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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

ASCLETIS ANNOUNCES ULTRA-LONG-ACTING SUBCUTANEOUS DEPOT MAINTENANCE FORMULATION OF SMALL MOLECULE GLP-1R AGONIST ASC30 DEMONSTRATED AN OBSERVED HALF-LIFE OF 75 DAYS IN PARTICIPANTS WITH OBESITY

– *Maintenance formulation of small molecule ASC30 demonstrated an observed half-life of 75 days in participants with obesity in the U.S. Phase Ib study.*

– *75-day observed half-life supports once-quarterly administration.*

– *Once-quarterly SQ administration of ASC30 is the most clinically advanced once-quarterly incretin drug and has the potential to address a highly unmet need as a maintenance therapy for chronic weight management, representing a significant patient population.*

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 ultra-long-acting subcutaneous (SQ) depot maintenance formulation of small molecule GLP-1 receptor (GLP-1R) agonist ASC30 demonstrated an observed half-life of 75 days in participants with obesity (body mass index (BMI) ≥ 30 kg/m^2) in a U.S. Phase Ib clinical study (NCT06679959), supporting once-quarterly administration as a maintenance therapy for chronic weight management. The ASC30 maintenance formulation was developed utilizing Ascletis' Ultra-Long-Acting Platform (ULAP).

After a single SQ injection of ASC30 (100 mg) maintenance formulation in eight participants with obesity, the median time for ASC30 to reach maximum concentrations (C_{max}) was 17 days post-dose. The time for ASC30 concentrations to reduce to fifty percent (50%) of ASC30's C_{max} was approximately 75 days post-dose, demonstrating an observed half-life of 75 days.

"Maintenance therapy represents a significant unmet medical need for chronic weight management," said Jinzi Jason Wu, Ph.D., Founder, Chairman of the Board and chief executive officer of Ascletis. "For example, after a period of treatment with once-weekly administered incretin drugs that help reach weight loss goals, patients prefer to switch to a once-quarterly

therapy to maintain the weight. Based on its promising pharmacokinetic parameters, including the ultra-long half-life, and good safety, we believe once-quarterly administration of ASC30 has the potential to help patients maintain their weight without rebound. Ultra-long-acting SQ depot maintenance formulation of ASC30 represents the most clinically advanced once-quarterly incretin drug and a potential major breakthrough in providing once-quarterly maintenance therapy for patients on chronic weight management, potentially enhancing compliance and quality of life."

Tolerability is key to maintenance therapies. During the 12-week period after a single SQ injection of ASC30 (100 mg) maintenance formulation, incidence rates of vomiting, nausea, diarrhea and constipation in ASC30-treated patients (N=8) were 0.0%, 0.0%, 12.5% and 12.5%, respectively, compared to 0.0%, 12.5%, 6.3% and 0.0%, in placebo-treated patients (N=16). The favorable gastrointestinal (GI) tolerability of ASC30 maintenance formulation resulted from the slow rate of rise to C_{max} and peak-to-trough (C_{max}-to-C_{trough}) ratio of approximately 2.5:1 during 12-week period post-dose. The trough concentrations (C_{trough}) of ASC30 were reached 84 days post-dose.

In the Phase Ib study, no serious adverse events (SAEs) were reported. There were no Grade 3 or higher adverse events (AEs) observed. GI-related AEs were rare and only Grade 1 among 100 mg ASC30 treated participants with obesity. There were no elevations of liver enzymes including alanine aminotransferase (ALT), aspartate aminotransferase (AST) and total bilirubin (TBL). There were no abnormal findings in laboratory tests, vital signs, ECGs (electrocardiograms, including QTc intervals), and physical exams. Table 1 summarizes the safety and tolerability profile of 100 mg ASC30 compared to placebo.

Table 1. Safety and tolerability profile of 100 mg ASC30 compared to placebo

Category	ASC30 maintenance formulation 100 mg (N=8) n (%)	Placebo (N=16) n (%)
Number of participants reporting at least one TEAE	8 (100%)	14 (87.5%)
Number of participants reporting TEAEs by severity		
Grade 1	7 (87.5%)	12 (75.0%)
Grade 2	1 (12.5%)	2 (12.5%)
Grade 3	0 (0.0%)	0 (0.0%)
Grade 4	0 (0.0%)	0 (0.0%)
Number of participants reporting SAEs	0 (0.0%)	0 (0.0%)
Overall discontinuation	0 (0.0%)	0 (0.0%)
Common GI-related TEAEs		
Vomiting	0 (0.0%)	0 (0.0%)
Nausea	0 (0.0%)	2 (12.5%)
Diarrhea	1 (12.5%)	1 (6.3%)
Constipation	1 (12.5%)	0 (0.0%)
Abdominal pain	0 (0.0%)	0 (0.0%)

Notes: TEAE(s): treatment-emergent adverse event (s); SAEs: serious adverse events; GI: gastrointestinal.

The clinical trial design including ASC30 maintenance dose selection is currently being evaluated including consultation with the regulatory authorities.

ASC30 ultra-long-acting SQ depot formulations demonstrated dose-proportional pharmacokinetic profiles that support both treatment and maintenance therapies. Reference is made to the announcement of the Company dated July 28, 2025, in which the Company announced, ASC30 ultra-long-acting SQ depot treatment formulation, also developed by Ascletis' ULAP, is being investigated as a once-monthly treatment therapy in a Phase IIa study (NCT06679959) in the U.S. in participants with obesity (BMI ≥ 30 kg/m^2) or overweight (BMI ≥ 27 kg/m^2 but < 30 kg/m^2) with at least one weight-related comorbidity. Topline data of ASC30 treatment formulation of Phase IIa study are expected in the first quarter of 2026. ASC30 treatment formulation demonstrated an observed half-life of 46 days in participants with obesity, supporting once-monthly administration to treat obesity.

Based on the properties of small molecules, peptides and proteins/antibodies, Ascletis can design, through its proprietary ULAP technology, various release constants (k) of drugs in SQ depots to precisely release SQ injected drugs slowly over desired dosing intervals to reduce peak-to-trough ratios and improve clinical outcomes.

ASC30 was discovered and developed in-house at Ascletis as a first and only investigational small molecule GLP-1R biased agonist designed to be administered once daily orally and once monthly to once quarterly subcutaneously as a treatment therapy and a maintenance therapy for chronic weight management.

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 without patent extensions.

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.

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

Hong Kong
September 9, 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.