CStone Pharmaceuticals

基石藥業

(Incorporated in the Cayman Islands with limited liability)

(**Stock Code: 2616**)

VOLUNTARY ANNOUNCEMENT

CSTONE SUBMITS NEW DRUG APPLICATION FOR TIBSOVO® IN TAIWAN FOR THE TREATMENT OF RELAPSED/REFRACTORY AML

CStone Pharmaceuticals (the "**Company**" or "**CStone**") announces that a new drug application ("**NDA**") for TIBSOVO® (ivosidenib) has been submitted by a third-party to the Taiwan Food and Drug Administration ("**TFDA**") as the first to-be-approved treatment of adult patients with relapsed or refractory ("**R/R**") acute myeloid leukemia ("**AML**") with a susceptible isocitrate dehydrogenase 1 ("**IDH1**") mutation. The application is the first market filing for CStone since its inception in 2015. TIBSOVO® is a first-in-class, oral, potent and selective inhibitor of the mutant IDH1 enzyme. The TFDA awarded TIBSOVO® the NDA filing priority review status on April 24, 2019.

Dr. Frank Ningjun Jiang, chairman, executive director and chief executive officer of CStone, commented: "The NDA filing for TIBSOVO® in Taiwan is a significant milestone for the Company. TIBSOVO® has the potential to become our first commercial product, and CStone is now taking the first step towards becoming a commercial-stage company. There are no currently approved treatments for AML patients with IDH1 mutation in the Greater China region. We are already actively building a commercial team and will be fully committed to introducing this product to patients in Greater China as quickly as we can for the sufferers who otherwise would have no treatment options."

AML is the most common acute leukemia affecting adults and is characterized by rapid disease progression. There are approximately 20,000 new cases of AML in the U.S., with a five-year survival rate of 27%, as compared to over 30,000 annual cases in China and a five-year survival rate below 20%. The incidence rate in Taiwan is 4 per 100,000 people, equating to around 800 annual cases, with a five-year survival rate of 26%.

The prognosis for elderly and R/R AML patients after current available treatment is poor and around 6%-10% of all AML cases have the IDH1 mutation.

Discovered by CStone's partner, Agios Pharmaceuticals, Inc. (NASDAQ: AGIO) ("**Agios**"), TIBSOVO® was first approved by the U.S. Food and Drug Administration ("**FDA**") for adults with R/R AML with a susceptible IDH1 mutation in 2018, and secured approval for a supplemental new drug application in 2019 for the treatment of newly diagnosed AML patients with an IDH mutation who are ⩾ 75 years old or have comorbidities that preclude the use of intensive induction chemotherapy. The FDA also granted Breakthrough Therapy Designation for TIBSOVO® in combination with Azacitidine for this population of newly diagnosed AML patients with an IDH mutation who are ⩾ 75 years old or have comorbidities that preclude the use of intensive induction chemotherapy.

The efficacy of TIBSOVO® was evaluated in 174 adult patients with R/R AML with an IDH1 mutation. TIBSOVO® was given orally at a starting dose of 500 mg daily until disease progression, development of unacceptable toxicity, or undergoing hematopoietic stem cell transplantation. Trial data to support filing showed that TIBSOVO® as a monotherapy to treat R/R AML patients with an IDH1 mutation achieved complete remission (CR) and complete remission with partial hematologic improvement (CRh) rate of 32.8% (57 of 174 patients) (95% CI: 25.8, 40.3). The median duration of CR+CRh is 8.2 months (95% CI: range 5.6, 12 months).

The safety profile of single-agent TIBSOVO® was evaluated in 179 patients with R/R AML with an IDH1 mutation treated with a dose of 500 mg daily. The median duration of exposure to TIBSOVO® was 3.9 months (range 0.1 to 39.5 months). In the clinical trial, 19% (34/179) of patients treated with TIBSOVO® experienced differentiation syndrome, which can be fatal if not treated. QTc interval prolongation and Guillain-Barré Syndrome occurred in patients treated with TIBSOVO®. The most common adverse reactions (⩾20%) of any grade were fatigue, leukocytosis, arthralgia, diarrhea, dyspnea, edema, nausea, mucositis, electrocardiogram QT prolonged, rash, pyrexia, cough and constipation. The most frequent serious adverse reactions (⩾5%) were differentiation syndrome (10%), leukocytosis (10%) and electrocardiogram QT prolonged (7%).

In June 2018, CStone and Agios announced an exclusive collaboration and license agreement for the development and commercialization of TIBSOVO® in Mainland China, Hong Kong, Macau and Taiwan (Greater China).

About TIBSOVO® (ivosidenib)

TIBSOVO® (ivosidenib) is an IDH1 inhibitor indicated as a treatment for AML in the United States with a susceptible IDH1 mutation under the following conditions:

- in patients with newly diagnosed IDH1-susceptible AML who are ⩾ 75 years old or have comorbidities that preclude the use of intensive induction chemotherapy; and
- in adult patients with R/R AML with a susceptible IDH1 mutation as detected by an FDA-approved test.

For more information about TIBSOVO® (ivosidenib), please visit: www.tibsovo.com.

About CStone

CStone is a biopharmaceutical company focused on developing and commercializing innovative immuno-oncology and precision medicine 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 with a strategic emphasis on immuno-oncology combination therapies. Currently, 4 late-stage candidates are at or near pivotal trials. With an experienced team, a rich pipeline, a robust clinical development-driven business model and substantial funding, CStone's vision is to become globally recognized as a leading Chinese 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

Hong Kong, June 3, 2019

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. Guobin Zhang and Dr. Lian Yong Chen as non-executive Directors, and Dr. Paul Herbert Chew, Mr. Ting Yuk Anthony Wu and Mr. Hongbin Sun as independent non-executive Directors.