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 SELECTS A BEST-IN-CLASS ONCE-MONTHLY SUBCUTANEOUSLY ADMINISTERED GLP-1R/GIPR DUAL PEPTIDE AGONIST, ASC35, FOR CLINICAL DEVELOPMENT

- *In head-to-head non-human primate (NHP) studies, average observed half-life of ASC35 was approximately 14 days, 6-fold longer than tirzepatide, which supports once-monthly subcutaneous (SQ) dosing in humans.*

- *In head-to-head NHP studies, drug exposures of ASC35 intravenous (I.V.) and SQ administration were approximately 80% and 70% greater than tirzepatide I.V. and SQ administration, respectively.*

- *ASC35 was approximately 4-fold more potent than tirzepatide for both GLP-1 receptor (GLP-1R) and GIP receptor (GIPR) in vitro.*

- *ASC35 demonstrated approximately 71% greater relative body weight reduction compared to tirzepatide in a head-to-head diet-induced obese (DIO) mouse study.*

- *Submission of an Investigational New Drug Application (IND) for ASC35 to the U.S. Food and Drug Administration (FDA) is expected in the second quarter of 2026.*

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 that it has selected ASC35, a once-monthly, potentially best-in-class subcutaneously administered GLP-1 receptor (GLP-1R)/GIP receptor (GIPR) dual peptide agonist, as a clinical development candidate. Ascletis expects to submit an Investigational New Drug Application (IND) for ASC35 for the treatment of obesity to the U.S. Food and Drug Administration (FDA) in the second quarter of 2026.

ASC35, a GLP-1R and GIPR dual peptide agonist, was discovered and developed in-house utilizing Ascletis' Artificial Intelligence-Assisted Structure-Based Drug Discovery (AISBDD) and Ultra-Long-Acting Platform (ULAP) technologies. ASC35 was approximately 4-fold more potent than tirzepatide for both GLP-1R and GIPR *in vitro*. ASC35 is engineered for a longer observed half-life (as measured by time to 50% C_{max}) and higher bioavailability per milligram of peptide, compared to once-weekly administered tirzepatide, to support once-monthly SQ dosing, with injection volume of one milliliter or less. These engineered properties also allow for scalability advantages in manufacturing.

In head-to-head non-human primate (NHP) studies, ASC35 slow-release SQ depot formulations had an average observed half-life of approximately 14 days, 6-fold longer than tirzepatide in its FDA-authorized SQ formulation. In head-to-head NHP studies, drug exposures (as measured by the area under curve) of ASC35 intravenous (I.V.) and SQ administration were approximately 80% and 70% greater than tirzepatide I.V. and SQ administration, respectively. The pharmacokinetic relationship between NHPs and humans is well established by multiple peptide agonists. For example, tirzepatide's 56-hour half-life in NHPs translates into a half-life of 128 hours (5.3 days) in humans[1]. Therefore, the observed half-life of ASC35 in humans may be predicted to be 30 days or longer based on NHP studies. These preclinical data support ASC35 as a once-monthly treatment for obesity in humans. The longer observed half-life and a flatter pharmacokinetic profile of ASC35 in NHPs compared to other peptide incretins may also translate into a better gastrointestinal tolerability in humans.

In a head-to-head diet-induced obese (DIO) mouse study, which is well established as being highly predictive of human efficacy, dosed with equal molar concentrations of ASC35 and tirzepatide, ASC35 reduced body weight by 33.6%, compared to 19.6% for tirzepatide, a relative increase in efficacy of 71% (Table 1). This superior weight loss per milligram of peptide may also provide scalability advantages in manufacturing.

Table 1. ASC35 demonstrated statistically and significantly more weight loss than tirzepatide in DIO mice

Group	Dosing	Total body weight change from baseline	Greater relative weight loss versus tirzepatide
Obese mice treated with vehicle	Vehicle, SQ, QD	0.4%	-
Obese mice treated with ASC35	3 nmol/kg, SQ, QD	-33.6% (p <0.0001 vs vehicle)	71% (p <0.0001 vs tirzepatide)
Obese mice treated with tirzepatide	3 nmol/kg, SQ, QD	-19.6% (p <0.0001 vs vehicle)	-

Note: Treatment duration: 14 days; DIO mice/Obese mice: diet-induced obese mice; SQ: subcutaneous; QD: once daily.

ASC35's superior *in vitro* potency, longer observed half-life, better SQ bioavailability and greater weight loss compared to tirzepatide demonstrate its potential as a best-in-class treatment for obesity.

"The selection of our first peptide agonist for clinical development demonstrates our commitment to innovation and complements our portfolio of small molecule candidates for the treatment of obesity and other metabolic diseases," said Jinzi Jason Wu, Ph.D., Founder, Chairman of the Board and chief executive officer of Ascletis, "The preclinical characterization of ASC35 suggests best-in-class efficacy with once-monthly dosing resulting in superior weight loss and a more versatile and patient friendly titration schedule."

Potential Combination Studies with ASC35

ASC35 is being developed as a monotherapy and in combination for the treatment of cardio-metabolic diseases including obesity, diabetes and metabolic dysfunction-associated steatohepatitis (MASH). Ascletis plans to combine ASC35, a GLP-1R/GIPR dual agonist, with its ASC36, a once-monthly subcutaneously administered amylin receptor peptide agonist to treat obesity and diabetes. Ascletis also plans to combine ASC35 with its once-monthly SQ ASC47, an adipose-targeted thyroid hormone receptor beta (THRβ) agonist, to treat multiple metabolic diseases such as obesity and MASH.

Ascletis' AISBDD and ULAP technologies enable the Company to design, optimize and develop multiple once-monthly SQ ultra-long-acting peptides, including ASC35 and ASC36. Based on the properties of peptides, the Company can design, through its proprietary ULAP technology, various slow-release constants (*k*) for peptides in SQ depots to precisely release injected peptides over desired dosing intervals to reduce peak-to-trough ratios and improve clinical outcomes.

[1] Jennifer A Martin et al, Absorption, distribution, metabolism, and excretion of tirzepatide in humans, rats, and monkeys, European Journal of Pharmaceutical Sciences 202 (2024) 106895, https://doi.org/10.1016/j.ejps.2024.106895

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 ASC35, ASC36 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
October 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.