CStone Pharmaceuticals

基石藥業

(Incorporated in the Cayman Islands with limited liability)

(**Stock Code: 2616**)

VOLUNTARY ANNOUNCEMENT
CSTONE PRESENTS CLINICAL DATA FROM THE CHINA REGISTRATIONAL BRIDGING STUDY ON IVOSIDENIB IN PATIENTS WITH RELAPSED/REFRACTORY ACUTE MYELOID LEUKEMIA (R/R AML) WITH A SUSCEPTIBLE IDH1 MUTATION AT THE 2021 ESMO CONGRESS

Key Highlights:

- The data showed that ivosidenib demonstrated clinical efficacy in the treatment of Chinese adults with relapsed/refractory acute myeloid leukemia ("**R/R AML**") with a susceptible isocitrate dehydrogenase 1 ("**IDH1**") mutation. It was clear that ivosidenib was well tolerated and had a manageable safety profile

- In August 2021, the National Medical Products Administration ("**NMPA**") of China accepted the new drug application ("**NDA**") of ivosidenib for the treatment of adults with R/R AML with a susceptible IDH1 mutation, and this NDA has been considered for priority review

CStone Pharmaceuticals (the "**Company**" or "**CStone**") is pleased to announce that the company has presented the clinical data from the China registrational bridging study CS3010-101 of its first-in-class drug ivosidenib (TIBSOVO®, the brand name in the U.S.) in a proffered paper presentation at the 2021 European Society for Medical Oncology ("**ESMO**") Congress.

CS3010-101 is an ongoing phase I, multi-center, single-arm study in China, which aims to evaluate the pharmacokinetic ("**PK**"), pharmacodynamics ("**PD**"), safety, and clinical efficacy of orally administrated ivosidenib in Chinese adult patients with R/R AML with a susceptible IDH1 mutation. And as the bridging study of the global pivotal AG120-C-001 study, it provides data on R/R AML patients in China.

Summary of the Presentation:

- Session title: Hematological malignancies
- Date: 19:30-19:40 (Beijing time), September 20, 2021
- Format: Proffered Paper Presentation
- Title: Ivosidenib in Chinese patients with R/R AML with a susceptible IDH1 mutation: results from a registrational bridging study
- Presentation number: 825O
- Principal Investigator: Professor Wang Jianxiang, Institute of Hematology and Blood Diseases Hospital, Chinese Academy of Medical Sciences
- Presenter: Dr. Sun Mingyuan, Institute of Hematology and Blood Diseases Hospital, Chinese Academy of Medical Sciences

Efficacy: ivosidenib demonstrated clinical efficacy in the treatment of Chinese adults with R/R AML with a susceptible IDH1 mutation

- In 30 evaluable patients, the primary efficacy endpoint of complete remission ("**CR**") plus complete remission with partial hematologic recovery ("**CRh**") ("**CR+CRh**") rate was 36.7% (11/30, with all 11 patients achieving CR). The median time to CR+CRh was 3.68 months, and 12-month duration rate of CR+CRh is 90.9%.
- Two patients received hematopoietic stem cell transplantation ("**HSCT**") after achieving responses of CR or CRh.
- The median event-free survival ("**EFS**") was 5.52 months and the median overall survival ("**OS**") was 9.10 months.

Safety: ivosidenib was well tolerated and had a manageable safety profile

- The incidence of Grade≥3 treatment emergent adverse events ("**TEAEs**") was 86.7%, and the incidence of TEAEs leading to permanent discontinuation was 10%.
- Ivosidenib had a well-tolerated safety profile, and no new safety signals were detected. Adverse events of special interest can be effectively monitored and controlled through protocol guidance and routine clinical management.

Professor Wang Jianxiang from the Institute of Hematology & Blood Diseases Hospital, Chinese Academy of Medical Sciences, the Principal Investigator of CS3010-101 in China, said, "As there are limited treatment options for AML patients with IDH1 mutations, patients have a low 5-year survival rate and poor quality of life. Ivosidenib is a targeted, potent, oral inhibitor for the treatment of IDH1 mutant cancers, and we are glad that China bridging study has achieved the desired results as ivosidenib demonstrated superior efficacy and safety. I hope it will benefit Chinese AML patients as soon as possible."

Dr. Jason Yang, Chief Medical Officer of CStone, said, "We are pleased that the positive data of ivosidenib in the treatment of Chinese patients with R/R AML were presented in a proffered paper presentation at the ESMO congress. It marks that ivosidenib has been highly recognized by the global scientific community. We will work closely with the NMPA of China to bring it to Chinese patients as early as possible which is our third first-in-class drug in the following of GAVRETO® and AYVAKIT®."

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

In July 2021, the China registrational study CS3010-101 of ivosidenib met the pre-specified endpoints in Chinese patients with R/R AML who have a susceptible IDH1 mutation. The results demonstrated efficacy and manageable safety profile of ivosidenib, which were consistent with previously reported data from the global study population.

In August 2021, the NMPA of China accepted the NDA of ivosidenib for the treatment of adults with R/R AML with a susceptible IDH1 mutation, and this NDA has been considered for priority review.

About TIBSOVO (ivosidenib tablets)

The U.S. Food and Drug Administration ("**FDA**") has granted Breakthrough Therapy Designation for TIBSOVO (ivosidenib tablets) in combination with azacytidine for the treatment of newly diagnosed susceptible IDH1-mutant AML adult patients who are not less than 75 years old or who have comorbidities that preclude the use of intensive induction chemotherapy; and Breakthrough Therapy Designation for TIBSOVO for the treatment of adult patients with relapsed and refractory myelodysplastic syndrome ("**MDS**") with a susceptible IDH1 mutation.

In August 2021, Servier, a global independent pharmaceutical Group governed by a Foundation, announced the global Phase III double blinded placebo controlled AGILE study of TIBSOVO in combination with the chemotherapy azacitidine in adult patients with previously untreated IDH1-mutated AML met its primary endpoint of EFS. Treatment with TIBSOVO in combination with azacitidine compared to azacitidine in combination with placebo demonstrated a statistically significant improvement in EFS. Additionally, the trial met all key secondary endpoints, including CR rate, OS, CR and CRh rate and objective response rate ("**ORR**"). The safety profile of TIBSOVO in combination with azacitidine was consistent with previously published data. The study recently halted further enrollment based on the recommendation of the Independent Data Monitoring Committee ("**IDMC**"), as a clinical difference was noted between the treatment groups.

In August 2021, Servier announced the FDA approved TIBSOVO for the treatment of adult patients with previously treated, locally advanced or metastatic cholangiocarcinoma with an IDH1 mutation as detected by an FDA-approved test. TIBSOVO is the first and only targeted therapy approved for patients with previously treated IDH1-mutated cholangiocarcinoma.

TIBSOVO is also approved in the U.S. as monotherapy for the treatment of adults with IDH1-mutated R/R AML and for adults with newly diagnosed IDH1-mutated AML who are not less than 75 years old or who have comorbidities that preclude the use of intensive induction chemotherapy.

Servier has an exclusive license agreement with CStone for the development and commercialization of TIBSOVO in Mainland China, Taiwan, China, Hong Kong, Macau and Singapore.

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 Mainland 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, China. 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, September 21, 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. Qun Zhao, 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.