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 ENTERS THE OBESITY DRUG SPACE WITH ANNOUNCEMENT OF TWO ONGOING U.S. PHASE I CLINICAL TRIALS UTILIZING ITS SMALL MOLECULE GLP-1R AGONIST ASC30 FOR BOTH ONCE-MONTHLY SUBCUTANEOUS INJECTION AND ONCE-DAILY ORAL TABLET FOR THE TREATMENT OF OBESITY

- *ASC30 is the first and only small molecule GLP-1 receptor (GLP-1R) agonist that can be dosed once-monthly subcutaneously and once-daily orally to treat obesity*

- *ASC30 is two– to threefold more potent, in vitro, than orforglipron and stimulated significantly greater insulin secretion when compared with orforglipron in non-human primates (NHPs)*

- *ASC30 single dose subcutaneous injection demonstrated sustained weight loss over one month in NHPs supporting once-monthly administration in humans*

- *ASC30 oral once-daily dosing demonstrated sustained weight loss in NHPs supporting once-daily oral administration in humans*

- *Topline data from ongoing U.S. Phase I clinical trials of ASC30 once-monthly subcutaneous injection and once-daily oral tablet to treat obesity expected first quarter 2025*

- *ASC30 has the potential to be a first-in-class and best-in-class small molecule GLP-1R agonist to treat obesity given its superior NHP data, as well as once-monthly and once-daily dosing*

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 of directors (the "**Board**") of the Company announces completion of initial dosing in its two recently initiated U.S. Phase I clinical trials for ASC30, the first and only small molecule GLP-1 receptor (GLP-1R) agonist that can be dosed once monthly subcutaneously and once-daily orally for the treatment of obesity. Ascletis received clearance for its Investigational New Drug (IND) applications from the U.S. Food and Drug Administration (FDA) in July 2024 for ASC30 tablets and September 2024 for ASC30 injection. The Company expects topline data from both U.S. Phase I clinical trials in the first quarter of 2025.

ASC30 was discovered and developed in-house at Ascletis as a GLP-1R biased small molecule agonist without β-arrestin recruitment. ASC30 has unique and differentiated properties that enable the administration of one small molecule as both a once-monthly subcutaneous injection and a once-daily oral tablet. ASC30 has two- to threefold better *in vitro* potency against GLP-1R when compared head-to-head with orforglipron. In the intravenous glucose tolerant test (IVGTT) in non-human primates (NHPs), ASC30 (1.5 mg/kg dose) stimulated statistically and significantly more insulin secretion when compared head-to-head with orforglipron (6 mg/kg dose).

In animal models, ASC30 injection showed a half-life of up to 25 days, supporting once-monthly injection in humans. In NHPs, a single dose of ASC30 subcutaneous injection demonstrated sustained and favorable weight loss over one month compared to six weekly doses of an antibody-peptide conjugate.

ASC30 once-monthly subcutaneous injection has potentially strong competitive advantages (less frequent injections and/or lower cost of goods) against weekly injected peptide GLP-1 drugs and monthly injected antibody-peptide conjugate drug candidate.

ASC30 once-daily tablets have the potential to be the best-in-class GLP-1R small molecule agonist given its superior pharmacokinetic (PK) profile and greater potency against GLP-1R. In animal models, ASC30 tablets had a half-life of up to 36 hours, supporting once-daily oral dosing. In NHPs, once-daily oral dosing of ASC30 demonstrated significant weight loss. Utilizing Ascletis' proprietary technology, the relative bioavailability of ASC30 tablets was 99% at steady state in animal models.

In obesity and diabetes markets, both once-monthly injections and oral once-daily administration are attractive to patients, who may choose to switch from injections to oral drugs or vice versa based on chronic weight management approach, lifestyle and convenience. As one small molecule, ASC30 offers both once-monthly injection and once-daily oral dosing options. Furthermore, the ASC30 oral tablet and injection offer same or similar safety profiles to enhance ease of switching between both options.

Two ASC30 Phase I Clinical Studies for the Treatment of Obesity

The Phase I study of ASC30 once-monthly subcutaneous injection is a randomized, double-blind, placebo-controlled, single ascending dose (5 cohorts) study being conducted in the U.S. to evaluate the safety, tolerability, PK and efficacy of ASC30 in participants with obesity over 16 weeks. In cohort 1, two patients with obesity have been successfully dosed with ASC30 once-monthly injection and demonstrated good safety and tolerability.

The Phase I study of ASC30 once-daily tablets is a randomized, double-blind, placebo-controlled, single ascending dose (6 cohorts) and multiple ascending dose (3 cohorts, 28 daily oral doses) study being conducted in the U.S. to evaluate the safety, tolerability, PK and efficacy of ASC30 in participants with obesity. In cohort 1, all eight obese patients (six on drug and two on placebo) have been successfully dosed with ASC30 tablets and demonstrated good safety and tolerability.

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 subcutaneous injection and oral tablet administrations. ASC30 is a new molecular entity (NME), with U.S. and global compound patent protection until 2044.

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, market 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

Hangzhou, the People's Republic of China
September 17, 2024

As at the date of this announcement, the Board of Directors of the Company comprises Dr. Jinzi Jason WU and Mrs. Judy Hejingdao WU, as executive Directors; Dr. Yizhen WEI, Mr. Jiong GU and Ms. Lin HUA, as independent non-executive Directors.