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## **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's MDM2-p53 Inhibitor APG-115 Granted Fast Track Designation by the US FDA for the Treatment of Relapsed/Refractory Unresectable or Metastatic Melanoma**

Ascentage Pharma Group International (the “**Company**” or “**Ascentage Pharma**”) is pleased to announce that its novel MDM2-p53 inhibitor alrizomadlin (APG-115) under development has been granted a Fast Track Designation (FTD) by the US Food and Drug Administration (FDA) for the treatment of patients with unresectable or metastatic melanoma, relapsed/refractory to prior immuno-oncologic agent (IO) treatments. Previously, APG-115 was already granted five Orphan Drug Designations (ODDs) by the US FDA, one of which was for the treatment of stage IIB-IV melanoma.

Melanoma is a potentially deadly dermatologic malignancy that has been increasingly prevalent globally. The current lifetime risk of developing melanoma is 1 in 63 in the US<sup>1</sup>. In 2019, an estimated 96,480 patients have been diagnosed with melanoma and about 7,230 patients with melanoma have died in the United States<sup>2</sup>. Advanced melanoma presents an enormous clinical challenge as it is prone to metastasis and lacks survival benefit from chemotherapies. Immune checkpoint inhibitors (ICIs) are currently recommended for the first-line treatment of most patients with metastasized melanoma<sup>3</sup>. Although approximately 35% to 60% of the patients have a response evaluation criterion in solid tumors (RECIST) response to ICIs, there are still 40% to 65% of the patients who have shown minimal or no RECIST response at the outset, and among which 43% develop acquired resistance in the three years after receiving ICIs<sup>4</sup>. Therefore, patients who failed on or developed acquired resistance to ICIs are in urgent need of new treatment options.

This FTD for APG-115 is based on combined preclinical results and preliminary clinical data from an ongoing Phase II study (APG-115-US-002, NCT03611868). Those preliminary clinical data were released in an oral report at the 2021 American Society of Clinical Oncology (ASCO) Annual Meeting, and showed that APG-115 has favorable antitumor activity and a manageable safety profile. The cohort of patients with PD-1/PD-L1 inhibitor-resistant melanoma treated with APG-115 in combination with pembrolizumab achieved one case of complete response (CR), an objective response rate (ORR) of 24.1%, and a disease control rate (DCR) of 55.2%.

The FTD expedites the development and review of drug candidates to treat serious diseases/conditions that present urgent unmet clinical needs. This FTD for APG-115 will create opportunities that could accelerate the clinical development and review for this drug candidate in various manners, including more frequent communications and meetings with the FDA during its clinical development; and if relevant standards are met, to be allowed to enter Rolling Review, a process that allows a company to submit New Drug Applications (NDAs) by sections, rather than waiting until all required materials become available. This FTD also paves the way for APG-115 to potentially obtain Accelerated Approval and Priority Review designations in the future.

### **About APG-115**

Being developed by Ascentage Pharma, APG-115 is an orally administered, selective, small-molecule inhibitor of the MDM2 protein. 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 clinical development in China and is currently being investigated in multiple Phase Ib/II clinical studies in solid tumors and hematologic malignancies in China, the US and Australia. To date, APG-115 has been granted a total of five Orphan Drug Designations (ODDs) by the US FDA for the treatment of gastric cancer, acute myeloid leukemia, soft tissue sarcoma, retinoblastoma, and stage IIB-IV melanoma.

### **About Ascentage Pharma**

Ascentage Pharma is a China-based, globally focused, clinical-stage biotechnology company engaged in developing novel therapies for cancers, CHB (Chronic hepatitis B), and age-related diseases. On October 28, 2019, Ascentage Pharma became listed on the Main Board of The Stock Exchange of Hong Kong Limited with the stock code: 6855.HK.

Ascentage Pharma has its own platform for developing therapeutics that inhibit protein-protein interactions to restore apoptosis or programmed cell death. The company has built a pipeline of eight type I small molecule clinical drug candidates which have entered the clinical development stage, including novel, highly potent Bcl-2 inhibitors, as well as candidates aimed at IAP and MDM2-p53 pathways, and next-generation tyrosine kinase inhibitors (TKIs). Ascentage Pharma is also the only company in the world with active clinical programs targeting all key apoptosis regulators. The Company is conducting more than 40 Phase I/II clinical trials in China, the US and Australia. HQP1351, the Company's core drug candidate developed for the treatment of drug-resistant chronic myeloid leukemia (CML), has been granted an Orphan Drug Designation (ODD) and a Fast Track Designation (FTD) by the US FDA, and a New Drug Application (NDA) for the drug candidate has been submitted and subsequently granted Priority Review by the Center for Drug Evaluation (CDE) in China. As at the date of this announcement, Ascentage Pharma has obtained a total of twelve ODDs from the US FDA for four of the Company's investigational drug candidates.

**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 successfully.

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

Suzhou, People's Republic of China, September 23, 2021

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

## References

1. *Stephanie C, Christy S, Jessica W. Epidemiology and Risk Factors of Melanoma. Surg Clin North Am. 2020 Feb;100(1):1–12.*
2. *Cancer Facts & Figures 2019. American Cancer Society. Link: <https://www.cancer.org/research/cancer-facts-statistics/all-cancer-facts-figures/cancer-facts-figures-2019.html>*
3. *National Comprehensive Cancer Network (NCCN®) Guidelines for the Treatment of Cancers, Version 2.2021*
4. *Tuba G, James W, Richard S, et al. Primary and Acquired Resistance to Immune Checkpoint Inhibitors in Metastatic Melanoma. Clin Cancer Res. 2018 Mar 15;24(6):1260-1270.*