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Skye Bioscience Doses First Cohort of Participants in Phase 1 Clinical Trial of SBI-100 Ophthalmic Emulsion

San Diego, California--(Newsfile Corp. - December 16, 2022) - Skye Bioscience, Inc. (OTCQB: SKYE) ("Skye" or the "Company"), a pharmaceutical company developing a proprietary, synthetic cannabinoid derivative to treat glaucoma and ocular hypertension, has completed dosing of SBI-100 Ophthalmic Emulsion ("OE") in the first cohort of healthy participants in the single ascending dose ("SAD") part of its Phase 1 study being conducted by CMAX Clinical Research in Adelaide, Australia.

The objective for this randomized, double-masked, placebo-controlled, single and multiple ascending dose study is to evaluate the safety, tolerability and pharmacokinetics of SBI-100 OE. Changes in intraocular pressure will also be evaluated. In this two-part study, a total of approximately 48 subjects are divided into three single ascending dose and three multiple ascending dose cohorts. In each cohort of eight participants, six will be administered SBI-100 OE and two placebo.

In the first SAD cohort, participants were administered a single topical dose of SBI-100 OE at a concentration of 0.5%. Participants are subsequently monitored for safety and tolerability over three days following dose administration. In the second and third cohorts of the SAD arm, participants will receive a single dose of SBI-100 OE at 1.0% and 2.0%, respectively. Recruitment of the second cohort will begin in January, with dosing planned for February.

"This first-in-human Phase 1 trial is a significant milestone for Skye and SBI-100 Ophthalmic Emulsion. We are pleased to complete this step of administering drug in our first study participants," said Punit Dhillon, CEO and Chair of Skye. "We believe there is substantial evidence that targeting the CB1 receptor in the eye can reduce intraocular pressure and potentially represents a new drug class to help treat patients with glaucoma. We look forward to seeing the safety, tolerability and other characteristics of this molecule in this study."

Skye announced that it had submitted an Investigational New Drug application for SBI-100 OE to the U.S. Food and Drug Administration on November 15, 2022. Once opened, the IND will allow the Company to conduct clinical trials in the United States. The Company intends to initiate a Phase 2 study in participants with primary open angle glaucoma and ocular hypertension in the United States in the first half of 2023.

About Glaucoma and SBI-100 Ophthalmic Emulsion

About 70 million people globally suffer from the debilitating effects of glaucoma, according to the Glaucoma Research Foundation and even more suffer from ocular hypertension, as

represented by the 3% of the US population reported by the British Journal of Ophthalmology. There is a need for a new class of drugs that relies on different mechanisms to affect disease progression.

Increased intraocular pressure (IOP) is a key risk factor in the progression of glaucoma. The first observations that consuming cannabis lowered IOP in humans took place in the early 1970s, which led to a significant amount of research on the effects of cannabinoids in the eye. Independent studies demonstrated that activation of the cannabinoid receptor-type 1 (CB1R) in ocular tissue mediates IOP-lowering. However, no cannabinoid-related drug has been approved for clinical use in the eye due primarily to the shortcomings of current delivery methods of CB1R agonists to the eye in a therapeutically beneficial dose. When cannabinoids are administered systemically, they can lower IOP but also result in undesirable psychotropic effects. In high doses they can also cause detrimental cardiovascular effects. Alternatively, extracted natural cannabinoids delivered topically as an eye drop do not penetrate ocular tissue well enough to effectively lower IOP, likely due to the lipophilic, or oily, properties of natural cannabinoids and the aqueous, or watery, surface of the eye.

To address these challenges, Skye is developing SBI-100 OE, a proprietary, synthetic cannabinoid derivative possessing a novel molecular structure and formulation that was rationally designed to enable better penetration of ocular tissue and effective topical delivery of a CB1R agonist. In preclinical studies involving three different species, a nanoemulsion formulation of the drug applied topically to the eye resulted in enhanced therapeutic efficacy and duration of response in lowering IOP. Importantly, these studies demonstrated advantages compared to today's standard of care that, if clinically validated in subsequent efficacy studies, may offer a suitable therapeutic window to be a new class of medicine for glaucoma.

About Skye Bioscience
Skye Bioscience is a pharmaceutical company unlocking the potential of cannabinoids through the development of its proprietary cannabinoid derivatives to treat diseases with significant unmet needs. The Company's lead program, SBI-100 OE, is focused on developing a treatment for glaucoma, the world's leading cause of irreversible blindness. For more information, please visit: www.skyebioscience.com.

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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.

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