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

INSIDE INFORMATION

ASCLETIS ANNOUNCES POSITIVE TOPLINE RESULTS OF U.S. PHASE IB MULTIPLE ASCENDING DOSE STUDY OF SMALL MOLECULE ORAL GLP-1R AGONIST ASC30 AND SUBMISSION OF 13-WEEK PHASE IIA STUDY PROTOCOL TO FDA

– *ASC30 oral once-daily tablet demonstrated a 6.5% placebo-adjusted mean body weight reduction from baseline after four-week treatment using weekly doses with titrations of 2 mg, 10 mg, 20 mg, and 40 mg doses.*

– *ASC30 oral once-daily tablet also demonstrated a 4.5% placebo-adjusted mean body weight reduction from baseline after four-week treatment using weekly doses with titrations of 2 mg, 5 mg, 10 mg, and 20 mg doses. No vomiting was seen in this dose group.*

– *Data from three different weekly titration schemes in the Phase Ib trial support utilizing a "lower starting dose and slower titration" strategy for a 13-week Phase IIa study design of ASC30 oral once-daily tablet.*

This announcement is made by Ascletis Pharma Inc. (the "**Company**" or "**Ascletis**") pursuant to Rule 13.09(2) of the Rules Governing the Listing of Securities on The Stock Exchange of Hong Kong Limited (the "**Listing Rules**") and the Inside Information Provisions (as defined in the Listing Rules) under Part XIVA of the Securities and Futures Ordinance (Chapter 571 of the Laws of Hong Kong).

The board (the "**Board**") of directors (the "**Directors**") of the Company announces positive topline results of 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). The Phase Ib MAD study consisted of three cohorts, each with a different weekly titration scheme, for a total of four-week treatment and one-week follow up. Scheme 1 (mid starting dose, slow titration: 2 mg, 5 mg, 10 mg, and 20 mg); Scheme 2 (mid starting dose, normal titration: 2 mg, 10 mg, 20 mg, and 40 mg); and Scheme 3 (high starting dose, fast titration: 5 mg, 15 mg, 30 mg, and 60 mg). Based on single ascending dose (SAD) data in participants with obesity, Schemes 1 and 2 were designed to investigate tolerability and efficacy. All participants with obesity stayed at the clinical site from day 1 to day 2 and from day 27 to day 29. For other days during the study, participants maintained their habitual eating and physical activity patterns as out-patients.

Mean body weight reductions from baseline for Scheme 1 (mid starting dose, slow titration: 2 mg, 5 mg, 10 mg, and 20 mg) and Scheme 2 (mid starting dose, normal titration: 2 mg, 10 mg, 20 mg, and 40 mg) were 4.3% (n=7, p=0.0002 vs placebo) and 6.3% (n=8, p<0.0001 vs placebo), respectively, after four-week treatment. No weight plateau was observed. Mean body weight increase from baseline for placebo was 0.2% (n=6, two placebos from each of three schemes). Placebo adjusted mean body weight reductions for Schemes 1 and 2 from baseline were 4.5% and 6.5%, respectively. The maximum body weight reductions from baseline were 7.6% and 9.1% for Schemes 1 and 2, respectively. ASC30 oral once-daily tablet was generally safe and well tolerated among Schemes 1 and 2, with a favorable safety profile. The majority of gastrointestinal (GI)-related adverse events (AEs) were mild (Grade 1) and short-lived. Schemes 1 and 2 demonstrated improved or comparable GI tolerability to the GLP-1 class such as orforglipron. For example, Scheme 1 had no incidences of vomiting.

After reviewing the safety and efficacy results of the first two dosing schemes, a third dosing scheme (high starting dose, fast titration: 5 mg, 15 mg, 30 mg, and 60 mg) was designed to help validate the optimal combination of tolerability and efficacy seen in Schemes 1 and 2. Mean body weight reduction from baseline for Scheme 3 was 4.8% (n=7, p=0.0015 vs placebo) after four-week treatment. Placebo-adjusted mean body weight reduction from baseline was 5.0%. The maximum body weight reduction from baseline was 9.3%. In Scheme 3, there were two outliers, each with body weight reduction of 1.8% from baseline, which were not seen in Schemes 1 or 2. Excluding these two outliers, placebo-adjusted mean body weight reduction from baseline in Scheme 3 was 6.1%, comparable to Scheme 2. The maximum body weight reduction from baseline of Scheme 3 was also comparable to Scheme 2 (9.3% and 9.1%, respectively). Moreover, the GI tolerability observed in Scheme 3 was less than that of Schemes 1 and 2, due to its high starting dose, fast titration design.

For all the above mentioned three schemes, no serious adverse events (SAEs) were reported. There were no Grade 3 or higher 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.

Both tolerability and efficacy data from the ASC30 tablet Phase Ib study support a “lower starting dose and slower titration” strategy for a 13-week Phase IIa study design of ASC30 oral once-daily tablet. The 13-week Phase IIa study protocol, which has a low starting dose and slow weekly titration to the desired maintenance doses, has been submitted to the U.S. Food and Drug Administration (FDA) following a preliminary consultation with FDA. The Company expects to initiate the 13-week Phase IIa study in the U.S. at the beginning of the third quarter of 2025.

ASC30 was discovered and developed in-house at Ascletis as a first and only investigational small molecule GLP-1 receptor (GLP-1R) biased agonist designed to be dosed once daily orally and once monthly subcutaneously for the treatment of obesity.

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.

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.

Shareholders and potential investors of the Company are advised to exercise caution when dealing in the securities of the Company.

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

Hong Kong, the People's Republic of China
April 23, 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.