October 25, 2023

Skye Bioscience Announces Positive Phase 1 Trial Results for SBI-100 Ophthalmic Emulsion, Its First-in-Class CB1 Agonist Being Developed for the Treatment of Glaucoma

• SBI-100 OE is well tolerated, with low rate of hyperaemia (8.4%)
• Reduced intraocular pressure (23% mean reduction) in healthy volunteers with higher baseline IOP (>17 mm Hg)

San Diego, California--(Newsfile Corp. - October 25, 2023) - Skye Bioscience, Inc. (OTCQB: SKYE) ("Skye" or the "Company"), a pharmaceutical company developing drugs targeting the endocannabinoid system, initially focused on the CB1 receptor to address glaucoma and metabolic conditions, is pleased to report successful results from its Phase 1 clinical trial assessing the safety and pharmacokinetics of SBI-100 Ophthalmic Emulsion ("OE"). This first-in-class cannabinoid type 1 receptor ("CB1") agonist, is a prodrug uniquely formulated as an eye drop, and is being developed as a potential new mechanism to address unmet needs in the treatment of glaucoma.

"Our Skye team is proud to have completed our first human trial of an ophthalmic drug targeting the CB1 receptor and accomplishing a major step on our journey to provide ophthalmology healthcare professionals, and their glaucoma patients, access to a new class of medicine," said Punit Dhillon, CEO and Chair of Skye. "There remain notable unmet needs in the treatment regimen for glaucoma. In particular, hyperaemia is a common side effect of anti-glaucoma therapy and is a major reason for patients discontinuing treatment with prostaglandin analogues. We believe that SBI-100 OE has a distinct potential role to play as a new mechanism for this disease."

Data from the Phase 1 clinical trial will be discussed in detail during the Company's virtual Investor Day, "CB1 Axis: Unlocking the Pharmaceutical Potential of the Endocannabinoid System", at 8:00am ET. To register, click here.

Summary of Trial Results

Hyperaemia

- One of 24 (4.2%) healthy volunteers in the single ascending dose ("SAD") arm and 2 of 24 (8.4%) in the multiple ascending dose ("MAD") arm of the SBI-100 OE study experienced hyperaemia, or red eyes.
- No participants receiving placebo experienced hyperaemia.

Safety and tolerability

- Discomfort/pain upon administration of SBI-100 OE was reported and any discomfort was transient and resolved on average in less than 15 minutes.
- SBI-100 OE was deemed safe, well-tolerated, with no drug-related serious adverse events and treatment-related adverse events were consistent with topically-applied eye treatments. No study participants dropped out due to SBI-100 OE.

Pharmacokinetics and systemic presence of THC in blood

- While SBI-100 OE was detected systemically, with exposures increasing with increasing concentrations of drug, no THC, the active pharmaceutical ingredient of SBI-100 OE, or its more psychoactive metabolite, 11-OH-THC, were detected in the plasma across all cohorts, except one patient in the 1.0% SBI-100 OE cohort.
- Lack of THC and 11-OH-THC detected in plasma support the minimal systemic side effects observed.

Intraocular pressure ("IOP") lowering

- No differences were observed in reducing IOP between placebo and active. The lack of meaningful reduction in IOP is possibly due to the low average baseline IOP in both groups.
- A subgroup analysis of study participants in the MAD arm with a higher baseline IOP, defined as 17mmHg or greater, was completed. Five of the 18 participants who were administered SBI-100 OE met this criteria. These study participants experienced a reduction in IOP ranging from 14%-31%, with a mean reduction of 23%. One participant with higher baseline IOP receiving placebo experienced IOP-lowering of 14%.

"On all counts, the results of this first human study of SBI-100 Ophthalmic Emulsion provide an encouraging outcome for the future of this program," said Tu Diep, Skye's Chief Development Officer. "These data suggest a beneficial safety profile compared to currently approved glaucoma drugs. Observing an incidence of hyperaemia below 10% could be a very important differentiating characteristic compared to competitive glaucoma drugs. Importantly, the lack of systemic side effects and generally nominal discomfort is very favorable."

"With respect to our evaluation of intraocular pressure, our primary goal was to monitor for increases in pressure resulting from drug administration to ensure the safety of our patients, and in this regard we did not see any increases in IOP. On the other hand, while meaningful reductions of intraocular pressure using IOP-lowering drugs are not generally expected in healthy populations, and while we must acknowledge that our evaluation of a higher-baseline-IOP subset of participants was not pre-specified in the trial design, we are encouraged by this first signal in humans that participants in the MAD arm with higher baseline IOP saw noticeable reductions in IOP. This is in line with historical research that has shown the ability of THC to lower intraocular pressure."

"Lowering intraocular pressure can prevent or reduce progression of disease in glaucoma and is accepted as an approvable clinical endpoint. We look forward to starting our placebo-controlled, double masked, randomized Phase 2a proof-of-concept study and reporting our first interim efficacy data in patients with elevated IOP early in 2024. We are also laying the groundwork for a Phase 2b study of SBI-100 OE compared to an active drug control, which

we plan to start later in 2024."

SBI-100 Ophthalmic Emulsion Trial Phase 1 Trial Design

- This Phase 1 trial was a randomized, double-masked, placebo-controlled study to evaluate the safety, tolerability and pharmacokinetics of SBI-100 OE with different dosing regimens in 48 healthy volunteers.
- Changes in intraocular pressure were measured to monitor for safety considerations.
- Participants were randomized into single ascending dose ("SAD") or multiple ascending dose ("MAD") arms, with three cohorts per arm and eight participants per cohort.
- In each cohort, six participants received SBI-100 OE and two placebo.
- SBI-100 OE was administered topically in one eye at ascending dose concentrations of 0.5%, 1.0% and 2.0% in the respective cohorts of the two arms.
- In the SAD arm, participants were administered a single dose per cohort.
- In the MAD arm, participants were administered a single dose in the morning and evening (approximately 12 hours later) for five days. They were monitored at the clinical research unit for a total of seven days (including the five days of dosing).

Next Steps: Initiation of SBI-100 OE Phase 2a Study

- SBI-100 OE Phase 2 will be a double-masked, randomized, placebo-controlled clinical study 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 compared to placebo in patients with elevated intraocular pressure.
- Data from the Phase 1 study support the use of 0.5% and 1.0% concentrations of SBI-100 OE. Patients will receive drug at these concentrations or placebo.
- Site initiation visits will be completed this week and patient enrollment is expected to begin in November.
- Interim analysis of intraocular pressure data is expected to be reported in Q1 2024 following completion of 50% of treated patients.

About SBI-100 Ophthalmic Emulsion

Skye's SBI-100 OE possesses a novel molecular structure and nanoemulsion formulation that were designed to enable effective topical delivery and better penetration of a CB1 agonist into ocular tissue. In preclinical studies involving three different species, the drug resulted in enhanced therapeutic efficacy and duration of response in lowering intraocular pressure, 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, initially through modulation of the CB1 receptor. Backed by leading biotechnology venture investors, Skye's strategy leverages biologic targets with substantial human proof of mechanism for the development of first- and only-in-class therapeutics with significant clinical and commercial differentiation. Nimacimab, a negative allosteric modulating antibody, inhibits peripheral CB1 with unprecedented safety and tolerability. Skye plans to start a Phase 2 basket study of nimacimab for cardio-metabolic disease, including an

assessment of obesity/weight loss, in Q1 2024. SBI-100 Ophthalmic Emulsion is a CB1 agonist that is a potential treatment for glaucoma; it will start Phase 2 in Q4 2023, with an interim data readout in Q1 2024. For more information, please visit: https://www.skyebioscience.com.

CONTACT

Investor Relations
ir@skyebioscience.com
(858) 410-0266

LifeSci Advisors, Mike Moyer
mmoyer@lifesciadvisors.com
617-308-4306

FORWARD-LOOKING STATEMENTS

This press release contains forward-looking statements, including statements regarding our product development, business strategy, 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/185167

SOURCE Skye Bioscience, Inc.