CStone Pharmaceuticals

基石藥業

(Incorporated in the Cayman Islands with limited liability)

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VOLUNTARY ANNOUNCEMENT
CSTONE ANNOUNCED RESULTS FROM PHASE III AGILE DATA OF TIBSOVO® (IVOSIDENIB TABLETS) IN COMBINATION WITH AZACITIDINE FOR PATIENTS WITH PREVIOUSLY UNTREATED IDH1-MUTATED ACUTE MYELOID LEUKEMIA PUBLISHED IN THE NEW ENGLAND JOURNAL OF MEDICINE

CStone Pharmaceuticals (the "**Company**" or "**CStone**") is pleased to announce the publication of results from the Phase III AGILE trial of TIBSOVO® (ivosidenib tablets) in the New England Journal of Medicine (NEJM). The AGILE trial is a global Phase III double blinded placebo-controlled study in adults with previously untreated isocitrate dehydrogenase-1 ("**IDH1**") -mutated acute myeloid leukemia ("**AML**") comparing TIBSOVO in combination with the azacitidine to azacitidine in combination with placebo. The study met the primary and all key secondary endpoints including overall survival ("**OS**"). Servier is actively working with the U.S. Food and Drug Administration ("**FDA**") and health authorities across the globe to potentially bring this new indication to market, and CStone is pursuing submission for this indication in China as well.

Key Highlights

- Results from the Phase III AGILE trial present a significant advancement for patients dealing with previously untreated IDH1-mutated AML.

- Global Phase III trial of TIBSOVO® (ivosidenib tablets) met its primary endpoint of event-free survival ("**EFS**") and all key secondary endpoints, complete remission ("**CR**") rate, OS, complete remission and complete remission with partial hematologic recovery rate ("**CR+CRh rate**") and objective response rate ("**ORR**").

AML is a cancer of the blood and bone marrow marked by rapid disease progression and is the most common acute leukemia affecting adults with approximately 20,000 new cases estimated in the U.S. each year.[1,2] In China, there are about 75.3 thousand new cases of leukemia each year and

approximately 59% are AML patients. The majority of patients with AML eventually relapse. Relapsed or refractory AML has a poor prognosis.[3] The five-year survival rate is approximately 29.5%.[1] IDH mutations are present in about 6 to 10 percent of AML cases.[4]

Dr. Jason Yang, Chief Medical Officer of CStone, said, "We are thrilled that the publication of the compelling Phase III AGILE study data in NEJM, which reinforces the clinical importance of these results. Patients with IDH1 mutant AML have a poor prognosis, especially for newly diagnosed patients who are not eligible for intensive chemotherapy. TIBSOVO® in combination with azacitidine provide a new treatment option for this group of patients and we plan to communicate with the National Medical Products Administration ("**NMPA**") of China with an aim to bring this innovative therapy to more Chinese patients as soon as possible."

The data from the global Phase III AGILE study, showed TIBSOVO® is the first IDH1 mutation specific targeted therapy to demonstrate improved EFS and OS in combination with azacitidine compared to azacitidine plus placebo. Treatment with TIBSOVO® in combination with azacitidine demonstrated a statistically significant improvement in EFS (hazard ratio [HR] = 0.33, 95% confidence interval [CI]: 0.16, 0.69, 1-sided P = 0.0011).5,6 The combination of TIBSOVO with azacitidine showed a statistically significant improvement in overall survival (HR = 0.44 [95% CI 0.27, 0.73]; 1-sided P = 0.0005), with a median OS of 24.0 months vs. 7.9 months in the placebo + azacitidine arm.

In addition, CR rate was 47.2% (n = 34/72) for TIBSOVO® in combination with azacitidine vs. 14.9% (n = 11/74) for placebo plus azacitidine (P < 0.0001). CR + CR with partial hematologic recovery rate (CR + CRh rate) was 52.8% (n = 38/72) for TIBSOVO® in combination with azacitidine vs. 17.6% (n = 13/74) for placebo plus azacitidine (P < 0.0001). ORR was 62.5% (n = 45/72) for TIBSOVO® in combination with azacitidine vs. 18.9% (n = 14/74) for placebo plus azacitidine (P < 0.0001).

On July 19, 2019, CStone announced that the first patient in China was dosed in AGILE, the global registrational Phase III study of TIBSOVO®. 16 centers in China participated in this global study.

Servier is the owner of TIBSOVO®'s rights and has granted an exclusive license to CStone to develop and commercialize the product in Mainland China, Taiwan, Hong Kong, Macau and Singapore. Currently, the NMPA has approved the new drug application ("**NDA**") of TIBSOVO® (ivosidenib tablets) for the treatment of adult patients with relapsed/refractory AML ("**R/R AML**") who have a susceptible IDH1 mutation.

About NCT03173248 AGILE Phase III AML Trial

The AGILE trial is a global, Phase III, multicenter, double-blind, randomized, placebo-controlled clinical trial designed to evaluate the efficacy and safety of TIBSOVO in combination with azacitidine compared with placebo in combination with azacitidine, in adults with previously untreated IDH1-mutated AML who are not candidates for intensive chemotherapy (not less than 75 years old or who have comorbidities that preclude the use of intensive induction chemotherapy). The study's primary endpoint is EFS, defined as the time from randomization until treatment failure, relapse from remission, or death from any cause, whichever occurs first. Treatment failure is defined as failure to achieve CR by Week 24.

Key secondary endpoints included CR rate, defined as the proportion of participants who achieve a CR; OS, defined as the time from date of randomization to the date of death due to any cause; CR and complete remission with partial hematologic recovery (CRh) rate, defined as the proportion of participants who achieve a CR or CRh; and ORR, defined as the rate of CR, CR with incomplete hematologic recovery (CRi) (including CR with incomplete platelet recovery [CRp]), partial

remission (PR), and morphologic leukemia-free state (MLFS).

About AML

AML, a cancer of blood and bone marrow characterized by rapid disease progression, is the most common acute leukemia affecting adults, with approximately 20,000 new cases in the U.S., and 43,000 cases in Europe each year.[1,2,7] In China, there are about 75.3 thousand new cases of Leukemia each year and approximately 59% are AML patients. AML incidence significantly increases with age, and the median age of diagnosis is 68.[1] The vast majority of patients do not respond to chemotherapy and progress to relapsed/refractory AML.[3] The five-year survival rate is approximately 29.5%.[1] For 6 to 10 percent of AML patients, the mutated IDH1 enzyme blocks normal blood stem cell differentiation, contributing to the genesis of acute leukemia.[4]

About TIBSOVO® (ivosidenib tablets)

TIBSOVO® is an oral targeted IDH1 inhibitor. The NMPA has approved the NDA of TIBSOVO® for the treatment of adult patients with R/R AML who have a susceptible IDH1 mutation.

In China, TIBSOVO was selected in the list of the third batch of Overseas New Drugs Urgently Needed in Clinical Settings by the Center for Drug Evaluation, NMPA in China, and granted fast-track designation. As a potent and highly selective first-in-class oral IDH1 inhibitor, TIBSOVO was also recommended by the 2020 edition of the CSCO Guidelines for Diagnosis and Treatment of Hematological Malignancies due to its proven clinical advantages.

TIBSOVO® is currently approved in the U.S. as monotherapy for the treatment for the treatment of adults with IDH1-mutant R/R AML, and for adults with newly-diagnosed AML with a susceptible IDH1 mutation as detected by an FDA-approved test in adult patients who are not less than 75 years old or who have comorbidities that preclude use of intensive induction chemotherapy. In 2021, TIBSOVO® was the first and only targeted therapy approved for patients with previously treated locally advanced or metastatic cholangiocarcinoma with an IDH1-mutation as detected by an FDA-approved test.

The FDA has granted Breakthrough Therapy Designation for TIBSOVO® in combination with azacitidine for this indication and Breakthrough Therapy Designation for TIBSOVO® for the treatment of adult patients with relapsed or refractory myelodysplastic syndrome (MDS) with a susceptible IDH1 mutation.

About CStone

CStone is a biopharmaceutical company focused on researching, developing and commercializing innovative immuno-oncology and precision medicines to address the unmet medical needs of cancer patients in China and worldwide. Established in 2015, CStone has assembled a world-class management team with extensive experience in innovative drug development, clinical research, and commercialization. The Company has built an oncology-focused pipeline of 15 drug candidates with a strategic emphasis on immuno-oncology combination therapies. Currently, CStone has received seven NDA approvals for four drugs. Multiple late-stage drug candidates are now under pivotal clinical trials or registration. CStone's vision is to become globally recognized as a world-renowned biopharmaceutical company by bringing innovative oncology therapies to cancer patients worldwide.

For more information about CStone, please visit: www.cstonepharma.com.

By Order of the Board
CStone Pharmaceuticals
Dr. Frank Ningjun Jiang
Chairman

Suzhou, the People's Republic of China, April 22, 2022

As at the date of this announcement, the board of directors of the Company comprises Dr. Frank Ningjun Jiang as Chairman and executive director, Dr. Wei Li, Mr. Kenneth Walton Hitchner III, Mr. Yanling Cao, Mr. Xianghong Lin and Mr. Edward Hu as non-executive directors, and Dr. Paul Herbert Chew, Mr. Ting Yuk Anthony Wu and Mr. Hongbin Sun as independent non-executive directors.

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