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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)

Inside Information

Ascentage Pharma Announces Approval by NMPA for China's First Approved Third-Generation BCR-ABL TKI HQP1351 (Olverembatinib)

Ascentage Pharma Group International (the “**Company**” or “**Ascentage Pharma**”) is making this announcement pursuant to Rule 13.09 of the Rules Governing the Listing of Securities on The Stock Exchange of Hong Kong Limited (the “**Listing Rules**”) and the Inside Information Provisions (as defined in the Listing Rules) under Part XIVA of the Securities and Futures Ordinance (Chapter 571 of the Laws of Hong Kong).

Ascentage Group International (the “**Company**” or “**Ascentage Pharma**”) is pleased to announce that the novel class I drug candidate olverembatinib of Guangzhou HealthQuest Pharma Co., Ltd., Inc., a wholly-owned subsidiary of Ascentage Pharma, has been approved by the China National Medical Products Administration (NMPA) for the treatment of adult patients with tyrosine kinase inhibitor (TKI)-resistant chronic phase chronic myeloid leukemia (CML-CP) or accelerated-phase CML (CML-AP) harboring the T315I mutation as confirmed by a validated diagnostic test.

Developed by Ascentage Pharma with support from the National Major New Drug Discovery and Manufacturing program, olverembatinib is a potentially best-in-class drug that will be co-commercialized in the China market by Ascentage Pharma and Innovent Biologics, Inc. (“**Innovent**”), for the benefit of more patients and their families. As China's first third-generation BCL-ABL TKI developed for the treatment of TKI-resistant CML, this approval fills an important treatment gap in T315I-mutant CML, and marks a major milestone signifying that Ascentage Pharma has successfully entered the commercialization-stage.

This approval for olverembatinib is based on the results from two pivotal Phase II studies — the HQP1351CC201 study and the HQP1351CC202 study. These results showed that olverembatinib is efficacious and well-tolerated in patients with TKI-resistant CML-CP and CML-AP harboring the T315I mutation, and the probability and depth of clinical response is expected to increase with prolonged treatment period.

CML is a hematologic malignancy of the white blood cells. The introduction of BCR-ABL TKIs have significantly improved the clinical management of CML. However, acquired resistance to TKIs remains a major challenge in the treatment of CML. BCR-ABL tyrosine kinase mutations represent a key mechanism of acquired drug resistance; T315I, which is the most common drug-resistant mutation, occurs in about 25% of patients with drug-resistant CML. Patients with T315I-mutant CML are resistant to both first-and second-generation BCR-ABL inhibitors, hence presenting an urgent unmet medical need for an effective treatment.

According to the collaboration and license agreement entered into with Innovent Biologics on July 14, 2021, the Company and Innovent will be jointly responsible for the commercialization olverembatinib in China. Both parties will leverage advantages in clinical development, market coverage and channel networks, building up an experienced and focused commercial team in hematologic oncology, facilitating the rolling out of olverembatinib to hospitals and pharmacies at various tiers, in order to benefit Chinese patient population as soon as possible. For further details, please refer to the relevant announcement of the Company dated July 14, 2021.

About Chronic Myeloid Leukemia

Chronic myeloid leukemia (CML) is a malignancy caused by the clonal proliferation of hematopoietic stem cell in the bone marrow. Also referred to as chronic myelocytic leukemia, CML is one of the most common subtypes of chronic leukemia, accounting for 15% of all leukemia cases in adults¹⁻². According to epidemiology data, the onset of CML in Chinese patients happens at a younger age than that in the West; the median age of onset of CML in China is around 45–50 years old, while it is 67 years old in the West³.

The commercialization of BCR-ABL tyrosine kinase inhibitors (TKIs) has significantly improved the clinical management of CML. However, acquired resistance to TKIs remains a major challenge in the treatment of CML. BCR-ABL tyrosine kinase mutations represent a key mechanism of acquired drug resistance; T315I, which is the most common drug-resistant mutation, occurs in about 25% of patients with drug-resistant CML. Patients with T315I-mutant CML are resistant to both first-and second-generation BCR-ABL inhibitors, therefore the mutation had long been a clinical obstacle undermining patients' long-term survival.

About Olverembatinib

Developed by Ascentage Pharma with support from the National Major New Drug Discovery and Manufacturing program, the orally active, third-generation BCR-ABL inhibitor olverembatinib is the first China-approved third-generation BCR-ABL inhibitor targeting drug-resistant chronic myeloid leukemia (CML). Olverembatinib can effectively target a spectrum of BCR-ABL mutants, including the T315I mutation.

In October 2020, olverembatinib was granted the Priority Review status by the Center for Drug Evaluation (CDE) of NMPA in China for the treatment of adult patients resistant to TKIs and with T315I-mutant chronic phase CML (CML-CP) and accelerated phase CML (CML-AP). In March 2021, it was granted the Breakthrough Therapy designation by the CDE. In the overseas, olverembatinib was cleared by the US FDA in July 2019 to directly enter a Phase Ib study. In May 2020, olverembatinib was sequentially granted an Orphan Drug designation and Fast Track designation by the US FDA. In November 2021, olverembatinib was granted an Orphan Designation by the European Union. Furthermore, since 2018, the clinical results of olverembatinib have been selected for oral presentations at the American Society of Hematology (ASH) Annual Meetings for four consecutive years, and was nominated for “Best of ASH” in 2019.

On July 14, 2021, Ascentage Pharma and Innovent entered into the collaboration and license agreement regarding the joint development and commercialization of olverembatinib in China. For further details, please refer to the relevant announcement of the Company dated July 14, 2021.

Results from the two pivotal Phase II studies

- ***The HQP1351CC201 study in patients with CML-CP***
 - HQP1351CC201 is an open-label, multicenter, single-arm Phase II designed to evaluate the safety and efficacy of patients with T315I-mutant CML-CP who have received prior treatment with BCR-ABL1 TKIs. The primary endpoint of the study is major cytogenetic response (MCyR).
 - As of data cut-off date of August 25, 2020, the median duration of follow-up in patients with CML-CP was 13.0 months (range: 7.2–16.3). Of the 31 patients evaluable for hematologic responses, all 31 (100%) patients achieved a complete hematologic response (CHR); In the 41 patients evaluable for cytogenetic responses, 31 (75.6%) patients achieved a MCyR, including 28 (68.3%) with complete cytogenetic response (CCyR), and 3 (7.3%) with partial cytogenetic response (PCyR); Among the 41 patients evaluable for molecular responses, 23 (56.1%) achieved a major molecular response (MMR). The 12-month progression-free survival (PFS) was 85.7% (95% CI: [63.6%–94.9%]) and the overall survival (OS) was 100% (95% CI: [100.0%–100.0%]).

- ***The HQP1351CC202 study in patients with CML-AP***
 - HQP1351CC202 is an open-label, multicenter, single-arm Phase II designed to evaluate the safety and efficacy of patients with T315I-mutant CML-AP and resistance to TKIs developed on prior treatment with BCR-ABL1 TKIs. The primary endpoint of the study is major hematologic response (MaHR).
 - As of data cut-off date of July 27, 2020, the median duration of follow-up in patients with CML-AP was 14.3 months (range: 6.6–15.2). Of the 17 patients evaluable for hematologic responses, 12 (70.6%) patients achieved a major hematologic response (MaHR), including 11 (64.7%) with CHR and 1 (5.9%) with no evidence of leukemia (NEL); Among the 17 evaluable patients, 8 (47.1%) achieved a MCyR, all of whom achieved (47.1%) a CCyR, and another 7 (41.2%) achieved MMR. The 12-month PFS was 73.3% (95% CI: [43.3%–89.1%]), and the 12-month OS was 88.2% (95% CI: [60.6%–96.9%]).

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, and dual Bcl-2/Bcl-xL 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 three known classes of key apoptosis regulators. The Company is conducting more than 40 Phase I/II clinical trials in China, the US, Australia and Europe. Olverembatinib, the Company's core drug candidate developed for the treatment of drug-resistant chronic myeloid leukemia (CML), was granted Priority Review status and a Breakthrough Therapy Designation (BTD) by the Center for Drug Evaluation (CDE) of China National Medical Products Administration (NMPA), and is already approved for the indication. In addition, Olverembatinib has also been granted an Orphan Drug Designation (ODD) and a Fast Track Designation (FTD) by the US FDA, and an Orphan Designation by the EU. As at the date of this announcement, Ascentage Pharma has obtained a total of 12 ODDs from the US FDA and 1 ODD from the EU for four of the Company's investigational drug candidates. The Company has been designated for multiple major national R&D projects in China, including five Major New Drug Development Projects, one Enterprise Innovative Drug Incubator Base status, four Innovative Drug Research and Development Programs, and one Major Project for the Prevention and Treatment of Infectious Diseases.

Leveraging its robust research and development capabilities, Ascentage Pharma has built a portfolio of global intellectual property rights, and entered into global partnerships with numerous leading biotechnology and pharmaceutical companies and research institutes such as UNITY Biotechnology, MD Anderson Cancer Center, Mayo Clinic, Dana-Farber Cancer Institute, MSD, and AstraZeneca. The Company has built a global and talented team with experience in the research and development of innovative drugs and clinical development, and is setting up its commercial manufacturing and sales and marketing teams with high standards. Ascentage Pharma aims to continuously strengthen its research and development capabilities and accelerate the clinical development progress of its product pipeline to fulfil its mission of ‘addressing unmet clinical needs of patients in China and around the world’ for the benefit of more patients.

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

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

Suzhou, People’s Republic of China, November 25, 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 National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Chronic Myelogenous Leukemia, V.2.2008[DB/OL]. NCCN Web Site. 8-28-2007.[2007-10-25]
- ² HehlmannR, HochhausA, BaccaraniM, et al. Chronic myeloid leukaemia[J]. Lancet, 2007, 370 (9584): 342-350.
- ³ The guidelines for diagnosis and treatment of chronic myelogenous leukemia in China (2020 edition). Zhonghua Xue Ye Xue Za Zhi. 2020 May; 41(5): 353-364.