January 9, 2024

Skye Bioscience Receives IND Clearance for Phase 2 Clinical Trial of Nimacimab in Obesity and Chronic Kidney Disease

Phase 2 trial to assess impact of peripherally-acting CB1 inhibitor on weight loss and metabolic biomarkers related to co-morbid obesity and chronic kidney disease

San Francisco, California--(Newsfile Corp. - January 9, 2024) - Skye Bioscience, Inc. (OTCQB: SKYE) ("Skye" or the "Company"), a pharmaceutical company developing drugs targeting the endocannabinoid system, has received clearance of its Investigational New Drug ("IND") application with the U.S. Food and Drug Administration ("FDA") to initiate a Phase 2 clinical trial of nimacimab in patients with obesity and chronic kidney disease. Skye plans to initiate the Phase 2 trial in mid-2024.

Nimacimab is a negative allosteric-modulating antibody targeting the cannabinoid 1 receptor ("CB1"), which has been implicated as an important target in cardiometabolic diseases including obesity and renal complications. The high correlation of these comorbid conditions, with 80% of patients with kidney disease being obese and 30% of obese patients having kidney disease, represents an opportunity for a mechanism that can affect their common underlying disease processes.

Nimacimab was observed to have very limited accumulation in the CNS in pre-clinical studies, a safety issue in earlier generations of CB1 inhibitors. Safety and tolerability assessments from the completed Phase 1b study of nimacimab in non-alcoholic fatty liver disease ("NAFLD") patients with diabetes or prediabetes demonstrated no serious adverse events, no early terminations of treatment due to adverse events, and no adverse events of concern occurring in a dose-dependent manner. Encouraging trends were observed in exploratory biomarkers including cholesterol, liver enzymes and liver function in patients receiving nimacimab versus placebo after the four-week dosing period. Moreover, pharmacokinetic assessment of nimacimab highlighted a half-life of approximately three weeks, potentially allowing for monthly dosing, which would offer a competitive advantage over once-a-week subcutaneous dosing of current peptidic GLP-1 receptor agonists.

Additionally, third-party research has strongly indicated the role of CB1 inhibition in modifying insulin and leptin sensitivity, preserving lean mass, and ultimately augmenting durability of weight loss. With nimacimab's differentiated characteristics, this novel molecule may provide an important alternative as a single or combination therapy targeting obesity and other metabolic, inflammatory and fibrotic conditions.

"We believe that the encouraging safety profile of nimacimab from preclinical and clinical studies exceeds that of small molecule CB1 inhibitors and that this class of drug offers the potential to treat a range of metabolic conditions," said Tu Diep, Chief Development Officer of Skye. "We look forward to evaluating multiple meaningful clinical endpoints in the Phase 2 trial, including weight loss, changes in albuminuria related to kidney function, and other

biomarkers, in order to guide the future development of nimacimab."

"With the growth of GLP-1 agonists we are also seeing large pharmaceutical companies acquiring drugs with complementary mechanisms of action to treat obesity," said Punit Dhillon, CEO and Chair of Skye. "We see peripheral CB1 inhibition playing a strong role in future combination therapies and are advancing nimacimab as a key possible component of such combinations."

About the Endocannabinoid System and Peripheral CB1 Inhibition for Weight Loss

The endocannabinoid system ("ECS") has emerged as one of the most relevant regulators of energy balance. The ECS acts through two cannabinoid receptors: types 1 and 2 (CB1 and CB2). CB1 is widely expressed in the CNS and brain but is also expressed in peripheral tissues such as adipose tissue, skeletal muscle, and in the liver, kidney, gut, and pancreas. In obese states, CB1 agonists such as anandamide (AEA) and 2-arachidonoyl-glycerol (2-AG), the body's naturally-produced endocannabinoids, are increased and may exert unfavorable effects on insulin-sensitive tissues. Peripheral inhibition of CB1 has been shown to cause a reduction in food intake and sustained weight loss through multiple mechanisms, including increasing incretin expression in the gut and reducing ghrelin expression. The ECS also contributes to the control of lipid and glucose metabolism, and it is well established that blockade of CB1 receptors enhances insulin sensitivity in both humans and rodents.

Clinically, early development of small molecule drugs that blocked CB1 appeared encouraging with the approval of rimonabant (Sanofi) in Europe for weight loss and obesity. However, it was soon removed from the market because of side effects related to the high exposure of the drug to the CNS and brain, which resulted in safety issues such as depression, anxiety and suicidal ideation. A new class of drugs are now designed to only target CB1 in the periphery, while avoiding the CNS.

About Nimacimab

Nimacimab is a first-in-class humanized monoclonal antibody that acts as a negative allosteric modulator to inhibit CB1 signaling in the periphery. Inhibition of CB1 has shown anti-fibrotic, anti-inflammatory, and metabolic mechanisms of action with potential to address a broad range of diseases with notable unmet medical needs such as obesity, chronic kidney disease, and non-alcoholic steatohepatitis (NASH).

Preclinical studies over 26 weeks showed that nimacimab has very limited accumulation in the brain.

The safety and tolerability assessments from the completed Phase 1b study of nimacimab in non-alcoholic fatty liver disease ("NAFLD") patients with diabetes or prediabetes demonstrated no serious adverse events, no early terminations of treatment due to adverse events, and no adverse events of concern occurring in a dose-dependent manner. The most frequently reported treatment-emergent adverse events (>5% of subjects) in the pooled nimacimab and placebo groups were diarrhea, headache, dizziness (9.5 vs. 5.0%), upper respiratory tract infection, nausea and vomiting. Encouraging trends were observed in exploratory biomarkers of cholesterol, liver enzymes and liver function in patients receiving nimacimab versus placebo after the three-week dosing period.

The promising PK data of approximately 21 days from the Phase 1 study suggests that nimacimab can be dosed once-a-month subcutaneously, which would potentially offer a competitive advantage over once-a-week subcutaneous dosing of current peptidic GLP-1 receptor agonists or even orally dosed GLP-1 receptor agonists due to their less desirable tolerability profile.

About Skye Bioscience

Skye is focused on unlocking the pharmaceutical potential of the endocannabinoid system to treat diseases with inflammatory, fibrotic, and metabolic processes. Backed by leading life science venture investors, Skye's strategy leverages biologic targets with substantial human proof of mechanism for the development of first-in-class therapeutics with significant clinical and commercial differentiation. Nimacimab, a negative allosteric modulating antibody that inhibits peripheral CB1, showed a favorable safety and tolerability profile in a Phase 1 study. Skye plans to start a Phase 2 study in obesity and chronic kidney disease for nimacimab in mid-2024. SBI-100 Ophthalmic Emulsion, a CB1 agonist, is currently being studied in a Phase 2 study of patients with glaucoma and ocular hypertension. For more information, please visit: https://www.skyebioscience.com.

CONTACT

Investor Relations
ir@skyebioscience.com
(858) 410-0266

LifeSci Advisors, Mike Moyer
mmoyer@lifesciadvisors.com
617-308-4306

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.

To view the source version of this press release, please visit
https://www.newsfilecorp.com/release/193647

SOURCE Skye Bioscience, Inc.