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Ascletis Pharma Inc.
歌禮製藥有限公司
(incorporated in the Cayman Islands with limited liability)
(Stock Code: 1672)

VOLUNTARY ANNOUNCEMENT

ASCLETIS PRESENTS FULL ANALYSIS OF PHASE IB STUDY OF ASC30 ORAL TABLET, PHASE IB STUDY OF ASC30 INJECTION, AND PRECLINICAL STUDY OF COMBINATION OF ASC31 AND ASC47 AT OBESITYWEEK® 2025

- *Positive data from Phase Ib study of ASC30 oral tablet demonstrated up to 6.5% placebo-adjusted mean body weight reduction; safe and well tolerated with only mild-to-moderate gastrointestinal (GI) adverse events (AEs) across all multiple ascending dose (MAD) cohorts.*

- *Phase Ib study data of ASC30 subcutaneous (SQ) injection showed that observed half-life reached 46 days for the treatment formulation (Injection A) and 75 days for the maintenance formulation (Injection B).*

- *Combination of ASC47 and ASC31, a novel peptide agonist targeting both GLP-1R and GIPR, significantly outperformed both tirzepatide and ASC31 monotherapy in promoting weight loss, body fat loss, and muscle preservation in diet-induced obesity (DIO) mouse studies.*

- *Presentations further highlight the promising efficacy and safety profiles of Ascletis' diverse obesity pipeline and validate its proprietary Artificial Intelligence-Assisted Structure-Based Drug Discovery (AISBDD) and Ultra-Long-Acting Platform (ULAP) technologies.*

This announcement is made by Ascletis Pharma Inc. (the "**Company**" or "**Ascletis**", together with its subsidiaries, the "**Group**") on a voluntary basis for the purpose of keeping the shareholders of the Company and potential investors abreast of the latest business development of the Group.

The board (the "**Board**") of directors (the "**Directors**") of the Company announces multiple poster presentations of the full analysis of the Phase Ib study of ASC30 once-daily oral tablet, Phase Ib study of ASC30 once-monthly injection, and preclinical study of the combination of ASC31 and ASC47 at ObesityWeek® 2025 in Atlanta, Georgia.

Abstract Title: A full analysis of 28-Day MAD Study of Oral GLP-1R Biased Small Molecule Agonist ASC30 for obesity

Results:

Efficacy: Body weight changes from baseline were 6.3% reduction (multiple ascending dose (MAD) 2, n=8, 40 mg), 4.3% reduction (MAD 1, n=7, 20 mg), and 0.2% increase (placebo, n=6). No plateau was observed at Day 29. Body weight change from baseline was 4.8% reduction for MAD 3 (n=7, 60 mg), with the maximum body weight change being 9.3% reduction in this cohort. Excluding two outliers, the mean body weight change from baseline was 5.9% reduction for MAD 3.

GI Tolerability: In the MAD study, MAD 1 (20 mg cohort) showed no vomiting, while MAD 2 (40 mg cohort) had events. Titrating from 2 mg to 5 mg did not cause vomiting in MAD 1, but titrating from 2 mg to 10 mg did result in vomiting in MAD 2. Compared with MAD 2, MAD 3 showed no increasing trend in severity or incidence of gastrointestinal (GI) adverse events (AEs), despite two discontinuations due to principal investigator's decisions, and one discontinuation due to subject withdrawal.

Safety: No serious adverse events (SAEs) or Grade ≥ 3 AEs, including GI events, were observed. Labs, vitals, ECGs (QTc), and physical exams were normal. No hepatic safety signals were detected across all MAD cohorts.

Conclusion: ASC30 once-daily oral tablet demonstrated up to 6.5% placebo-adjusted mean body weight reduction from baseline after 28-day treatment. The highest dose level (MAD 3, 60 mg) exhibited up to 9.3% body weight reduction, showed no increasing trend in severity or incidence in GI AEs. ASC30 was safe and well tolerated with only mild-to-moderate GI AEs across all MAD cohorts. The safety profile of ASC30 tablets was consistent with or better than that of the GLP-1R agonist class.

Abstract Title: ASC30, a Once-Monthly SQ Injected Small Molecule GLP-1RA in Participants with Obesity: A Ph Ib Study

Results: The observed half-life (time for ASC30 concentrations to reduce to fifty percent (50%) of ASC30's C_{max}) reached 46 days and 75 days, for ASC30 subcutaneous (SQ) treatment formulation (Injection A) and ASC30 SQ maintenance formulation (Injection B), respectively. C_{max}-to-C_{day29} ratio of 1.5:1, supports ASC30 SQ treatment formulation monthly dosing, while C_{max}-to-C_{day85} ratio of 2.5:1, supports ASC30 SQ maintenance formulation quarterly dosing.

No SAEs or Grade ≥ 3 AEs were observed. GI-related AEs were mild to moderate. Labs, vitals, ECGs (QTc), and physical exams were normal. No hepatic safety signals were detected across all cohorts.

Conclusion: ASC30 ultra-long-acting, slow-release SQ depot formulations demonstrated 46-day observed half-life (treatment formulation) and 75-day observed half-life (maintenance formulation), supporting both once-monthly treatment and once-quarterly maintenance therapies.

ASC30 SQ formulations were well tolerated, with only mild-to-moderate treatment-emergent adverse events (TEAEs), comparable or superior to those observed with GLP-1R agonists. Developed with Ascletis' Ultra-Long-Acting Platform (ULAP) technology, ASC30 treatment and maintenance formulations represent a potential breakthrough in chronic weight management by improving treatment convenience, adherence, and quality of life.

Abstract Title: GLP-1R/GIPR Peptide Agonist ASC31 + ASC47 Shows 119.6% More Weight Loss than Tirzepatide in DIO Mice

Results: The combination of ASC47 plus ASC31 resulted in a 44.8% reduction in weight compared to a 19.1% reduction for ASC31 monotherapy. This was a 134% greater reduction than ASC31 alone. The combination of ASC47 plus tirzepatide resulted in a 38.1% reduction in weight compared to a 20.4% reduction for tirzepatide alone. This was an 87% greater reduction in weight compared to tirzepatide alone. The mean greater reduction in weight of ASC31 in combination with ASC47 compared to ASC31 alone (134%) is statistically significantly higher than that of tirzepatide plus ASC47 compared to tirzepatide alone (87%).

Conclusion: The combination of ASC47 and ASC31 significantly outperformed both tirzepatide and ASC31 monotherapy in promoting weight loss, body fat loss, and muscle preservation. The combination of ASC47 with either ASC31 or tirzepatide restored the body composition of obese mice to the level of healthy non-obese mice. ASC31 is a dual GLP-1R and GIPR peptide agonist. ASC47 is a small molecule thyroid hormone receptor beta (THRβ)-selective agonist and was designed with unique and differentiated properties to enable targeted delivery to adipose tissue.

Detailed data presented at ObesityWeek® 2025 can be found at Ascletis' website (link).

"These presentations highlight the exciting efficacy and safety profiles of our diverse obesity pipeline of both small molecules and peptides and validate our proprietary AISBDD and ULAP technologies," said Jinzi Jason Wu, Ph.D., Founder, Chairman of the Board and chief executive officer of Ascletis. "As we advance clinical development of ASC30, ASC31, and ASC47, we remain focused on close discussion with strategic partners to ensure that Ascletis is best positioned to address the needs of patients with obesity globally."

About ASC30

ASC30 is an investigational GLP-1R biased small molecule agonist and has unique and differentiated properties that enable the same small molecule for both oral tablet and subcutaneous injection administrations. ASC30 is a new chemical entity (NCE), with U.S. and global compound patent protection until 2044 without patent extensions.

About ASC31

ASC31 is an in-house discovered and developed novel peptide agonist targeting both GLP-1R and GIPR, which demonstrated a favorable pharmacokinetic profile in non-human primates as well as promising *in vitro* activities and *in vivo* efficacy in the diet-induced obese (DIO) mice. ASC31 is part of Ascletis' discovery efforts to apply its Ultra-Long-Acting Platform (ULAP) to in-house discovered novel subcutaneously (SQ) injectable peptides and oral peptides.

About ASC47

ASC47 is an adipose-targeted, once-monthly SQ injected THRβ-selective small molecule agonist, discovered and developed in-house at Ascletis. ASC47 possesses unique and differentiated properties to enable adipose targeting, resulting in dose-dependent high drug concentrations in the adipose tissue.

Cautionary Statement required by Rule 18A.05 of the Rules Governing the Listing of Securities on The Stock Exchange of Hong Kong Limited: We cannot guarantee that we will be able to ultimately develop, manufacture and/or commercialize ASC30, ASC31 and/or ASC47 successfully.

By order of the Board
Ascletis Pharma Inc.
歌禮製藥有限公司
Jinzi Jason WU
Chairman

Hong Kong
November 5, 2025

As at the date of this announcement, the Board comprises Dr. Jinzi Jason WU and Mrs. Judy Hejingdao WU, as executive Directors; and Dr. Yizhen WEI, Mr. Jiong GU and Ms. Lin HUA, as independent non-executive Directors.