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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 U.S. IND FILING OF ORAL ANTIVIRAL ASC10 FOR MONKEYPOX INDICATION

- *ASC10 has two indications: monkeypox and SARS-CoV-2 virus infections. The Investigational New Drug (IND) application of the latter was approved by the U.S. Food and Drug Administration (FDA) in August 2022 and Phase Ib clinical trial in COVID-19 patients is underway in the U.S.*
- *Preclinical studies shows that ASC10 has potent antiviral activities against both monkeypox and SARS-CoV-2 viruses*
- *The IND filing of ASC10 for monkeypox indication in the U.S. will further broaden Ascletis' pipeline portfolio in viral diseases*

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 that the Investigational New Drug (IND) application of ASC10, an oral antiviral drug candidate targeting viral polymerase of monkeypox virus, has been filed with the U.S. Food and Drug Administration (FDA).

ASC10 is an orally bioavailable and broad antiviral spectrum 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) or EIDD-1931. Ascletis has filed multiple patent applications globally for ASC10 and its use in viral diseases including monkeypox virus infection.

The data from the *in vitro* antiviral cellular assay with infectious monkeypox virus demonstrated that ASC10-A has potent antiviral activity against monkeypox virus, suggesting that ASC10 has the potential to be an effective treatment of monkeypox virus infection. This study was conducted at IIT Research Institute, headquartered at Illinois Institute of Technology in Chicago, U.S. and sponsored by Ascletis.

In August 2022, a research paper was published by Dr. Watashi et al. at the National Institute of Infectious Diseases, Tokyo, Japan^[1]. In this research, Dr. Watashi et al. tested 132 drugs and showed that molnupiravir (active metabolite ASC10-A) and other two drugs have potent cellular antiviral activity in the infectious monkeypox virus assay. The rest of 129 drugs such as remdesivir, favipiravir, sofosbuvir and ribavirin, etc. do not have antiviral activities against monkeypox virus.

Monkeypox virus is an orthopoxvirus that causes a disease with symptoms similar to smallpox^[2]. As of October 26, 2022, there had been over 75,000^[3] confirmed cases globally and monkeypox virus had been spread in over 100 countries^[3] according to data from World Health Organization (WHO). In particular, a total of 28,061^[4] confirmed monkeypox/orthopoxvirus cases have been reported in the U.S. In China, the first confirmed case was reported on September 19, 2022. WHO assesses the risk of monkeypox virus in the European Region and the Region of the Americas as high^[3].

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. Studies have demonstrated^[5,6] that ASC10-A has potent cellular antiviral activity against various Omicron variants (BA.1 EC₅₀=0.3 µM; BA.2 EC₅₀=0.25 µM; BA.5 EC₅₀=0.23 µM; BA.2.75 EC₅₀=0.90 µM). The Phase Ib clinical trial in COVID-19 patients is underway in the U.S.

^[1] Daisuke Akazawa, Hirofumi Ohashi, Takayuki Hishiki, et al. Potential anti-monkeypox virus activity of atovaquone, mefloquine, and molnupiravir, and their potential use as treatments. bioRxiv preprint. <https://doi.org/10.1101/2022.08.02.502485>

^[2] https://www.who.int/health-topics/monkeypox/#tab=tab_1

^[3] https://worldhealthorg.shinyapps.io/mpx_global/

^[4] <https://www.cdc.gov/poxvirus/monkeypox/response/2022/index.html>

^[5] Takashita E, Yamayoshi S, Fukushi S, et al. Efficacy of Antiviral Agents against the Omicron Subvariant BA.2.75. *N Engl J Med.* 2022; 387(13): 1236-1238

^[6] In-house studies

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
October 26, 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.