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 POSTER PRESENTATION DESCRIBING POSITIVE INTERIM 12-WEEK RESULTS FROM ONGOING 52-WEEK PHASE II CLINICAL TRIAL OF ONCE-DAILY ASC41 IN PATIENTS WITH BIOPSY-CONFIRMED MASH AT EASL CONGRESS 2024

– *Up to 68.2% mean relative reduction in liver fat content from baseline among biopsy-confirmed metabolic dysfunction-associated steatohepatitis (MASH) patients receiving 12-week treatment of ASC41*

– *Significant and clinically meaningful reductions in liver fat, alanine aminotransferase (ALT), aspartate aminotransferase (AST) and lipids as well as excellent safety and tolerability profile demonstrated by ASC41 in MASH patients*

This announcement is made by Ascletis Pharma Inc. (the "**Company**" or "**Ascletis**", together with its subsidiaries, the "**Group**") on a voluntary basis for the purpose of keeping the shareholders of the Company and potential investors abreast of the latest business development of the Group.

The board of directors (the "**Board**") of the Company announces that, on June 11, 2024, Gannex Pharma Co., Ltd. ("**Gannex**"), a wholly-owned subsidiary of the Company, dedicated to the research and development and commercialization of new drugs in the field of metabolic dysfunction-associated steatohepatitis (MASH), announced a poster presentation at the European Association for the Study of the Liver (EASL) Congress 2024, held June 5-8, 2024 in Milan, Italy. A copy of the poster is available under the Posters/Publications page of Gannex's website at www.gannexpharma.com.

The poster presentation titled, "*ASC41, a selective THRβ agonist significantly reduces liver fat and ALT in biopsy-confirmed MASH patients after 12-week treatment: an interim analysis of a 52-week serial liver biopsy study*", describes significant and clinically meaningful reductions in liver fat, alanine aminotransferase (ALT) and aspartate aminotransferase (AST) in biopsy-confirmed MASH patients receiving 12-week treatment of ASC41 tablet, among which the data of ALT and AST notably differentiates ASC41 from other thyroid hormone receptor β (THRβ) agonists currently at clinical or commercial stages. In addition, baseline characteristics from Phase II clinical trials were comparable between ASC41, conducted in China, and resmetirom, except for lower body mass index (BMI) and more males for ASC41. Please refer to Table 1 below for more details.

Table 1. Baseline Characteristics

Characteristics	ASC41 Phase 2			Resmetirom Phase 2[1]	
	PBO (n=14)	2 mg (n=13)	4 mg (n=15)	Placebo (n=41)	60/80 mg (n=84)
Age, years	41.2 (11.6)	36.1 (11.0)	34.7 (6.5)	47.3 (11.7)	51.8 (10.4)
Male, n (%)	9 (64.3%)	12 (92.3%)	13 (86.7%)	24 (59%)	38 (45%)
MRI-proton density fat fraction, % fat fraction (SD)	18.2% (6.7)	17.8% (5.4)	18.9% (7.9)	19.6% (8.2)	20.2% (6.8)
Diabetes, n (%)	4 (28.6%)	3 (23.1%)	3 (20.0%)	13 (32%)	36 (43%)
Body-mass index, kg/m^2	28.7 (3.1)	29.7 (4.8)	30.4 (5.1)	33.6 (5.8)	35.8 (6.2)
ALT (U/L)	77.6 (56.2)	65.9 (31.2)	84.8 (32.6)	60.1 (32.2)	50.0 (29.2)
AST (U/L)	47.9 (31.6)	44.2 (23.0)	53.8 (18.2)	38.0 (20.7)	35.1 (17.7)
HDL-C (mg/dL)	44.8 (8.7)	58.4 (6.0)	41.5 (6.3)	45.2 (13.4)	43.8 (12.5)
LDL-C (mg/dL)	116.0 (25.4)	127.5 (24.6)	122.61 (25.1)	116.9 (30.0)	111.3 (30.4)
TG (mg/dL)	156.8 (54.0)	180.4 (74.3)	228.6 (126.5)	161.1 (75.2)	178.5 (82.4)

Data are mean (SD) or n (%) unless otherwise stated.

[1] Harrison, S. A., et al.[J] Lancet, (2019).DOI: 10.1016/s0140-6736(19)32517-6.

In Table 1, "PBO" stands for placebo, "MRI" stands for magnetic resonance imaging, "ALT" stands for alanine aminotransferase, "AST" stands for aspartate aminotransferase, "HDL-C" stands for high-density lipoprotein cholesterol, "LDL-C" stands for low-density lipoprotein cholesterol and "TG" stands for triglycerides.

ASC41, a once-daily oral tablet, is a liver targeted small molecule and is highly THRβ-selective. The oral tablet formulation was developed utilizing Ascletis' in-house proprietary technology. Three Phase I or Ib studies in China were completed in healthy or obese subjects with elevated low-density lipoprotein cholesterol (LDL-C) > 110 mg/dL. A U.S. Phase I study demonstrated no clinically significant drug-drug interactions between ASC41/ASC41-A and most frequently used antidepressants and statins, as well as no significant difference in drug exposure between Americans and Chinese at the same dose.

Table 2. Changes from Baseline (CFB) in LFC, Liver Enzymes and Lipids Biomarkers at Week 12

Parameters	Placebo (n = 14)	ASC41 Tablet	
		2 mg, QD (n = 13)	4 mg, QD (n = 15)
Mean relative CFB in LFC	-13.1%	-55.0% (p = 0.0001)	-68.2% (p < 0.0001)
Percentage of patients achieving LFC reduction ≥ 30%	21.4%	92.3% (p = 0.0002)	93.3% (p < 0.0001)
Percentage of patients achieving LFC reduction ≥ 50%	21.4%	46.2% (p = 0.24)	86.7% (p = 0.0004)
Percentage of patients achieving ≤ 5% absolute LFC	0.0%	30.8% (p = 0.16)	66.7% (p = 0.0017)
Mean relative CFB in ALT	5.2%	-8.5% (p = 0.61)	-32.6% (p = 0.0051)
Percentage of patients achieving ALT reduction > 17 U/L	21.4%	30.8% (p = 0.68)	73.3% (p = 0.0052)
Mean relative CFB in AST	17.3%	-3.6% (p = 0.67)	-24.2% (p = 0.041)
Mean relative CFB in LDL-C	4.3%	-19.4% (p = 0.0002)	-23.4% (p < 0.0001)
Mean relative CFB in TC	3.4%	-16.8% (p < 0.0001)	-20.0% (p < 0.0001)
Mean relative CFB in TG	3.9%	-30.6% (p = 0.0001)	-42.6% (p < 0.0001)

In Table 2, "LFC" stands for liver fat content, "ALT" stands for alanine aminotransferase, "AST" stands for aspartate aminotransferase, "LDL-C" stands for low-density lipoprotein cholesterol, "TC" stands for total cholesterol and "TG" stands for triglycerides.

ASC41 was generally well tolerated, with adverse events (AEs) being grade 1 in majority across all cohorts in the Phase II clinical trial, including the placebo cohort (see Table 3). No treatment-related serious adverse event (SAE) was reported in any patients receiving ASC41 treatment or placebo. As in prior studies, ASC41 demonstrated excellent gastrointestinal (GI) tolerability.

Table 3. Safety Data

Event, n (%)	Placebo (n = 14)	ASC41 Tablet	
		2 mg, QD (n = 13)	4 mg, QD (n = 15)
TEAEs	13 (92.9%)	13 (100%)	15 (100%)
Drug-related TEAEs	6 (42.9%)	7 (53.9%)	7 (46.7%)
Grade 1	6 (42.9%)	7 (53.9%)	7 (46.7%)
Drug-related GI AEs	2 (14.3%)	3 (23.1%)	1 (6.7%)
Nausea	0 (0.0%)	0 (0.0%)	0 (0.0%)
Vomiting	0 (0.0%)	0 (0.0%)	0 (0.0%)
Diarrhea	1 (7.1%)	3 (23.1%)	1 (6.7%)
Abdominal distension	1 (7.1%)	0 (0.0%)	0 (0.0%)
Abdominal pain (upper)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Constipation	0 (0.0%)	0 (0.0%)	0 (0.0%)
Dyspepsia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Frequent bowel movements	0 (0.0%)	0 (0.0%)	0 (0.0%)

In Table 3, "TEAEs" stands for treatment emergent adverse events, "GI" stands for gastrointestinal, "AEs" stands for adverse events and "QD" stands for every day.

About ASC41

ASC41, a once-daily oral tablet in clinical development for the treatment of MASH, is a liver targeted small molecule which is converted into its active metabolite, ASC41-A, a potent and highly selective THRβ agonist. ASC41 tablet was developed using Ascletis' in-house proprietary formulation technology. The patent of ASC41 tablet formulation has been granted in the U.S.

About the Phase II Clinical Trial

The randomized, double-blind, placebo-controlled and multi-center Phase II clinical trial (ClinicalTrials.gov: NCT05462353) is being conducted in China and is expected to enroll approximately 180 liver biopsy-confirmed MASH patients to be randomized into two treatment cohorts of ASC41 tablet (2 mg or 4 mg), once-daily and one placebo control cohort at the ratio of 1:1:1 for 52-week treatment and 4-week follow-up. Enrollment included patients with at least 7.5% liver fat content at baseline as measured by magnetic resonance imaging proton density fat fraction (MRI-PDFF), as well as F2 and F3 liver fibrosis. The study allows up to 15% of enrolled patients to have F1 liver fibrosis. Two liver biopsies will be performed, one at baseline and the other at the end of 52-week treatment. MRI-PDFF will be performed at baseline, Week 12 and Week 52, respectively. The pre-specified interim analysis was conducted when 42 enrolled patients completed 12-week treatment of ASC41 tablet or placebo. Primary objective is a histological reduction in nonalcoholic fatty liver disease (NAFLD) activity score (NAS) ≥ 2 points that results from reduction of necro-inflammation (inflammation or ballooning) without worsening fibrosis. Secondary objectives include MASH resolution and fibrosis improvement.

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 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 11, 2024

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.