May 17, 2021

Skye Bioscience's THCVHS Demonstrates Superior Therapeutic Benefit Compared to Glaucoma Standard of Care, both as Combination and Single Agent, in Preclinical Study

- THCVHS combined with netarsudil (Rhopressa®) achieves an average maximum intraocular pressure (IOP) reduction of 32.4% and maintains an average IOP reduction of 26.5% at 9 hours, significantly better than any single drug or combination tested
- THCVHS demonstrates superior IOP-lowering and duration relative to glaucoma standard of care, latanoprost

San Diego, Calif, May 17, 2021 (GLOBE NEWSWIRE) -- Skye Bioscience, Inc. (OTCQB: SKYE) ("SKYE" or the "Company"), a biopharmaceutical company developing proprietary, synthetic cannabinoid-derived molecules to treat glaucoma and other diseases with significant unmet need, announced that in a preclinical study assessing intraocular pressure (IOP)-lowering effects of its novel prodrug, THCVHS combined with netarsudil demonstrated the most significant IOP-lowering effects and duration of activity compared to all other tested single and combined treatments. Data from this study also highlighted THCVHS' superior IOP-lowering capability and duration of activity as a single agent compared to the current standard of care for the treatment of glaucoma, latanoprost.

Elevated IOP is a key risk factor in the progression of glaucoma and the result of fluid build-up in the anterior compartment of the eye. Although current therapies attempt to lower IOP by decreasing fluid production or increasing fluid drainage, many patients respond poorly to specific drugs, build tolerance, or do not experience sufficient lowering of IOP to slow disease progression. More than half of patients eventually require two or more drugs to adequately control their IOP. This leaves a significant need and opportunity for new drugs and classes of therapies, especially ones that increase the magnitude and duration of therapeutic effects.

Previous studies conducted with the University of Mississippi (UM) established that THCVHS decreased IOP significantly and over a longer duration than the top two commercially available treatments, latanoprost and timolol. Clinical evidence suggests that combining different classes of IOP-lowering drugs can provide additional benefit for some patients. This new study was designed, in collaboration with UM, to determine the benefit of combining THCVHS with other classes of IOP-lowering drugs, specifically a prostaglandin analogue (latanoprost) and a rho kinase inhibitor (netarsudil).

This study demonstrated that THCVHS combined with netarsudil achieved superior IOP-

lowering and durability compared to latanoprost. Latanoprost's average maximum IOP-lowering effect was 21.3% and it returned to baseline after 9 hours; THCVHS combined with netarsudil achieved an average maximum IOP-lowering effect of 32.4% and retained an average reduction in IPO of 26.5% at 9 hours. The data also showed superior IOP-lowering compared to netarsudil combined with latanoprost.

This study also reaffirmed THCVHS' superior ability to significantly lower IOP over a longer duration compared to latanoprost: THCVHS achieved an average maximum reduction in IOP of 27.5% and maintained an average reduction in IOP of 21.1% after 9 hours, at which point latanoprost had returned to baseline.

"Our group has had significant experience formulating THCVHS for a variety of therapeutic indications and continues to discover new therapeutic applications for this promising molecule," said Soumyajit Majumdar, PhD, Professor, Department of Pharmaceutics and Drug Delivery at University of Mississippi. "This study again highlights THCVHS' superiority as a single agent over latanoprost to lower intraocular pressure, including its ability to maintain a significant therapeutic effect beyond nine hours. Importantly, the data also suggests the potential to further enhance the intraocular-pressure-lowering capabilities of THCVHS by combining it with specific alternative classes of IOP-lowering drugs. We anticipate sharing the complete set of data as part of a manuscript to be submitted to a peer-reviewed academic journal."

"This new study provides positive new observations regarding THCVHS' potential to provide advantageous therapeutic benefits for patients, both as a single agent and combined with other drugs, and we plan to fully investigate these possibilities," said Punit Dhillon, Skye Bioscience, CEO. "These data suggest there is strong potential for THCVHS to be a once-a-day treatment, a desirable outcome for glaucoma treatments. With our recently announced progression on manufacturing and imminent toxicology studies, we continue our progress toward our first-in-human trial for THCVHS that is intended to start later this year."

Study design

This study was conducted in collaboration with the University of Mississippi using three in vivo groups. Each group received a single 50 µL dose of THCVHS, latanoprost or netarsudil once daily for the first five days and then a combination of two different drugs once daily for the next five days. In the combined drug study, the second drug was administered 15 minutes after administering the first drug. IOP was measured over the course of 24 hours on days 1, 3 and 5 using single drug treatment and days 6, 8 and 10 using combination drug treatment. The study was performed with the following treatment regimens:

Single Drug Regimens

- Group 1: THCVHS 1.0%
- Group 2: latanoprost 0.005%
- Group 3: netarsudil 0.02%

Combined Drug Regimens

- Group 1: THCVHS 1.0% followed by netarsudil 0.02%

- Group 2: latanoprost 0.005% followed by THCVHS 1.0%
- Group 3: netarsudil 0.02% followed by latanoprost 0.005%

About THCVHS
THCVHS, a proprietary prodrug of tetrahydrocannabinol (THC), is a topical ocular formulation under development to treat glaucoma. Developed with rational drug design and biochemical engineering, THCVHS is a proprietary synthetic molecule that enables local delivery of the drug into the eye and reduces the potential for systemic side effects. In preclinical studies, THCVHS demonstrated superior lowering of intraocular pressure, a major risk factor related to irreversible vision loss, compared to the standard-of-care glaucoma treatment.

About the University of Mississippi
The University of Mississippi, the state's flagship institution, 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.

UM's research interests include studies of the botanical, pharmacological and chemical properties of the cannabis plant. Since 1968, the marijuana research lab at University of Mississippi's School of Pharmacy has been the only facility in the United States permitted by the federal government's National Institute on Drug Abuse to cultivate cannabis for research purposes.

About Skye Bioscience
Skye Bioscience Inc. is a biopharmaceutical company unlocking the pharmaceutical potential of cannabinoids through the development of its proprietary, cannabinoid-derived molecules to treat diseases with significant unmet needs. The company's lead program, THCVHS, 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.

CONTACT
Karam Takhar
VP, Corporate Development & Investor Relations
Email: ir@skyebioscience.com
Phone: (858) 410-0266

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.