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 ASC47, A MUSCLE-PRESERVING WEIGHT LOSS DRUG CANDIDATE FOR TREATMENT OF OBESITY, DEMONSTRATED GREATER EFFICACY WITH TIRZEPATIDE THAN SEMAGLUTIDE IN A PRECLINICAL MODEL

- *The combination of ASC47 low dose with tirzepatide in diet-induced obese (DIO) mice resulted in an 87% greater reduction in body weight compared to tirzepatide monotherapy.*

- *ASC47 low dose in combination with tirzepatide demonstrated statistically significantly greater increase in efficacy than ASC47 low dose in combination with semaglutide, 87% vs 55%, respectively, in the DIO mouse model.*

- *The combination of ASC47 low dose with tirzepatide also restored the body composition of obese mice to the level of healthy non-obese mice. At the end of treatment, the percentage of total muscle mass over the total body weight of obese mice treated with the combination of ASC47 low dose with tirzepatide was similar to healthy non-obese mice, 60.4% vs 62.0% respectively.*

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 encouraging efficacy results from its study in diet-induced obese (DIO) mice combining ASC47, a first-in-class muscle-preserving weight loss drug candidate for the treatment of obesity, with tirzepatide.

ASC47 is an adipose-targeted, once-monthly subcutaneously (SQ) injected thyroid hormone receptor beta (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.

The objective of the DIO mouse study was to compare a low dose of ASC47 (9 mg/kg, single dose) combined with tirzepatide (3 nmol/kg, SQ, once daily) against tirzepatide monotherapy (3 nmol/kg, SQ, once daily). The treatment duration in the DIO mice was 14 days. Results showed that the combination of ASC47 low dose with tirzepatide was superior to tirzepatide monotherapy, with an average total body weight reduction of 38.1% compared to 20.4%, achieving 87% more relative weight loss compared to tirzepatide monotherapy (Table 1). In comparison, the combination of ASC47 low dose with semaglutide demonstrated statistically significantly lower efficacy (p=0.006) in the DIO mouse study, showing a 55% greater reduction in body weight compared to semaglutide monotherapy.

Table 1. ASC47 low dose demonstrated greater efficacy with tirzepatide than semaglutide

Group	Dosing	Total body weight change from baseline	Greater body weight reduction of combination vs monotherapy
Obese mice treated with tirzepatide	Tirzepatide, 3 nmol/kg, SQ, QD	-20.4%	–
Obese mice treated with ASC47 low dose combination with tirzepatide	ASC47, 9 mg/kg, SQ, a single dose + tirzepatide, 3 nmol/kg, SQ, QD	-38.1% (p<0.0001 vs tirzepatide monotherapy)	87%
Obese mice treated with semaglutide	Semaglutide, 30 nmol/kg, SQ, QD	-23.1%	–
Obese mice treated with ASC47 low dose combination with semaglutide	ASC47, 9 mg/kg, SQ, a single dose + semaglutide, 30 nmol/kg, SQ, QD	-35.9% (p<0.0001 vs semaglutide monotherapy)	55%

Note: Treatment duration: 14 days for tirzepatide monotherapy and ASC47/tirzepatide combination therapy; 28 days for semaglutide monotherapy and ASC47/semaglutide combination therapy; Obese mice: diet-induced obese mice; SQ: subcutaneous; QD: once daily.

The combination of ASC47 low dose with tirzepatide also restored the body composition of obese mice to the level of healthy non-obese mice. At the end of treatment, the percentage of total muscle mass over the total body weight of obese mice treated with ASC47 low dose and tirzepatide (60.4%) was similar to healthy non-obese mice (62.0%), indicating healthy weight loss. Tirzepatide monotherapy was unable to restore body composition to healthy levels.

"These preclinical data build upon a body of evidence demonstrating the potential of ASC47 as an important therapeutic approach for the treatment of obesity." said Jinzi Jason Wu, Ph.D., Founder, Chairman of the Board and chief executive officer of Ascletis, "With topline data in participants with obesity from the combination study of ASC47 with semaglutide coming soon, we look forward to the combinations of ASC47 with other incretin drugs including tirzepatide in future clinical trials."

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.

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

Hong Kong
August 13, 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.