May 5, 2022

Skye Bioscience Reports Enhanced Intraocular Pressure-Lowering of SBI-100 Formulation Published in Peer-Reviewed Journal

International Journal of Pharmaceutics reports advantageous performance of glaucoma drug candidate compared to standard of care in preclinical study

San Diego, California, May 05, 2022 (GLOBE NEWSWIRE) -- Skye Bioscience, Inc. (OTCQB: SKYE) ("Skye" or the "Company"), a pharmaceutical company developing proprietary, synthetic cannabinoid derivatives to treat glaucoma and other diseases with significant unmet need, announced that the peer-reviewed journal *International Journal of Pharmaceutics* published preclinical data demonstrating stronger and longer-lasting reduction of intraocular pressure (IOP) when Skye's proprietary molecule, SBI-100, is formulated as a nanoemulsion containing the mucoadhesive agent Carbopol® 940.

The results of the research were published March 2022 in a paper, "Impact of mucoadhesive agent inclusion on the intraocular pressure lowering profile of Δ9-tetrahydrocannabinol-valine-hemisuccinate loaded nanoemulsions in New Zealand white rabbits," authored by C. Sweeney et al. from the University of Mississippi (UM).

Skye, in collaboration with UM, previously published preclinical data demonstrating SBI-100 formulated as a nanoemulsion (THC-VHS-NE) achieved greater reduction of intraocular pressure in non-pigmented rabbits than both latanoprost and timilol[1], the current first and second line treatments for glaucoma, respectively. The current study was undertaken to determine if the inclusion of a mucoadhesive agent could prolong the intensity and duration of action of the THC-VHS-NE formulation through increased residence time or penetration, or both, to potentially achieve once- or twice- a day dosing.

In this study sponsored by Skye, researchers at the University of Mississippi compared the reduction of IOP in normotensive rabbits with a single treatment of THC-VHS-NEC (SBI-100 formulated as a nanoemulsion with Carbopol® 940) compared to latanoprost, the commercial standard of care; THC-NEC (native THC formulated as a nanoemulsion with Carbopol® 940); and THC-VHS-NE (SBI-100 formulated as just a nanoemulsion). When comparing each treatment group, THC-VHS-NEC, Skye's SBI-100 Opthalmic Emulsion, demonstrated the greatest intensity and duration of IOP-lowering.

"Skye has been working aggressively to optimize a formulation of SBI-100 to advance toward a first in-human study, which is planned to start this quarter. We previously reported strong preclinical results that highlighted the superior IOP-lowering of our unique molecule formulated as just a nanoemulsion compared to other established commercial glaucoma

drugs. This further evolution of our formulation, generating even more robust results, gives us strong conviction as we step into the clinic with SBI-100 Ophthalmic Emulsion," said Punit Dhillon, CEO and Chair of Skye.

"Our aim with this program is to advance a new class of glaucoma treatment with a once or twice a day dosing regimen. Positive, prior third-party research relevant to our molecule and this preclinical work informed our selection of the best formulation of SBI-100 for this application. We appreciate that these results are peer-reviewed by a recognized scientific journal."

In comparison to THC-VHS-NE, THC-NEC and commercial latanoprost, THC-VHS-NEC (SBI-100 Ophthalmic Emulsion) exhibited a prolonged duration of action. THC-NEC and THC-VHS-NE formulations respectively produced an average maximum drop in IOP of 3.7 mmHg at 60 minutes and 4.8 mmHg at 150 min, while the IOP-lowering effect lasted for 240 and 360 min, respectively, in the treated eye (Fig. 4). In contrast, SBI-100 Ophthalmic Emulsion lowered IOP by 4.5 mmHg at 60 min and maintained this drop for at least 480 min in the treated eye.

A significant difference ($p < 0.05$) in IOP-lowering was also observed between SBI-100 Ophthalmic Emulsion and commercial latanoprost ophthalmic solution. The average maximum drop in IOP with SBI-100 Ophthalmic Emulsion (THC-VHS-NEC) of 4.5 mmHg at 60 min was almost twice that obtained with commercial latanoprost ophthalmic solution (2.3 mmHg) at 60 min. Moreover, latanoprost maintained IOP 10% below baseline for only 360 min, whereas SBI-100 Ophthalmic Emulsion maintained the IOP- lowering effect for at least 480 min ($p < 0.05$).

[1] Sweeney, C., Dudhipala, N., Thakkar, R. et al. Effect of surfactant concentration and sterilization process on intraocular pressure–lowering activity of Δ9-tetrahydrocannabinol-valine-hemisuccinate (NB1111) nanoemulsions. Drug Deliv. and Transl. Res. 11, 2096–2107 (2021). https://doi.org/10.1007/s13346-020-00871-9
** SBI-100 has previously also been referred to as THCVHS and/or NB1111

About the University of Mississippi
The University of Mississippi, the state's flagship university, is among the elite group of R-1: Doctoral Universities - Highest Research Activity in the Carnegie Classification. The university has a long history of producing leaders in public service, academics, research and business. Its 15 academic divisions include a major medical school, nationally recognized schools of accountancy, law and pharmacy, and an Honors College acclaimed for a blend of academic rigor, experiential learning and opportunities for community action. Over 50 years ago, the university was awarded the first federal government contract to cultivate cannabis for research.

About Skye Bioscience
Skye Bioscience, Inc. is a pharmaceutical company unlocking the potential of cannabinoids through the development of its proprietary cannabinoid derivatives to treat diseases with significant unmet need. The Company's lead program, SBI-100, is focused on treating glaucoma, a disease with no cure and 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.

Source: Skye Bioscience, Inc.