亞盛醫藥
Ascentage Pharma

ASCENTAGE PHARMA GROUP INTERNATIONAL
亞盛醫藥集團

(Incorporated in the Cayman Islands with limited liability)
(Stock Code: 6855)

Voluntary Announcement

Phase IIa clinical study of APG-115 as single agent or in combination with APG-2575 receives clearances in China and the U.S.

Ascentage Pharma Group International (the "**Company**" or "**Ascentage Pharma**") is pleased to announce that the Center for Drug Evaluation (CDE) of China National Medical Products Administration (NMPA) has approved a clinical study of the Company's class 1 novel MDM2-p53 inhibitor APG-115, as a single agent or in combination with the Company's other class 1 novel Bcl-2 inhibitor APG-2575, and will commence the Phase IIa clinical study for the treatment of patients with relapsed/refractory T-cell prolymphocytic leukemia (R/R T-PLL). Previously, such study plan has already received clearance from the U.S. Food and Drug Administration (FDA).

This global multicenter, open-label Phase IIa clinical study was designed to evaluate the safety, pharmacokinetics, and preliminary efficacy of APG-115 as a single agent or in combination with APG-2575 for the treatment of patients with R/R T-PLL.

T-PLL is an aggressive T-cell leukemia[1]. Ataxic telangiectasia mutation (ATM) caused by the deletion or missense mutation of 11q23 occurs in up to 80–90% of patients with T-PLL[2]. Ascentage Pharma's pre-clinical study discovered that in patient-derived xenograft (PDX) models harboring the ATM mutation, APG-115 demonstrated impressive antitumor activity; in a panel of cancer cell line or patient-derived xenograft models (CDX) or PDX representing human hematologic or solid malignancies, APG-115, in combination with APG-2575 has demonstrated potent synergistic effect and significantly enhanced antitumor activities. It is worth noting that such combination produced a response rate of 100% in xenograft models of MV-4-11 acute myeloid leukemia (AML) and Z138 mantle cell lymphoma (MCL) cell lines.

APG-115 is an orally administered, selective, small-molecule inhibitor of the MDM2 protein under the development of Ascentage Pharma. APG-115 has strong binding affinity to MDM2 and is designed to activate tumor suppression activity of p53 by blocking the MDM2-p53 protein-protein interaction. APG-115 is the first MDM2-p53 inhibitor entering into clinical stage in China, with multiple ongoing clinical studies in solid tumors and hematologic malignancies in China and the U.S..

The Company believes concurrent inhibition of both MDM2-TP53 and BCL-2 apoptosis pathways by the combination of APG-115 and APG-2575 has great clinical significance in triggering 'synthetic lethality' and effectively induces cell death by simultaneously blocking two important nodes of both apoptosis pathways[3]. Apart from that, both APG-115 and APG-2575 are orally bioavailable targeted agents, and the combination may provide a chemo-free treatment option for patients with T-PLL. Hence, the clinical application value is high. Further, the combination treatment in R/R T-PLL is a pioneer therapy worldwide. The Company hopes its relevant research can deliver a clinical breakthrough for patients with T-PPL and benefit more patients earlier and quicker.

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 obtain further approval for, or ultimately market APG-115 and APG-2575 successfully.

By order of the Board
Ascentage Pharma Group International
Dr. Yang Dajun
Chairman and Executive Director

Suzhou, People's Republic of China, December 2, 2020

As at the date of this announcement, the Board of Directors of the Company comprises Dr. Yang Dajun as Chairman and executive Director, Dr. Wang Shaomeng, Dr. Tian Yuan, Mr. Zhao Qun, Dr. Lu Simon Dazhong and Mr. Liu Qian as non-executive Directors, and Mr. Ye Changqing, Dr. Yin Zheng and Mr. Ren Wei as independent non-executive Directors.

References:

1. Swerdlow SH, Campo E, Pileri SA, et al. The 2016 revision of the World Health Organization classification of lymphoid neoplasms. Blood. 2016;127(20):2375–2390.

2. Schrader A, Crispatzu G, Oberbeck S, et al. Actionable perturbations of damage responses by TCL1/ATM and epigenetic lesions form the basis of T-PLL. Nat Commun. 2018;9(1):697.

3. Pan R, Ruvolo V, Mu H, et al. Synthetic Lethality of Combined Bcl-2 Inhibition and p53 Activation in AML: Mechanisms and Superior Antileukemic Efficacy. Cancer Cell. 2017 Dec 11; 32(6): 748–760. e6.