CStone Pharmaceuticals

基石藥業

(Incorporated in the Cayman Islands with limited liability)

(**Stock Code: 2616**)

VOLUNTARY ANNOUNCEMENT

CSTONE'S PARTNER BLUEPRINT MEDICINES ANNOUNCED TOP-LINE DATA FROM PHASE I/II ARROW TRIAL IN RET-ALTERED THYROID CANCERS AND COMPLETION OF ROLLING NDA SUBMISSION TO U.S. FDA FOR PRALSETINIB FOR RET FUSION-POSITIVE NON-SMALL CELL LUNG CANCER

The partner of CStone Pharmaceuticals (the "**Company**" or "**CStone**"), Blueprint Medicines Corporation (NASDAQ: BPMC) ("**Blueprint Medicines**"), announced on April 1, 2020 the compilation of top-line data for pralsetinib in patients with RET-mutant medullary thyroid cancer ("**MTC**"), supporting plans to submit a new drug application ("**NDA**") to the U.S. Food and Drug Administration ("**U.S. FDA**") in the second quarter of 2020. In addition, Blueprint Medicines announced the completion of its rolling NDA submission to the U.S. FDA for pralsetinib for the treatment of patients with RET fusion-positive non-small cell lung cancer ("**NSCLC**").

The key updates include:

- Top-line ARROW trial data for pralsetinib show 60% overall response rate ("**ORR**") and 18-month duration of response rate of 90% in previously treated RET-mutant medullary thyroid cancer; Blueprint Medicines plans to submit an NDA to U.S. FDA in the second quarter of 2020;
- The ORR reaches 74% in treatment-naïve RET-mutant MTC and the ORR reaches 89% in RET fusion-positive thyroid cancer;
- An NDA has been submitted to U.S. FDA for pralsetinib for RET fusion-positive NSCLC.

Blueprint Medicines has entered into an exclusive collaboration and license agreement with CStone for the development and commercialization of pralsetinib, avapritinib and fisogatinib in mainland China, Hong Kong, Macau and Taiwan. Blueprint Medicines retains development and commercial rights for all three licensed products in the rest of the world.

Currently, as part of the global ARROW studies, CStone is conducting in China Phase I/II trial of pralsetinib for the treatment of RET-altered NSCLC, MTC and other advanced solid tumors. CStone has completed the enrollment of a cohort of patients in China with RET fusion-positive NSCLC previously treated with platinum-based chemotherapy, and expects an NDA submission for this indication in China in the second half of 2020. Furthermore, an additional registrational cohort of patients with RET fusion-positive NSCLC naïve to platinum-based chemotherapy has been initiated by the Company in China.

Top-line Data from Phase I/II ARROW Trial in RET-Altered Thyroid Cancers

Top-line results announced today support Blueprint Medicines' plans to submit an NDA to the U.S. FDA for pralsetinib in patients with RET-mutant MTC previously treated with an approved multi-kinase inhibitor in the second quarter of 2020. The registration endpoints are ORR and duration of response ("**DOR**"), based on independent central radiology and Response Evaluation Criteria in Solid Tumors version 1.1 ("**RECIST 1.1**") criteria.

Top-line efficacy data were reported for patients who were treated with pralsetinib and evaluable for response assessment according to RECIST 1.1, as determined by blinded independent central review. All patients received the proposed indicated dose of 400 mg once daily ("**QD**"). All results were cut off as of February 13, 2020.

In 53 patients with RET-mutant MTC previously treated with cabozantinib or vandetanib, the ORR was 60% (95% CI: 46-74%) with one response pending confirmation. 98% of all patients had tumor shrinkage. The median DOR was not reached (95% CI: not estimable), and the 18-month DOR rate was 90% (95% CI: 77-100%).

In addition, the top-line data showed robust clinical activity in treatment-naïve patients, supporting the potential of pralsetinib across lines of therapy. In 19 patients with RET-mutant MTC who had not received prior systemic treatment, the confirmed ORR was 74% (95% CI: 49-91%), and all patients had tumor shrinkage. The median DOR was not reached (95% CI: 7 months, not estimable), with 12 of 14 responders remaining in response for up to 15 months as of the data cut-off date.

In nine patients with RET fusion-positive thyroid cancer, the confirmed ORR was 89% (95% CI: 52-100%) and all patients had tumor shrinkage. The median DOR was not reached (95% CI: 8 months, not estimable), with seven of eight responders remaining in response for up to 20 months as of the data cut-off date.

Top-line safety data were consistent with those previously reported. Pralsetinib was well-tolerated and most treatment-related adverse events ("**AEs**") were Grade 1 or 2. Among all patients enrolled in the ARROW trial treated at the proposed indicated dose of 400 mg QD (N=438), only 4% discontinued treatment with pralsetinib due to treatment-related AEs.

Blueprint Medicines plans to present the full data at a scientific meeting this year.

NDA Submission to U.S. FDA for Pralsetinib for RET Fusion-Positive NSCLC

Blueprint Medicines completed the rolling NDA submission to the U.S. FDA for pralsetinib for RET fusion-positive NSCLC. Blueprint Medicines requested priority review for the application, which, if granted, could result in a six-month review process.

About Pralsetinib

Pralsetinib is an investigational, once-daily oral precision therapy specifically designed for highly potent and selective targeting of oncogenic RET alterations. Blueprint Medicines is developing pralsetinib for the treatment of patients with RET-altered NSCLC, MTC and other solid tumors.

Pralsetinib was designed by Blueprint Medicines' research team, leveraging on proprietary compound library of the company. In preclinical studies, pralsetinib consistently demonstrated sub-nanomolar potency against the most common RET fusions, activating mutations and predicted resistance mutations. In addition, pralsetinib demonstrated markedly improved selectivity for RET compared to pharmacologically relevant kinases, including approximately 90-fold improved potency for RET versus VEGFR2. By suppressing primary and secondary mutants, pralsetinib has the potential to overcome and prevent the emergence of clinical resistance. Blueprint Medicines believes this approach will enable durable clinical responses across a diverse range of RET alterations, with a favorable safety profile.

About CStone

CStone is a biopharmaceutical company focused on 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, five late-stage candidates are at 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

Suzhou, People's Republic of China, April 2, 2020

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.