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Skye Bioscience Highlights Novel Synthetic Cannabinoid-based Library Capable of Modulating the Endocannabinoid System to Treat Ocular Diseases at ARVO 2024 Annual Meeting

Poster presentation details screening approach allowing selection of candidate molecules applicable to dry eye disease and chronic ocular pain, with potential to identify therapeutic candidates with novel mechanisms of action for other ocular pathologies

SAN DIEGO, May 10, 2024 (GLOBE NEWSWIRE) -- Skye Bioscience, Inc. (Nasdaq: SKYE) ("Skye"), a clinical-stage biotechnology company focused on the discovery, development and commercialization of novel classes of therapeutic drugs that modulate the endocannabinoid system (ECS), today announced that it presented new data in a poster titled "Development and screening of a novel library of synthetic endocannabinoid agonists and inhibitors to advance a potential therapy to treat dry eye disease and chronic ocular pain" on May 9th at the ARVO (Association of Research in Vision and Ophthalmology) 2024 Annual Meeting.

"The endocannabinoid system offers unique opportunities to address unmet medical needs with new mechanisms of action. At ARVO we showcased Skye's development and screening of a novel library of synthetic agonists and inhibitors that could potentially fulfill some of these opportunities," said Punit Dhillon, Chief Executive Officer and Chairman of Skye.

Key highlights

a. Presented biological ECS screening program focused on pathways relevant to dry eye disease (DED) and chronic ocular pain
b. Three synthetic cannabinoid-based compounds relevant to DED and chronic ocular pain have been identified for further pharmaceutical development
c. Conclusion: a unique screening approach has the potential to provide a new class of therapeutics with novel mechanisms of action for the treatment of diverse ocular pathologies.

Chris Twitty, PhD, Chief Scientific Officer of Skye, added: "Skye's strategy is to develop advanced pharmaceutical drugs capable of modulating the endocannabinoid system to positively impact ocular pathologies. The study's evaluation of a novel synthetic cannabinoid-based library with biologically relevant cell types, targets, and pathways enabled the selection of candidate molecules applicable to DED and chronic ocular pain. Ultimately, we selected cannabinerol and two non-electrophilic indolic adducts of

cannabidiolquinone and cannabigeroquinone that warrant further interrogation and pharmaceutical development."

Study details

A rigorous *in vitro* screening platform based on modulation of pathways relevant to cannabinoid biology in the context of ocular pathologies was designed to interrogate a library of 98 synthetic cannabinoid-based molecules for their potential to treat ocular diseases. Immortalized human ocular cell lines and stable modified HEK cells were used to measure activation/inhibition of specific cannabinoid receptors, including CB1, CB2, GPR55, and TRPV1. The library was initially interrogated using a threshold of relevant biological activity. The resulting 38 compounds were scored based on EC_{50}/IC_{50} of signaling (CB1/2/TRPV1/PPARg/NF-kB) and inhibition of ROS and HIF-1a in human epithelial and endothelial (corneal/conjunctival) cells. These compounds were also interrogated for chemical/developability attributes, which helped provide the rationale for ultimately selecting three lead candidate molecules.

About Skye Bioscience

Skye is focused on unlocking the pharmaceutical potential of the endocannabinoid system to treat diseases with metabolic, inflammatory, and fibrotic 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 that inhibits peripheral CB1, showed a favorable safety and tolerability profile in a Phase 1 study. Skye plans to start a Phase 2 clinical trial in obesity comparing monotherapy and combination arms of Nimacimab and a GLP-1R agonist in mid-2024. Enrollment has been completed for a Phase 2 clinical trial of SBI-100 Ophthalmic Emulsion, a CB1 agonist currently being studied in patients with glaucoma and ocular hypertension. Topline data for this study is expected in Q2 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

Media Inquiries
LifeSci Communications, Michael Fitzhugh
mfitzhugh@lifescicomms.com
(628) 234-3889

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.

Source: Skye Bioscience, Inc.