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Skye Bioscience Launches Phase 2 CBeyond Clinical Trial of its Differentiated CB1 Inhibitor, Nimacimab, in Patients with Obesity

CBeyond™ will assess nimacimab's ability to safely induce weight loss, and will also evaluate a combination of a GLP-1 receptor agonist plus nimacimab

SAN DIEGO, Aug. 22, 2024 (GLOBE NEWSWIRE) -- Skye Bioscience, Inc. (Nasdaq: SKYE) ("Skye"), a clinical-stage biopharmaceutical company focused on unlocking new therapeutic pathways for metabolic health, has started screening patients for a Phase 2 clinical trial (*CBeyond*™) of its novel peripheral CB1 inhibitor, nimacimab, a negative allosteric modulating antibody. The study will assess the ability of nimacimab as a next-generation weight loss therapeutic to safely and effectively reduce weight in patients with obesity. It will assess parameters increasingly viewed as important to the long-term quality and/or sustainability of weight loss, including gastrointestinal tolerability (GI) and lean mass retention.

"There is clearly a need for alternative mechanisms of action that can provide physicians and patients with improved overall health outcomes in the pursuit of weight loss beyond those achieved with GLP-1 and GIP drugs. We believe that peripheral CB1 inhibition, and nimacimab, a unique biologic drug within the class, have attributes that may help provide such outcomes, and we look forward to our goals of reporting interim data from this Phase 2 obesity trial in Q2 of 2025 and final data in Q4 of 2025," said Punit Dhillon, Chief Executive Officer of Skye. "CB1 inhibition research has shown its potential to directly promote energy expenditure and fat breakdown[1], improve leptin sensitivity[2] , and peripherally modulate hunger and satiety [3]. We are pleased to be assessing nimacimab as a monotherapy but to also undertake a preliminary evaluation of our peripheral CB1 inhibitor in combination with a GLP-1 drug."

"As we evaluate CB1 inhibition as a possible alternative mechanism for weight loss, we believe it is important to consider health outcomes beyond GI intolerance and muscle loss, such as neuropsychiatric adverse events, that may compromise the long-term use of these drugs that is necessary for sustainable results," added Tu Diep, Chief Development Officer of Skye. "The first-generation CB1 inhibitor, rimonabant, was a small molecule that acted on the CNS. While showing efficacy in reducing weight [4], it also indicated dose-related psychiatric adverse events [5] including anxiety, depressed mood, depression and suicidality. Current second-generation CB1 inhibitors, small molecules that may be more peripherally restricted than rimonabant, continue to show accumulation in the brain[6] in preclinical models, which suggest a potential lingering safety issue with this approach. Nimacimab, a

monoclonal antibody (large molecule), is significantly more restricted from the brain[7] and there were no psychiatric adverse events in our preclinical studies[7] or Phase 1 study[7] in patients with nonalcoholic fatty liver disease (NAFLD). We believe that nimacimab's positive safety and tolerability profile places Skye at a competitive advantage over small molecule CB1 inhibitors."

"We are most honored to participate in this study of nimacimab as an adjunct therapy for the treatment of obesity. This innovative approach, targeting the CB1 receptor, is a logical next step following the results in promising early trials," said Harold Edward Bays, MD, Medical Director/President of Louisville Metabolic and Atherosclerosis Research Center/Your Body Goal. "We hope investigations into this additional mechanism of action will ultimately broaden the treatment options for patients living with obesity."

CBeyond™ Phase 2 Clinical Trial Design

The clinical trial protocol for this Phase 2 study of nimacimab consists of the following elements:

- 120 patients across four treatment groups will be enrolled.
    - 80 patients will receive either nimacimab 200 mg or nimacimab-matching placebo subcutaneously once-weekly in a double-blinded design.
    - 40 patients will receive either nimacimab + Wegovy® or nimacimab-matching placebo + Wegovy® once-weekly in a partially-blinded design. Wegovy® will be administered once-weekly according to the prescribing information, up to a maximum weekly dose of 2.4 mg.
- Patients will be treated for 26 weeks and further evaluated for an additional 13 weeks.
- Primary endpoint: evaluation of weight loss in the nimacimab arm vs. placebo. Designed to detect a difference in mean weight loss of 8% between active and placebo with 80% power.
- Secondary endpoints: safety and tolerability; neuropsychiatric and cognitive evaluation; change in body composition by dual-energy X-ray absorptiometry (DEXA).
- Exploratory endpoints: change in key metabolic parameters including triglycerides, insulin sensitivity, and leptin sensitivity; evaluation of combination of nimacimab and Wegovy®; evaluation of difference in weight loss between nimacimab and Wegovy®; evaluation of difference in body composition between nimacimab and Wegovy®; improvement in sleep.
- The study will evaluate patients with obesity (≥ 30 kg/m2 to ≤ 45 kg/m2) OR overweight (≥ 27 kg/m2 and < 30 kg/m2) with clinically confirmed diagnosis of at least one of the following weight-related co-morbidities: dyslipidemia, cardiovascular disease, obstructive sleep apnea (OSA) syndrome, or controlled arterial hypertension, among other inclusion criteria.
- A subset of 40 patients encompassing all arms of the study will additionally be assessed for sleep quality by EEG quantification of sleep patterns. Disruptions in sleep quality can be associated with sleep apnea, a condition for which obesity is a major risk factor. Multi-night data will be collected following screening, and in weeks 13, 26, and the follow-up period. Data will be collected and assessed using Beacon Biosignal's FDA 510(k)-cleared Dreem Headband and its advanced sleep monitoring technology platform.

- Patients with diabetes will be excluded.
- This study is being conducted at 18 clinical trial sites in the U.S.
- Interim data will be reported after 50% of enrolled patients have completed the treatment period. Final data will be reported following completion of treatment and follow-up of all enrolled patients.

1 Ruiz de Azua et al., J Clin Invest. 2017
2 Tam et al., JCI. 2010; Tam et al., Cell Metabolism 2012
3 Tam et al., JCI. 2010; Tam et al., Cell Metabolism 2012
4 RBC Capital Markets (February 2024); Després et al., NEJM. 2005
5 FDA Briefing Document, NDA 21-888, Zimulti (rimonabant) Tablets, 20 mg, Sanofi Aventis, Advisory Committee – June 13, 2007
6 Liu et al., ACS Pharmacol Transl Sci. 2021.
7 Skye data.

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 unmet medical needs such as obesity, chronic kidney disease, and metabolic dysfunction-associated steatohepatitis (MASH).

In July 2024 Skye conducted an Obesity KOL event with key opinion leaders and Skye management which highlighted the mechanisms of peripheral CB1 inhibition and the attributes and potential role of nimacimab in the obesity therapeutic landscape. The presentation and a replay of the call are available on the Company's website.

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 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: https://www.skyebioscience.com. Connect with us on X and LinkedIn.

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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, including statements regarding our product development, business strategy, the timing of clinical trials, the timing of receipt of interim and final data and the therapeutic potential of our therapeutic candidates. 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 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.