CStone Pharmaceuticals
基石藥業
(Incorporated in the Cayman Islands with limited liability)
(**Stock Code: 2616**)

VOLUNTARY ANNOUNCEMENT
CSTONE ANNOUNCED THE NMPA APPROVAL OF GAVRETO® (PRALSETINIB) FOR THE TREATMENT OF ADVANCED OR METASTATIC RET-MUTANT MEDULLARY THYROID CANCER AND RET FUSION-POSITIVE THYROID CANCER

CStone Pharmaceuticals (the "**Company**" or "**CStone**") is pleased to announce that the National Medical Products Administration ("**NMPA**") of China has approved the supplemental new drug application ("**sNDA**") of selective rearranged during transfection ("**RET**") inhibitor GAVRETO® (pralsetinib). The approval expanded the labeled indications of GAVRETO in China to include adult and pediatric patients 12 years of age and older with advanced or metastatic RET-mutant medullary thyroid cancer ("**MTC**") who requires systemic therapy, and adult and pediatric patients 12 years of age and older with advanced or metastatic RET fusion-positive thyroid cancer ("**TC**") who requires systemic therapy and radioactive iodine-refractory (if radioactive iodine treatment is appropriate).

Key Highlights

- GAVRETO® is the first and only selective RET inhibitor approved in China for the treatment of RET-mutant MTC and RET fusion-positive TC.

- The labeled indications of GAVRETO® have been expanded after it was approved by the NMPA in March 2021 for the treatment of locally advanced or metastatic RET fusion-positive non-small cell lung cancer ("**NSCLC**") after platinum-based chemotherapy.

Dr. Frank Jiang, Chairman and CEO of CStone, said, "We are very glad about the sNDA approval of GAVRETO®, which will provide a new treatment option for Chinese patients with advanced RET-mutant medullary thyroid cancer and RET fusion-positive thyroid cancer. We also want to extend our special thanks to the NMPA for the priority review. CStone is always committed to developing innovative therapies to address the unmet medical needs of cancer patients. We will continue to enhance the clinical value and potential of our pipeline, and step up efforts to provide patients

worldwide with high-quality, innovative drugs."

Professor Ming Gao, a Principal Investigator of the ARROW study and President of Tianjin Union Medical Center, said "The incidence rate of thyroid cancer has been rising in recent years. There are limited treatment options clinically for the treatment of MTC, and there is an urgent need for precision therapies, especially for patients with RET-mutant MTC. GAVRETO® demonstrated robust and durable anti-tumor activity in Chinese patients with advanced or metastatic RET-mutant MTC, with overall safety consistent with the results seen in the global ARROW study. With this expansion of GAVRETO®'s labeled indications, we look forward to addressing unmet clinical needs of thyroid cancer patients."

Dr. Jason Yang, Chief Medical Officer of CStone, said "The NMPA approval of the sNDA is another key milestone for us after GAVRETO® was approved for the treatment of patients with locally advanced or metastatic RET fusion-positive NSCLC. We'd like to thank all patients and investigators who contributed to the clinical study of GAVRETO® in the expanded indications. We will continue to advance clinical research of GAVRETO® for the treatment of multiple types of cancers so that we can quickly bring forward this innovative therapy to help benefit more patients."

The sNDA approval is based on results from the global phase I/II ARROW trial, 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. As of the data cutoff date of April 12, 2021, a total of 28 patients with advanced RET-mutant MTC were enrolled in the China MTC registrational bridging cohort of the global ARROW study and received a starting GAVRETO® dose of 400mg once daily. The study results showed that the confirmed objective response rate ("**ORR**") of 26 RET-mutant MTC patients with measurable disease at baseline was 73.1%, including 3 with complete response (CR) and 16 with partial responses (PR). The disease control rate (DCR) was 84.6% and responses were observed regardless of RET mutation genotype. Among the 19 patients with confirmed response, the median duration of response ("**DOR**") was not reached, and the 9-month DOR rate was 100%. Calcitonin and carcinoembryonic antigen (CEA) levels were substantially reduced. GAVRETO® was generally well-tolerated, with no new safety signals detected. The results for the China registrational bridging cohort were presented during a late breaking oral abstract session at the 90th Annual Meeting of the American Thyroid Association 2021.

About RET-altered TC

TC 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, in 2020, there were about 220,000 new cases of TC and the number of new cases in females reached about 170,000 in China [1]. The incidence of TC ranked 4th among all malignant tumors in females in urban areas.

TC is clinically divided into multiple subtypes, including papillary, follicular, undifferentiated and medullary. The treatment and prognosis of different types of TC 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 TC. Approximately 10 - 20% of patients with papillary TC (the most common type of TC) carry RET fusions and approximately 90% of patients with advanced MTC (approximately 2 - 5% of TC) carry RET mutations.

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 and for the treatment of adult and pediatric patients 12 years of age and older with advanced or metastatic RET-mutant MTC who requires systemic therapy, and adult and pediatric patients 12 years of age and older with advanced or metastatic RET fusion-positive TC who requires systemic therapy and radioactive iodine-refractory (if radioactive iodine treatment is appropriate).

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 TC 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.

The European Commission has granted conditional marketing authorization for GAVRETO as a monotherapy for the treatment of adult patients with RET fusion-positive advanced NSCLC not previously treated with a RET inhibitor.

GAVRETO® is not approved for the treatment of any other indication in China, U.S. or Europe.

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.

Discovered by CStone's partner Blueprint Medicines Corporation (NASDAQ: BPMC) ("**Blueprint Medicines**"), GAVRETO® is a potent and selective RET inhibitor. 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.

Blueprint Medicines and Roche are co-developing GAVRETO globally (excluding Greater China) for the treatment of patients with RET-altered NSCLC, TC 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 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 seven NDA approvals for its four drugs. 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, March 14, 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.

**Statement: only for medical and healthcare professionals communication use.*

Notes:

1. https://gco.iarc.fr/today/data/factsheets/populations/160-china-fact-sheets.pdf.