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

## ASCENTAGE PHARMA ANNOUNCES IND APPROVAL IN CHINA FOR PHASE I STUDY OF APG-5918 IN PATIENTS WITH ADVANCED SOLID TUMORS OR HEMATOLOGIC MALIGNANCIES

Ascentage Pharma Group International (the "**Company**" or "**Ascentage Pharma**") is pleased to announce that its novel inhibitor of the embryonic ectoderm development (EED) protein, APG-5918, has been approved by the Center for Drug Evaluation (CDE) of China National Medical Products Administration (NMPA) to enter a Phase I study in patients with advanced solid tumors or hematologic malignancies. Following the recent clearance for the study in the US for advanced solid tumors or hematologic malignancies, this approval in China marks another milestone for the Company's strategy of simultaneous clinical development in the two countries. APG-5918 is the first domestically developed novel EED inhibitor entering clinical development in China.

This multicenter, open-label Phase I dose-escalation and dose-expansion study is designed to assess the safety, pharmacokinetics, and efficacy of orally administered APG-5918 in patients with advanced solid tumors or hematologic malignancies. Prof. Ruihua Xu, President and Director of Sun Yat-Sen University Cancer Center, and President of the Chinese Society of Clinical Oncology, will be the principal investigator of this study.

EZH2, which is highly expressed in multiple tumors in humans, was found to promote the development and progression of tumors, and targeted inhibition of EZH2's methyltransferase activity has already proved to be an effective mechanistic approach for cancer treatment. However, the secondary mutation of EZH2 may lead to acquired drug resistances, while the homologous EZH1 also has methyltransferase (MTase) activity that could limit the effects of EZH2 inhibitors. Studies have shown that the PRC2 complex's component proteins and EZH2's histone (MTase; HMTase) activities are highly dependent on the scaffold and modulating effects of EED. Compounds with inhibitory effects on EED, a subunit of PRC2, can disrupt the protein-to-protein interaction between EED and EZH2, culminating in damaged PRC2 functions, H3K27me3-induced silencing of PRC2 expressions, and blockade of the triple-methylation of H3K27.[1] Therefore, allosteric targeting of EED has in recent years gained a great deal of traction as a promising approach for inhibiting the replacement of inactivated PRC2.

Discovered and developed by Ascentage Pharma, APG-5918 is an orally active, potent, selective, small-molecule EED inhibitor with high binding affinity. APG-5918 can regulate the epigenetics of tumors and the tumor microenvironment, and therefore has broad therapeutic potential for the treatment of hematologic malignancies, solid tumors, and nononcologic conditions. APG-5918 can selectively bind to the H3K27me3 domain of the EED protein, leading to the conformational changes to H3K27me3's binding pockets in the EED protein, which can then block EED from interacting with the histone methyltransferase EZH2. Preliminary data showed that APG-5918 has *in vitro* antiproliferative activity in various tumor cell lines and antitumor activity in patient-derived xenograft (PDX)/cell line-derived xenograft (CDX) models of EZH1-mutant B-cell non-Hodgkin lymphoma, IN1-negative malignant rhabdoid tumor, BAP1-mutant mesothelioma and prostate cancer.

**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-5918 successfully.

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

Suzhou, People's Republic of China, November 10, 2022

*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 and Dr. Lu Simon Dazhong as non-executive Directors, and Mr. Ye Changqing, Dr. Yin Zheng, Mr. Ren Wei and Dr. David Sidransky as independent non-executive Directors.*

**Reference**

1. Erokhin M, Chetverina O, Győrffy B, Tatarskiy V V, Mogila V, Shtil AA, et al. Clinical correlations of polycomb repressive complex 2 in different tumor types. Cancers 2021;13:3155.