September 27, 2023

Skye Bioscience Receives Clinical Site Approvals for Glaucoma Phase 2a Trial

Patient enrollment starting in Q4 2023 for proof-of-concept P2a study of CB1 agonist

Phase 1 study complete and data will be reported in October

San Diego, California--(Newsfile Corp. - September 27, 2023) - Skye Bioscience, Inc. (OTCQB: SKYED) ("Skye" or the "Company"), a pharmaceutical company developing drugs targeting the endocannabinoid system, initially through modulation of the CB1 receptor, to address diseases including glaucoma and metabolic conditions, announces that the U.S. Drug Enforcement Agency ("DEA"), after reviewing the physical security and diversion prevention plans for Skye's investigational drug product, has authorized three clinical trial sites in SBI-100-201 in Pennsylvania and California to administer SBI-100 Ophthalmic Emulsion ("OE") in the Phase 2a study. All sites have also been approved by the central Investigational Review Board (IRB) to conduct this study. SBI-100 OE is an ophthalmic emulsion that delivers SBI-100, a prodrug which converts into tetrahydrocannabinol ("THC"). This active pharmaceutical ingredient, currently designated as a Schedule 1 controlled substance, is being developed by Skye to lower intraocular pressure ("IOP") associated with glaucoma and ocular hypertension.

Site initiation visits for the Phase 2a study will commence in October. Skye plans for patient enrollment to begin in Q4, with an interim analysis of the intraocular pressure data when 50% of enrollment has been reached. The initial analysis of this data is tentatively expected in Q1 2024.

Study SBI-100-201 is a double-masked, randomized, placebo-controlled clinical study of SBI-100 OE that is planned to include 54 patients with primary open-angle glaucoma ("POAG") or ocular hypertension ("OHT"). The primary objective is to evaluate the safety and effectiveness of two dose levels of SBI-100 OE when compared to placebo in patients with elevated intraocular pressure. Patients will receive SBI-100 OE at a 1.0% concentration, 0.5% concentration or placebo dose.

"After starting the interaction with the DEA early in the year, obtaining approval for all the sites is one of the last key items off our preparation checklist," said Tu Diep, Chief Development Officer. "SBI-100 Ophthalmic Emulsion is a new medicine that has the potential to fulfill a vital role, initially, we believe, as a second-line therapy. Key opinion leaders have indicated newer options are missing from their therapeutic regimen for glaucoma and ocular hypertension. Our recent August financing fully funded this Phase 2a study and we should progress relatively quickly to first data."

Moreover, safety data for Skye's Phase 1 study of SBI-100 OE in healthy volunteers will be reported in October. While Skye previously reported on the lack of serious adverse events or adverse events of concern, the full dataset will provide an evaluation of specific topical adverse side effects from SBI-100 OE eye drops. Additionally, this report will discuss the

systemic exposure to SBI-100 OE and its metabolite, THC, and any potential psychotropic side effects that may have occurred, if any.

"Given the potential safety concerns around the use of a controlled substance like THC, a positive outcome for this first-in-human safety study is critical for the development of SBI-100 OE," added Mr. Diep. "We look forward to reporting this first human data from SBI-100 Ophthalmic Emulsion.

"Like prostaglandins and beta blockers which generally do not reduce IOP in healthy individuals, we similarly do not expect to see impacts on intraocular pressure in healthy volunteers treated in our Phase 1 study. However, we look forward to the Phase 2a efficacy and safety results of SBI-100 OE in patients with glaucoma and ocular hypertension from our planned interim analysis early in 2024."

About SBI-100 Ophthalmic Emulsion

Skye's SBI-100 OE possesses a novel molecular structure and nanoemulsion formulation designed to enable effective topical delivery and better penetration of a CB1R agonist into ocular tissue. In preclinical studies involving three different species, the drug resulted in enhanced therapeutic efficacy and duration of response in lowering IOP, comparing favorably to the standard of care for treating glaucoma.

About Skye Bioscience
Skye is focused on unlocking the pharmaceutical potential of the endocannabinoid system to treat diseases with inflammatory, fibrotic, and metabolic 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, inhibits peripheral CB1 with unprecedented safety and tolerability. A Phase 2 cardio-metabolic related indication study is expected to start in Q1 2024. Skye is also evaluating potential development paths for nimacimab related to obesity and weight loss. SBI-100 Ophthalmic Emulsion is a CB1 agonist that is a potential treatment for glaucoma and is expected to start a Phase 2 clinical trial in Q4 2023. For more information, please visit: https://www.skyebioscience.com.

CONTACT
Investor Relations
Email: ir@skyebioscience.com
Phone: (858) 410-0266

FORWARD LOOKING STATEMENTS
This letter contains forward-looking statements, including statements regarding our product development, business strategy, the timing of clinical trials, and commercialization of cannabinoid-derived therapeutics. 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 Skye's most recent annual or quarterly report filed with the Securities and Exchange Commission. Except as expressly required by law, Skye disclaims any intent or obligation to update these forward-looking statements.

To view the source version of this press release, please visit https://www.newsfilecorp.com/release/182032

SOURCE Skye Bioscience, Inc.