CStone Pharmaceuticals

基石藥業

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VOLUNTARY ANNOUNCEMENT
CSTONE PRESENTS REGISTRATIONAL BRIDGING STUDY DATA FOR GAVRETO® (PRALSETINIB) HIGHLIGHTING EFFICACY AND SAFETY IN CHINESE PATIENTS WITH ADVANCED RET FUSION-POSITIVE NON-SMALL CELL LUNG CANCER AT IASLC WCLC 2021

CStone Pharmaceuticals (the "**Company**" or "**CStone**") is pleased to announce that efficacy and safety data from a cohort of Chinese patients with rearranged during transfection ("**RET**") fusion-positive non-small cell lung cancer ("**NSCLC**") in a global trial of GAVRETO® (pralsetinib) were reported in an oral presentation at the IASLC 2021 World Conference on Lung Cancer ("**WCLC**"), hosted by the International Association for the Study of Lung Cancer. The results show that GAVRETO had robust and durable anti-tumor activity and a generally well-tolerated safety profile in patients enrolled at China sites who had advanced RET fusion-positive NSCLC, with no new safety signals detected. This is also the first time that data on GAVRETO for the first-line treatment of Chinese patients with RET fusion-positive NSCLC have been presented at an international academic conference. CStone plans to submit a supplemental new drug application ("**sNDA**") for this indication to the National Medical Products Administration ("**NMPA**") of China.

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

The ARROW study (ClinicalTrials.gov identifier: NCT03037385) 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 medullary thyroid cancer ("**MTC**") and other advanced solid tumors with RET fusions.

As of a data cutoff date of April 12, 2021, a total of 68 patients with advanced RET fusion-positive

NSCLC from 10 sites were enrolled in the China cohort of the global ARROW study, and received a starting GAVRETO dose of 400 mg once daily. Among these patients, 37 patients received prior platinum-based chemotherapy, and 31 patients received no prior systemic treatment. Tumor response was assessed by blinded independent central review ("**BICR**") using Response Evaluation Criteria in Solid Tumors ("**RECIST**") version 1.1.

Efficacy: GAVRETO is a promising targeted therapy with rapid and durable clinical activity in Chinese patients with RET fusion-positive NSCLC regardless of prior therapy.

- For patients who have previously received platinum-based chemotherapy (n=33, measurable disease at baseline):
    - The confirmed overall response rate ("**ORR**") was 66.7%, including 1 complete response ("**CR**") and 21 partial responses ("**PR**"). The disease control rate ("**DCR**") reached 93.9%.
    - Among 22 patients with confirmed response, the median time to first response was 1.89 months.
- For patients who have not received prior systemic treatment (n=30, measurable disease at baseline):
    - The confirmed ORR was 80%, including 2 CRs and 22 PRs. The DCR was 86.7%.
    - Among 24 patients with confirmed response, the median time to first response was 1.87 months.

Safety: GAVRETO was generally well-tolerated with a manageable safety profile

- GAVRETO was generally well-tolerated. The overall safety in Chinese patients was manageable, with no new safety signal detected.

Professor Yi-Long Wu of Guangdong Provincial People's Hospital, a Principal Investigator of the ARROW study, said, "As the first RET inhibitor approved in China, GAVRETO fills a gap for the treatment of patients with RET fusion-positive NSCLC. The updated data not only further demonstrate that GAVRETO had proven efficacy and well-tolerated safety in second-line treatment settings, but more importantly show it had even better anti-tumor activity in Chinese patients with RET fusion-positive advanced NSCLC with no new safety signal detected. I look forward to seeing GAVRETO benefit more Chinese patients in the future."

Professor Qing Zhou, professor of Guangdong Provincial People's Hospital, the presenter for this report, said, "Since reporting data on GAVRETO for the second-line treatment of Chinese patients with RET fusion-positive NSCLC at last year's WCLC, the updated results showed durable responses that have deepened over time. It is also the first data readout at a medical meeting for GAVRETO for the first-line treatment of Chinese patients with RET fusion-positive NSCLC. I am encouraged by the positive data, which support the potential of GAVRETO as a new standard treatment for Chinese patients with RET fusion-positive NSCLC."

Dr. Jason Yang, Chief Medical Officer of CStone, said, "We are very excited that GAVRETO has shown remarkable tumor response, rapid onset of efficacy, and duration of response in Chinese patients with RET fusion-positive advanced NSCLC in both first-line and second-line treatment settings, with a manageable safety profile. We plan to submit an sNDA for GAVRETO as a first-line treatment of RET fusion-positive NSCLC to the NMPA of China, and we will continue to explore

the potential of GAVRETO in other solid tumors driven by RET alterations."

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 GAVRETO (pralsetinib)

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

In April 2021, the NMPA of China accepted the sNDA of GAVRETO 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 thyroid cancers who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate).

GAVRETO has been 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 have received accelerated approval based on ORR and duration of response. 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 United States by the FDA.

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 United States, and Roche has exclusive commercialization rights for GAVRETO outside of the U.S. (excluding Greater China). The European Medicines Agency has validated a marketing authorization application for GAVRETO for the treatment of RET fusion-positive NSCLC, and the review is still in progress. The FDA has 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 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 9, 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.