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 FIRST SUBJECT DOSED IN THE U.S. DRUG-DRUG INTERACTION STUDY OF FXR AGONIST ASC42 FOR TREATMENT OF PRIMARY BILIARY CHOLANGITIS

- *Enrollment of the total 12 subjects is expected to be completed in August 2022*
- *The DDI study on ASC42 in the U.S. is expected to be completed by the beginning of the fourth quarter 2022*
- *This DDI study and ongoing Phase II clinical trial in PBC patients in China will provide more evidence to support upcoming Phase III clinical trials in China, the U.S. and the European Union*

The board of directors (the "**Board**") of Ascletis Pharma Inc. (the "**Company**" or "**Ascletis**") announces that it has completed the first subject dosing in the U.S. drug-drug interaction (DDI) study of Farnesoid X receptor (FXR) agonist ASC42 for treatment of primary biliary cholangitis (PBC). This DDI study is expected to enroll 12 subjects in total in August 2022 and be completed by the beginning of the fourth quarter 2022 in the U.S. The DDI study and ongoing Phase II clinical trial in PBC patients in China will provide more evidence to support upcoming Phase III clinical trials in China, the U.S. and the European Union for treatment of PBC. ASC42 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.

PBC is a chronic autoimmune cholestatic disease and frequently progresses to liver fibrosis and cirrhosis requiring liver transplantation or resulting in death. In response to the increasing incidence, Asian Pacific Association for the Study of the Liver (APASL) developed the clinical practice guidance on the diagnosis and management of patients with PBC in 2022. PBC is gaining extensive attention as both the incidence and prevalence has showed an increasing tendency globally[1].

An epidemiology study indicates that there were approximately 120,000 PBC patients in the U.S. in 2014[2]. Ursodeoxycholic acid (UDCA) is the standard treatment for PBC, however, approximately 40% PBC patients have an inadequate response to or are unable to tolerate UDCA[3]. For those patients with insufficient UDCA response or intolerance, Obeticholic Acid (OCA) is the only approved medicine in the U.S. while it has not been approved in China yet. Additionally, OCA may significantly cause pruritus and low density lipoprotein cholesterol (LDL-C) levels to rise.

ASC42 is an in-house developed, novel non-steroidal, selective, potent FXR agonist with best-in-class potential and global intellectual property. Previous Phase I clinical trial in the U.S. (ClinicalTrials.gov Identifier: NCT04679129) demonstrated that ASC42 might be a potentially best-in-class PBC drug candidate as LDL-C levels were in normal range with no pruritus occurrence, and FXR target engagement biomarker FGF19 increased 1,780% when ASC42 was dosed at 15 mg, once daily (QD) during the 14-day treatment.

Currently, FXR agonist ASC42 is in Phase II clinical trial in China. The Phase II study (ClinicalTrials.gov Identifier: NCT05190523) consists of three ASC42 active treatment arms (5 mg, 10 mg and 15 mg) and one placebo control arm at the ratio of 1:1:1:1 and is expected to enroll a total of 100 patients who have an inadequate response to or are unable to tolerate UDCA. The treatment duration is 12 weeks.

Gannex intends to initiate Phase III clinical trials in China, the U.S. and the European Union after the completion of the ongoing Phase II clinical trial in China.

[1] Lv T, Chen S, Li M, et al. Regional variation and temporal trend of primary biliary cholangitis epidemiology: A systematic review and meta-analysis. J Gastroenterol Hepatol. 2020;36:1423-1434.

[2] Lu M, Zhou Y, Haller I V, et al. Increasing Prevalence of Primary Biliary Cholangitis and Reduced Mortality With Treatment [J]. Clin Gastroenterol Hepatol 2018, 16(8): 1342-50 e1. DOI: 10.1016/j.cgh.2017.12.033.

[3] Lindor K D, Bowlus C L, Boyer J, et al. Primary Biliary Cholangitis: 2018 Practice Guidance from the American Association for the Study of Liver Diseases [J]. Hepatology 2019, 69(1): 394-419. DOI: 10.1002/hep.30145.

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
August 16, 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.