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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

Novel Bcl-2 Inhibitor Lisoftoclax Approved by China NMPA for Treatment of Adult CLL/SLL Patients

Ascentage Pharma Group International (the “**Company**” or “**Ascentage Pharma**”) is pleased to announce that its proprietary novel Bcl-2 selective inhibitor lisoftoclax (APG-2575) has been approved by China’s National Medical Products Administration (NMPA) for the treatment of adult patients with chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) who have previously received at least one systemic therapy including Bruton’s tyrosine kinase (BTK) inhibitors, which makes lisoftoclax the first Bcl-2 inhibitor receiving conditional approval and marketing authorization for the treatment of patients with CLL/SLL in China, and the second Bcl-2 inhibitor approved globally.

Lisoftoclax is a proprietary, novel, orally administered small-molecule Bcl-2 selective inhibitor developed by Ascentage Pharma to treat patients with malignancies by selectively blocking the antiapoptotic protein Bcl-2, thereby restoring the normal apoptosis process in cancer cells. In the clinical trials, lisoftoclax exhibits broad therapeutic potentials in multiple hematologic malignancies and solid tumors, particularly in CLL/SLL, both as a monotherapy and in combination treatments. Furthermore, lisoftoclax is Ascentage Pharma’s second commercialized novel drug, following olverembatinib. This approval for lisoftoclax underscores Ascentage Pharma’s outstanding capabilities in global clinical development and innovation, marking another major milestone in the Company’s successful development of its pipeline.

This approval is based on the results from a pivotal registrational Phase II study (APG2575CC201) that was designed to evaluate the efficacy and safety of lisaftoclax monotherapy in patients with relapsed or refractory CLL/SLL, with the overall response rate (ORR) as the primary endpoint. Lisaftoclax demonstrated compelling efficacy and an ORR that met the prespecified endpoint in patients who were previously treated with BTK inhibitors and/or immunochemotherapy. Meanwhile, lisaftoclax showed a favorable safety profile with no tumor lysis syndrome (TLS) occurring during the study, a low incidence of hematologic toxicities which were manageable, and a low incidence of non-hematologic toxicities which were mostly grade 1-2.

The Company is currently conducting 4 global registrational Phase III trials: the GLORA study of lisaftoclax in combination with BTK inhibitors in patients with CLL/SLL previously treated with BTK inhibitors; the GLORA-2 study in patients with newly diagnosed CLL/SLL; the GLORA-3 study in newly diagnosed, elderly and unfit patients with acute myelogenous leukemia (AML); and the GLORA-4 study in patients with newly diagnosed higher risk myelodysplastic syndrome (MDS).

CLL/SLL is a hematologic malignancy caused by mature B-cell neoplasms. It primarily affects older populations, with over 100,000 new diagnoses reported globally each year¹. In China, where the incidence rate of CLL/SLL is lower than that in the western countries, the disease is occurring at a rapidly rising rate, with a younger age of onset and higher aggressiveness². As the current primary option and cornerstone for the first-line treatment of CLL/SLL, BTK inhibitors have significantly improved treatment outcomes for patients. However, BTK inhibitors still face a range of issues such as limited ability to induce deep responses, high risk of relapse in mid- and long-term treatment, toxicities and intolerability associated with prolonged treatment, thus necessitating safer and more effective treatment options for the patients with CLL/SLL.

The introduction of Bcl-2 inhibitors has further revolutionized the treatment of CLL/SLL. The apoptosis suppressor factor Bcl-2, commonly overexpressed in various hematologic malignancies, particularly CLL/SLL, is a key mechanism by which tumor cells evade apoptosis. However, the discovery of Bcl-2 inhibitor as a therapeutic target is highly challenging primarily because its mechanism of action is based on the protein-protein interaction (PPI). The binding interface of Bcl-2 is relatively large, making it difficult for small-molecule inhibitors to exert blocking effects. Additionally, the Bcl-2 protein is located on the mitochondria, which with double-membrane structure, are among the most complex and challenging cellular components as it requires drugs to first penetrate the cell membrane before they can further act on the target. Prior to this, no Bcl-2 inhibitor had been approved for the treatment of CLL/SLL in China. This approval of lisaftoclax represents a milestone achieved through over a decade of committed research and clinical development by Ascentage Pharma and fills a treatment gap in CLL/SLL, bringing renewed hope to many patients in China.

Cautionary Statement required by Rule 18A.05 of the Listing Rules: We cannot guarantee that lisaftoclax will ultimately be successfully developed and marketed.

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

Suzhou, the PRC, July 10, 2025

As at the date of this announcement, the Board comprises Dr. Yang Dajun as chairman and executive Director, Dr. Wang Shaomeng and Dr. Lu Simon Dazhong as non-executive Directors^{Note}, and Mr. Ye Changqing, Mr. Ren Wei, Dr. David Sidransky, Ms. Marina S. Bozilenko, Dr. Debra Yu and Marc E. Lippman, MD as independent non-executive Directors.

Note: Dr. Wang Shaomeng and Dr. Lu Simon Dazhong are independent directors under NASDAQ rules.

References

1. Yao, Y., Lin, X., Li, F., et al. The global burden and attributable risk factors of chronic lymphocytic leukemia in 204 countries and territories from 1990 to 2019: analysis based on the global burden of disease study 2019. Biomed Eng Online. 2022 Jan 11;21(1):4. DOI: 10.1186/s12938-021-00973-6
2. Liu Peng. Practice guidelines for the diagnosis and treatment of chronic lymphocytic leukemia/small lymphocytic lymphoma in Zhongshan Hospital, Fudan University (v1.2018). [J]. Chin J Clin Med, 2018, 25(1): 157-160. DOI 10.12015/j. issn. 1008-6358. 2018. 20180