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Skye Bioscience Completes CMC and GLP Production for THCVHS Lead Program

- **Novel glaucoma drug ready for next development phase - GLP toxicology study – on critical path to first human clinical trial**
- **Ongoing development of THCVHS includes near-term preclinical comparison with and in combination with leading glaucoma treatments and an assessment of neuroprotective properties**

San Diego, Calif, April 22, 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, has established its Chemical, Manufacture and Controls (CMC) procedures for the production of THCVHS drug product suitable for Good Laboratory Practice (GLP) non-clinical research. This is a key step in advancing the Company’s planned Phase 1 study for its lead drug candidate, THCVHS, a novel prodrug of THC for the treatment of glaucoma.

“Our team has worked diligently to advance THCVHS into the clinic. CMC is an integral part of any drug development program that ensures pharmaceutical products are consistent between batches. While necessary for all drug development, having accomplished CMC is critical to ensure a new drug will be manufactured efficiently and effectively. Adding a pandemic into the equation adds complexity but finalizing the CMC process in this short timeframe is a testament to our team’s experience, expertise and shared passion to drive this program forward,” Punit Dhillon, Skye’s CEO and Chair.

CMC is an essential part of the drug development life cycle. CMC includes the development of specific manufacturing processes, establishment of product characteristics, as well as product testing and stability which must be defined before receiving approval to proceed with human studies. The CMC work established during the early stages of discovery and preclinical development will set the foundation for later stages of clinical development and will eventually be an important factor in marketing approval for a drug.

GLP toxicology studies are required by the Therapeutic Goods Administration (TGA), the Australian equivalent of the US Food and Drug Administration (FDA), and must be provided before moving into human testing. These data will also be a significant part of a future Investigational New Drug (IND) application with the FDA, which will allow the company to conduct a human trial in the United States.

“Now that we have successfully manufactured THCVHS drug product suitable for our GLP toxicology studies and at a scale we intend to use for our Phase 1 study, our selected contract research organization (CRO), Calvert Laboratories Inc, will initiate our planned GLP toxicology studies as soon as it is issued its pending Drug Enforcement Agency (DEA)

license for THCVHS. Next, our team will establish Good Manufacturing Practices (GMP), such as master batch records, operational controls, and facility specific procedures, to support our CMC in advance of producing clinical trial material for the Phase 1 study."

Additional Updates on the THCVHS Program

- Preclinical pharmacology studies of THCVHS in rabbits has been completed. These studies compared THCVHS' effect on intraocular pressure (IOP) versus netarsudil and latanoprost and evaluated the potential additive and synergistic effects of THCVHS with these agents. A manuscript is being drafted to summarize this data and the company looks forward to reporting results before the end of the quarter.
- Regulatory requirements for the neuroprotection study being conducted by the CRO, Experimentica UAB, have been received. The company is in the process of shipping drug material, which will allow for the CRO to initiate the study imminently.
- A genotoxicity study underway will validate that THCVHS has no effect on the genetic material of cells that may lead to mutations that could cause cancer. This is another data set required by the Australian TGA, as well as the US FDA, before receiving regulatory clearance to conduct human clinical trials.
- The company plans to initiate its first-in-human Phase 1 study of THCVHS for the treatment of glaucoma before the end of the year.

About THCVHS
THCVHS, a proprietary prodrug of tetrahydrocannabinol (THC), is a topical formulation under development to treat glaucoma. Through the application of rational drug design, Skye has chemically modified THC to create a unique synthetic molecule with the intent to safely realize the known positive effects of THC. THCVHS enables enhanced local delivery of the drug into the eye, reduced systemic side effects and the potential for neuroprotection. In preclinical studies, THCVHS demonstrated superior lowering of intraocular pressure, a key cause of vision loss, compared to the top commercially marketed classes of drugs that represent 80% of a nearly $7 billion global market opportunity. Skye expects key preclinical data in the first half of 2021 and initiation of its first-in-human Phase 1 study before the end of the year.

About Glaucoma and THCVHS
Glaucoma is a group of eye diseases that can cause vision loss and blindness by damaging the optic nerve in the back of the eye. Damage to the optic nerve can be caused by increased intraocular pressure (IOP) due to improper drainage and/or overproduction of fluid in the eye. There are over one million fibers that form the optic nerve. These can become damaged when rising pressure in the eye causes a direct crush injury or deprives these fibers of oxygen or nutrients from neighboring blood vessels. The damage is irreversible, leading to progressive vision loss and blindness if left untreated.

Currently approved therapies are focused on lowering IOP to sustain the nerve fibers and prevent a process of programmed cell death or apoptosis. These therapies are applied by eyedrop, with dosages ranging from once daily to up to three times per day, depending on the class of medicine used. The goal of these therapies is either to enhance drainage out of the eye or lower fluid production inside the eye.

Globally, more than half of those treated for glaucoma require two or more drug classes to manage their disease and are often referred to as a non-responder market. The elusive goal in managing glaucoma is going beyond just lowering IOP to also providing direct neuroprotection to these optic nerve cells to preserve vision.

Cannabinoids are also known to have neuroprotective qualities. Multiple third-party preclinical studies have proved the utility of cannabinoids, in particularly THC, in preventing programmed cell death of the cells forming the optic nerve.

The potential dual activity of THCVHS (lowering of IOP and potential for neuroprotection) would make it a valuable therapy not only for hypertensive glaucoma, which involves increased IOP, but also for patients with normotensive glaucoma, which does not involve elevated IOP, through direct neuroprotection of the optic nerve.

About the Glaucoma Market
Glaucoma is the leading cause of irreversible blindness globally, affecting nearly 80 million people and expected to increase to over 110 million people by 2040. It currently accounts for over $2.5 billion in pharmaceutical prescription sales in the US and projections estimate the worldwide market could exceed $11 billion by 2027 as the prevalence of this eye disease increases, especially in Asia. Current therapies focus on lowering intraocular pressure to help preserve retinal ganglion cells that form the optic nerve. The two major goals in developing a cannabinoid-based therapy for glaucoma are to not only lower intraocular pressure but exert a direct neuroprotective effect on the cells forming the optic nerve to preserve vision for affected patients, a capability that current drugs are unable to provide.

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. In preclinical studies, THCVHS, demonstrated intraocular pressure lowering capabilities in patients with glaucoma or elevated intraocular pressure that is superior to the current standard of care. For more information, please visit: 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.