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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

ORAL SMALL MOLECULE AMYLIN RECEPTOR AGONIST ASC39 DEMONSTRATED ELORALINTIDE-LIKE AMYLIN SELECTIVITY AND EFFICACY IN PRECLINICAL MODELS

- *In a head-to-head cyclic adenosine monophosphate (cAMP) activation assay vs. eloralintide, oral small molecule amylin receptor agonist ASC39 demonstrated similar selectivity and potency to that of eloralintide. EC_{50} for human amylin 1 receptor (hAMY1R) was 21.4 pM and 21.2 pM for ASC39 and eloralintide, respectively. EC_{50} for human calcitonin receptor (hCTR) was 846.1 pM and 1,350.8 pM for ASC39 and eloralintide, respectively. These data indicate ASC39 and eloralintide have similar selectivity for hAMY1R over hCTR.*

- *In a head-to-head diet-induced obese (DIO) rat study vs. eloralintide, efficacy of ASC39 oral dosing was comparable to that of eloralintide, demonstrating significant placebo adjusted weight loss of 6.6% and 5.6% for ASC39 and eloralintide, respectively.*

- *Submission of an Investigational New Drug Application (IND) to the U.S. Food and Drug Administration (FDA) for ASC39 oral tablets is expected in the third 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 ASC39, a potent and amylin-selective oral small molecule amylin receptor agonist, as a clinical development candidate. Ascletis expects to submit an Investigational New Drug Application (IND) to the U.S. Food and Drug Administration (FDA) for ASC39 oral tablets for the treatment of obesity in the third quarter of 2026.

ASC39 has a unique chemical scaffold that was discovered in-house utilizing Ascletis' Artificial Intelligence-assisted Structure-Based Drug Discovery (AISBDD) technology. In a head-to-head cyclic adenosine monophosphate (cAMP) activation assay comparing ASC39 to eloralintide, EC_{50} (half maximal effective concentration) for human amylin 1 receptor (hAMY1R) was 21.4 pM and 21.2 pM for ASC39 and eloralintide (an amylin peptide analog), respectively. EC_{50} for human calcitonin receptor (hCTR) was 846.1 pM and 1,350.8 pM for ASC39 and eloralintide, respectively. These data indicate that ASC39 is highly selective for hAMY1R over hCTR with comparable selectivity to eloralintide. ASC39 and eloralintide were 40-fold and 64-fold, respectively more selective for hAMY1R over hCTR.

In a head-to-head diet-induced obese (DIO) rat study, compared with placebo (vehicle)-treated obese rats, oral daily administration of ASC39 resulted in statistically significant weight loss which was comparable to eloralintide (Table 1). Once-daily oral administration of 5 mg/kg ASC39 for 6 consecutive days produced significant placebo adjusted weight loss of 6.6%. Once-every-three-day subcutaneous (SQ) administration of 3 nmol/kg eloralintide for 6 consecutive days produced significant placebo adjusted weight loss of 5.6%, which is consistent with the literature data[1].

Table 1. Once-daily oral administration of ASC39 for 6 consecutive days produced statistically significant body weight reduction, with an efficacy comparable to that of eloralintide.

Group	Dosing	Total body weight change from baseline
Obese rats treated with vehicle	Vehicle, PO, QD	0.6%
Obese rats treated with eloralintide	3 nmol/kg, SQ, Q3D	-5.0% (p<0.0001 vs obese rats treated with vehicle)
Obese rats treated with ASC39	5 mg/kg, PO, QD	-6.0% (p<0.0001 vs obese rats treated with vehicle)

Notes:

a. SQ: subcutaneous; PO: oral administration; Q3D: once every 3 days; QD: once daily.

b. The body weight on Day 1 was set as the baseline.

c. Obese rats: diet-induced obese rats.

ASC39 demonstrated favorable pharmacokinetic profiles in rats and non-human primates (NHPs), supporting once-daily oral dosing in humans.

"Ascletis is committed to developing treatment options for patients living with obesity," said Jinzi Jason Wu, Ph.D., Founder, Chairman of the Board and chief executive officer of Ascletis. "As such, we are excited to be advancing the first oral small molecule eloralintide-like selective amylin receptor agonist into the clinic later this year. We believe ASC39 may provide efficacy and safety similar to Eli Lilly's eloralintide with the patient convenience and commercial scalability of a once-daily oral small molecule."

ASC39, a potent and amylin-selective oral small molecule amylin receptor agonist, is being developed as a monotherapy and in combination with ASC30, Ascletis' oral small molecule, Phase III ready GLP-1, for the treatment of metabolic diseases including obesity. This new oral small molecule amylin is in addition to Ascletis' current amylin peptide portfolio that includes ASC36, a once-monthly to once quarterly SQ amylin peptide for monotherapy and a fixed dosed combination of ASC36 and once-monthly ASC35, a GLP-1/GIP SQ peptide.

[1] Briere DA, Qu H, Lansu K, et al. Eloralintide (LY3841136), a novel amylin receptor agonist for the treatment of obesity: From discovery to clinical proof of concept. Mol Metab. 2025;102:102271. doi:10.1016/j.molmet.2025.102271

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 ASC39 successfully.

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

Hong Kong
March 17, 2026

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.