January 29, 2024

Skye Bioscience Announces $50.25 Million Private Placement Equity Financing

Financing co-led by a leading life science investor and 5AM Ventures expected to fully fund obesity Phase 2 trial assessing nimacimab, Skye's differentiated peripheral CB1 inhibitor, in combination with a GLP-1R agonist

San Diego, California--(Newsfile Corp. - January 29, 2024) - Skye Bioscience, Inc. (OTCQB: SKYE) ("the Company"), a clinical stage biotechnology company focused on the discovery, development and commercialization of novel classes of therapeutic drugs that modulate the endocannabinoid system, today announced that it has entered into a securities purchase agreement for the sale of (i) 11,822,124 shares of its common stock at $2.305 per share and (ii) to certain investors, in lieu of common stock, pre-funded warrants to purchase up to 9,978,739 shares of common stock at a price of $2.3049 per pre-funded warrant in a private placement (the "PIPE") to certain qualified institutional buyers. The pre-funded warrants will have an exercise price of $0.001 per share, will be exercisable immediately and will be exercisable until exercised in full. Gross proceeds from the PIPE are expected to be $50.25 million, before deducting any placement agent fees and offering-related expenses. The PIPE financing is expected to close on January 31, 2024, subject to the satisfaction of customary closing conditions.

The PIPE financing was co-led by a life sciences-focused investor and 5AM Ventures, with participation from Ally Bridge Group, Sphera Healthcare, Altium Capital, Driehaus Capital Management and other institutional investors.

Piper Sandler is acting as the lead placement agent and Oppenheimer & Co. is acting as a placement agent for the PIPE financing.

The Company expects the PIPE financing net proceeds to fund its operations into early 2026 through a set of key milestones and operations encompassing:

- Phase 2 clinical trial for nimacimab in obesity: anticipating starting mid-year 2024; interim data expected in Q1 2025; preliminary topline data expected in 2025
- Phase 2a clinical trial for SBI-100 Ophthalmic Emulsion ("OE") in glaucoma and ocular hypertension: currently enrolling; interim data expected Q1 2024; preliminary topline data Q2 2024
- Phase 2b trial of SBI-100 OE for glaucoma and ocular hypertension: anticipating starting H2 2024; preliminary topline data expected in 2025
- Ongoing R&D, general corporate purposes and working capital.

As an update to its previously announced clinical development plans, Skye is planning a Phase 2 trial that will randomize approximately 200 obese patients into four equal-sized arms in which they will be administered either 1) nimacimab (200 mg), 2) GLP-1R agonist (2.4 mg), 3) a combination of nimacimab and GLP-1R agonist, or 4) placebo for 26 weeks with a 12-week follow-up. The primary endpoint will be percent change in weight from baseline at week 26. Secondary endpoints include safety and tolerability, change in waist

circumference, change in body composition, change in fasting triglycerides and cholesterol, and change in A1c (a measure of blood sugar). This planned Phase 2 clinical trial design is not finalized and remains subject to change based on further input from advisors and the U.S. FDA.

"CB1-modulating therapies have potential to meaningfully impact the treatment of obesity and glaucoma, and Skye's technology and development plans have resonated with a strong syndicate of specialist life science investors and resulted in funding through multiple Phase 2 catalysts," said Punit Dhillon, CEO and Chair of Skye. "We appreciate the engagement of the new investors and ongoing support of our existing investors who have enabled us to accelerate our programs and enhance Skye's value proposition.

He added: "As the obesity market witnesses remarkable clinical and commercial outcomes with new drugs, it is revealing opportunities for mechanisms that complement weight loss beyond incretin-based appetite suppression such as promoting loss of fat tissue while preserving lean mass, as well as enhancing leptin and insulin sensitivity. The merit of peripheral CB1 inhibition to possibly enable such outcomes is scientifically well-validated and nimacimab, as a negative allosteric modulating antibody, stands out with its distinguishing characteristics within this mechanistic category. This funding allows us to pursue a high-impact clinical strategy for nimacimab and places us among the most advanced programs evaluating a peripheral CB1 inhibitor in comparison to and in combination with a GLP-1 drug for obesity.

"We also look forward to near-term data from our currently-enrolling Phase 2a trial of SBI-100 OE, which showed positive efficacy signals in a subset of patients in our Phase 1 trial, and advancing a Phase 2b trial comparing SBI-100 OE against a standard of care drug. Key opinion leaders have strongly indicated the need for an alternative class of intraocular pressure-lowering drug, and with only one new class commercialized in the last roughly 25 years (Rhopressa, 2017), there is a compelling opportunity for SBI-100 OE, which, like nimacimab, involves a mechanism of action with compelling prior evidence of utility and an excellent safety profile in human studies to date."

The securities being issued and sold in the PIPE have not been registered under the Securities Act of 1933, as amended (the "Securities Act"), or the securities laws of any state, and may not be offered or sold in the United States, except pursuant to an effective registration statement or an applicable exemption from the registration requirements of the Securities Act. The Company has agreed to file a registration statement with the Securities and Exchange Commission registering the resale of the shares of common stock and shares of common stock underlying the pre-funded warrant shares issued in this PIPE within 60 days of signing.

This press release shall not constitute an offer to sell or the solicitation of an offer to buy any securities described herein, nor shall there be any sale of these securities in any state or jurisdiction in which such offer, solicitation or sale would be unlawful prior to the registration or qualification under the securities laws of any such state or jurisdiction.

About Skye Bioscience, Inc.

Skye is focused on unlocking the pharmaceutical potential of the endocannabinoid system to treat diseases with metabolic, inflammatory, and fibrotic processes. Backed by leading life

science venture investors, Skye's strategy leverages biologic targets with substantial human proof of mechanism for the development of first-in-class therapeutics with significant clinical and commercial differentiation. Nimacimab, a negative allosteric modulating antibody that inhibits peripheral CB1, showed a favorable safety and tolerability profile in a Phase 1 study. Skye plans to start a Phase 2 clinical trial in obesity comparing monotherapy and combination arms of nimacimab and a GLP-1R agonist in mid-2024. SBI-100 Ophthalmic Emulsion, a CB1 agonist, is currently being studied in a Phase 2 clinical trial of patients with glaucoma and ocular hypertension, with interim data expected in Q1 2024. For more information, please visit: https://www.skyebioscience.com.

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Forward-Looking Statements

This release contains forward-looking statements, including statements regarding timing of closing and whether the conditions for the closing of the PIPE will be satisfied, the intended use of proceeds from the PIPE, the Company's cash runway, anticipated timelines and milestones with respect to the Company's product development programs, business strategy, and expected plans with respect to clinical trials, including the timing of patient enrollment and clinical trial data updates. Such statements and other statements in this press release that are not descriptions of historical facts are forward-looking statements that are based on management's current expectations and assumptions and are subject to risks and uncertainties. If such risks or uncertainties materialize or such assumptions prove incorrect, our business, operating results, financial condition, and stock price could be materially negatively affected. In some cases, forward-looking statements can be identified by terminology including "anticipated," "plans," "goal," "focus," "aims," "intends," "believes," "can," "could," "challenge," "predictable," "will," "would," "may" or the negative of these terms or other comparable terminology. We operate in a rapidly changing environment, and new risks emerge from time to time. As a result, 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 the Company may make. Risks and uncertainties that may cause actual results to differ materially include, among others, our capital resources, uncertainty regarding the results of future testing and development efforts and other risks that are described in the Risk Factors section of the Company's most recent annual or quarterly report filed with the Securities and Exchange Commission. Except as expressly required by law, the Company disclaims any intent or obligation to update these forward-looking statements.

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