CStone Pharmaceuticals

基石藥業

(Incorporated in the Cayman Islands with limited liability)

(**Stock Code: 2616**)

VOLUNTARY ANNOUNCEMENT
CSTONE'S PARTNER SERVIER ANNOUNCED PHASE III DATA SHOWING THAT TIBSOVO® (IVOSIDENIB TABLETS) IN COMBINATION WITH AZACITIDINE SIGNIFICANTLY IMPROVES EVENT-FREE SURVIVAL AND OVERALL SURVIVAL IN PATIENTS WITH PREVIOUSLY UNTREATED IDH1-MUTATED ACUTE MYELOID LEUKEMIA

The partner of CStone Pharmaceuticals (the "**Company**" or "**CStone**"), Servier, announced Phase III data from the global AGILE study on December 12, 2021, demonstrating that TIBSOVO® (ivosidenib tablets) in combination with the chemotherapy azacitidine significantly improved event-free survival ("**EFS**") and overall survival ("**OS**") in adults with previously untreated isocitrate dehydrogenase 1 ("**IDH1**")-mutated acute myeloid leukemia ("**AML**") compared to azacitidine plus placebo. These data will be presented in an oral session on Monday, December 13, 2021 from 2:45 - 4:15 PM ET (Abstract No.697) and featured in the official press program during the 63rd American Society of Hematology Annual Meeting and Exposition.

Key Highlights

- TIBSOVO in combination with azacitidine compared to placebo plus azacitidine also demonstrated significant improvement in complete remission ("**CR**") rate, CR and complete remission with partial hematologic recovery ("**CRh**") rate and objective response rate ("**ORR**").

- Safety profile was favorable and consistent with previously published data.

- Data from the Phase III AGILE trial of patients with previously untreated IDH1-mutated AML will be presented in an oral session on Monday, December 13, 2021, and featured in the official press program of the 63rd American Society of Hematology Annual Meeting.

Treatment with TIBSOVO in combination with azacitidine demonstrated a statistically significant improvement in EFS (hazard ratio ["**HR**"] = 0.33 [95% CI 0.16, 0.69], 1-sided P = 0.0011). In addition, the combination of TIBSOVO with azacitidine showed a statistically significant improvement in OS (HR = 0.44 [95% CI 0.27, 0.73]; 1-sided P = 0.0005), with a median OS of 24.0 months in the ivosidenib + azacitidine arm vs. 7.9 months in the placebo + azacitidine arm.

Servier has an exclusive license agreement with CStone for the development and commercialization of TIBSOVO in Mainland China, Taiwan, Hong Kong, Macau and Singapore. On July 19, 2019, CStone announced that the first patient in China was dosed in AGILE, the global registrational Phase III study of ivosidenib. 16 centers in China participated in this study.

Professor Wang Jianxiang with the Institute of Hematology & Blood Diseases Hospital, Chinese Academy of Medical Sciences, the Principal Investigator of AGILE in China, said: "AML is a rapidly progressing and life-threatening hematological malignancy. The prognosis is poor in newly diagnosed elderly patients who have conditions that preclude use of intensive induction chemotherapy. For them, our goal of treatment is to prolong OS. The impressive clinical benefit following treatment with the TIBSOVO combination will provide a new option for patients with previously untreated IDH1-mutated AML."

Dr. Jason Yang, Chief Medical Officer of CStone, said, "We are excited to bring a new treatment option to patients with previously untreated IDH1-mutated AML. These findings demonstrated growing evidence of significant clinical benefits in patients with AML and IDH1 mutations, and it will help advance precision treatment of AML, greatly increase patients' survival rate. Meanwhile, we plan to communicate with the National Medical Products Administration ("**NMPA**") of China with an aim to bring this innovative treatment to Chinese patients as soon as possible."

Additional Study Results:

Investigators reported on results of key secondary endpoints of the AGILE trial including:

- 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 + 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 ($p < 0.0001$).

Common all-grade adverse events ("**AEs**") occurring in more than 20% of patients receiving TIBSOVO in combination with azacitidine vs. placebo plus azacitidine were nausea (42.3% vs. 38.4%), vomiting (40.8% vs. 26.0%), diarrhea (35.2% vs. 35.6%), pyrexia (33.8% vs. 39.7%), anemia (31.0% vs. 28.8%), febrile neutropenia (28.2% vs. 34.2%), thrombocytopenia (28.2% vs. 20.5%), neutropenia (28.2% vs. 16.4%), constipation (26.8% vs. 52.1%) and pneumonia (23.9% vs. 31.5%).

TIBSOVO is currently approved in the U.S. as monotherapy for the treatment of adults with IDH1-mutant relapsed or refractory AML ("**R/R AML**"), and for adults with newly diagnosed IDH1-mutant AML who are not less than 75 years old or who have comorbidities that preclude the use of intensive induction chemotherapy. Recently, TIBSOVO was approved as a first and only targeted therapy for patients with previously treated IDH1-mutated cholangiocarcinoma.

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 of China, and granted for 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. Meanwhile, the NMPA of China has accepted the new drug application ("**NDA**") of TIBSOVO in adult patients with R/R AML who have a susceptible IDH1 mutation and this NDA has been granted priority review.

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 patients with newly diagnosed IDH1 mutant AML who are not candidates for intensive 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.

Other 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 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 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 in the U.S., and 43,000 cases in Europe each year. The majority of patients with AML eventually relapse. R/R AML has a poor prognosis. The five-year survival rate is approximately 27%. For 6% to 10% of AML patients, the mutated IDH1 enzyme blocks normal blood stem cell differentiation, contributing to the genesis of acute leukemia.

About TIBSOVO® (ivosidenib tablets)

TIBSOVO is an IDH1 inhibitor indicated for the treatment of adult patients with a susceptible IDH1 mutation as detected by an FDA-approved test with:

AML

- Newly-diagnosed AML who are not less than 75 years old or who have comorbidities that preclude use of intensive induction chemotherapy.
- R/R AML.

Locally Advanced or Metastatic Cholangiocarcinoma

- Locally advanced or metastatic cholangiocarcinoma who have been previously treated.

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 three drug approvals in Greater China, including two in Mainland China and one in Taiwan. 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, December 12, 2021

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.