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Skye Bioscience Receives Human Research Ethics Committee Approval to Start Multiple Ascending Dose Arm of Phase 1 Study of SBI-100 Ophthalmic Emulsion

San Diego, California--(Newsfile Corp. - March 15, 2023) - Skye Bioscience, Inc. (OTCQB: SKYE) ("Skye" or the "Company"), a pharmaceutical company developing a proprietary, synthetic cannabinoid derivative to treat glaucoma, reports that the human research ethics committee ("HREC") in Australia has approved the initiation of the multiple ascending dose ("MAD") arm of Skye's Phase 1 study of SBI-100 Ophthalmic Emulsion ("OE"). Skye expects to dose the first MAD cohort in April.

In a similar fashion to the single ascending dose ("SAD") arm (that has completed dosing), each of the three MAD cohorts will consist of eight healthy participants, six to be randomized to SBI-100 OE and two randomized to placebo. Participants receiving SBI-100 OE will receive drug concentrations of 0.5%, 1.0%, and 2.0% per respective cohort. Each participant in the MAD arm will be administered a topical dose of SBI-100 OE or placebo twice a day for five consecutive days and monitored for safety for approximately five days after the last dose administration. This differs from SAD's regimen of a single treatment followed by three days of safety monitoring.

In the SAD arm, 18 of 24 total participants across the three cohorts were dosed with SBI-100 OE. The study's safety review committee ("SRC") completed its review of the first two cohorts and determined that the drug was well-tolerated, with no drug-related serious adverse events and expected mild to moderate adverse events. During the review of cohort two, the SRC also agreed to the advancement of the study into the MAD arm. Although MAD cohort 1 has been approved by the SRC, the committee will meet and perform a comprehensive review of all SAD data.

"With HREC approval of our submission to advance our Phase 1 study into the multiple ascending dose arm, we are now lined up to start dosing in April the fourth of six total cohorts in this study of our novel synthetic cannabinoid derivative, SBI-100 Ophthalmic Emulsion," said Punit Dhillon, Chief Executive Officer and Chair of Skye.

About SBI-100 Ophthalmic Emulsion

Skye's SBI-100 OE represents a new class of therapeutic in the form of a proprietary, synthetic cannabinoid derivative possessing a novel molecular structure and formulation that was designed to enable better penetration of ocular tissue and effective delivery of a CB1R agonist into the eye. In preclinical studies involving three different species, a nanoemulsion formulation of the drug topically applied to the eye resulted in enhanced therapeutic efficacy and duration of response in lowering IOP. These studies demonstrated favorable attributes

of SBI-100 OE compared to today's standard of care for treating glaucoma. If clinically validated in future efficacy studies, the favorable attributes may offer a suitable therapeutic window to be a new class of medicine for glaucoma.

The first observations that consuming cannabis lowered IOP in humans occurred in the early 1970s, which led to 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 primarily due to the shortcomings of available 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 and other effects. Alternatively, extracted natural cannabinoids administered 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.

About Glaucoma

Over 60 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. Increased intraocular pressure (IOP) is a key risk factor in the progression of glaucoma. Approved drugs are often subject to growing patient tolerance to the drug and other side effects. There is a need for a new class of drug that relies on different mechanisms of action to affect these diseases.

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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