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Skye Bioscience Demonstrates Prominent Role of Peripheral CB1 Inhibition and Achieves Significant Weight Loss with Novel CB1-inhibiting Antibody, Nimacimab, in Preclinical Model

Peripherally-restricted nimacimab achieves significant dose-dependent weight loss, fat mass reduction, lean mass preservation, and glycemic control in diet-induced obesity model

Preliminary data shows that nimacimab achieves desired metabolic outcomes without central inhibition and its risk of neuropsychiatric adverse events

SAN DIEGO, Nov. 04, 2024 (GLOBE NEWSWIRE) -- Skye Bioscience, Inc. (Nasdaq: SKYE) ("Skye"), a clinical-stage biopharmaceutical company focused on unlocking new therapeutic pathways for metabolic health, today announced preliminary data from a diet-induced obesity (DIO) model in mice. Skye's CB1-inhibiting antibody, nimacimab, achieved significant dose-dependent weight loss of up to 16% compared to vehicle, highlighting a novel peripherally-driven mechanism for inducing weight loss and other metabolic benefits.

Skye developed a DIO model using a transgenic mouse expressing the human CB1 receptor (hCB1R). After establishing this newly-developed model, the goal of this initial study was to assess the effects of its peripherally-targeting CB1 inhibitor on weight loss and other metabolic parameters. Five groups of mice were treated for 35 days with vehicle, 10 nmol/kg semaglutide, or nimacimab at 7.5 mg/kg, 24 mg/kg or 75 mg/kg, respectively. Key initial findings include:

- Dose-dependent weight loss with nimacimab of 4.5%, 11.4% and 16.0% compared to vehicle
- Significant fat mass loss with lean mass preservation
- Dose-dependent improvement in glucose tolerance.

Chris Twitty, PhD, Chief Scientific Officer of Skye, commented, "This is the first-ever reported assessment of an antibody-based peripherally-restricted CB1 inhibitor using a DIO model. These results are preliminary and we continue to refine this model, however, the data are very encouraging and provide the first direct evidence supporting our hypothesis that peripheral CB1 inhibition is the primary driver of weight loss whereas central CB1 inhibition contributes minimally to efficacy yet promotes neuropsychiatric adverse events. With this DIO model developed, we are continuing to assess different parameters and look forward to presenting further preclinical data in the future."

Puneet Arora, MD, Chief Medical Officer of Skye, said, "It is evident from the clinical studies of small molecule CB1 inhibitors that even modest exposure to the brain can cause

concerning neuropsychiatric adverse events. We believe that the promising data from these experiments combined with our Phase 1 data, which showed no significant neuropsychiatric adverse events, places nimacimab as the most promising candidate to realize the therapeutic potential of CB1 inhibition. We believe the mechanism of action of nimacimab is complementary to that of incretin mimetics such as GLP-1 receptor agonists. In addition, nimacimab offers the potential of a safe and well-tolerated alternative to the currently approved weight loss drugs."

Additional data will be presented during ObesityWeek and available as a recorded presentation on the Company's website under Investor Relations.

About Skye Bioscience

Skye is focused on unlocking new therapeutic pathways for metabolic health through the development of next-generation molecules that modulate G-protein-coupled receptors. Skye's strategy leverages biologic targets with substantial human proof of mechanism for the development of first-in-class therapeutics with clinical and commercial differentiation. Skye is conducting a Phase 2 clinical trial (ClinicalTrials.gov: NCT06577090) in obesity for nimacimab, a negative allosteric modulating antibody that peripherally inhibits CB1. This study is also assessing the combination of nimacimab and a GLP-1R agonist (Wegovy®). For more information, please visit: www.skyebioscience.com. Connect with us on X and LinkedIn.

CONTACTS

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 press release contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. 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. These forward looking statements include, but are not limited to: statements regarding our product development, statements regarding the superior safety and tolerability profile of nimacimab relative to other small molecule CB1 inhibitors, statements relating to any expectations regarding the safety, efficacy, tolerability or dosing of nimacimab, including based on Skye's DIO model, statements regarding the ability of

nimacimab to treat obesity or related indications, statements regarding the timing of receipt of interim and final data from Skye's Phase 2 obesity study of nimacimab, as well as additional preclinical data, and statements regarding the therapeutic potential of antibody-based peripherally-restricted CB1 inhibitors. 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. 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 Company's periodic filings with the Securities and Exchange Commission, including in the "Risk Factors" section of Skye's most recent Annual Report on Form 10-K and Quarterly Report on Form 10-Q. Except as expressly required by law, Skye disclaims any intent or obligation to update these forward-looking statements.

Source: Skye Bioscience, Inc.