CStone Pharmaceuticals

基石藥業

(Incorporated in the Cayman Islands with limited liability)

(Stock Code: 2616)

VOLUNTARY ANNOUNCEMENT
CSTONE ANNOUNCED POSITIVE REGISTRATIONAL STUDY OF GAVRETO® (PRALSETINIB) IN CHINESE PATIENTS WITH RET-MUTANT MEDULLARY THYROID CANCER

CStone Pharmaceuticals (the "**Company**" or "**CStone**") is pleased to announce positive results from China registrational study of the global pivotal Phase I/II ARROW clinical trial of the rearranged during transfection ("**RET**") inhibitor GAVRETO® (pralsetinib), showing deep and durable anti-tumor activity in Chinese patients with advanced or metastatic RET-mutant medullary thyroid cancer ("**MTC**"), consistent with previously reported results in the global ARROW study. The safety data observed in Chinese patients is similar with results shown in global patients. This marks another milestone for GAVRETO® in the field of RET-altered thyroid cancer, following the medicine's approval in China in March this year for the treatment of adult patients with locally advanced or metastatic RET fusion-positive non-small cell lung cancer ("**NSCLC**") after platinum-based chemotherapy. GAVRETO is a potent and selective RET inhibitor discovered by CStone's partner Blueprint Medicines Corporation (NASDAQ: BPMC) ("**Blueprint Medicines**").

Key Highlights

- Key efficacy data for GAVRETO® showed deep and durable anti-tumor activity in Chinese patients with advanced or metastatic RET-mutant MTC

- In March 2021, GAVRETO® was approved by the National Medical Products Administration ("**NMPA**") of China for the treatment of patients with locally advanced or metastatic RET fusion-positive NSCLC after platinum-based chemotherapy

- Top-line results in RET-mutant MTC mark another milestone for GAVRETO® after approval for subset of lung cancer patients. The NMPA of China has accepted the supplemental New Drug Application of GAVRETO® with Priority Review Designation on a rolling submission basis for the treatment of patients with advanced or metastatic RET-mutant MTC and RET

fusion-positive thyroid cancer

Professor Ming Gao, Principal Investigator of the ARROW study and President of Tianjin Union Medical Center, said, "In recent years, there is an increasing incidence of thyroid cancer, but treatment options are extremely limited for patients with RET-mutant MTC. RET-targeting precision therapies in thyroid cancer indication have not been approved in China yet. We are very glad that the pivotal clinical study of GAVRETO® in Chinese patients with RET-mutant MTC has achieved positive results. We look forward to GAVRETO® potentially addressing unmet medical needs and benefiting patients with thyroid cancer."

Dr. Jason Yang, Chief Medical Officer of CStone, said, "We are pleased to see the excellent efficacy and safety profiles of GAVRETO® in Chinese thyroid cancer patients with RET-mutant MTC. The NMPA of China accepted the supplemental New Drug Application of GAVRETO® with priority review designation for the treatment of patients with advanced or metastatic RET-mutant MTC and RET fusion-positive thyroid cancer in April 2021. We look forward to the potential approval of GAVRETO® for this indication, so the treatment may benefit Chinese patients with thyroid cancer soon."

Detailed study data will be presented at a future international academic conference. GAVRETO® has previously been granted Breakthrough Therapy Designation by the Center for Drug Evaluation, the NMPA of China, for the treatment of advanced or metastatic RET-mutant MTC. The NMPA of China has previously accepted the supplemental New Drug Application of GAVRETO® with Priority Review Designation on a rolling submission basis for the treatment of patients with advanced or metastatic RET-mutant MTC and RET fusion-positive thyroid cancer.

CStone has an exclusive collaboration and license agreement with Blueprint Medicines for the development and commercialization of GAVRETO® in Greater China, which encompasses Mainland China, Hong Kong, Macau, and Taiwan.

About the ARROW Study

The ARROW study is a global Phase I/II clinical study designed to evaluate the safety, tolerability and efficacy of GAVRETO® in patients with RET fusion-positive NSCLC, RET-mutant MTC and other advanced solid tumors with RET fusions.

Results from the ARROW trial in global patients with RET-mutant MTC were presented at the European Society for Medical Oncology Virtual Congress in September 2020. As of a data cutoff date of February 13, 2020, the results showed that GAVRETO® had robust and durable anti-tumor activity in response-evaluable patients who received a starting dose of 400 mg once daily. In 53 patients previously treated with cabozantinib or vandetanib, the overall response rate ("**ORR**") was 60 percent (95% CI: 46%, 74%) with one response pending confirmation, and the median duration of response ("**DOR**") was not reached (95% CI: not reached, not reached). In 19 systemic treatment-naïve patients who were ineligible for standard therapy per the study protocol, the confirmed ORR was 74 percent (95% CI: 49%, 91%), and the median DOR was not reached (95% CI: 7 months, not reached). In 438 ARROW trial patients across RET-altered tumor types, the most common treatment-related adverse events reported by investigators (≥ 15 percent) were increased aspartate aminotransferase, anemia, increased alanine aminotransferase, constipation, hypertension, decreased white blood cell count, neutropenia, decreased neutrophil count and hyperphosphatemia.

About Thyroid Cancer

Thyroid cancer is the most common endocrine malignancy with significantly increasing incidence in recent years. According to the latest estimates on the global burden of cancer released by International Agency for Research on Cancer ("**IARC**"), in 2020, there were about 220,000 new cases of thyroid

cancer and the number of new cases in females reached about 170,000 in China. The incidence of thyroid cancer ranked 4th among all malignant tumors in females in urban areas.

Thyroid cancer is clinically divided into multiple subtypes, including papillary, follicular, undifferentiated and medullary. The treatment and prognosis of different types of thyroid cancer vary according to the characteristics of the tumor.

RET fusions and mutations are key disease drivers in many cancer types (including NSCLC and several types of thyroid cancer). Approximately 10-20% of patients with papillary thyroid cancer (the most common type of thyroid cancer) carry RET fusions, and approximately 90% of patients with advanced MTC (approximately 2-5% of thyroid cancers) carry RET mutations. There is currently no effective approved standard treatment regimen for patients with RET-mutant MTC in China.

About GAVRETO® (pralsetinib)

GAVRETO® (pralsetinib) is a once-daily oral targeted therapy approved by the NMPA for the treatment of adults with locally advanced or metastatic RET fusion-positive NSCLC after platinum-based chemotherapy.

GAVRETO™ is approved by the U.S. Food and Drug Administration ("**FDA**") for the treatment of three indications: adult patients with metastatic RET fusion-positive NSCLC as detected by an FDA approved test, adult and pediatric patients 12 years of age and older with advanced or metastatic RET-mutant MTC, and adult and pediatric patients 12 years of age and older with advanced or metastatic RET fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate). These indications are approved under accelerated approval based on ORR and DOR. Continued approval for these indications may be contingent upon verification and description of clinical benefit in confirmatory trials.

GAVRETO® is not approved for the treatment of any other indication in China by the NMPA or in the U.S. by the FDA, or for any indication in any other jurisdiction by any other health authority.

GAVRETO® is designed to selectively and potently target oncogenic RET alterations, including secondary RET mutations predicted to drive resistance to treatment. In preclinical studies, GAVRETO® inhibited RET at lower concentrations than other pharmacologically relevant kinases, including VEGFR2, FGFR2, and JAK2.

Blueprint Medicines and Roche are co-developing GAVRETO® globally (excluding Greater China) for the treatment of patients with RET-altered NSCLC, thyroid cancer, and other solid tumors. Blueprint Medicines and Genentech, a member of the Roche Group, are co-commercializing GAVRETO in the U.S., and Roche has exclusive commercialization rights for GAVRETO outside of the U.S. (excluding greater China). The European Medicines Agency validated a marketing authorization application for GAVRETO® for the treatment of RET fusion-positive NSCLC, and the review is ongoing. The FDA granted breakthrough therapy designation to GAVRETO® for the treatment of RET fusion-positive NSCLC that has progressed following platinum-based chemotherapy and for RET mutation-positive MTC that requires systemic treatment and for which there are no alternative treatments.

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, People's Republic of China, June 28, 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 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.