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 POSITIVE PHASE I CLINICAL RESULTS OF ORAL RDRP INHIBITOR ASC10 FOR COVID-19

– *The exposure of active drug ASC10-A after twice daily dosing 800 mg double prodrug ASC10 in Chinese subjects was 94% of that after twice daily dosing 800 mg single prodrug molnupiravir in Japanese subjects*

– *Based on Ascletis' Phase I results of ASC10 and molnupiravir's clinical efficacy data in American, Japanese and Chinese patients, 800 mg twice daily of ASC10 is selected for the registrational trial*

– *All doses of ASC10 including 800 mg twice daily were safe and well tolerated in Chinese subjects. Safety profiles between ASC10 and placebo treatments were comparable*

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 positive topline results from its Phase I multiple ascending dose (MAD) study (NCT05523141) in healthy subjects for oral RNA-dependent RNA polymerase (RdRp) inhibitor ASC10 for COVID-19 treatment. ASC10 is an innovative orally available double prodrug, which has a new and differentiated chemical structure from the single prodrug molnupiravir. After oral dosing, both ASC10 and molnupiravir are rapidly and completely converted *in vivo* into the same active drug ASC10-A, also known as β-D-N4-hydroxycytidine (NHC). Double prodrug approach significantly increased oral bioavailability of active drug ASC10-A.

The Phase I data demonstrated that all doses of ASC10 including 800 mg twice daily were safe and well tolerated in Chinese subjects. Safety profiles between ASC10 and placebo treatments were comparable. The exposure of active drug ASC10-A after twice daily dosing 800 mg double prodrug ASC10 in Chinese subjects was 94% of that after twice daily dosing 800 mg single prodrug molnupiravir in Japanese subjects[1]. The plasma concentrations of the double prodrug ASC10 in Chinese subjects were below detection limit (0.2 ng/mL) after 800 mg dosing. Similarly, the plasma concentrations of the single prodrug molnupiravir in American subjects were negligible after 800 mg dosing[2].

After the body weight normalization, the exposures of active drug ASC10-A are also equivalent between 800 mg double prodrug ASC10 in Chinese subjects and 800 mg single prodrug molnupiravir in American subjects[2].

The food had no effect on ASC10-A's exposure, indicating that ASC10 can be taken with or without food.

Molnupiravir has been approved or authorized for the emergent use in many countries including Japan and the U.S. Furthermore, recent publication indicated that molnupiravir demonstrated exciting clinical efficacy against omicron infections in Chinese patients[3].

Based on Ascletis' Phase I results of ASC10 and molnupiravir's clinical efficacy data in American[4], Japanese and Chinese patients, 800 mg twice daily is selected for the registrational trial.

The active drug ASC10-A has potent antiviral activity against various Omicron variants such as BA.5 and BA.2.75. Ascletis has filed multiple patent applications for ASC10 and its use globally. ASC10 oral tablet formulation for the clinical study was developed with in-house proprietary technology of Ascletis.

[1] Nakamura et al., Clin Transl Sci. 2022;00:1-12
[2] Painter et al., Antimicrobial Agents and Chemotherapy, May 2021, Volume 65, Issue 5, e02428-20
[3] Zou et al., Frontiers in Pharmacology, June 2022, Volume 13, Article 939573
[4] Bernal et al., The New England Journal of Medicine, December 16, 2021

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 commercialize ASC10 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
December 12, 2022

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.