

Skye Bioscience's Novel Cannabinoid Derivative Reduces Pain in Animal Model; Results Published in Scientific Journal

San Diego, California--(Newsfile Corp. - April 3, 2023) - Skye Bioscience, Inc. (OTCQB: SKYE) ("Skye" or the "Company"), a pharmaceutical company developing a proprietary, synthetic cannabinoid derivative to treat glaucoma, reports that in a preclinical study using one of its experimental cannabinoid-derivative molecules, cannabidiol monovalinate hemisuccinate ("CBD-Val-HS"), called SBI-200, researchers observed significantly decreased pain responses in relevant animal pain models.

In contrast to cannabidiol ("CBD"), treatment of mice with SBI-200 resulted in significant analgesic effects compared to saline placebo in two different animal pain models. Interestingly, in a hot plate model, SBI-200 yielded an anti-pain effect equivalent to an analgesic dose (3.0 mg/kg) of oxycodone. Additionally, in a second model that emulates acute visceral pain, SBI-200, although less effective than oxycodone, was additive across both sub-analgesic and analgesic doses of oxycodone, suggesting Skye's novel molecule may address pain via an alternate mechanism than opiate-based pain modifiers.

"This early-stage research shows that our novel derivative of CBD provided a positive pain-reducing effect alone as well as in combination with oxycodone. While oxycodone is considered the gold standard analgesic, particularly for acute pain, given its addictive nature and other side effects, a cannabinoid derivative such as SBI-200 may be a potential alternative or complementary pain modifier," said Punit Dhillon, Chief Executive Officer of Skye.

"Skye has significantly expanded its experimental work focused on engaging cannabinoid receptors pertinent to a myriad of important diseases and conditions. This study highlights another therapeutic area that the endocannabinoid system may positively modulate. Beyond systemic pain management, these data are also relevant to ophthalmologic pathologies that often require management of both neuropathic and nociceptive-based pain, which aligns with and further supports the advancement of Skye's R&D pipeline."

This research was conducted by researchers at the University of Mississippi, which licensed the development and commercialization rights to SBI-200. The results of this study were published in the scientific journal *Cannabis and Cannabinoid Research* in a paper titled, "Differential Effects of Cannabidiol and a Novel Cannabidiol Analog on Oxycodone Place Preference and Analgesia in Mice: an Opioid Abuse Deterrent with Analgesic Properties," Harris, Hanna et al, Volume 7, Number 6, 2022.

CBD-Val-HS is a proprietary analog of CBD that has demonstrated biological activity that is both pharmacologically and therapeutically distinct from CBD in various preclinical models.

About Skye Bioscience

Skye Bioscience is a pharmaceutical company unlocking the potential of cannabinoids through the development of its proprietary cannabinoid derivatives to treat diseases with significant unmet needs. The Company's lead program, SBI-100 OE, is focused on developing a treatment for glaucoma, the world's leading cause of irreversible blindness. For more information, please visit: www.skyebioscience.com.

CONTACT

Investor Relations

Email: ir@skyebioscience.com

Phone: (858) 410-0266

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.



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