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 CLINICAL AND PRECLINICAL DATA OF FOUR NASH PROGRAMS TO BE PRESENTED IN ORAL OR POSTER PRESENTATION AT THE LIVER MEETING® 2021 BY AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

The board of directors (the "**Board**") of Ascletis Pharma Inc. (the "**Company**") is pleased to announce that the latest clinical and preclinical data of four NASH programs (ASC40/TVB-2640 co-authored with Sagimet Biosciences Inc., ASC41, ASC42 and ASC43F) of its wholly-owned subsidiary, Gannex Pharma Co., Ltd. (甘萊製藥有限公司，"**Gannex**") will be presented in oral or poster presentation at The Liver Meeting® 2021 of American Association for the Study of Liver Diseases (AASLD). The Liver Meeting® is one of the world's premier meetings on liver disease and will be held from November 12, 2021 to November 15, 2021.

The abstracts to be presented at The Liver Meeting® 2021 are as follows:

NOVEL, FIRST-IN-CLASS, FATTY ACID SYNTHASE (FASN) INHIBITOR TVB-2640 DEMONSTRATES ROBUST CLINICAL EFFICACY AND SAFETY IN A GLOBAL PHASE 2 RANDOMIZED PLACEBO-CONTROLLED NASH TRIAL (FASCINATE-1) CONDUCTED IN THE US AND CHINA

Presentation Type: Oral, Parallel Session

Publication Number: 141

Session Title: Parallel 21: NAFLD and NASH: Clinical Trials of Novel Therapeutics

Presenting Author: Dr. Rohit Loomba, MD, University of California

Session Broadcast Date and Time: Sunday, November 14, 2021, 6:30-8:00 PM EST

Highlights:

- *TVB-2640 is an oral, once-daily, first-in-class small molecule FASN inhibitor that reduces excess liver fat, inhibits inflammatory and fibrogenic pathways.*
- *Subjects with MRI-PDFF ≥8% and fibrosis (MRE ≥2.5 kPa or biopsy F1-F3) were randomized 2:1 to TVB-2640 or placebo once daily (US N=99; China N=30) for 12 weeks to access the efficacy and safety of TVB-2640.*
- *TVB-2640 was well-tolerated, with no AEs ≥ Gr. 3 and no on treatment SAEs.*
- *PK profiles (50mg) were similar in the U.S. and China.*
- *TVB-2640 reduced liver fat and decreased alanine aminotransferase (ALT) in both populations, that combined had a relative PDFF reduction of 28.2% (50mg, N=48) at W12 v. 6.4% placebo (N=19, p=0.019) and absolute PDFF reduction of 5% v. 1.6% placebo (p<0.0001). The PDFF response rates were 56% (50mg) v. 15% placebo.*

A PHASE Ib STUDY TO EVALUATE THE SAFETY, TOLERABILITY, PHARMACOKINETICS AND PHARMACODYNAMICS OF ASC41, A THR-β AGONIST, FOR 28-DAYS IN OVERWEIGHT AND OBESE SUBJECTS WITH ELEVATED LDL-C, A POPULATION CHARACTERISTIC OF NAFLD

Presentation Type: Poster Presentation

Publication Number: 1851

Session Title: NAFLD and NASH: Experimental: Clinical

Presentation time: Friday, November 12, 2021, 6:00-11:55 AM EST

Highlights:

- *ASC41 is a small molecule, hepatic targeting, potent and selective thyroid hormone receptor beta (THRβ) agonist prodrug, which is converted to its pharmacologically active metabolite ASC41-A by CYP3A4 in the liver.*

- *Twenty overweight and obese subjects with elevated low density lipoprotein cholesterol (LDL-C) (>110 mg/dL) were treated with ASC41 10mg oral tablets or matching placebo tablets with the ratio of 3:1 once daily in this randomized, double-blind, placebo controlled clinical study to evaluate the safety, tolerability, pharmacokinetics and lipid lowering potential of ASC41 oral tablets.*

- *Compared with placebo, lipid parameters (LDL-C, TG, TC, Apo-B, and LP (a)) for those treated with ASC41 showed clinically meaningful and statistically significant reductions ($P<0.05$).*

- *ASC41 was tolerable and had a benign adverse event (AE) profile with no serious adverse reactions and no adverse reactions above Grade 3.*

ASC42, A NOVEL NON-STEROIDAL FXR AGONIST, DEMONSTRATES A NORMAL CHOLESTEROL PROFILE AND LACK OF PRURITUS AT THERAPEUTIC DOSES IN A 14-DAY PHASE I RANDOMIZED, DOUBLE-BLIND, PLACEBO CONTROLLED STUDY IN HEALTHY VOLUNTEERS

Presentation Type: Poster Presentation

Publication Number: 1854

Session Title: NAFLD and NASH: Experimental: Clinical

Presentation time: Friday, November 12, 2021, 6:00-11:55 AM EST

Highlights:

- *ASC42 is a potent, orally available, non-steroidal farnesoid X receptor (FXR) agonist under clinical development for NASH.*
- *Sixty-four healthy volunteers (8 cohorts n=8 (6 active:2 placebo)) were dosed with 5-200mg (single-ascending doses) and 14 days of 5-50mg qd (multi-ascending doses), to evaluate the safety and tolerability of ASC42 and to establish the PK and PD profiles of ASC42.*
- *No pruritus was observed during the 14-day treatment at the human therapeutic dose of 15mg.*
- *ASC42 for 14-days was well tolerated and safe, without elevated ALT/aspartate aminotransferase (AST) or lipid parameter abnormalities at doses within the therapeutic dose range.*
- *FXR targets activated biomarker of fibroblast growth factor 19 (FGF19) levels increased 1,632% from baseline at Day-14 with the dose of 15mg.*
- *FXR targets activated biomarker of 7α-hydroxy-4-cholesten-3-one (C4) levels decreased 93% from baseline at Day-14 with the Dose of 15mg.*
- *Based on the study data, 15mg qd has been selected as one of 3 doses to be studied in the Phase II trial in patients with NASH.*

ASC43F TABLET AS A ONE-PILL, ONCE-A-DAY FIXED-DOSE COMBINATION (FDC) OF ASC41, A THR-β AGONIST, AND ASC42, AN FXR AGONIST, DEMONSTRATED COMPARABLE DISSOLUTION PROFILES AND IN VIVO PHARMACOKINETICS VS. SINGLE ASC41 AND ASC42 TABLET

Presentation Type: Poster Presentation

Publication Number: 1762

Session Title: NAFLD and NASH: Experimental: Basic

Presentation time: Friday, November 12, 2021, 6:00-11:55 AM EST

Highlights:

- *ASC43F is a One-Pill, Once-a-Day FDC of ASC41, an oral hepatic targeting THR-β agonist prodrug, and ASC42, a non-steroidal, selective, potent, oral FXR agonist.*
- *Three male beagle dogs were dosed with ASC42 tablet (15mg), ASC41 tablet (5mg) and ASC43F tablet (ASC42/ASC41 15mg/5mg) in a cross-over study design with a 5-day washout period to evaluate in vivo PK. Dissolution profiles of ASC43F tablets were compared with those of single ASC41 and ASC42 tablets.*
- *In beagle dogs, the PK parameters of ASC42 and ASC41A in/from ASC43F tablets remained approximately unchanged as compared to those of single ASC41 and ASC42 tablets.*
- *The dissolution profiles of ASC41/ASC42 in ASC43F tablets were similar to those of single ASC41 and ASC42 tablets using 4 different pH dissolution media.*
- *The stability data demonstrated that ASC43F tablets were stable in the accelerated condition of 40℃/75%RH for 4.5 months (equivalent to 1.5 years in the normal condition).*

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 ASC22, ASC40, 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
October 13, 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.