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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 FDA CLEARANCE OF ORAL RDRP INHIBITOR ASC10 TO CONDUCT A RANDOMIZED, PLACEBO CONTROLLED PHASE Ib STUDY IN MILD-TO-MODERATE COVID-19 PATIENTS

- *ASC10 is an oral double prodrug that is rapidly and completely converted in vivo into the active metabolite ASC10-A, which is the same active metabolite of molnupiravir*

- *Ascletis has filed multiple patent applications for ASC10 and its use globally. Compared with molnupiravir, ASC10 has a new and differentiated chemical structure*

- *FDA recommended that Ascletis directly conduct the first clinical study of ASC10 in mild-to-moderate COVID-19 patients rather than in healthy subjects*

The board of directors (the "**Board**") of Ascletis Pharma Inc. (the "**Company**" or "**Ascletis**") announces that the U.S. Food and Drug Administration (FDA) has approved its Investigational New Drug (IND) application for ASC10, an oral drug candidate targeting RNA-dependent RNA polymerase (RdRp) for COVID-19, to conduct the Phase Ib clinical trial in mild-to-moderate COVID-19 patients. Ascletis will immediately initiate the clinical trial in patients to collect ASC10's clinical safety, pharmacokinetics and preliminary efficacy data.

ASC10 is an orally bioavailable double prodrug which has a new and differentiated chemical structure from the single prodrug molnupiravir. After oral administration, both ASC10 and molnupiravir are rapidly and completely converted *in vivo* into the same active metabolite ASC10-A, also known as β-D-N4-hydroxycytidine (NHC). ASC10 was discovered and developed in-house. 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.

By applying a double prodrug strategy, ASC10's permeability in Caco-2 cells (human colorectal adenocarcinoma cells) and active metabolite exposure in monkeys reached 3.2-fold and 2.1-fold of molnupiravir's, respectively. In the SARS-CoV-2 infected mouse models, ASC10 at 240 mg/kg twice daily led to a 4.0 log reduction in viral titer in lungs, equivalent to molnupiravir at 500 mg/kg twice daily[1]. Preclinical studies demonstrated that ASC10-A has potent cellular antiviral activity against Omicron variant (EC_{50} = 0.3 μM), Delta variant (EC_{50} = 0.5 μM) and wildtype virus (EC_{50} = 0.7 μM). It also suggested that there were no drug-drug interactions between ASC10 and other common medicines.

[1] Wahl, et al., Nature. 2021 March ; 591(7850): 451 -457.

FDA recommended that Ascletis directly conduct the first clinical study of ASC10 in mild-to-moderate COVID-19 patients rather than in healthy subjects. This study is a randomized, placebo controlled Phase Ib clinical trial to determine the safety, tolerability, pharmacokinetics and preliminary efficacy in multiple ascending doses of ASC10 tablets (200 mg, 400 mg or 800 mg twice daily) in mild-to-moderate COVID-19 patients for 5.5-day treatment with 28-day monitoring. Previously, molnupiravir was granted Emergency Use Authorization by FDA for 800 mg twice daily.

Currently, Ascletis is actively communicating with regulatory authorities to explore the possibility of further accelerating the clinical development of ASC10.

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
August 3, 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.