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Skye's CB1 Inhibitor, Nimacimab, Demonstrates Superior Weight Loss and Differentiated Mechanisms from Monlunabant, and Continues to Show Enhanced Combination with Tirzepatide with Durable Post-Treatment Weight Maintenance in DIO Model

- **Skye shares new preclinical DIO data at virtual KOL event**
- **Nimacimab + tirzepatide demonstrates over 40% weight loss in multiple preclinical DIO studies**
- **Nimacimab demonstrates durable post-treatment weight loss compared to tirzepatide**
- **Nimacimab reduced rebound weight gain following treatment with tirzepatide or nimacimab + tirzepatide**
- **Nimacimab outperformed monlunabant head-to-head, and is uniquely positioned as a well-tolerated therapeutic to potentially induce healthier and sustained weight loss, both as a monotherapy, combination and maintenance therapy**
- **Top-line data from Phase 2 CBeyond^{TM} study expected to be reported in late Q3/early Q4 2025**

SAN DIEGO, Sept. 04, 2025 (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, today reported results from two new preclinical diet induced obesity mouse (DIO) studies evaluating nimacimab, a peripherally-acting CB1-inhibiting monoclonal antibody. The first study measured the efficacy and weight regain dynamics ("rebound") of monlunabant, a small molecule CB1 inhibitor, versus nimacimab, and demonstrated similar or better weight loss than monlunabant, while showing a superior post-treatment maintenance of weight loss, reinforcing a potentially differentiated mechanism. The second study re-evaluated the combination of nimacimab, this time with both optimal and sub-optimal doses of tirzepatide, and continued to show enhanced weight loss effects compared to tirzepatide alone, while also limiting rebound after treatment with tirzepatide is stopped. Importantly, these studies position nimacimab as a potential stand alone, combination and maintenance therapy in the obesity drug development landscape.

Key takeaways from Skye's preclinical DIO data readouts:

1. **Nimacimab is differentiated from monlunabant** As a truly peripherally restricted

CB1 inhibitor which has potential to have a superior safety and tolerability profile compared to the small molecules like monlunabant, these preclinical DIO studies have shown that nimacimab can potentially not only drive weight loss similar to, if not better than, monlunabant, but also shows a differentiated post-treatment weight maintenance profile that suggests potential broader metabolic effects beyond reduced calorie intake.

2. **Nimacimab enhances weight loss when combined with tirzepatide**: when combined with both low-dose and high-dose tirzepatide, nimacimab has demonstrated in multiple preclinical DIO studies that it can result in 40%+ weight loss.
3. **Nimacimab blunts rebound following treatment with tirzepatide**: There is significant weight regain when treatment with tirzepatide is ended. Nimacimab has demonstrated an ability to blunt this "rebound" effect by over 50% in preclinical DIO models.

"These two new in vivo studies advance a clear story: nimacimab can potentially both amplify and sustain weight loss, amplify in combination with GLP-1 therapy, and potentially sustain by limiting rebound when treatment is ended," said Punit Dhillon, Chief Executive Officer of Skye. "We believe the ability to switch to or maintain nimacimab after GLP-1 treatment aligns with real-world needs where durability and adherence remain critical due to a variety of factors including GI tolerability of the incretin-based anti-obesity medicines."

"Mechanistically, we see what peripheral CB1 inhibition should deliver - improved metabolic homeostasis with less compensatory rebound with treatment withdrawal," said Chris Twitty, Ph.D., Chief Scientific Officer. "Notably, nimacimab compared favorably to monlunabant promoting more durable weight loss upon treatment discontinuation, reinforcing our differentiation versus small-molecule CB1 approaches."

Skye will review these findings during its KOL event today, September 4, 2025 (webcast), where academic and clinical experts will discuss how combining and sequencing peripherally-acting CB1 antagonism with GLP-1s could improve the magnitude, tolerability, and maintenance of weight loss.

Detailed slide decks and figure sets for the two new pre-clinical studies, the repeat DIO combination/maintenance study of nimacimab with tirzepatide and the in vivo nimacimab dose-titration study versus monlunabant, along with additional nimacimab pre-clinical data with voiceover are available on Skye's website under the Spotlight page.

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 2a 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.

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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. 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,” “potential” or the negative of these terms or other comparable terminology. These forward looking statements include, but are not limited to: statements relating to any expectations regarding the efficacy and therapeutic potential of nimacimab as a monotherapy or in combination with a GLP-1 targeted drug or other incretin drugs, statements regarding the potential of CB1 inhibition to address certain unmet needs of patients on GLP-1 weight loss drugs, statements regarding the timing of receipt of data from Skye’s Phase 2a obesity study, including its extension study, statements regarding the ability of nimacimab to perform in humans in a manner consistent with preclinical DIO data, statements regarding the potential market opportunities of nimacimab and statements regarding nimacimab’s potential to have a superior safety and tolerability profile compared to the small molecules like monlunabant,. 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 that could cause our actual results to differ materially from those expressed or implied by such forward-looking statements. 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. Risks and uncertainties that may cause actual results to differ materially include, among others: that preclinical data are not predictive of, may be inconsistent with, or more favorable than, data generated from future or ongoing clinical trial of nimacimab, including the Phase 2a study of nimacimab, competition from third parties that are developing products for similar uses, Skye’s ability to obtain, maintain and protect its intellectual property, Skye’s dependence on third parties for development and manufacture of product candidates, Skye’s ability to manage expenses and to obtain additional funding when needed to support its business activities, as well as those risks more fully described in the section entitled “Risk Factors” 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.