CStone Pharmaceuticals

(Incorporated in the Cayman Islands with limited liability)
(Stock Code: 2616)

VOLUNTARY ANNOUNCEMENT

CSTONE’S PARTNER BLUEPRINT MEDICINES PRESENTED UPDATED PART 1 DATA FROM PIONEER TRIAL OF AVAPRITINIB SHOWING ROBUST REDUCTIONS IN CUTANEOUS DISEASE SYMPTOMS IN PATIENTS WITH INDOLENT SYSTEMIC MASTOCYTOSIS

The partner of CStone Pharmaceuticals (the “Company” or “CStone”), Blueprint Medicines Corporation (NASDAQ: BPMC) (“Blueprint Medicines”), announced on June 6 updated clinical data from part 1 of the PIONEER trial showing robust and consistent clinical activity for avapritinib across multiple qualitative and quantitative measures of cutaneous disease in patients with indolent systemic mastocytosis (“ISM”). Additional data showed avapritinib treatment resulted in deepening improvements in overall disease symptoms, as measured by the ISM symptom assessment form (“ISM-SAF”) total symptom score (“TSS”), and was well-tolerated through 24 weeks of follow-up. These data were presented during the European Academy of Allergy and Clinical Immunology (“EAACI”) Digital Congress 2020.


Systemic Mastocytosis (“SM”) is a rare disease driven by the KIT D816V mutation in nearly all patients and characterized by uncontrolled mast cell proliferation and activation. The disorder can lead to debilitating systemic, gastrointestinal and neurocognitive symptoms, including life-threatening anaphylaxis. Additional skin manifestations such as itching, flushing and pigmented skin lesions are common and can significantly impact quality of life. Avapritinib is a potent and highly selective inhibitor of D816V mutant KIT.
Blueprint Medicines has an exclusive collaboration and license agreement with CStone for the development and commercialization of pralsetinib, avapritinib and fisogatinib in Mainland of the People’s Republic of China, Hong Kong Special Administrative Region, Macau Special Administrative Region and Taiwan. Blueprint Medicines retains development and commercial rights for all three licensed products in the rest of the world.

The key updates include:

- Updated PIONEER trial data in patients with ISM showed response rate of 60% for avapritinib versus 0% for placebo at 24 weeks, with response defined as ≥30% reduction in total symptom score;

- Plan to present updated data from EXPLORER trial of avapritinib in patients with advanced SM (“AdvSM”) at the European Hematology Association Virtual Congress on June 12.

**Highlights from the EAACI Presentation of PIONEER Trial Data**

Previously reported data from part 2 of the PIONEER trial showed that treatment with avapritinib was well-tolerated and resulted in robust and clinically meaningful improvements on measures of mast cell burden, disease symptoms and patient-reported quality of life through 16 weeks. Based on these data, avapritinib 25 mg once daily (“QD”) was selected as the recommended part 2 dose. Updated data on disease symptoms through 24 weeks and new skin assessment results were reported in the EAACI presentation.

**Updated clinical activity and safety data**

As of March 31, 2020, updated data from part 1 of the PIONEER trial showed a deepening of symptom reductions in patients treated with avapritinib through 24 weeks of follow-up. The mean percent change from baseline in ISM- SAF TSS was -35 percent in patients treated with avapritinib 25 mg QD (n=10) compared to -4 percent in patients treated with placebo. In addition, the mean percent change from baseline in ISM-SAF skin domain score was -38 percent for avapritinib 25 mg QD versus +11 percent for placebo.

The updated data also showed a 60 percent response rate in patients treated with avapritinib 25 mg QD compared to a 0 percent response rate in patients treated with placebo at 24 weeks, with response defined as a 30 percent or greater reduction in ISM-SAF TSS. Based on these data and feedback from the Food and Drug Administration of the United States (“USFDA”), Blueprint Medicines has selected response rate at 24 weeks as the primary endpoint for the registration-enabling part 2 of the PIONEER trial and plans to enroll approximately 200 patients. Blueprint Medicines continues to plan to initiate patient screening in part 2 of the PIONEER trial in June 2020.

As of March 31, 2020, avapritinib 25 mg QD was well-tolerated and safety results were consistent with previously reported data, with no grade ≥3 adverse events or discontinuations due to adverse events.

**Additional clinical activity data on measures of skin disease**

High-resolution skin photographs were taken at baseline and every 12 weeks during treatment for patients with significant cutaneous involvement who consented to photography. To assess changes in skin disease,
photographs were assessed by a blinded independent review committee and a computational image analysis algorithm. Images and data as of March 31, 2020 were evaluated by the independent committee.

Based on skin photography at 24 weeks or the last available assessment, results showed that skin lesions lightened in 71 percent of patients treated with avapritinib (n=17; all doses) compared to 25 percent of patients treated with placebo (n=8), per blinded review by the independent committee. In addition, the median percent change from baseline in most affected surface area was -35 percent for avapritinib (n=18; all doses) compared to -8 percent for placebo (n=8), based on a computational image analysis algorithm.

Mast cell infiltration in skin lesions was also assessed by lesional skin biopsies obtained at baseline and 12 weeks. The median percent change from baseline in mast cell infiltration was -46 percent for avapritinib (n=18; all doses) compared to +51 percent for placebo (n=7).

**About avapritinib**

avapritinib is a kinase inhibitor approved by the USFDA under the brand name AYVAKIT™ for the treatment of adults with unresectable or metastatic gastrointestinal stromal tumor (“GIST”) harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations.

avapritinib is not approved for the treatment of any other indication, including SM, in the U.S. by the USFDA or for any indication in any other jurisdiction by any other health authority.

Blueprint Medicines is developing avapritinib globally for the treatment of advanced, smoldering and indolent SM. The USFDA granted a breakthrough therapy designation to avapritinib for the treatment of advanced SM, including the subtypes of aggressive SM, SM with an associated hematologic neoplasm and mast cell leukemia.

**About the Phase 2 PIONEER Trial**

PIONEER is a randomized, double-blind, placebo-controlled and registration-enabling trial evaluating avapritinib in patients with indolent and smoldering SM. The trial includes three parts: dose-finding part 1, registration-enabling part 2 and long-term treatment part 3. All patients who complete parts 1 or 2 will have an opportunity to continue to receive treatment with avapritinib in part 3. Key trial endpoints include the change in patient-reported disease symptoms as measured by the ISM-SAF TSS, quantitative measures of mast cell burden and safety. Part 1 has completed patient enrollment. Blueprint Medicines plans to initiate patient screening for part 2 in June 2020 at sites in the United States, Canada and European Union.

**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 at the end of 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.
Suzhou, People’s Republic of China, June 17, 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.