

Hong Kong Exchanges and Clearing Limited and The Stock Exchange of Hong Kong Limited take no responsibility for the contents of this announcement, make no representation as to its accuracy or completeness and expressly disclaim any liability whatsoever for any loss howsoever arising from or in reliance upon the whole or any part of the contents of this announcement.



ASCENTAGE PHARMA GROUP INTERNATIONAL

亞盛醫藥集團

(Incorporated in the Cayman Islands with limited liability)

(Stock Code: 6855)

Voluntary Announcement

Entry into of an agreement with the University of Michigan to obtain an exclusive license for a MDM2 Protein Degradar using PROTACs Technology

Ascentage Pharma Group International (the “**Company**” or “**Ascentage Pharma**”) is pleased to announce that it has entered into an agreement with the University of Michigan, through which the Company shall obtain the exclusive global rights to a MDM2 protein degrader developed using the Proteolysis-Targeting Chimeras (PROTACs) technology. The drug candidate has entered into IND-enabling studies.

MDM2 is a key regulator of the tumor suppressor p53 and one of the most potent inhibitors of apoptosis discovered thus far. It has high expression in tumors and plays a key role in the occurrence and development of tumors¹. The PROTACs technology has emerged as a new approach that induces the degradation of targeted proteins through the ubiquitin-proteasome system (UPS), and it has received widespread interest from both the scientific community and the industry since its introduction. Compared to conventional “occupancy-driven” pharmacological modality, the “event-driven” PROTACs technology has many advantages, such as high potency, high selectivity, with catalytic mode of action, and the ability to target undruggable proteins².

Dr. Shaomeng Wang, Ph.D., co-founder of Ascentage Pharma and chairman of its scientific advisory board, and Warner-Lambert/Parke-Davis professor in medicine, professor of internal medicine, pharmacology and medicinal chemistry of the University of Michigan, and director of the Michigan Center for Therapeutic Innovation, is a leading researcher in the field. Through structure-function studies of their previously developed MDM2 inhibitors using the PROTACs technology, Professor Shaomeng Wang’s research team has obtained potent and efficacious MDM2 degraders that could effectively induce rapid degradation of MDM2. The lead MDM2 degrader has achieved complete and durable tumor regression in a xenograft tumor model in mice³.

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 MDM2 protein degrader successfully.

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

Suzhou, People's Republic of China, November 30, 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. Zhao, Y.; Aguilar, A.; Bernard, D.; Wang, S. Small-molecule inhibitors of the MDM2-p53 protein-protein interaction (MDM2 inhibitors) in clinical trials for cancer treatment. *J. Med. Chem.* 2015, 58, 1038–1052.
2. Lai, A. C.; Crews, C. M. Induced protein degradation: an emerging drug discovery paradigm. *Nat Rev. Drug Discov.* 2017, 16, 101-114.
3. Ryan P. Wurz and Victor J. Cee. Targeted Degradation of MDM2 as a New Approach to Improve the Efficacy of MDM2-p53 Inhibitors. *J. Med. Chem.* 2019, 62, 445–447.