November 16, 2022

Skye Bioscience Initiates First-in-Human Phase 1 Clinical Trial for SBI-100

- **Recruitment for cohort 1 has begun**

- **Clinical trial material manufactured and shipped to Australia**

San Diego, California--(Newsfile Corp. - November 16, 2022) - Skye Bioscience, Inc. (OTCQB: SKYE) ("Skye" or the "Company"), a pharmaceutical company developing a proprietary, synthetic cannabinoid derivative to treat glaucoma, has initiated screening for its first-in-human Phase 1 trial of SBI-100 Ophthalmic Emulsion ("SBI-100 OE"). As previously announced, this study has received all regulatory approvals to initiate in Australia and will be conducted at CMAX Clinical Research, Skye's contract clinical trial unit in Adelaide, Australia.

The primary endpoints for this randomized, double-masked, placebo-controlled study are to assess safety and tolerability of the drug in healthy volunteers. The secondary endpoint is to assess pharmacokinetics. The study will also measure changes to intraocular pressure in the eye. A total of 48 subjects will be topically administered SBI-100 OE or placebo on a single eye in single ascending dose (SAD) and multiple ascending dose (MAD) arms. Eight participants will be enrolled in each of six total cohorts. In each cohort, six participants will be administered SBI-100 Ophthalmic Emulsion and two will receive placebo. Recruitment of participants for this study has begun and the first cohort is expected to be enrolled in December.

"The initiation of this first-in-human Phase 1 trial for SBI-100 OE marks an important milestone for Skye. It is also a milestone for the pharmaceutical industry since this is the first CB1 receptor agonist eye-drop entering into human studies. We have been finalizing the last steps to start enrollment and are now counting down to dosing the first cohort of study participants," said Punit Dhillon, CEO and Chair of Skye. "Our aim is to potentially offer patients with glaucoma a treatment alternative with improved outcomes and we are pleased to initiate our first clinical study in pursuit of that goal. The data obtained through this Phase 1 trial will be important to our future development plans for this program."

Since meeting regulatory requirements to begin the Phase 1 clinical study and completing clinical material production, as announced in prior news releases, Skye has worked closely with its contract manufacturers, DEA and other Australian regulatory authorities to ensure the appropriate permits were obtained to legally ship SBI-100 OE internationally for clinical trial purposes.

About SBI-100 Ophthalmic Emulsion

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. 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 developed 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 also demonstrated advantages compared to today's standard of care and, if clinically validated in subsequent efficacy studies, may provide 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.

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/144472

SOURCE Skye Bioscience, Inc.