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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 ANNOUNCES FAVORABLE AND DIFFERENTIATED PHARMACOKINETIC PROFILE OF ASC30 ORAL ONCE-DAILY TABLET IN ITS U.S. PHASE IB MULTIPLE ASCENDING DOSE STUDY

- *ASC30 oral once-daily tablet demonstrated approximately 2.3-fold to 3.3-fold greater drug exposure than orforglipron in a cross-trial comparison.*

- *Higher drug exposure and favorable tolerability profile positions ASC30 oral once-daily tablet favorably compared to orforglipron.*

- *Topline data from the Ascletis' U.S. Phase IIa study for ASC30 in participants with obesity or overweight are expected in the fourth quarter of 2025.*

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 promising topline pharmacokinetic (PK) data from its randomized, double-blind, placebo-controlled Phase Ib multiple ascending dose (MAD) study (NCT06680440), conducted in the U.S., of ASC30 oral once-daily tablet in participants with obesity (body mass index (BMI): 30-40 kg/m^2). At steady state, ASC30 demonstrated drug exposures (area under the curve over 0-24 hours or AUC_{0-24h}) of 3,560 ng·h/mL and 5,060 ng·h/mL for cohort 1 (20 mg) and cohort 2 (40 mg), respectively, in the Phase Ib MAD study. These drug exposure data are consistent with placebo-adjusted mean body weight reduction from baseline of 4.5% for cohort 1 (20 mg) and 6.5% for cohort 2 (40 mg) after 28-day treatment, indicating higher drug exposures are associated with greater weight loss.

Based on a cross-trial comparison, 20 mg and 40 mg ASC30 oral once-daily tablet demonstrated greater drug exposure of approximately 2.3-fold and 3.3-fold, respectively, of orforglipron oral once-daily capsule (24 mg cohort, $AUC_{0\text{-}24h}$ 1,520 ng·h/mL)[1]. After 28-day treatment, orforglipron (24 mg cohort, $AUC_{0\text{-}24h}$ 1,520 ng·h/mL) resulted in only 3.6% placebo-adjusted mean body weight reduction from baseline[1]. Despite high drug exposure of ASC30 in cohort 1 (20 mg, $AUC_{0\text{-}24h}$ 3,560 ng·h/mL), there were no incidences of vomiting in cohort 1 (20 mg), whereas orforglipron 24 mg cohort ($AUC_{0\text{-}24h}$ 1,520 ng·h/mL) had 18% vomiting[1], suggesting the Ascletis' chemical lead and formulation optimization strategies played a role in tolerability improvement.

In the Phase Ib MAD study, ASC30 oral once-daily tablet was safe and well tolerated with no serious adverse events (SAEs) reported and no Grade 3 or higher adverse events (AEs) including GI-related AEs observed. There were no elevations of liver enzymes including alanine aminotransferase (ALT), aspartate aminotransferase (AST) and total bilirubin (TBL) during the treatment. There were no abnormal findings in laboratory tests, vital signs, ECGs (electrocardiograms, including QTc intervals), and physical exams.

"Based on recent clinical data published to date, we believe higher drug exposure leads to greater weight loss for small molecule GLP-1 receptor (GLP-1R) agonists including orforglipron," said Jinzi Jason Wu, Ph.D., Founder, Chairman of the Board and chief executive officer of Ascletis. "I am pleased to see that the higher drug exposures of ASC30 seen in a head-to-head study in non-human primates with orforglipron translated to humans at approximately 2.3-fold to 3.3-fold greater than orforglipron in a cross-trial comparison. Given that higher drug exposures of ASC30 produced more weight loss in participants with obesity, we believe that ASC30 oral once-daily tablet may potentially be competitive and differentiated for the treatment of obesity compared to orforglipron."

Reference is made to the announcement of the Company dated August 5, 2025, in which the Company announced that it completed enrollment in its U.S. Phase IIa study for ASC30 in 125 participants with obesity or overweight, with topline data expected in the fourth quarter of 2025.

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.

[1] Pratt E, Ma X, Liu R, et al. Orforglipron (LY3502970), a novel, oral non-peptide glucagon-like peptide-1 receptor agonist: A Phase 1a, blinded, placebo-controlled, randomized, single- and multiple-ascending-dose study in healthy participants. Diabetes Obes Metab. 2023;25(9):2634-2641. doi:10.1111/dom.15184.

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 successfully.

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

Hong Kong
August 28, 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.