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

Olverembatinib Recommended for a Breakthrough Therapy Designation in China for the Treatment of SDH-Deficient GIST

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 recommended olverembatinib (HQP1351), Ascentage Pharma's novel drug candidate, for a Breakthrough Therapy Designation (BTD) for the treatment of patients with succinate dehydrogenase (SDH)-deficient gastrointestinal stromal tumor (GIST) who had received first-line treatment.

This marks the second BTD granted to olverembatinib by the CDE, with the first one granted in March 2021 for the treatment of patients with chronic-phase chronic myeloid leukemia (CML-CP) resistant and/or intolerant to first- and second-generation tyrosine kinase inhibitors (TKIs). Furthermore, olverembatinib has received two Priority Review Designations from the CDE.

BTDs are commonly granted to innovative drugs and modified novel drugs that are intended for the prevention or treatment of serious life-threatening diseases and/or conditions that severely impact the quality of life for which there is no existing treatment or where sufficient evidence indicates advantages over currently available treatment options. Drugs that have been granted BTDs are prioritized by the CDE in communications and exchange, and in receiving guidance to advance the drug development progress. Furthermore, BTD-designated drugs will be eligible for Priority Review status and conditional approvals upon submission of a New Drug Application (NDA). In conclusion, granting of BTDs effectively accelerates development and commercialization of innovative drugs and modified novel drugs presenting significant clinical value or addressing urgent unmet clinical needs.

GIST is a type of malignancy that arises in mesenchymal tissues of the gastrointestinal tract, and most patients with GIST harbor *KIT* or *PDGFRA* mutations. The introduction of TKIs has significantly improved the prognosis of these patients. However, patients with SHD-deficient GIST, a rare subtype of GIST, still have considerable unmet medical needs. It is known to the research community that patients with SDH-deficient GIST are commonly insensitive to existing TKIs. Although patients with early-stage localized disease can benefit from surgical treatment, most of them eventually experience relapse[1-5]. At present, there is no standard of care for patients with relapsed or advanced SDH-deficient GIST[1-5], whose 5-year event-free survival (EFS) is only 24%[4].

Olverembatinib is a type 1 novel, orally active, potent third-generation BCR-ABL1 inhibitor. As the first and only China-approved third-generation BCR-ABL inhibitor, olverembatinib is indicated for the treatment of adult patients with TKI-resistant chronic-phase chronic myeloid leukemia (CML-CP) or accelerated-phase CML (CML-AP) harboring the T315I mutation. While being clinically developed and adopted for the treatment of hematologic malignancies, olverembatinib also showed potent antitumor activity against GIST in preclinical models and early clinical studies, including particularly promising efficacy in patients with SDH-deficient GIST. Results from an ongoing Phase Ib/II study of olverembatinib in China showed an impressive clinical benefit rate (CBR) of 93.8% in patients with this subtype of GIST[6]. Based on these promising results, the study was selected for presentations at the American Society of Clinical Oncology (ASCO) Annual Meeting for two consecutive years.

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

Suzhou, People's Republic of China, May 31, 2023

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.

References:

1. Mantese G. Gastrointestinal stromal tumor: epidemiology, diagnosis, and treatment. Curr Opin Gastroenterol. 2019; 35(6): 555-559.

2. Call JW, Wang Y, Rothschild S, et al. Treatment responses in SDH-deficient GIST. LRG Science, https://liferaftgroup.org/2019/08/treatmentresponses-in-sdh-deficient-gist.

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4. Weldon CB, Madenci AL, Boikos SA, et al. Surgical Management of Wild-Type Gastrointestinal Stromal Tumors: A Report From the National Institutes of Health Pediatric and Wildtype GIST Clinic. J Clin Oncol. 2017; 35(5): 523-528.

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