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 POSITIVE TOPLINE RESULTS OF THE U.S. PHASE I TRIAL OF NASH DRUG ASC42, AN FXR AGONIST

- *No pruritus observed during 14-day treatment of the once-daily human therapeutic dose of 15 mg.*
- *FXR target engagement biomarker FGF19 increased 1,632% on Day 14 of treatment with 15 mg, once-daily.*
- *FXR target engagement biomarker C4 decreased 93% on Day 14 of treatment with 15 mg, once-daily.*
- *Mean LDL-C values remained within the normal range during 14-day, once daily treatment with 15 mg.*
- *There were no treatment-emergent ALT and AST elevations during 14-day, once daily treatment with 15 mg.*
- *Doses selected for Phase II trial in patients with NASH, which will be initiated by the end of 2021*

The board of directors (the "**Board**") of Ascletis Pharma Inc. (the "**Company**") is pleased to announce positive topline results of safety and pharmacodynamic biomarkers from the U.S. Phase I trial of NASH drug farnesoid X receptor (FXR) agonist ASC42 of Gannex Pharma Co., Ltd. (甘萊製藥有限公司, "**Gannex**"), a wholly-owned subsidiary of the Company.

The ASC42 Phase I trial in the U.S. was a first-in-human, randomized, placebo-controlled, double-blind single-ascending dose (SAD), multiple-ascending dose (MAD), and food effect trial in 64 healthy subjects receiving ASC42 or matching placebo. Doses in the SAD portion ranged from 5 to 200 mg doses and in the MAD portion ranged from 5 to 50 mg administered once-daily for 14 days. The food effect on ASC42 pharmacokinetics was studied with a dose of 15 mg. The primary objective was to evaluate the safety, pharmacokinetics and pharmacodynamics of ASC42 versus placebo. Biomarkers for FXR target engagement were assessed through measurement of 7α-hydroxy-4-cholesten-3-one (C4), a blood biomarker of bile acid synthesis that decreases with FXR activation, and Fibroblast Growth Factor 19 (FGF19), a hormone produced after FXR activation in the intestine that regulates bile acid synthesis as well as glucose and lipid metabolism.

Based on both mouse and rat NASH animal models, the predicted human therapeutic dose was 15 mg once-daily. ASC42 Phase I topline data showed that during 14-day treatment with 15 mg once-daily, Day 1 and Day 14 FGF19 levels increased 1,195% and 1,632% from the pre-dose level, respectively; Day 1 and Day 14 C4 levels decreased 88% and 93% from the baseline, respectively. Based on these data, 15 mg once-daily dose has been selected as one of three doses to be studied in the Phase II trial in patients with NASH, which will be initiated by the end of 2021. The magnitude of FGF19 increase and/or C4 decrease may be used to project potential levels of liver fat reduction in patients with NASH, with a ≥30% relative liver fat reduction on MRI-PDFF potentially correlating with an increased likelihood of histologic benefit.

Overall, ASC42 was safe and tolerated and there were no study drug related SAEs or premature discontinuations. Notably, there was no pruritus, mean LDL-C values remained within normal limits and there were no treatment-emergent ALT and AST elevations for 14-day, once daily dosing with 15 mg.

In addition, there was no significant food effect on the pharmacokinetic profile of ASC42 with a high fat meal.

ASC42 is an in-house developed, novel non-steroidal, selective, potent FXR agonist with best-in-class potential. ASC42 is an oral tablet formulation developed with in-house proprietary technology and is stable at room temperature. ASC42 is expected to be used alone and in combination with thyroid hormone receptor beta (THR-β) agonist ASC41 or fatty acid synthase (FASN) inhibitor ASC40.

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
June 16, 2021

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.