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 FIRST PATIENT DOSED IN THE PHASE II CLINICAL TRIAL OF ASC42, AN IN-HOUSE DEVELOPED, BEST-IN-CLASS FXR AGONIST FOR CHRONIC HEPATITIS B INDICATION

- *ASC42 is a Novel anti-viral candidate for HBV functional cure through inhibiting the transcription of HBV cccDNA into HBV RNA and reducing the HBV cccDNA stability*

- *Combination of anti-viral candidate ASC42 with immunotherapy such as ASC22 (subcutaneously injected PD-L1 antibody) may offer an opportunity for synergistic effect, leading to high rate of HBV functional cure*

- *ASC42 is a best-in-class FXR agonist with no pruritus observed and LDL-C remained within normal range at the human therapeutic dose of 15 mg*

The board of directors (the "**Board**") of Ascletis Pharma Inc. (the "**Company**" or "**Ascletis**") is pleased to announce the dosing of the first patient in the Phase II clinical trial of ASC42 for chronic hepatitis B (CHB) indication.

The Phase II clinical trial (ClinicalTrials.gov Identifier: NCT05107778) is a multi-center, randomized, single-blind, placebo-controlled study in China to evaluate safety and efficacy of ASC42 tablets in combination with Entecavir and pegylated interferon-α-2a (PEG-IFN-α-2a) in subjects with CHB. About 45 CHB patients will be enrolled and receive ASC42 tablets (10 mg or 15 mg) or matching placebo orally once daily in combination with Entecavir (0.5 mg, orally once daily) and PEG-IFN-α-2a (180 μg, subcutaneous injection once a week) for 12 weeks, and serum hepatitis B surface antigen (HBsAg) and hepatitis B virus (HBV) pregenomic RNA (pgRNA) change from baseline will be measured during 12-week intervention period and 24-week follow-up period.

ASC42 is an in-house developed, selective, potent farnesoid X receptor (FXR) agonist with best-in-class potential. The U.S. Phase I trial (ClinicalTrials.gov Identifier: NCT04679129) of ASC42 indicated that there was no pruritus observed and LDC-C values remained within normal range during 14-day treatment of the once-daily human therapeutic dose of 15 mg while FXR target engagement biomarker Fibroblast Growth Factor 19 (FGF19) increased 1,780% and 7α-hydroxy-4-cholesten-3-one (C4) decreased 91% on Day 14.

As an FXR agonist, ASC42 has unique mechanism of action against HBV: ASC42 inhibits the transcription of HBV covalently closed circular DNA (cccDNA) into HBV RNA, which in turn inhibits the translation of HBV RNA into HBsAg. ASC42 may also reduce HBV cccDNA stability. Both *in vitro* primary human hepatocyte (PHH) cells and *in vivo* AAV/HBV mouse studies demonstrated that ASC42 significantly inhibited serum HBsAg and pgRNA, indicating that ASC42 has therapeutic potential to functionally cure CHB.

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 ASC42 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
January 11, 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.