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Skye Bioscience Treats First Patient in Nimacimab Higher-Dose Expansion Study Evaluating Exposure-Response to Inform Phase 2b Dose Selection for GLP-1 Combination Development

Topline safety and pharmacokinetic data expected in Q4 2026; an independent Data Monitoring Committee is overseeing the study

SAN DIEGO, April 02, 2026 (GLOBE NEWSWIRE) -- Skye Bioscience, Inc. (Nasdaq: SKYE) ("Skye") a clinical-stage biotechnology company focused on unlocking new therapeutic pathways for obesity and other metabolic health disorders, has treated the first patient in its Part C expansion study of the CBeyond Phase 2a trial to characterize safety and pharmacokinetics (PK) at exposures designed to challenge the peripheral restriction of nimacimab through intravenous (IV) administration over 16 weeks of treatment. These doses will set the benchmark for the safety profile of nimacimab and support higher dosing in combination with incretin therapies.

The expansion study comprises two cohorts of nimacimab monotherapy (400 mg IV and 600 mg IV) compared to placebo administered weekly over 15 weeks (16 doses), with a 12 week follow-up period, to generate preliminary safety and PK data with administration of higher doses. Based on the Company's translational work, 400 mg IV and 600 mg IV correspond to approximately ~700 mg and 1,000 mg subcutaneous dosing, respectively, and are projected to achieve substantially higher peripheral tissue exposure than the 200 mg subcutaneous dose tested in the Phase 2a study. Within each dose cohort, 8 participants will be randomized in a 3:1 ratio to nimacimab (n=6) or placebo (n=2). Enrollment in Cohort 2 (600 mg IV) is contingent on a favorable safety review of the first participants completing four weeks of treatment in Cohort 1 (400 mg IV) by an independent Cohort Review Committee. We expect to report topline data from the expansion study in the fourth quarter of 2026.

"The data generated over the past year have sharpened our understanding of nimacimab's dose-response relationship and strengthened the case for higher-exposure evaluation," said Punit Dhillon, President and CEO of Skye. "In combination with semaglutide, nimacimab demonstrated 22.3% mean weight loss at 52 weeks with no plateau observed, clean tolerability, and a differentiated body-composition and weight-maintenance profile - all at what we now believe was a suboptimal dose based on our biodistribution work showing that peripheral tissue exposure, not serum levels alone, drives efficacy. Part C is designed to test that thesis directly: if higher exposure produces the expected PK step-up while preserving the CNS-sparing safety profile, we will have a substantially stronger basis for Phase 2b dose selection."

Mr. Dhillon continued, "We have received written feedback from the FDA in response to our

Type C meeting request, which addressed our proposed Phase 2b clinical trial design including dose, treatment duration, endpoints, and patient selection criteria for a potential add-on development path with incretin therapy. We are using this regulatory input alongside our ongoing data analysis to refine the Phase 2b protocol. Final trial design and timing remain subject to the outcome of the Part C data, completion of our regulatory review, and capital considerations."

Clinical Context

Part C follows the completion of the Phase 2a CBeyond trial and its extension, which evaluated nimacimab at 200 mg subcutaneous weekly as both monotherapy and in combination with semaglutide (Wegovy® 2.4 mg). Key findings from the completed study program include: 22.3% mean weight loss at 52 weeks in the combination arm with no plateau observed; statistically significant improvements in waist circumference and lean-to-fat mass ratio versus semaglutide alone at 26 weeks; over 50% reduction in weight regain during the 13-week off-treatment follow-up period in the combination cohort versus semaglutide alone; and no drug-related neuropsychiatric adverse events in any treatment arm through the full study period. Nimacimab monotherapy at 200 mg weekly produced modest weight loss, which the Company attributes to insufficient peripheral tissue exposure based on subsequent translational analysis. Part C is designed to resolve this exposure question at doses modeled to approach or achieve the peripheral target-engagement threshold.

About Nimacimab

Nimacimab is a potential first-in-class, peripherally-restricted monoclonal antibody inhibitor of the CB1 receptor. Unlike previous CB1-targeting drugs, nimacimab is designed to avoid central nervous system penetration, potentially limiting neuropsychiatric side effects seen with small-molecule antagonists. As a non-incretin, non-peptide agent, nimacimab acts independently of the GLP-1 pathway and has demonstrated additive effects in combination with semaglutide in the Phase 2a CBeyond trial. The Company is developing nimacimab as a potential orthogonal add-on therapy for patients with obesity who are experienced on or have plateaued with GLP-1-based treatment, targeting clinically meaningful incremental weight loss, improved body composition, and reduced weight regain without added gastrointestinal or neuropsychiatric burden.

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 2a clinical trial (ClinicalTrials.gov: NCT06577090) in obesity and overweight 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.

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FORWARD LOOKING STATEMENTS

This press release includes “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this press release other than statements of historical fact should be considered forward-looking statements, including, without limitation, statements relating to: the potential for higher dosing of nimacimab to achieve increased efficacy; the potential for the combination of nimacimab and semaglutide to deepen weight loss and mitigate weight rebound; the potential for future weight loss beyond 52 weeks; plans to advance nimacimab into the next stage of development to optimize dosing; future clinical development of nimacimab, including the initiation and design of any future clinical trials; the expected timing for reporting topline data from the Phase 2a extension study; the ability of nimacimab to drive weight loss without neuropsychiatric and other adverse events; the potential for nimacimab to be a first-in-class drug; the potential for Skye to develop a leading orthogonal platform to intensify incretin outcomes and help patients achieve more durable metabolic benefit; the commercially competitive nature of nimacimab combined with semaglutide; and the potential for nimacimab to be a long term option in obesity and related metabolic diseases. When used herein, words including “anticipate,” “believe,” “can,” “continue,” “could,” “designed,” “estimate,” “expect,” “forecast,” “goal,” “intend,” “may,” “might,” “plan,” “planning,” “possible,” “potential,” “predict,” “project,” “should,” “target,” “will,” “would” and similar expressions are intended to identify forward-looking statements, though not all forward-looking statements use these words or expressions. All forward-looking statements are based upon Skye’s current expectations and various assumptions. Skye believes there is a reasonable basis for its expectations and beliefs, but they are inherently uncertain. Skye may not realize its expectations, and its beliefs may not prove correct. Actual results could differ materially from those described or implied by such forward-looking statements as a result of various important risks and uncertainties, including, without limitation, the initiation and design of any future clinical trials will be impacted by Skye’s capital resources, Skye’s ability to obtain additional sources of capital needed to run an additional Phase 2 clinical trial, program considerations and potentially other factors outside the Skye’s control; the potential for additional weight loss after 52 weeks may not ultimately be observed; there is no guarantee that higher dosing of nimacimab will achieve increased efficacy, and likewise it is possible that higher dosing will produce adversely different safety and tolerability results than those observed to date; Skye’s dependence on third parties in connection with product manufacturing; research and preclinical and clinical testing; Skye’s ability to advance, obtain

regulatory approval of and ultimately commercialize nimacimab, competitive products or approaches limiting the commercial value of nimacimab; the timing and results of preclinical and clinical trials; Skye's ability to fund development activities and achieve development goals; the impact of any global pandemics, inflation, supply chain issues, government shutdowns, high interest rates, adverse regulatory changes; Skye's ability to protect its intellectual property; risks associated with Skye's common stock and the other important factors discussed under the caption "Risk Factors" in Skye's filings with the Securities and Exchange Commission, including in its Annual Report on Form 10-K for the year ended December 31, 2024, which are accessible on the SEC's website at www.sec.gov and the Investors section of Skye's website. Any such forward-looking statements represent management's estimates as of the date of this press release. While Skye may elect to update such forward-looking statements at some point in the future, except as required by law, it disclaims any obligation to do so, even if subsequent events cause Skye's views to change. These forward-looking statements should not be relied upon as representing Skye's views as of any date subsequent to the date of this press release.

Source: Skye Bioscience, Inc.