Ascletis Pharma Inc.
歌禮製藥有限公司
(incorporated in the Cayman Islands with limited liability)
(Stock Code: 1672)

VOLUNTARY ANNOUNCEMENT

GANNEX ANNOUNCES COMPLETION OF THE U.S. PHASE I TRIAL OF ASC43F, AN IN-HOUSE DEVELOPED FIRST-IN-CLASS DUAL TARGETING FIXED-DOSE COMBINATION TABLET FOR NASH

- *ASC43F was safe and well tolerated in healthy subjects with no clinically significant study drug related adverse events*

- *Pharmacokinetic parameters of ASC41 and ASC42 from ASC43F are similar to those of ASC41 and ASC42 monotherapy*

- *Phase I trial completed two months after the U.S. IND approval, demonstrating execution excellence*

The board of directors (the "**Board**") of Ascletis Pharma Inc. (the "**Company**" or "**Ascletis**") is pleased to announce the completion of the U.S. Phase I trial of ASC43F, an in-house developed, first-in-class dual targeting fixed-dose combination (FDC) tablet for non-alcoholic steatohepatitis (NASH). ASC43F is a drug candidate of Gannex Pharma Co., Ltd. (甘萊製藥有限公司, "**Gannex**"), a wholly-owned subsidiary of the Company.

ASC43F is a once-a-day (QD), single tablet, FDC of 5 mg ASC41, a thyroid hormone receptor beta (THRβ) agonist, and 15 mg ASC42, a farnesoid X receptor (FXR) agonist. The U.S. Phase I trial (ClinicalTrials.gov Identifier: NCT05118516) was an open-label, single-dose study evaluating the safety, tolerability and pharmacokinetics of ASC43F in healthy subjects. The results showed that ASC43F was safe and well tolerated, without clinically significant adverse effects. The pharmacokinetic parameters of ASC41 and ASC42 from ASC43F are similar to those of ASC41 and ASC42 as monotherapy.

The positive results from the Phase I study of ASC43F support continued development of this promising dual targeting FDC into NASH patients. ASC41 and ASC42 have complementary mechanisms of action as THRβ agonists have shown primarily anti-metabolic effects, while FXR agonists have shown primarily anti-fibrotic, as well as anti-inflammatory effects. Thus, a combination of these two molecules can potentially work synergistically, targeting all NASH components – steatosis, ballooning, inflammation and fibrosis. In addition, a THRβ agonist combined with an FXR agonist may reduce potential adverse events, such as lowering atherogenic risks, by decreasing the elevated LDL-C that has been associated with other FXR agonists.

Previous Phase I studies in the U.S. and China have shown ASC41 at 5 mg to be safe and well tolerated in both healthy volunteers, overweight and obese subjects and patients with non-alcoholic fatty liver disease (NAFLD). In these studies, ASC41 significantly reduced low density lipoprotein cholesterol (LDL-C), triglyceride (TG), and total cholesterol (TC) in overweight and obese subjects with elevated LDL-C, a population that is characteristics of NASH.

Previous Phase I clinical data indicated that ASC42 was safe and well tolerated, with no pruritus and with LDC-C values remaining within normal range during 14-day treatment with once-daily therapeutic dose of 15 mg. FXR target engagement biomarkers Fibroblast Growth Factor 19 (FGF19) increased 1,780% and 7α-hydroxy-4-cholesten-3-one (C4) decreased 91% on Day 14 of treatment with 15 mg, once-daily dose.

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 ASC41, ASC42 and ASC43F 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 4, 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.