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Skye Bioscience Treats First Patient in Glaucoma Phase 2 Study of SBI-100 Ophthalmic Emulsion

- SBI-100 Ophthalmic Emulsion, a CB1 agonist/activator delivered as a topical eye drop, was developed to treat patients with elevated intraocular pressure
- Phase 2 study evaluating efficacy and safety using two concentrations of SBI-100 OE vs. placebo, dosing twice a day for 14 days
- Analysis of IOP data from 50% of patients enrolled in Phase 2 study to be performed in Q1 2024

SAN DIEGO, Nov. 28, 2023 (GLOBE NEWSWIRE) -- Skye Bioscience, Inc. (OTCQB: SKYE) ("Skye" or the "Company"), a pharmaceutical company developing drugs targeting the endocannabinoid system, focusing on glaucoma and metabolic conditions, has treated the first patient in its Phase 2 clinical trial evaluating SBI-100 Ophthalmic Emulsion's ("OE") ability to lower intraocular pressure ("IOP"), safety and relevant biomarkers, in patients with primary open-angle glaucoma ("POAG") or ocular hypertension ("OHT"). SBI-100 OE is a synthetic prodrug of tetrahydrocannabinol ("THC") that is able to bind and activate CB1 receptors in key ocular tissues.

"Skye's clinical pipeline targets the endocannabinoid system, which has seen growing development and M&A attention. We are advancing the next generation of investigational drugs targeting the endocannabinoid system's CB1 receptor," said Punit Dhillon, Skye's CEO and Chairman. "Key opinion leaders have indicated that there is a need for an alternative class of glaucoma medicine to serve patients that fail approved treatments and that potentially offers an improved safety profile. SBI-100 OE represents an opportunity to develop a first-in-class alternative with differentiated therapeutic characteristics. Following our encouraging Phase 1 results, we look forward to assessing initial Phase 2 IOP results in Q1 2024."

SBI-100 Ophthalmic Emulsion Phase 2 Study Design

- Double-masked, randomized, placebo-controlled study treating approximately 54 patients with elevated intraocular pressure (between 21mmHg and 36mmHg) diagnosed with POAG or OHT.
- Primary endpoints: assess change in diurnal IOP vs placebo, and ocular and systemic safety.
- Secondary endpoints: assess ocular hypotensive efficacy at individual time points and application comfort.
- Dosing: 0.5% or 1.0% concentrations of SBI-100 OE, or placebo.
- Patients will be treated with one drop in each eye, twice a day, in the morning and the evening (about 12 hours apart), for 14 days.
- Description of Phase 2 study on ClinicalTrials.gov:NCT06144918

"We have long been aware of THC's ability to lower intraocular pressure, however, the true

capabilities were confounded by the psychotropic effects of inhaled/ingested delivery. Localized ocular delivery via topical drop enables optimal evaluation with less risk of the systemic (psychotropic) effect, allowing for concise assessment of the IOP lowering potential," said Dr. David Wirta, MD, a principal investigator of this study. "This Phase 2 study provides an avenue to confirm IOP-lowering ability and advance the potential for SBI-100 OE in treating ophthalmic disorders. We are excited to be apart of the evolution of SBI-100's capabilities within the ophthalmic realm."

SBI-100 OE Phase 1 Trial Results

In October 2023, Skye reported data from its first clinical study of SBI-100 OE, with the following highlights:

- SBI-100 OE was deemed safe, well-tolerated, and no serious adverse events were reported (drug related and non-drug related).
- No participants dropped out due to SBI-100. Reported adverse events were consistent with topically applied eye treatments.
- Discomfort/pain after drop instillation was the most commonly reported adverse event, but was transient and resolved in less than 15 minutes.
- SBI-100 was detected in the blood, consistent with exposure dose concentration, however, none of the active ingredient (THC) and minimum amounts of the psychoactive metabolite (11-OH-THC) were detected. The lack of detection supports minimal systemic side effects.
- Low rate of hyperaemia (red eyes) of 8.4% compared to other leading classes of glaucoma drugs.
- Mean reduction of intraocular pressure of 23.9% in subset of healthy volunteers with higher baseline IOP (>17 mm Hg)

SBI-100 OE

SBI-100 OE is a synthetic THC prodrug which can cross the corneal membrane, where it is converted into tetrahydrocannabinol ("THC"). This active form of SBI-100 OE is able to bind and activate CB1 receptors in key ocular tissues, which may help to lower intraocular pressure in patients suffering from glaucoma and ocular hypertension.

Past studies have shown that activation of the CB1 receptor using THC is able to notably reduce intraocular pressure, but not without psychotropic and other side effects. SBI-100 OE's novel molecular structure and proprietary nanoemulsion eyedrop formulation was designed to enable topical delivery and enhance bioavailability of a CB1 agonist in ocular tissue. In preclinical studies involving three different species, SBI-100 OE lowered IOP to a level and duration that compared favorably to the standard of care for treating glaucoma. Skye's Phase 1 study of SBI-100 OE showed that the drug was safe and well-tolerated, with no psychotropic effects, and provided an encouraging preliminary indication of IOP-lowering in a subset of healthy volunteers with higher baseline IOP.

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, is planned to start a Phase 2 cardiometabolic-focused study encompassing obesity in H1 2024. SBI-100 Ophthalmic Emulsion, a CB1 agonist that is a potential treatment for glaucoma, is in a Phase 2 study. For more information, please visit: https://www.skyebioscience.com.

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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.

Source: Skye Bioscience, Inc.