimab in obesity, and we plan to launch a Phase 2 clinical trial to evaluate nimacimab for the treatment of obesity as monotherapy compared against placebo, as well as evaluate the combination of nimacimab and a GLP-1 agonist in Q3 2024, with final data in late 2025. We are also continuing clinical development of SBI-100 OE for glaucoma and ocular hypertension, with the first data read out from our recently completed Phase 2a trial anticipated in Q2 2024.

Merger, 2023 Private Placement and Note Financing

On August 18, 2023, we completed the acquisition of Bird Rock Bio, Inc., a Delaware corporation ("Bird Rock") in accordance with the terms of the Agreement and Plan of Merger and Reorganization, dated August 15, 2023 (the "Merger Agreement") by and among us, Aquila Merger Sub, Inc. ("Merger Sub") and Bird Rock. Pursuant to the Merger Agreement, Merger Sub merged with and into Bird Rock, with Bird Rock surviving such merger as a wholly owned subsidiary of the Company (the "Merger").

Pursuant to the Merger Agreement, we issued to certain former stockholders of Bird Rock, an aggregate of 6,100,822 shares (the "Merger Shares") of our Common Stock in a transaction exempt from registration under the Securities Act in reliance on Section 4(a)(2) and Rule 506 of Regulation D thereunder.

In connection with the Merger Agreement, on August 15, 2023, we entered into a Securities Purchase Agreement, by and between us and the institutional investors identified therein (the "2023 Purchase Agreement"), pursuant to which we issued and sold an aggregate of (i) 2,325,537 shares (the "2023 Shares") of our Common Stock at a price of \$5.16 per share and (ii) accompanying warrants (each a "2023 Warrant" and collectively, the "2023 Warrants") to purchase up to 2,325,537 shares of our Common Stock (the "2023 Private Placement"). The 2023 Warrants are exercisable at an exercise price of \$5.16 per share, subject to adjustment as set forth therein. The 2023 Warrants have a term of ten years from the date of issuance. The shares issuable upon exercise of the 2023 Warrants will become eligible for sale by the selling securityholders under this prospectus only when the 2023 Warrants are exercised. We cannot predict when or whether any of the selling securityholders who hold 2023 Warrants will exercise such warrants.

Additionally, on August 15, 2023, we entered into a Secured Note and Warrant Purchase Agreement (the “Note Purchase Agreement” and such transactions, the “Note Financing”) with MFDI, LLC (“MFDI”), pursuant to which we issued to MFDI (i) a secured convertible promissory note (the “MFDI Note”) in the principal amount of \$5.0 million and (ii) an accompanying warrant to purchase up to 340,000 shares of Common Stock (the “MFDI Warrant”). The conversion rate for the MFDI Note is currently \$5.16 per share of Common Stock (the “Conversion Rate”). The MFDI Note bears interest at a rate of 10% per year and all interest accrued under the MFDI Note will be payable quarterly within 30 days of the last day of each calendar quarter. During the term of the MFDI Note, MFDI will be permitted to convert the MFDI Note into shares of Common Stock at any time at the then applicable Conversion Rate. The Company may prepay the principal or interest outstanding under the MFDI Note at any time without penalty. The MFDI Warrant is exercisable at an exercise price of \$5.16 per share, subject to adjustment as set forth therein. The MFDI Warrant has a term of ten years from the date of issuance. The shares issuable upon exercise of the MFDI Warrant will become eligible for sale by the selling securityholders under this prospectus only when the MFDI Warrant is exercised. We cannot predict when or whether the selling securityholders who holds the MFDI Warrant will exercise such warrant.

Under the terms of the MFDI Warrant and the warrant issued to MFDI in connection with the 2023 Private Placement, we may not effect the exercise of any such warrant, and MFDI will not be entitled to exercise any portion of any such warrant, if, upon giving effect to such exercise, the aggregate number of shares of our Common Stock beneficially owned by the holder (together with its affiliates, any other persons acting as a group together with the holder or any of the holder’s affiliates, and any other persons whose beneficial ownership of our Common Stock would or could be aggregated with the holder’s for purposes of Section 13(d) or Section 16 of the Exchange Act) would exceed 4.99% of the number of shares of our Common Stock outstanding immediately after giving effect to the exercise, as such percentage ownership is determined in accordance with the terms of such warrant, which percentage may be increased or decreased at the holder’s election upon 61 days’ notice to us subject to the terms of such warrants..

On August 15, 2023, in connection with the execution of the Merger Agreement, the 2023 Purchase Agreement and the Note Purchase Agreement, the Company entered into a Registration Rights Agreement (the “2023 Registration Rights Agreement”) with the selling securityholders named in this prospectus pursuant to which we agreed to file a registration statement with the SEC covering the resale of the Merger Shares, the 2023 Shares and the shares of Common Stock issuable upon exercise or conversion of the Warrants, the MFDI Warrant and the MFDI Note (the “2023 Registrable Securities”). We agreed to file such registration statement no later than 180 days after the date of the 2023 Registration Rights Agreement and to use reasonable best efforts to have such registration statement declared effective as promptly as possible thereafter, and in any event no later than 30 days following such filing date (or 60 days following such filing date in the event the SEC reviews and has written comments to the registration statement). The investors holding a majority of the 2023 Registrable Securities purchased under the 2023 Purchase Agreement (the “Required Holders”) subsequently executed a waiver on January 29, 2024, in which the Required Holders agreed to waive the Company’s obligation to file a registration statement pursuant to the 2023 Registration Rights Agreement until 60 days after the date of the 2024 Registration Rights Agreement (as defined below). We have granted the selling securityholders customary indemnification rights in connection with such registration statement. The selling securityholders have also granted us customary indemnification rights in connection with such registration statement. The registration statement of which this prospectus is a part has been filed in accordance with the 2023 Registration Rights Agreement.

For more information regarding the Merger, the 2023 Private Placement and the Note Financing, see our Current Report on Form 8-K filed with the SEC on August 21, 2023.

January 2024 Private Placement

On January 29, 2024, we entered into a Securities Purchase Agreement, by and between us and the institutional investors identified therein (the “January 2024 Purchase Agreement”), pursuant to which we issued and sold an aggregate of (i) 11,713,664 shares (the “January 2024 Shares” and together with the Merger Shares and the 2023 Shares, the “Shares”) of our Common Stock at a price of \$2.31 per share and (ii) to certain investors, in lieu of shares of our Common Stock, pre-funded warrants (the “Pre-Funded Warrants” and together with the 2023 Warrants and the MFDI Warrant, the “Warrants”) to purchase 9,978,739 shares of our Common Stock at a price of \$2.31 per

Pre-Funded Warrant (the “January 2024 Private Placement”). The closing of the issuance and sale of these securities was consummated on January 31, 2024. Each Pre-Funded Warrant has an exercise price of \$0.001 per share, is exercisable immediately and is exercisable until the Pre-Funded Warrant is exercised in full. The shares issuable upon exercise of the Pre-Funded Warrants will become eligible for sale by the selling securityholders under this prospectus only when the Pre-Funded Warrants are exercised. We cannot predict when or whether any of the selling securityholders who hold Pre-Funded Warrants will exercise their Pre-Funded Warrants.

Under the terms of the Pre-Funded Warrant, we may not effect the exercise of any such warrant, and a holder will not be entitled to exercise any portion of any such warrant, if, upon giving effect to such exercise, the aggregate number of shares of our Common Stock beneficially owned by the holder (together with its affiliates, any other persons acting as a group together with the holder or any of the holder’s affiliates, and any other persons whose beneficial ownership of our Common Stock would or could be aggregated with the holder’s for purposes of Section 13(d) or Section 16 of the Exchange Act) would exceed 4.99% of the number of shares of our Common Stock outstanding immediately after giving effect to the exercise, as such percentage ownership is determined in accordance with the terms of such warrant, which percentage may be increased or decreased at the holder’s election upon 61 days’ notice to us subject to the terms of such warrants, provided that such percentage may in no event exceed 19.99%. We refer to such percentage limitation as the Beneficial Ownership Limitation.

In connection with the January 2024 Private Placement, we entered into a registration rights agreement with the selling securityholders named in this prospectus, dated as of January 29, 2024 (the “January 2024 Registration Rights Agreement”), pursuant to which we agreed to file a registration statement with the SEC covering the resale of the January 2024 Shares and the shares of Common Stock issuable upon exercise of the Pre-Funded Warrants sold in the January 2024 Private Placement. We agreed to file such registration statement no later than 60 days after the date of the January 2024 Registration Rights Agreement and to use reasonable best efforts to have the 2024 Registration Statement declared effective as promptly as possible thereafter, and in any event no later than 30 days following the filing date (or 60 days following the filing date in the event the SEC reviews and has written comments to the registration statement). We have granted the selling securityholders customary indemnification rights in connection with the registration statement. The selling securityholders have also granted us customary indemnification rights in connection with the registration statement. The registration statement of which this prospectus is a part has been filed in accordance with the January 2024 Registration Rights Agreement.

For more information regarding the January 2024 Private Placement, see our Current Report on Form 8-K filed with the SEC on January 29, 2024.

Corporate Information

We were incorporated in the State of Nevada on March 16, 2011. Our Common Stock is listed on the Nasdaq Global Market under the symbol “SKYE”. Our principal executive offices are located at 11250 El Camino Real, Suite 100, San Diego, CA 92130, and our telephone number is (858) 410-0266. In August 2019, we formed a subsidiary in Australia, called SKYE Bioscience Australia for the purpose of undertaking preclinical and clinical studies in Australia. Our website is located at <http://www.skyebioscience.com>. Our website and the information contained on, or that can be accessed through, the website will not be deemed to be incorporated by reference in, and are not considered part of, this prospectus. You should not rely on any such information in making your decision whether to purchase our Common Stock. Our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Exchange Act, are available free of charge on the investors section of our website as soon as reasonably practicable after we electronically file such material with, or furnish it to the SEC. The SEC also maintains a website that contains reports, proxy and information statements, and other information regarding the Company that we file electronically with the SEC. The address of the website is <http://www.sec.gov>.

Implications of Being a Smaller Reporting Company

We are a “smaller reporting company,” meaning that the market value of our stock held by non-affiliates is less than \$700 million as of our most recently completed second fiscal quarter and our annual revenue was less than \$100 million during our most recently completed fiscal year. We may continue to be a smaller reporting company if

either (i) the market value of our stock held by non-affiliates is less than \$250 million or (ii) our annual revenue was less than \$100 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than \$700 million as of our most recently completed second fiscal quarter. As a smaller reporting company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not smaller reporting companies.

THE OFFERING

Issuer

Skye Bioscience, Inc.

Shares of Common Stock offered for resale by the selling securityholders

Up to 33,753,271 shares of Common Stock, which consists of (i) 6,100,821 shares of Common Stock issued pursuant to the Merger Agreement, (ii) 2,325,537 shares of Common Stock issued pursuant to the 2023 Purchase Agreement, (iii) 2,325,537 shares of Common Stock issuable upon the exercise of the 2023 Warrants issued pursuant to the 2023 Purchase Agreement, (iv) 968,973 shares of Common Stock issuable upon conversion of the MFDI Note, (v) 340,000 shares of Common Stock issuable upon exercise of the MFDI Warrant, (vi) 11,713,664 shares of Common Stock issuable issued pursuant to the January 2024 Purchase Agreement, and (vii) 9,978,739 shares of Common Stock issuable upon exercise of the Pre Funded Warrants issued pursuant to the 2024 Purchase Agreement.

Use of Proceeds

The selling securityholders will receive all of the net proceeds from the sale of any securities sold by them pursuant to this prospectus. We will not receive any proceeds from these sales. We will, however, receive the net proceeds of any Warrants exercised for cash. See "[Use of Proceeds](#)" in this prospectus.

Market for our Common Stock

Our shares of Common Stock are traded on the Nasdaq Global Market.

Nasdaq Global Market Ticker Symbol

"SKYE"

Risk Factors

Any investment in our securities is speculative and involves a high degree of risk. You should carefully consider the information set forth under "[Risk Factors](#)", on page [6](#) of this prospectus and in our most recent Annual Report on Form 10-K, subsequent Quarterly Reports on Form 10-Q and Current Reports on Form 8-K and our other filings with the SEC.

RISK FACTORS

Investing in our Common Stock, involves a high degree of risk. You should carefully consider the risks and uncertainties described below, together with all of the other information incorporated by reference to our most recent Annual Report on Form 10-K, any subsequent Quarterly Reports on Form 10-Q or Current Reports on Form 8-K and all other information contained in or incorporated by reference into this prospectus, as updated by our subsequent filings under the Exchange Act, or the Securities Exchange Act of 1934, as amended, and the risk factors and other information contained in any applicable prospectus supplement before acquiring any of such securities. If any of the following risks actually occurs, our business, prospects, operating results and financial condition could suffer materially, the trading price of our Common Stock could decline and you could lose all or part of your investment. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently believe to be immaterial also may materially and adversely affect our business, prospects, operating results and financial condition. Please also refer to the section entitled “Cautionary Note Regarding Forward-Looking Statements” in this prospectus.

Our failure to meet the continued listing requirements of the Nasdaq could result in a delisting of our Common Stock.

If we fail to satisfy the continued listing requirements of the Nasdaq, such as the corporate governance requirements or the minimum closing bid price requirement, Nasdaq may take steps to delist our common stock. Such a delisting would likely have a negative effect on the price of our Common Stock and would impair your ability to sell or purchase our Common Stock when you wish to do so. In the event of a delisting, we can provide no assurance that any action taken by us to restore compliance with listing requirements would allow our Common Stock to become listed again, stabilize the market price or improve the liquidity of our Common Stock, prevent our Common Stock from dropping below the Nasdaq minimum bid price requirement or prevent future non-compliance with Nasdaq’s listing requirements.

USE OF PROCEEDS

We will not receive any cash proceeds from the possible resale from time to time of some or all of such shares of our Common Stock by the selling securityholders named in this prospectus. The proceeds from the offering are solely for the account of the selling securityholders. Upon any exercise of the Warrants for cash, the applicable selling securityholder would pay us the exercise price set forth in the applicable Warrant.

We will pay all expenses incident to the registration of the shares of our Common Stock offered herein.

PLAN OF DISTRIBUTION

The selling securityholders, which as used herein includes donees, pledgees, transferees or other successors-in-interest selling shares of Common Stock or interests in shares of Common Stock received after the date of this prospectus from a selling securityholder as a gift, pledge, partnership distribution or other transfer, may, from time to time, sell, transfer or otherwise dispose of any or all of their shares of Common Stock or interests in shares of Common Stock on any stock exchange, market or trading facility on which the shares are traded or in private transactions. These dispositions may be at fixed prices, at prevailing market prices at the time of sale, at prices related to the prevailing market price, at varying prices determined at the time of sale, or at negotiated prices.

The selling securityholders may use any one or more of the following methods when disposing of shares or interests therein:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the shares as agent, but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- short sales;
- through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise;
- broker-dealers may agree with the selling securityholders to sell a specified number of such shares at a stipulated price per share;
- a combination of any such methods of sale; and
- any other method permitted by applicable law.

The selling securityholders may, from time to time, pledge or grant a security interest in some or all of the shares of Common Stock owned by the selling securityholders and, if the selling securityholders default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the shares of Common Stock, from time to time, under this prospectus, or under an amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act, amending the selling securityholders list to include the pledgee, transferee or other successors in interest as selling securityholders under this prospectus. The selling securityholders also may transfer the shares of Common Stock in other circumstances, in which case the transferees, pledgees, donees or other successors in interest will be the selling beneficial owners for purposes of this prospectus.

In connection with the sale of our Common Stock or interests therein, the selling securityholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the Common Stock in the course of hedging the positions they assume. The selling securityholders may also sell shares of our Common Stock short and deliver these securities to close out their short positions, or loan or pledge the Common Stock to broker-dealers that in turn may sell these securities. The selling securityholders may also enter into option or other transactions with broker-dealers or other financial institutions or the creation of one or more derivative securities which require the delivery to such broker-dealer or other financial institution of shares offered by this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction).

The aggregate proceeds to the selling securityholders from the sale of the Common Stock offered by the selling securityholders will be the purchase price of the Common Stock less discounts or commissions, if any. Each of the

selling securityholders reserves the right to accept and, together with its agents from time to time, to reject, in whole or in part, any proposed purchase of Common Stock to be made directly or through agents. We will not receive any of the proceeds from this offering.

The selling securityholders also may resell all or a portion of the shares in open market transactions in reliance upon Rule 144 under the Securities Act, provided that the selling securityholders meet the criteria and conform to the requirements of that rule.

To the extent required, the shares of our Common Stock to be sold, the names of the selling securityholders, the respective purchase prices and public offering prices, the names of any agents or dealers, and any applicable commissions or discounts with respect to a particular offer will be set forth in an accompanying prospectus supplement or, if appropriate, a post-effective amendment to the registration statement that includes this prospectus.

In order to comply with the securities laws of some states, if applicable, the Common Stock may be sold in these jurisdictions only through registered or licensed brokers or dealers. In addition, in some states the Common Stock may not be sold unless it has been registered or qualified for sale or an exemption from registration or qualification requirements is available and is complied with.

We have advised the selling securityholders that the anti-manipulation rules of Regulation M under the Securities Exchange Act of 1934, as amended, may apply to sales of shares in the market and to the activities of the selling securityholders and their affiliates. In addition, to the extent applicable, we will make copies of this prospectus (as it may be supplemented or amended from time to time) available to the selling securityholders for the purpose of satisfying the prospectus delivery requirements of the Securities Act. The selling securityholders may indemnify any broker-dealer that participates in transactions involving the sale of the shares against certain liabilities, including liabilities arising under the Securities Act.

We have agreed to indemnify the selling securityholders against liabilities, including liabilities under the Securities Act and state securities laws, relating to the registration of the shares offered by this prospectus.

We have agreed with the selling securityholders to use commercially reasonable efforts to cause the registration statement of which this prospectus constitutes a part to become effective and to remain continuously effective until the earlier of (1) such time as all of the shares covered by this prospectus have been disposed of pursuant to and in accordance with such registration statement or (2) the date on which all of the shares may be sold without restriction pursuant to Rule 144 of the Securities Act.

DESCRIPTION OF SECURITIES

The following is a summary of the material features of the common stock of the Company. The following summary does not purport to be complete and is subject to and qualified in its entirety by the Nevada Revised Statutes and other applicable law, as well as the provisions of the Company's articles of incorporation, as amended and as currently in effect (the "Articles of Incorporation"), which are filed as Exhibit 3.1 to the Company's Annual Report on Form 10-K filed with the SEC on March 22, 2024, and the Company's amended and restated bylaws, as amended and as currently in effect (the "Bylaws"), which are filed as Exhibit 3.2 to the Company's Annual Report on Form 10-K filed with the Commission on March 31, 2023. The Company's stockholders are urged to read the Articles of Incorporation and Bylaws carefully and in their entirety.

Pursuant to the Articles of Incorporation, the total number of shares of all classes of stock that we have authority to issue is 100,200,000 consisting of 100,000,000 shares of common stock, par value \$0.001 per share and 200,000 shares of preferred stock, par value \$0.001 per share.

Common Stock

General

The holders of common stock of the Company are not entitled to pre-emptive or other similar subscription rights to purchase any of our securities. Our common stock is neither convertible nor redeemable. Unless the board of directors of the Company determines otherwise, the Company will issue all of its capital stock in uncertificated form.

Voting Rights

The holders of shares of our common stock are entitled to one non-cumulative vote per share.

Dividends and Distributions

Subject to preferences that may apply to any shares of the Company's preferred stock outstanding at the time, the holders of outstanding shares of common stock are entitled to receive dividends out of funds legally available at the times and in the amounts that the Company's board of directors may determine.

Liquidation Rights

Upon the Company's liquidation, dissolution or winding-up, the assets legally available for distribution to the Company's stockholders would be distributable ratably among the holders of common stock after payment of liquidation preferences on any Company preferred stock outstanding at that time and any creditors.

The rights, preferences and privileges of holders of common stock are subject to, and may be adversely affected by, the rights of holders of shares of any series of preferred stock that the Company may designate and issue in the future.

Rights of Repurchase

The Company will not have any rights to repurchase shares of its common stock.

Preemptive or Similar Rights

The common stock is not entitled to preemptive rights and is not subject to redemption.

Preferred Stock

The board of directors of the Company has authority to issue shares of Company preferred stock in one or more series, to fix for each such series such voting powers (full or limited, or no voting powers), designations, preferences, qualifications, limitations or restrictions thereof, including dividend rights, conversion rights, redemption privileges and liquidation preferences for the issue of such series all to the fullest extent permitted by the

Nevada Revised Statutes and any other applicable Law (“Nevada Law”). The issuance of Company preferred stock could have the effect of decreasing the trading price of the shares of common stock, restricting dividends on the Company’s capital stock, diluting the voting power of the common stock, impairing the liquidation rights of the Company’s capital stock, or delaying or preventing a change in control of the Company.

Anti-Takeover Provisions

The provisions of our Articles of Incorporation and Bylaws and of the NRS summarized below may have an anti-takeover effect and may delay, defer or prevent a tender offer or takeover attempt that a stockholder might consider in the stockholder’s best interest, including an attempt that might result in the stockholder’s receipt of a premium over the market price for the stockholder’s shares. These provisions are also designed, in part, to encourage persons seeking to acquire control of us to first negotiate with our board of directors, which could result in an improvement of their terms.

Blank Check Preferred Stock

Our Articles of Incorporation authorize the issuance of up to 200,000 shares of preferred stock in one or more series with such voting powers, designations, preferences, qualifications, limitations, restrictions and relative, participating, optional or other special rights, as are determined by our board of directors in accordance with Nevada law.

Board of Directors

Our Articles of Incorporation and Bylaws provide that the number of directors will be fixed from time to time exclusively pursuant to a resolution adopted by the board of directors.

Removal of Directors; Vacancies

Under NRS 78.335, one or more of the incumbent directors may be removed from office by the vote of stockholders representing two-thirds or more of the voting power of the issued and outstanding stock entitled to vote. Our Articles of Incorporation provide that subject to the rights of any one or more series of preferred stock then outstanding, any newly created position on the board of directors that results from an increase in the total number of directors and any vacancies on the board of directors will be filled only by the affirmative vote of a majority of the remaining directors, even if less than a quorum, by a sole remaining director, or by the stockholders entitled to vote thereon.

No Cumulative Voting

The NRS does not permit stockholders to cumulate their votes other than in the election of directors, and then only if expressly authorized by the corporation’s articles of incorporation. Our Articles of Incorporation do not permit cumulative voting.

Special Stockholder Meetings

Our Articles of Incorporation provide that except as otherwise required by law and subject to the rights of the holders of any series of preferred stock, special meetings of our stockholders may be called at any time only by or at the direction of (i) the board of directors, (ii) the chairman of the board of directors or (iii) two or more of the members of our board of directors. Our Bylaws prohibit the conduct of any business at a special meeting other than as specified in the notice for such meeting.

Requirements for Advance Notification of Director Nominations and Stockholder Proposals

Our Bylaws established advance notice procedures with respect to stockholder proposals and the nomination of candidates for election as directors, other than nominations made by or at the direction of the board of directors or a committee of the board of directors. In order for any matter to be properly brought before a meeting of our stockholders, the stockholder submitting the proposal or nomination will have to comply with advance notice requirements and provide us with certain information.

Exclusive Forum

Our Articles of Incorporation provide that to the fullest extent permitted by law, and unless the Company consents in writing to the selection of an alternative forum that the Eighth Judicial District Court of Clark County, Nevada shall be the sole and exclusive forum for any (i) derivative action or proceeding brought in the name or right of the corporation or on its behalf, (ii) action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, employees, consultants or agents to the corporation or any of our stockholders, (iii) any action arising or asserting a claim arising pursuant to the NRS or any provision of our Articles of Incorporation or Bylaws or (iv) any action to interpret, apply, enforce or determine the validity of the Articles of Incorporation or Bylaws, or (v) any action asserting a claim governed by the internal affairs doctrine.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is ClearTrust, LLC. The transfer agent's address is 16540 Pointe Village Dr, Suite 210, Lutz, Florida 33558, and its telephone number is 1-813-235-4490. Our shares of common stock were issued in uncertificated form only, subject to limited circumstances.

Nasdaq Global Market

Our common stock is traded on the Nasdaq Global Market under the symbol "SKYE."

SELLING SECURITYHOLDERS

The shares of our Common Stock being offered by the selling securityholders are those (i) that were issued to the selling securityholders in connection with the Merger, the 2023 Private Placement and the January 2024 Private Placement and (ii) issuable to the selling securityholders upon exercise of the Warrants and upon conversion of the MFDI Note. For additional information regarding the issuance of the Shares, the Warrants and the MFDI Note, see “*Prospectus Summary – Merger, 2023 and Private Placement*”, and “*Prospectus Summary – January 2024 Private Placement*” above. We are registering the resale of the Shares and shares of our Common Stock issuable upon exercise of the Warrants and conversion of the MFDI Note in order to permit the selling securityholders to offer the shares of our Common Stock for resale from time to time. Except for the ownership of the Shares, the Warrants and the MFDI Note, and for the selling securityholders whose other relationships are provided in “*Certain Relationships and Related Party Transactions*,” the selling securityholders have not had any material relationship with us within the past three years.

Beneficial ownership is determined in accordance with the rules of the SEC and includes voting or investment power with respect to our Common Stock. Generally, a person “beneficially owns” shares of our Common Stock if the person has or shares with others the right to vote those shares or to dispose of them, or if the person has the right to acquire voting or disposition rights within 60 days.

Except as set forth in the footnotes below, the following table sets forth, based on written representations from the selling securityholders, certain information as of the date hereof regarding the beneficial ownership of our Common Stock by the selling securityholders and the shares of Common Stock being offered by the selling securityholders. The applicable percentage ownership of Common Stock is based on 28,062,907 shares of Common Stock outstanding as of March 20, 2024. Information with respect to shares of Common Stock owned beneficially after the offering assumes the sale of all of the shares of Common Stock held by the selling securityholders or that may be acquired upon exercise of other securities.

In accordance with the terms of the 2023 Registration Rights Agreement and January 2024 Registration Rights Agreement, this prospectus generally covers the resale of the sum of (i) the number of shares of Common Stock issued to the selling securityholders in the Merger, the 2023 Private Placement and the January 2024 Private Placement and (ii) the maximum number of shares of Common Stock issuable upon exercise of the Warrants and conversion of the MFDI Note. This maximum amount is determined as if the outstanding Warrants were exercised in full as of the trading day immediately preceding the date this registration statement was initially filed with the SEC, subject to adjustment as provided in the 2023 Registration Rights Agreement and January 2024 Registration Rights Agreement and without regard to any limitations on the exercise of the Warrants.

Under the terms of the MFDI Warrant and that certain 2023 Warrant issued to MFDI in connection with the 2023 Private Placement, we may not effect the exercise of any such warrant, and MFDI will not be entitled to exercise any portion of any such warrant, if, upon giving effect to such exercise, the aggregate number of shares of our Common Stock beneficially owned by the holder (together with its affiliates, any other persons acting as a group together with the holder or any of the holder’s affiliates, and any other persons whose beneficial ownership of our Common Stock would or could be aggregated with the holder’s for purposes of Section 13(d) or Section 16 of the Exchange Act) would exceed 4.99% of the number of shares of our Common Stock outstanding immediately after giving effect to the exercise, as such percentage ownership is determined in accordance with the terms of such warrant, which percentage may be increased or decreased at the holder’s election upon 61 days’ notice to us subject to the terms of such warrants. The number of shares in the second and fifth columns reflect this limitation. The selling securityholders may sell all, some or none of their shares in this offering. See “*Plan of Distribution*.”

Under the terms of the Pre-Funded Warrants, we may not effect the exercise of any such warrant, and a holder will not be entitled to exercise any portion of any such warrant, if, upon giving effect to such exercise, the aggregate number of shares of our Common Stock beneficially owned by the holder (together with its affiliates, any other persons acting as a group together with the holder or any of the holder’s affiliates, and any other persons whose beneficial ownership of our Common Stock would or could be aggregated with the holder’s for purposes of Section 13(d) or Section 16 of the Exchange Act) would exceed 4.99% of the number of shares of our Common Stock outstanding immediately after giving effect to the exercise, as such percentage ownership is determined in

accordance with the terms of such warrant, which percentage may be increased or decreased at the holder's election upon 61 days' notice to us subject to the terms of such warrants, provided that such percentage may in no event exceed 19.99%. The number of shares in the second and fifth columns reflect this limitation. The selling securityholders may sell all, some or none of their shares in this offering. See "Plan of Distribution."

Name of Selling securityholders	Before Offering		Maximum Number of Shares of Common Stock Offered Pursuant to this Resale Offering	After Offering	
	Shares of Common Stock Beneficially Owned	Percentage of Outstanding Common Stock Beneficially Owned ⁽¹⁾		Shares of Common Stock Beneficially Owned	Percentage of Outstanding Common Stock Beneficially Owned ⁽¹⁾
Entities affiliated with 5AM Ventures VII, L.P. ⁽²⁾	11,884,898	40.29 %	11,434,898	450,000	1.60 %
Entities affiliated with Baker Bros. Advisors L.P. ⁽³⁾	1,447,626	4.99 %	8,677,166	500,000	1.78 %
Entities affiliated with Versant Venture Capital III, L.P. ⁽⁴⁾	2,530,950	8.86 %	2,530,950	—	*%
Ally Bridge MedAlpha Master Fund L.P. ⁽⁵⁾	1,427,518	4.99 %	2,169,253	15,161	*%
MFDI, LLC ⁽⁶⁾	1,463,745	4.99 %	1,502,769	96,184	*%
Entities affiliated with Sphera ⁽⁷⁾	1,481,518	5.35 %	1,281,518	200,000	*%
Logos Opportunities Fund IV LP ⁽⁸⁾	1,301,518	4.64 %	1,301,518	—	*%
Altium Growth Fund, LP ⁽⁹⁾	1,764,784	6.29 %	1,264,784	500,000	1.78 %
CVI Investments, Inc. ⁽¹⁰⁾	1,037,672	3.70 %	1,037,672	—	*%
Entities affiliated with Driehaus Capital Management LLC ⁽¹¹⁾	650,758	2.32 %	650,758	—	*%
GSK Equity Investments, Limited ⁽¹²⁾	694,739	2.48 %	694,739	—	*%
Global Life Sciences Solutions USA LLC ⁽¹³⁾	154,670	*%	154,670	—	*%
Aravis Biotech II L.P. KGK ⁽¹⁴⁾	198,497	*%	198,497	—	*%
argenx B.V. ⁽¹⁵⁾	55,680	*%	55,680	—	*%
Apposite Healthcare Fund LP ⁽¹⁶⁾	694,739	2.48 %	694,739	—	*%

(1) Based on a total of 28,062,907 shares of our Common Stock outstanding as of March 20, 2024.

(2) The shares reported under "Shares of Common Stock Beneficially Owned Prior to the Offering" consist of (i) 8,393,520 shares of Common Stock held by 5AM Ventures VII L.P. ("Ventures VII") and (ii) 1,705,393 shares of Common Stock issuable upon exercise of 2023 Warrants held by Ventures VII that are currently exercisable, (iii) 1,718,189 shares of Common Stock held by 5AM Ventures II, L.P. ("Ventures II") and (iv) 67,796 shares held by 5AM Co-Investors II ("Co-Investors II"). 5AM Partners VII, LLC ("Partners VII") serves as sole general partner of Ventures VII and shares voting and dispositive power over the securities held by Ventures VII. Andrew J. Schwab and Dr. Kush Parmar are managing members of Partners VII. Each of Partners VII, Andrew J. Schwab, Dr. Kush Parmar shares voting and dispositive power over the securities held by Ventures VII. 5AM Partners VI, LLC ("Partners VI") serves as sole general partner of Ventures II and Co-Investors II. Andrew J. Schwab, Dr. Scott Rocklage, Dr. John D. Diekman are managing members of Partners II. Each of Partners II, Andrew J. Schwab, Dr. Scott Rocklage, Dr. John D. Diekman shares voting and dispositive power over the securities held by Ventures II and Co-Investors II. Andrew J. Schwab, one of our directors, is an affiliate of Ventures VII, Ventures II, and Co-Investors II. Each of Partners VII, Partners II, Andrew J. Schwab, Dr. Kush Parmar, Dr. Scott Rocklage and Dr. John D. Diekman disclaim beneficial ownership of such shares except to the extent of its or their pecuniary interest therein. The address of all entities affiliated with Ventures VII is c/o 5AM Ventures, 4 Embarcadero Center, Suite 3110, San Francisco, CA 94111

(3) The shares reported under "Shares of Common Stock Beneficially Owned Prior to the Offering" consist of (i) 59,605 and 888,021 shares of Common Stock issuable upon exercise of Pre-Funded Warrants held by 667, L.P. ("667") and Baker Brothers Life Sciences, L.P. ("BBLS") and together with 667, the "Baker Funds") and (ii) 39,901 shares of Common Stock held by 667 and 460,099 shares of Common Stock held by BBLS. The Baker Funds are prohibited from exercising such Pre-Funded Warrants, if as a result of such exercise, the Baker Funds would beneficially own more than 4.99% of the number of shares of our Common Stock outstanding immediately after giving effect to the exercise. As a result, the shares reported under "Shares of Common Stock Beneficially Owned Prior to the Offering" do not include (a) 486,180 shares of Common Stock which may be acquired upon exercise of Pre-Funded Warrants held by 667, L.P. and (b) 7,243,360 shares

- of Common Stock which may be acquired upon exercise of Pre-Funded Warrants held by BBLs. The shares reported under “Shares of Common Stock Offered Pursuant to this Resale Offering” do not give effect to the Beneficial Ownership Limitation and consist of (i) 8,131,381 shares of Common Stock which may be acquired upon exercise of Pre-Funded Warrants held by BBLs and (ii) 545,785 shares of Common Stock which may be acquired upon exercise of Pre-Funded Warrants held by 667, L.P. Baker Bros. Advisors LP is the management company and investment advisor to the Baker Funds and has sole voting and investment power with respect to the shares held by the Baker Funds. Baker Bros. Advisors (GP) LLC is the sole general partner of Baker Bros. Advisors LP. Julian C. Baker and Felix J. Baker are managing members of Baker Bros. Advisors (GP) LLC. Baker Bros. Advisors (GP) LLC, Felix J. Baker, Julian C. Baker and Baker Bros. Advisors L.P. may be deemed to be beneficial owners of the securities directly held by the Baker Funds. Julian C. Baker, Felix J. Baker, Baker Bros. Advisors L.P. and Baker Bros. Advisors (GP) LLC disclaim beneficial ownership of all shares held by the Baker Funds, except to the extent of their indirect pecuniary interest therein. The business address of Baker Bros. Advisors LP, Baker Bros. Advisors (GP) LLC, Julian C. Baker and Felix J. Baker is 860 Washington Street, 3rd Floor, New York, NY 10014.
- (4) Consists of (i) 1,995,916 shares of Common Stock held by Versant Venture Capital III, L.P. (“Versant III”), (ii) 520,173 shares of Common Stock issuable upon exercise of 2023 Warrants held by Versant III that are currently exercisable, (iii) 11,788 shares of Common Stock held by Versant Side Fund III, L.P. (“Side Fund III”) and (iv) 3,073 shares of Common Stock issuable upon exercise of 2023 Warrants held by Side Fund III that are currently exercisable. Versant Ventures III, LLC (“Versant Ventures III”) is the sole general partner of Versant III and Side Fund III. The Managing Directors of Versant Ventures III, Brian Atwood, Bradley Bolzon, Samuel Colella, William Link, Barbara Lubash, Ross Jaffe, Robin Praeger, Rebecca Robertson, Charles Warden and Don Milder, have voting and investment control over the securities held by Versant III and Side Fund III and as a result may be deemed to have beneficial ownership over such securities. The address of all entities affiliated with Versant III is c/o Versant Ventures, One Sansome Street, Suite 1650, San Francisco, CA 94104.
- (5) The shares reported under “Shares of Common Stock Beneficially Owned Prior to the Offering” consist of (i) 882,841 shares of Common Stock and (ii) 544,677 shares of Common Stock issuable upon exercise of Pre-Funded Warrants held by Ally Bridge MedAlpha Master Fund L.P. (“MedAlpha”). MedAlpha is prohibited from exercising such Pre-Funded Warrants, if as a result of such exercise, MedAlpha would beneficially own more than 4.99% of the number of shares of our Common Stock outstanding immediately after giving effect to the exercise. As a result, the shares reported under “Shares of Common Stock Beneficially Owned Prior to the Offering” do not include (a) 756,896 shares of Common Stock which may be acquired upon exercise of Pre-Funded Warrants held by MedAlpha. The shares reported under “Shares of Common Stock Offered Pursuant to this Resale Offering” do not give effect to the Beneficial Ownership Limitation and consist of (i) 882,841 shares of Common Stock and (ii) 1,301,573 shares of Common Stock which may be acquired upon exercise of Pre-Funded Warrants held by MedAlpha. Mr. Fan Yu is the sole shareholder of ABG Management Ltd., which is the sole member of Ally Bridge Group (NY) LLC, which manages investments of MedAlpha. As such, each of the foregoing entities and Mr. Fan Yu may be deemed to share beneficial ownership of the shares held by MedAlpha. Each of them disclaims any such beneficial ownership.
- (6) The shares reported under “Shares of Common Stock Beneficially Owned Prior to the Offering” consist of (i) 193,082 shares of Common Stock held by MFDI, (ii) 301,690 shares of Common Stock issuable upon exercise of the 2023 Warrant and MFDI Warrant held by MFDI and (iii) 968,973 shares of Common Stock issuable upon conversion of the convertible promissory note held by MFDI. MFDI is prohibited from exercising such 2023 Warrant and MFDI Warrant, if as a result of such exercise, MFDI would beneficially own more than 4.99% of the number of shares of our Common Stock outstanding immediately after giving effect to the exercise. As a result, the shares reported under “Shares of Common Stock Beneficially Owned Prior to the Offering” do not include 135,208 shares of Common Stock which may be acquired upon exercise of the 2023 Warrant and the MFDI Warrants held by MFDI. The shares reported under “Maximum Number of Shares of Common Stock Offered Pursuant to this Resale Offering” do not give effect to the Beneficial Ownership Limitation and consist of (i) 96,898 shares of Common Stock, (ii) 436,898 shares issuable on exercise of the 2023 Warrant and the MFDI Warrant and (iii) 968,973 shares issuable upon the conversion of convertible debt, determined as of the date the registration statement of which this prospectus is a part was initially filed with the SEC. Baldev K. Munger and Kewal K. Munger have voting and investment power over these securities. Each of Baldev K. Munger and Kewal K. Munger disclaim beneficial ownership of these securities, except to the extent of each’s pecuniary interest in such securities, if any. The address of MFDI is 786 Road 188, Delano, CA 93215.
- (7) Does not include 4,000 shares of Common Stock previously sold by Sphera Global Healthcare Master Fund and 16,000 shares of Common Stock previously sold by Sphera Biotech Master Fund, L.P. pursuant to the Registration Statement. The shares reported under “Shares of Common Stock Beneficially Owned Prior to the Offering” consists of (i) 256,920 shares of Common Stock are held directly by Sphera Global Healthcare Master Fund, which has delegated its investment management authority to the Sphera Global Healthcare Management LP (the “Management Company”) and (ii) 1,244,598 shares of Common Stock are held directly by Sphera Biotech Master Fund, L.P., which has delegated its investment management authority to the Management Company. Accordingly, the Management Company may be deemed to have beneficial ownership of the shares held by each of Sphera Global Healthcare Master Fund and Sphera Biotech Master Fund. The Management Company disclaims beneficial ownership of such shares, except to the extent of its pecuniary interest therein. Their business address is 4 YitzhakSadeh, Building A, 29th Floor, Tel Aviv 6777520, Israel.
- (8) Logos Opportunities IV GP LLC (“Logos Opportunities GP”) is the general partner of Logos Opportunities Fund IV LP (“Logos Opportunities”). Arsani William and Graham Walmsley are the members of Logos Opportunities GP. Mr. William and Mr. Walmsley each disclaim beneficial ownership of these shares, except to the extent of each’s pecuniary interest in such shares, if any. The principal address of Logos Opportunities is 1 Letterman Drive, Building C, Suite C3-350, San Francisco, CA 94129.
- (9) Does not include 36,734 shares of Common Stock previously sold by Altium Growth Fund, LP pursuant to the Registration Statement. Altium Capital Management, LP, the investment manager of Altium Growth Fund, LP, has voting and investment power over these securities. Jacob Gottlieb is the managing member of Altium Capital Growth GP, LLC, which is the general partner of Altium Growth Fund, LP. Each of Altium Growth Fund, LP and Jacob Gottlieb disclaims beneficial ownership over these securities. The principal address of Altium Capital Management, LP is 152 West 57th Street, 20th Floor, New York, NY
- (10) Does not include 46,926 shares of Common Stock previously sold by CVI Investments, Inc. (“CVI”) pursuant to the Registration Statement. Heights Capital Management, Inc. (“Heights Capital”) serves as the investment manager to CVI and may be deemed to be the beneficial owner of all securities owned by CVI. Martin Kobinger, in his capacity as Investment Manager of Heights Capital, may also be deemed to have investment discretion and voting power over the securities held by CVI. Mr. Kobinger disclaims beneficial ownership of these securities except to the extent of their pecuniary interest therein. Their business address is 101 California Street, Suite 3250, San Francisco, California 94111.

- (11) Consists of (i) 487,418 shares of Common Stock held by Driehaus Life Sciences Master Fund, L.P. and (ii) 163,340 shares of Common Stock held by Driehaus Life Sciences (QP) Fund, L.P. Driehaus Capital Management LLC is the investment adviser of the Driehaus Entities. Michael Caldwell is a portfolio manager of the Driehaus Capital Management LLC and Alex Munns is the assistant portfolio manager of Driehaus Capital Management LLC, and may be deemed to have investment discretion and voting power over the shares held by the Driehaus Entities. Each of Michael Caldwell and Alex Munns disclaims beneficial ownership of these shares. The address of the foregoing entities is 25 E. Erie St., Chicago, IL 60611
- (12) Consists of shares of common stock owned by GSK Equity Investments, Limited (formerly S.R. One, Limited), which is an indirect wholly owned subsidiary of GSK plc. The address for GSK plc is 980 Great West Road, Brentford, Middlesex TW8 9GS, England.
- (13) Global Life Sciences Solutions USA LLC is an indirect, wholly owned subsidiary of Danaher Corporation. Danaher Corporation may be deemed to beneficially own the securities held by Global Life Sciences Solutions USA LLC. The address of Global Life Sciences Solutions USA LLC is 100 Results Way, Marlborough, MA 01752
- (14) The address of Aravis Biotech II L.P., KGK is Merkurstrasse 70, 8032 Zürich, Switzerland
- (15) The address of argenx B.V. (formerly known as arGEN-X B.V.) is Industriepark Zwijnaarde 7, 9052 Zwijnaarde Gent, Belgium.
- (16) Apposite Healthcare (GP) Limited, the general partner of Apposite Healthcare Fund, LP, has appointed Apposite Capital LLP as the manager of Apposite Healthcare Fund, L.P. Ford David Porter and Samuel Gray, partners of Apposite Capital LLP, share voting and investment power with respect to the shares held by Apposite Healthcare Fund, L.P. Each of such persons disclaims beneficial ownership of the shares held by Apposite Healthcare Fund, L.P., except to the extent of his pecuniary interest therein. The address for Apposite Healthcare Fund LP is c/o Apposite Capital LLP, 21 Whitefriars Street, London EC4Y 8JJ, United Kingdom.

EXPERTS

Marcum LLP, an independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the fiscal years ended December 31, 2023 and 2022, as set forth in their report which is incorporated herein by reference. Such financial statements have been incorporated by reference in reliance on the report of such firm given their authority as experts in accounting and auditing.

LEGAL MATTERS

Morrison & Foerster LLP is acting as counsel in connection with the registration of our securities under the Securities Act. The validity of our Common Stock offered hereby will be passed upon for us by Fennemore Craig, P.C

WHERE YOU CAN FIND ADDITIONAL INFORMATION

We are required to file annual, quarterly and current reports, proxy statements and other information with the SEC as required by the Exchange Act. You can read our SEC filings, including this prospectus, over the Internet at the SEC's website at www.sec.gov.

Our website address is www.skyebioscience.com. Through our website, we make available, free of charge, the following documents as soon as reasonably practicable after they are electronically filed with, or furnished to, the SEC, including our Annual Reports on Form 10-K; our proxy statements for our annual and special stockholder meetings; our Quarterly Reports on Form 10-Q; our Current Reports on Form 8-K; Forms 3, 4, and 5 and Schedules 13D and 13G with respect to our securities filed on behalf of our directors and our executive officers; and amendments to those documents. The information contained on, or that may be accessed through, our website is not a part of, and is not incorporated into, this prospectus.

INCORPORATION BY REFERENCE

The SEC allows us to incorporate by reference much of the information that we file with the SEC, which means that we can disclose important information to you by referring you to those publicly available documents. The information that we incorporate by reference in this prospectus is considered to be part of this prospectus. Because we are incorporating by reference future filings with the SEC, this prospectus is continually updated and those future filings may modify or supersede the information included or incorporated by reference in this prospectus. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus or in any document previously incorporated by reference have been modified or superseded. This prospectus incorporates by reference the documents listed below and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (in each case, other than those documents or the portions of those documents furnished pursuant to Items 2.02 or 7.01 of any Current Report on Form 8-K and, except as may be noted in any such Form 8-K, exhibits filed on such form that are related to such information), until the offering of the securities under the registration statement of which this prospectus forms a part is terminated or completed:

- our Annual Report on [Form 10-K](#) filed with the SEC on March 22, 2024;
- Our Current Reports on Form 8-K filed with the SEC on [January 29, 2024](#), [February 12, 2024](#), [March 4, 2024](#), and [March 13, 2024](#); and
- the description of our Common Stock contained in our Registration Statement on [Form 8-A](#) filed with the SEC on April 10, 2024, pursuant to Section 12(b) of the Exchange Act, including any amendment or report filed for the purpose of updating such description.

We will provide without charge to each person, including any beneficial owners, to whom this prospectus is delivered, upon his or her written or oral request, a copy of any or all documents referred to above which have been or may be incorporated by reference into this prospectus but not delivered with this prospectus, excluding exhibits to those documents unless they are specifically incorporated by reference into those documents. You may request a copy of these documents by writing or telephoning us at the following address.

Skye Bioscience, Inc.
11250 El Camino Real
Suite 100, San Diego, CA
(858) 410-0266
Attn: Investor Relations

PART II
INFORMATION NOT REQUIRED IN THE PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution.

The following is an itemized statement of the estimated amounts of all expenses payable by us in connection with the registration of the Common Stock, other than underwriting discounts and commissions. All amounts shown are estimates.

SEC Registration Fee	\$	61,627 ⁽¹⁾
Accounting Fees and Expenses		33,951
Legal Fees and Expenses		75,000
Legal Fees and Expenses paid on behalf of certain investors or agents		100,000
Printing Expenses		25,000
Miscellaneous Expenses		—
Total	\$	295,578

(1) Previously Paid

Item 15. Indemnification of Directors and Officers.

Section 78.7502 of the Nevada Revised Statutes (“NRS”) allows, and the Company wishes to adopt, discretionary indemnification of its directors, officers, employees, and agents as provided below.

Subsection (1) of Section 78.7502 of the NRS empowers a corporation to indemnify any person who was or is a party or is threatened to be made a party of any threatened, pending, or completed action, suit, or proceeding, whether civil, criminal, administrative, or investigative (other than an action by or in the right of the corporation) by reason of the fact that the person is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, or as a manager of a limited-liability company, against expenses (including attorneys’ fees), judgments, fines, and amounts paid in settlement actually and reasonably incurred by him or her in connection with the action, suit, or proceeding if the person (a) is not in breach of their fiduciary duty which breach involved intentional misconduct, fraud or a knowing violation of law, or (b) acted in good faith and in a manner in which he or she reasonably believed to be in, or not opposed to, the best interests of the corporation, and, with respect to any criminal action or proceeding, had no reasonable cause to believe the conduct was unlawful.

Subsection (2) of Section 78.7502 of the NRS empowers a corporation to indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending, or completed action or suit by or in the right of the corporation to procure a judgment in favor by reason of the fact that such person acted in any of the capacities set forth in subsection (1) enumerated above, against expenses, including amounts paid in settlement and attorneys’ fees actually and reasonably incurred by the person in connection with the defense or settlement of such action or suit if the person (a) was not in breach of their fiduciary duty, which breach involved intentional misconduct, fraud or a knowing violation of law, or (b) acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of the corporation except that no indemnification may be made for any claim, issue, or matter as to which such person shall have been adjudged by a court of competent jurisdiction, after exhaustion of any appeals taken therefrom, to be liable to the corporation or for amounts paid in settlement to the corporation, unless and only to the extent that the court in which the action or suit was brought or other court of competent jurisdiction determines upon application that in view of all the circumstances of the case, the person is fairly and reasonably entitled to indemnity for such expenses as the court deems proper.

Subsection (3) of Section 78.7502 of the NRS provides that, unless a court orders indemnification or amounts are advanced pursuant to NRS 78.751(2) or any discretionary indemnification under Subsections (1) or (2) of NRS 75.7502 must be authorized by a determination that such indemnification is proper. This determination must be

made by the stockholders, the majority vote of a quorum of the board of the directors not parties to the action, suit or proceeding, or a written opinion by independent legal counsel ordered by a majority of the directors who were not parties to the action, suit, or proceeding, or a quorum of directors who were not parties to the action, suit or proceeding cannot be obtained.

Subsection (1) of Section 78.751 of the NRS provides for mandatory indemnification of any person who is a director, officer, employee or agent to the extent that the person is successful on the merits or otherwise in defense of (i) any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative, including, without limitation, an action by or in the right of the corporation, by reason of the fact that the person is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise; or (ii) any claim, issue or matter therein, against expenses actually and reasonably incurred by the person in connection with defending the action, including, without limitation, attorney's fees.

Additionally, NRS 78.138(7) provides, with limited statutory exceptions relating to a director's duty when confronted with a change or potential change in control of the corporation, or unless the articles of incorporation or an amendment thereto (in each case filed on or after October 1, 2003) provide for greater individual liability, that a director or officer is not individually liable to a corporation or its stockholders or creditors for any damages as a result of any act or failure to act in his or her capacity as a director or officer unless it is proven that: (i) the presumption that a director has acted in good faith, on an informed basis and with a view to the interest of the corporation has been overcome; (ii) the act or failure to act constituted a breach of his or her fiduciary duties as a director or officer; and (iii) the breach of those duties involved intentional misconduct, fraud or a knowing violation of law.

Pursuant to the above indemnification provisions, our Articles of Incorporation and Bylaws provide that we must indemnify and advance expenses to our directors and officers to the fullest extent permitted under the NRS and other applicable law. In addition, we have entered into indemnification agreements with each of our directors and executive officers that require us to indemnify these persons to the full extent provided by the law as stated above.

Item 16. Exhibits

(a) The exhibits listed in the following Exhibit Index are filed as part of this Registration Statement.

Exhibit No.	Description
2.1	Agreement and Plan of Merger and Reorganization, dated August 15, 2023, by and among Skye Bioscience, Inc., Aquila Merger Sub, Inc., and Bird Rock Bio, Inc. (incorporated herein by reference to Exhibit 2.1 to the Current Report on Form 8-K of Skye Bioscience, Inc. filed with the SEC on August 21, 2023).
3.1	Articles of Incorporation of Skye Bioscience, Inc., as amended (incorporated by reference to Exhibit 3.1 to the Annual Report on Form 10-K of Skye Bioscience, Inc. filed with the SEC on March 22, 2023).
3.2	Amended and Restated Bylaws of Skye Bioscience, Inc. (incorporated herein by reference to Exhibit 3.2 to the Annual Report on Form 10-K of Skye Bioscience, Inc. filed with the SEC on March 2, 2021).
4.1	Form of Common Stock Purchase Warrant (incorporated herein by reference to Exhibit 4.1 to the Current Report on Form 8-K of Skye Bioscience, Inc. filed with the SEC on August 21, 2023).
4.2	Form of Secured Convertible Promissory Note issued by Skye Bioscience, Inc. to MFDI, LLC (incorporated herein by reference to Exhibit 4.2 to the Current Report on Form 8-K of Skye Bioscience, Inc. filed with the SEC on August 21, 2023)
4.3	Common Stock Purchase Warrant Issued by Skye Bioscience, Inc. to MFDI, LLC (incorporated herein by reference to Exhibit 4.3 to the Current Report on Form 8-K of Skye Bioscience, Inc. filed with the SEC on August 21, 2023)
4.4	Form of Pre-Funded Warrant (incorporated herein by reference to Exhibit 4.1 to the Current Report on Form 8-K of Skye Bioscience, Inc. filed with the SEC on January 29, 2024)
5.1†	Opinion of Fennemore Craig, P.C.
10.1	Securities Purchase Agreement, by and among Skye Bioscience, Inc. and the institutional investors listed on the signature pages thereto, dated as of January 29, 2024 (incorporated herein by reference to Exhibit 10.1 to the Current Report on Form 8-K of Skye Bioscience, Inc. filed with the SEC on January 29, 2024).
10.2	Registration Rights Agreement, by and among Skye Bioscience, Inc. and the institutional investors listed on the signature pages thereto, dated as of January 29, 2024 (incorporated herein by reference to Exhibit 10.2 to the Current Report on Form 8-K of Skye Bioscience, Inc. filed with the SEC on January 29, 2024).
10.3	Securities Purchase Agreement, by and among Skye Bioscience, Inc. and the institutional investors listed on the signature pages thereto, dated as of August 15, 2023 (incorporated herein by reference to Exhibit 10.1 to the Current Report on Form 8-K of Skye Bioscience, Inc. filed with the SEC on August 21, 2023).
10.4	Registration Rights Agreement, by and among Skye Bioscience, Inc. and the institutional investors listed on the signature pages thereto, dated as of August 15, 2023 (incorporated herein by reference to Exhibit 10.2 to the Current Report on Form 8-K of Skye Bioscience, Inc. filed with the SEC on August 21, 2023).
23.1†	Consent of Marcum LLP
23.2†	Consent of Fennemore Craig, P.C. (included in Exhibit 5.1).
24.1*	Power of Attorney (included on signature page of the initial registration statement).
107†	Filing Fee Table.

* Previously Filed

† Filed Herewith

Item 17. Undertakings

(a) The undersigned Registrant hereby undertakes:

- (1) to file, during any period in which offers or sales are being made, a post-effective amendment to this Registration Statement:
 - (i) to include any prospectus required by Section 10(a)(3) of the Securities Act;
 - (ii) to reflect in the prospectus any facts or events arising after the effective date of the Registration Statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the Registration Statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than 20% change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective Registration Statement; and
 - (iii) to include any material information with respect to the plan of distribution not previously disclosed in the Registration Statement or any material change to such information in the Registration Statement; provided, however, that paragraphs (a)(1)(i), (a)(1)(ii) and (a)(1)(iii) do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Commission by the Registrant pursuant to Section 13 or Section 15(d) of the Exchange Act that are incorporated by reference in the Registration Statement.

provided, however, that: Paragraphs (a)(1)(i), (a)(1)(ii) and (a)(1)(iii) of this section do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Commission by the registrant pursuant to Section 13 or Section 15(d) of the Exchange Act, that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.

- (2) that, for the purpose of determining any liability under the Securities Act, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.
- (3) to remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.
- (4) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser:
 - (i) Each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and
 - (ii) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5) or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii) or (x) for the purpose of providing the information required by Section 10(a) of the Securities Act shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the

registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof. Provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.

- (5) That, for the purpose of determining liability of the registrant under the Securities Act to any purchaser in the initial distribution of the securities, the undersigned Registrant undertakes that in a primary offering of securities of the undersigned Registrant pursuant to this Registration Statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned Registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:
- (i) any preliminary prospectus or prospectus of the undersigned Registrant relating to the offering required to be filed pursuant to Rule 424;
 - (ii) any free writing prospectus relating to the offering prepared by or on behalf of the undersigned Registrant or used or referred to by the undersigned Registrant;
 - (iii) the portion of any other free writing prospectus relating to the offering containing material information about the undersigned Registrant or its securities provided by or on behalf of the undersigned registrant; and
 - (iv) any other communication that is an offer in the offering made by the undersigned registrant to the purchaser.
- (b) The undersigned registrant hereby undertakes that, for purposes of determining any liability under the Securities Act of 1933, each filing of the registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof..
- (c) Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act of 1933 and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act of 1933 and will be governed by the final adjudication of such issue

SIGNATURES

Pursuant to the requirements of the Securities Act, the registrant has duly caused this Post-Effective Amendment No. 1 to the Registration Statement to be signed on its behalf by the undersigned thereunto duly authorized in the City of San Diego, State of California on April 24, 2024.

Skye Bioscience, Inc.
a Nevada corporation

April 24, 2024

By: /s/ Punit Dhillon
Its: Punit Dhillon
Chief Executive Officer, Director
(Principal Executive Officer)

Pursuant to the requirements of the Securities Act, this Post-Effective Amendment No. 1 to the Registration Statement has been signed by the following persons in the capacities and on the dates indicated.

By:	<u>/s/ Punit Dhillon</u> Punit Dhillon	April 24, 2024
Its:	Chief Executive Officer, Director (Principal Executive Officer)	
By:	<u>/s/ Kaitlyn Arsenault</u> Kaitlyn Arsenault	April 24, 2024
Its:	Chief Financial Officer (Principal Financial and Accounting Officer)	
By:	<u>*</u> Margaret Dalesandro	April 24, 2024
Its:	Director	
By:	<u>*</u> Deborah Charych	April 24, 2024
Its:	Director	
By:	<u>*</u> Praveen Tyle	April 24, 2024
Its:	Director	
By:	<u>*</u> Keith Ward	April 24, 2024
Its:	Director	
By:	<u>*</u> Andrew Schwab	April 24, 2024
Its:	Director	
By:	<u>*</u> Paul Grayson	April 24, 2024
Its:	Director	
By:	<u>*</u> Annalisa Jenkins	April 24, 2024
Its:	Director	
*By:	<u>/s/ Kaitlyn Arsenault</u> Kaitlyn Arsenault Attorney-in-fact	

Calculation of Filing Fee Tables

Form S-3
(Form Type)

Skye Bioscience, Inc.
(Exact Name of Registrant as Specified in its Charter)

Table 1: Newly Registered and Carry Forward Securities

	Security Type	Security Class Title	Fee Calculation or Carry Forward Rule	Amount Registered	Proposed Maximum Offering Price Per Unit	Maximum Aggregate Offering Price	Fee Rate	Amount of Registration Fee	Carry Forward Form Type	Carry Forward File Number	Carry Forward Initial effective date	Filing Fee Previously Paid In Connection with Unsold Securities to be Carried Forward
Newly Registered Securities												
Fees Previously Paid	Equity	Common Stock, par value \$0.0001 per share	Rule 457(c)	33,753,271	\$12.37	\$417,527,962.27	\$0.0001476	\$61,627.13				
Total Offering Amounts						\$417,527,962.27	\$0.0001476	\$61,627.13				
Total Fees Previously Paid								\$61,627.13				
Total Fee Offsets								—				
Net Fee Due								\$0.00				

(1) Pursuant to Rule 416(a) under the Securities Act, there are also being registered an indeterminable number of additional securities as may be issued to prevent dilution resulting from share splits, share dividends or similar transactions. Capitalized terms used herein have the meanings set forth in the Post-Effective Amendment to the Registration Statement on Form S-3 with which this Filing Fee Table is filed as Exhibit 107.

(2) Consists of (i) 6,100,821 shares of Common Stock issued pursuant to the Merger Agreement, (ii) 2,325,537 shares of Common Stock issued pursuant to the 2023 Purchase Agreement, (iii) 2,325,537 shares of Common Stock issuable upon the exercise of the 2023 Warrants, (iv) 968,973 shares of Common Stock issuable upon conversion of the MFDI Note, (v) 340,000 shares of Common Stock issuable upon exercise of the MFDI Warrant, (vi) 11,713,664 shares of Common Stock issued pursuant to the January 2024 Purchase Agreement, and (vii) 9,978,739 shares of Common Stock issuable upon exercise of the Pre-Funded Warrants issued pursuant to the January 2024 Purchase Agreement

(3) Pursuant to Rule 457(c) under the Securities Act, and solely for the purpose of calculating the registration fee, the proposed maximum offering price per share is \$12.37, which was the average of high and low prices of the Common Stock on March 20, 2024 on the OTCQB Marketplace operating by OTC Markets Group Inc.

April 24, 2024

Skye Bioscience, Inc.
11250 El Camino Real
Suite 100
San Diego, CA 92130

Re: Registration Statement on U.S. Securities Exchange Commission form S-3.

Ladies and Gentlemen:

We have acted as special Nevada counsel for Skye Bioscience, Inc., a Nevada corporation (the “*Company*”). We are providing this opinion in connection with the registration under the Securities Act of 1933, as amended (the “*Act*”), by the Company, by means of a post-effective amendment No. 1 to the registration statement filed on Form S-1 (File No. 333-278286), which amendment is to be filed on Form S-3 for the purpose of converting the original registration statement to a form S-3 registration statement (as it may be amended and supplemented, the “*Registration Statement*”), with the United States Securities and Exchange Commission (the “*Commission*”) relating to the registration of up to a total 33,753,272 shares of common stock, par value \$0.001 per share of the Company (collectively the “*Shares*”), consisting of all of the following:

1. 6,100,821 Shares issuable pursuant to the Agreement and Plan of Merger and Reorganization, dated August 15, 2023 (the “*Merger Agreement*”);
 2. 2,325,537 Shares issuable pursuant to that certain Securities Purchase Agreement, dated as of August 15, 2023, by and between the Company and the institutional investors identified therein (the “*2023 Purchase Agreement*”);
 3. 2,325,537 Shares issuable upon the exercise of the warrants issued pursuant to the 2023 Purchase Agreement (the “*2023 Warrants*”);
 4. 968,973 Shares issuable upon conversion of a secured convertible promissory note, dated as of August 15, 2023, by and between the Company and MFDI, LLC (the “*MFDI Note*”);
 5. 340,000 Shares issuable upon exercise of that certain warrant, dated as of August 15, 2023, by and between the Company and MFDI, LLC (the “*MFDI Warrant*”);
 6. 11,713,664 Shares issuable pursuant to that certain Securities Purchase Agreement, dated as of January 29, 2024, by and between the Company and the institutional investors identified therein (the “*2024 Purchase Agreement*”); and
-

FENNEMORE.

Sky Bioscience, Inc.

April 24, 2024

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7. 9,978,739 Shares issuable upon exercise of the pre-funded warrants (the “**Pre-Funded Warrants**” together with the 2023 Warrants and the MFDI Warrant, the “**Warrants**”) issued pursuant to the 2024 Purchase Agreement.

In connection with this opinion, we have examined and relied upon:

- (i) the Registration Statement,
- (ii) the Merger Agreement;
- (iii) the 2023 Purchase Agreement;
- (iv) the form of the 2023 Warrants;
- (v) the MFDI Note;
- (vi) the MFDI Warrant;
- (vii) the 2024 Purchase Agreement;
- (viii) the form of the Pre-Funded Warrants; and
- (ix) the Company’s Articles of Incorporation and Bylaws, each as amended and currently in effect, and the originals or copies certified to our satisfaction of such other documents, records, certificates, memoranda and other instruments as in our judgment are necessary or appropriate to enable us to render the opinion expressed below (the “**Organizational Documents**”).

We have examined originals or copies of such corporate records and certificates of public officials as we have deemed necessary or advisable for purposes of this opinion. We have relied upon the certificates of all corporate officials with respect to the accuracy of all matters contained therein. We have assumed the authenticity of all documents submitted to us as originals, the genuineness of all signatures, the legal capacity of natural persons and the conformity to originals of all copies of all documents submitted to us. We note that the Company reserved, and assume that it will continue to reserve, sufficient authorized but unissued shares of its common stock to allow for all of the above issuances.

On the basis of the foregoing, and in reliance thereon, we are of the opinion that the Shares have been duly authorized and, when issued and delivered pursuant to the Merger Agreement, the 2023 Purchase Agreement, the MFDI Note, the MFDI Warrant, and the 2024 Purchase Agreement, as applicable, the Shares will be validly issued, fully paid and nonassessable.

FENNEMORE.

Sky Bioscience, Inc.

April 24, 2024

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This opinion is issued in the State of Nevada. By issuing this opinion, Fennemore Craig, P.C. (i) shall not be deemed to be transacting business in any other state or jurisdiction other than the State of Nevada and (ii) does not consent to the jurisdiction of any state other than the State of Nevada. Nothing herein shall be deemed an opinion as the laws of any jurisdiction other than the State of Nevada except we express no opinion concerning any securities law or rule or any law or rule regulating the purchasers of the Shares.

We hereby consent to the inclusion of this opinion as Exhibit 5.1 to the Registration Statement and to the references to our firm therein. In giving our consent, we do not admit that we are in the category of persons whose consent is required under Section 7 of the Act or the rules and regulations thereunder.

The opinions expressed herein are given as of the date hereof, and we expressly decline any undertaking to revise or update any of the opinions subsequent to the date hereof or to advise you of any matter arising subsequent to the date hereof which would cause us to modify our opinions, in whole or in part. This opinion letter is provided for use in connection with the Registration Statement and may only be relied upon by the Company and its, agents, successors, and assigns. To the extent required, the Company and any of its respective permitted successors and assigns is permitted to show this letter to any auditor, accountant, attorney or other professional advisor or regulator. Delivery of this opinion letter pursuant to the previous sentence, however, shall not entitle the persons to whom it is delivered to rely on it. This letter may not be used or relied upon by any other person for any other purposes.

Very truly yours,

/s/ Fennemore Craig, P.C.

FENNEMORE CRAIG, P.C.

CETE/CDOL

INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM'S CONSENT

We consent to the inclusion in this Registration Statement of Skye Bioscience, Inc. on Form S-3 of our report dated March 21, 2024, with respect to our audits of the consolidated financial statements of Skye Bioscience, Inc. as of December 31, 2023 and 2022 and for the years ended December 31, 2023 and 2022, which report appears in the Prospectus, which is part of this Registration Statement. We also consent to the reference to our Firm under the heading "Experts" in such Prospectus.

/s/ Marcum LLP

Marcum LLP
East Hanover, New Jersey
April 24, 2024