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 PHASE IB STUDIES OF ASC47 MONOTHERAPY IN AUSTRALIA AND U.S. FDA CLEARANCE OF IND APPLICATION FOR ASC47 IN COMBINATION WITH SEMAGLUTIDE

- *ASC47, an adipose-targeted muscle-preserving weight loss drug candidate for the treatment of obesity, demonstrated a half-life of up to 26 days and 40 days, respectively, in Phase Ib single subcutaneous injection studies in healthy subjects with elevated low-density lipoprotein cholesterol (LDL-C) and patients with obesity, supporting once-monthly to once-bimonthly administration.*

- *ASC47 was safe and well tolerated in both healthy subjects with elevated LDL-C and patients with obesity.*

- *Previous preclinical data indicated that in a head-to-head diet-induced obese (DIO) mouse model, low dose ASC47 in combination with semaglutide demonstrated a 56.7% greater reduction in body weight compared to semaglutide monotherapy.*

- *U.S. Food and Drug Administration (FDA) clearance recognizes and supports a proof-of-concept clinical study of ASC47, an adipose-targeted thyroid hormone receptor beta (THRβ) selective agonist, in combination with an incretin drug.*

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 encouraging pharmacokinetic and weight loss data from its ASC47 Phase Ib single subcutaneous injection studies in Australia in healthy subjects with elevated low-density lipoprotein cholesterol (LDL-C) (Part I) and in patients with obesity (Part II) (NCT06427590).

ASC47, an adipose-targeted muscle-preserving weight loss drug candidate for the treatment of obesity, demonstrated a half-life of up to 26 days and 40 days, respectively, in Phase Ib single subcutaneous injection studies in healthy subjects with elevated LDL-C and patients with obesity, supporting once-monthly to once-bimonthly administration. Furthermore, ASC47 subcutaneous injection demonstrated dose-proportional drug exposures (area under curve or AUC) and C_{max} values. Similar drug exposures were observed between healthy subjects and patients with obesity.

ASC47 single subcutaneous injection (90 mg) in patients with obesity demonstrated a weight loss signal. Placebo-adjusted mean weight loss was 0.2% (day 29), 1.0% (day 43), and peaked at 1.7% (day 50), consistent with the speed of weight loss anticipated given ASC47's mechanism of action. One of the key mechanisms for ASC47 is through UCP-1-mediated thermogenesis which results in a slower rate of weight loss with the added benefit of muscle preservation, compared to incretin drugs. This slower rate of weight loss was seen in diet-induced obese (DIO) mouse models of ASC47 compared to incretin drugs. Muscle preservation of ASC47 treatment was also observed in DIO mouse models.

ASC47 single subcutaneous injections in healthy subjects with elevated LDL-C (10 mg, 30 mg, 90 mg) and patients with obesity (90 mg) showed clinically significant placebo-adjusted mean reductions in LDL-C (up to 22%) and total cholesterol (TC) (up to 16%), indicating target engagement in humans.

ASC47 single subcutaneous injection demonstrated good tolerability up to 90 mg with no serious adverse events (SAEs) and no discontinuations due to adverse events (AEs). The majority of AEs were mild (grade 1). There was no heart rate increase or abnormal liver enzyme changes.

The multiple ascending dose (MAD) study of ASC47 monotherapy for the treatment of obesity is expected to be initiated in the second half of 2025.

Reference is made to the announcement of the Company dated December 18, 2024, previous preclinical data indicated that in a head-to-head DIO mouse study, adipose-targeted low dose ASC47 (human equivalent dose of 20 mg) in combination with semaglutide demonstrated not only a 56.7% greater reduction in body weight compared to semaglutide monotherapy, but also muscle preservation.

The U.S. IND (Investigational New Drug) application for ASC47 in combination with semaglutide for the treatment of obesity, recently cleared by U.S. Food and Drug Administration (FDA), is supported by the above preclinical data of low dose ASC47 in combination with semaglutide and by the safety, tolerability and preliminary efficacy of the Phase Ib ASC47 monotherapy studies in Australia. The combination study will consist of three cohorts of patients with obesity (body mass index (BMI) $\geq$ 30 kg/m^2). Each cohort consists of a single low dose of ASC47 and four doses of semaglutide (0.5 mg, once weekly). Cohorts 1-3 have ASC47 low doses of 10 mg, 30 mg, and 60 mg, respectively. Each cohort has six patients treated with ASC47 in combination with semaglutide and two patients treated with matching placebo in combination with semaglutide. The first patient is expected to be dosed by the end of the second quarter of 2025.

The data from single doses of ASC47 in combination with semaglutide will be used to support the MAD study of combination therapy of ASC47 low doses and an incretin drug for the treatment of obesity, which is expected to be initiated by the end of 2025.

ASC47 is an adipose-targeted, ultra-long-acting subcutaneously (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.

ASC47 Phase I Studies in Australia for the Treatment of Obesity

Part I: Single ascending dose (SAD) study of ASC47 monotherapy in subjects with elevated LDL-C: Study objectives include safety, tolerability, target engagement and pharmacokinetics in subjects with elevated LDL-C receiving SAD of ultra-long-acting ASC47 monotherapy via SQ injections. Part I study consists of three cohorts (10 mg, 30 mg and 90 mg). Each of 10 mg and 30 mg cohorts has six subjects (four subjects treated with ASC47 and two subjects treated with matching placebo). 90 mg cohort has eight subjects (six subjects treated with ASC47 and two subjects treated with matching placebo).

Part II: ASC47 monotherapy study in patients with obesity: Study objectives include safety, tolerability, pharmacokinetics and preliminary efficacy in patients with obesity (BMI: 30-40 kg/m^2) receiving 90 mg single dose ASC47 monotherapy via SQ injections. 90 mg cohort has eight patients with obesity (six patients treated with ASC47 and two patients treated with matching placebo).

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 ASC47 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

Hangzhou, the People's Republic of China
March 12, 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.