CStone Pharmaceuticals

基石藥業

(Incorporated in the Cayman Islands with limited liability)

(Stock Code: 2616)

VOLUNTARY ANNOUNCEMENT
CSTONE ANNOUNCED THE ACCEPTANCE OF NEW DRUG APPLICATION (NDA) FOR PRALSETINIB FOR THE TREATMENT OF RET FUSION-POSITIVE NON-SMALL CELL LUNG CANCER (NSCLC) AND RET-ALTERED THYROID CANCERS IN TAIWAN, CHINA

CStone Pharmaceuticals (the "**Company**" or "**CStone**") is pleased to announce that the Taiwan Food and Drug Administration ("**TFDA**") has confirmed the acceptance of the new drug application ("**NDA**") for pralsetinib for the treatment of rearranged during transfection ("**RET**") fusion-positive locally advanced or metastatic non-small cell lung cancer ("**NSCLC**"), advanced or metastatic RET-mutant medullary thyroid cancer ("**MTC**"), and advanced or metastatic RET fusion-positive thyroid cancer ("**TC**") who are radioactive iodine-refractory (if radioactive iodine treatment is appropriate).

Discovered by CStone's partner Blueprint Medicines Corporation (NASDAQ: BPMC) ("**Blueprint Medicines**"), pralsetinib is a potent and selective RET inhibitor. CStone has an exclusive collaboration and license agreement with Blueprint Medicines for the development and commercialization of pralsetinib in Greater China, which encompasses Mainland China, Hong Kong, Macau and Taiwan.

Dr. Jason Yang, Chief Medical Officer of CStone, said, "We are very glad that the NDA of another innovative precision medicine, pralsetinib, is accepted in Taiwan, China for the treatment of NSCLC and TC, after AYVAKYT® (avapritinib) was approved for the treatment of unresectable or metastatic PDGFRA D842V mutant gastrointestinal stromal tumors last year. In the global phase 1/2 ARROW study, pralsetinib demonstrated robust and durable anti-tumor activity and a generally well-tolerated safety profile in patients with RET fusion-positive locally advanced or metastatic NSCLC and advanced or metastatic RET-altered MTC. We look forward to the potential approval of pralsetinib in Taiwan, China to help benefit more patients as quickly as possible."

The NDA acceptance of pralsetinib in Taiwan, China is based on the global phase I/II ARROW study, which is designed to evaluate the safety, tolerability and efficacy of pralsetinib 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 fusion-positive NSCLC were presented at the 2021 American Society of Clinical Oncology (ASCO) Annual Meeting in June 2021. As of the data cutoff date of November 6, 2020, pralsetinib showed durable clinical benefits in patients with RET fusion-positive NSCLC who had measurable disease at baseline and received a starting dose of 400 mg once daily. In 68 treatment-naïve patients, the overall response rate ("**ORR**") was 79 percent (95% CI: 68%, 88%). The complete response ("**CR**") rate was 6 percent, 10 percent of patients had complete regression of target tumors, and 74 percent of patients had a partial response ("**PR**"). The median duration of response ("**DOR**") was not reached (95% CI: 9.0 months, not reached). In 126 patients who previously received platinum-based chemotherapy, the ORR was 62 percent (95% CI: 53%, 70%). The CR rate was 4 percent, 12 percent of patients had complete regression of target tumors, and 58 percent of patients had a PR. The median DOR was 22.3 months (95% CI: 15.1 months, not reached). As of the data cutoff date, a total of 471 patients were enrolled in across tumor types with a pralsetinib dose starting at 400 mg once daily. The most common treatment-related adverse events ("**AEs**") reported by investigators were neutropenia, increased aspartate aminotransferase, anemia, decreased white blood cell count, increased alanine aminotransferase, hypertension, constipation and asthenia.

Results from the ARROW trial in global patients with RET-altered TC were published in The Lancet Diabetes and Endocrinology in August 2021. As of the data cutoff date of May 22, 2020, pralsetinib showed durable anti-tumor activity in patients with RET-altered TC who received a starting dose of 400 mg once daily. In 55 patients with RET-mutant MTC previously treated with cabozantinib or vandetanib, the ORR was 60 percent (95% CI: 46%, 73%), and the median DOR was not reached (95% CI: 15.1 months, not estimable). In 21 systemic treatment-naïve patients with RET-mutant MTC, the ORR was 71 percent (95% CI: 48%, 89%), and the median DOR was not reached (95% CI: not estimable, not estimable). In addition, the ORR was 89 percent (95% CI: 52%, 100%) in nine patients with RET fusion-positive TC, and the median DOR was not reached (95% CI: not estimable, not estimable). In 142 patients with RET-altered TC, the most common AEs were anemia, musculoskeletal pain, constipation, increased aspartate aminotransferase and hypertension.

About RET fusion-positive NSCLC

In recent years, China has had rising lung cancer incidence. According to the latest estimates on the global burden of cancer released by International Agency for Research on Cancer ("**IARC**"), in 2020, an estimated 0.82 million new lung cancer cases and 0.71 million new lung cancer deaths occurred in China. Among all Chinese cancer patients, lung cancer is the leading cause of cancer-related deaths. NSCLC is the most common type of lung cancer.

In lung cancer, there are a number of somatic mutations, including EGFR, ALK, and ROS1, that can be targeted with approved therapies. RET fusions account for 1 - 2% of NSCLC patients, the majority of whom are non-smokers.

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 IARC, 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. 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. There is currently no effective approved standard treatment regimen for patients with RET-mutant MTC in China.

About Pralsetinib

Pralsetinib is a once-daily oral targeted therapy approved by the National Medical Products Administration of China ("**NMPA**") under the brand name GAVRETO® for the treatment of adults with locally advanced or metastatic RET fusion-positive NSCLC after platinum-based chemotherapy.

In April 2021, the NMPA accepted the supplemental new drug application for pralsetinib with priority review designation for the treatment of patients with advanced or metastatic MTC who require systemic therapy, and advanced or metastatic RET fusion-positive TCs who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine 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.

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

Pralsetinib is designed to selectively and potently target oncogenic RET alterations, including secondary RET mutations predicted to drive resistance to treatment. In preclinical studies, pralsetinib 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, 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 pralsetinib 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 leading 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 six drug approvals. 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, February 17, 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.