CStone Pharmaceuticals

基石藥業

(Incorporated in the Cayman Islands with limited liability)

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VOLUNTARY ANNOUNCEMENT
CSTONE'S PARTNER BLUEPRINT MEDICINES PRESENTS REGISTRATIONAL DATA FROM PIONEER TRIAL OF AYVAKIT® (AVAPRITINIB) IN PATIENTS WITH INDOLENT SYSTEMIC MASTOCYTOSIS AT 2023 AAAAI ANNUAL MEETING

CStone Pharmaceuticals (the "**Company**" or "**CStone**") is pleased to announce that the partner of CStone, Blueprint Medicines Corporation (NASDAQ: BPMC) ("**Blueprint Medicines**") announced detailed results from the PIONEER trial of AYVAKIT® (avapritinib) in patients with indolent systemic mastocytosis (SM). As previously reported, AYVAKIT achieved statistically significant and clinically meaningful improvements on the primary and all key secondary endpoints. New results further highlight the benefits of AYVAKIT on pathological mast cell burden, disease symptoms – including total symptom score (TSS), most severe symptom and all individual symptoms – and quality of life. Across clinical measures, improvements continued to deepen over time in patients treated with AYVAKIT through 48 weeks. AYVAKIT was well-tolerated with a safety profile favorable to placebo, and 96 percent of patients in the AYVAKIT arm opted to continue treatment in the open-label extension study.

Key Highlights

- AYVAKIT achieved a statistically significant and clinically meaningful improvement in total symptom score that deepened over time, with improvements shown across all individual symptoms.
- AYVAKIT achieved a statistically significant and clinically meaningful improvement on the Mastocytosis Quality of Life Questionnaire (MC-QoL).
- AYVAKIT had a favorable safety profile compared to placebo, supporting potential for chronic treatment.

Based on these data, Blueprint Medicines submitted a supplemental new drug application (sNDA) for AYVAKIT to the U.S. Food and Drug Administration (FDA) and a type II variation marketing authorization application (MAA) for AYVAKYT® to the European Medicines Agency (EMA) for the treatment of patients with indolent SM. The FDA has granted priority review to the sNDA for AYVAKIT with a Prescription Drug User Fee Act (PDUFA) action date of May 22, 2023, and the EMA has validated the MAA for AYVAKYT.

Discovered by CStone's partner Blueprint Medicines, AYVAKIT (avapritinib) is a potent, selective and orally available inhibitor of KIT and PDGFRA mutant kinases. CStone has an exclusive collaboration and license agreement with Blueprint Medicines for the development and commercialization of AYVAKIT in Mainland China, Hong Kong, Macau and Taiwan.

Data Highlights from the PIONEER Trial

In the randomized, double-blind, placebo-controlled part of the PIONEER trial, 141 patients received AYVAKIT 25 mg once daily plus best supportive care and 71 patients received placebo plus best supportive care (placebo) at 49 sites in 13 countries. The study included adults with an indolent SM diagnosis confirmed by central pathology review, and moderate-to-severe symptom burden despite an optimized regimen of best supportive care. All patients were able to continue symptom-directed therapy throughout the trial and, following completion of the 24-week treatment period, had the option to receive AYVAKIT in an open-label extension study. Baseline patient demographics were balanced between treatment arms and reflected significant disease burden. Disease symptoms were assessed using the Indolent SM Symptom Assessment Form (ISM-SAF).

AYVAKIT achieved rapid, durable and statistically significant reductions on all measures of pathological mast cell burden compared to placebo at 24 weeks.

Outcome measure	AYVAKIT	Placebo	p-value
Proportion with ≥50% reduction in serum tryptase	53.9 %	0 %	p<0.0001
Proportion with ≥50% reduction in KIT D816V variant allele fraction	67.8 %	6.3 %	p<0.0001
Proportion with ≥50% reduction in bone marrow mast cell aggregates	52.8 %	22.8 %	p<0.0001

AYVAKIT achieved a statistically significant and clinically meaningful improvement in TSS compared to placebo at 24 weeks, with improvements observed across all symptoms measured by the ISM-SAF that deepened over time.

Outcome measure	AYVAKIT		Placebo	p-value
	24 weeks	48 weeks	24 weeks	24 weeks
Mean change in TSS	-15.6 points	-20.2 points	-9.2 points	p=0.003
Proportion with ≥30% reduction in TSS	45.4 %	60.7 %	29.6 %	p=0.009
Proportion with ≥50% reduction in TSS	24.8 %	39.3 %	9.9 %	p=0.005

- AYVAKIT achieved a statistically significant improvement in mean change in most severe symptom score compared to placebo at 24 weeks (p=0.015).

AYVAKIT achieved a statistically significant and clinically meaningful improvement in the mean percent change in Mastocytosis Quality of Life Questionnaire (MC-QoL) total score compared to placebo at 24 weeks.

Outcome measure	AYVAKIT	Placebo	p-value

Mean percent change in MC-QoL total score	-34.3 %	-17.9 %	p=0.001

AYVAKIT was well-tolerated with a favorable safety profile compared to placebo, supporting the potential for long-term treatment.

- Across treatment arms, most adverse events (AEs) were mild to moderate in severity, and treatment-related AEs leading to discontinuations were low for both arms (1.4% each).
- Serious AEs were reported more frequently in the placebo arm (11.3%) compared to the AYVAKIT arm (5.0%).
- The most common treatment-related AEs (≥5 percent) were headache (7.8% AYVAKIT vs. 9.9% placebo), nausea (6.4% AYVAKIT vs. 8.5% placebo), peripheral edema (6.4% AYVAKIT vs. 1.4% placebo), periorbital edema (6.4% AYVAKIT vs. 2.8% placebo) and dizziness (2.8% AYVAKIT vs. 7.0% placebo). Most edema AEs were Grade 1, and none led to treatment discontinuation.

These data were presented at the 2023 American Academy of Allergy, Asthma & Immunology (AAAAI) Annual Meeting, February 24 to 27.

About AYVAKIT (avapritinib)

Avapritinib (AYVAKIT) is a kinase inhibitor approved by the National Medical Products Administration (NMPA) of China for the treatment of adults with unresectable or metastatic GIST harboring the PDGFRA exon 18 mutation, including PDGFRA D842V mutations. Avapritinib was approved by the Department of Health (DOH), Hong Kong, China, and Taiwan Food and Drug Administration (TFDA) for the treatment of adults with unresectable or metastatic GIST harboring a PDGFRA D842V mutation.

The U.S. Food and Drug Administration (FDA) has approved avapritinib for the treatment of two indications: adults with advanced systemic mastocytosis (Advanced SM), including aggressive SM (ASM), SM with an associated hematological neoplasm (SM-AHN) and mast cell leukemia (MCL), and adults with unresectable or metastatic GIST harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations. This medicine is approved by the European Commission under the brand name AYVAKYT for the treatment of adults with ASM, SM-AHN or MCL, after at least one systemic therapy, and adults with unresectable or metastatic GIST harboring the PDGFRA D842V mutation.

AYVAKIT/AYVAKYT is not approved for the treatment of any other indication in the U.S., Europe or Greater China. The FDA granted breakthrough therapy designation to AYVAKIT for the treatment of moderate to severe indolent SM.

About Systemic Mastocytosis

Systemic mastocytosis (SM) is a rare disease driven by the KIT D816V mutation in about 95 percent of cases. Uncontrolled proliferation and activation of mast cells result in chronic, severe and often unpredictable symptoms across multiple organ systems. Most of those affected have non-advanced (indolent or smoldering) SM, and among these patients, the vast majority have indolent SM. A broad range of symptoms, including anaphylaxis, maculopapular rash, pruritis, diarrhea, brain fog, fatigue and bone pain, frequently persist in patients with non-advanced SM despite treatment with multiple symptom-directed therapies. This burden of disease can lead to a profound, negative impact on quality of life. Patients often live in fear of severe, unexpected symptoms, have limited ability to work or perform daily activities, and isolate themselves to protect against unpredictable triggers. Currently, there are no approved therapies for the treatment of non-advanced SM.

A minority of patients have advanced SM, which encompasses a group of high-risk SM subtypes including ASM, SM-AHN and MCL. In addition to mast cell activation symptoms, advanced SM is associated with organ damage due to mast cell infiltration and poor survival.

About the PIONEER Trial

PIONEER is a randomized, double-blind, placebo-controlled, registrational trial evaluating AYVAKIT in patients with indolent SM. The trial includes three parts: dose-finding Part 1, registrational Part 2 and open-label extension Part 3. Key trial endpoints include the change in patient-reported disease symptoms as assessed by the ISM-SAF TSS, patient-reported quality of life, measures of mast cell burden and safety. Patients who completed Part 1 or 2 were eligible to participate in Part 3. All patients receive AYVAKIT treatment during Part 3, including those rolling over from the placebo arm.

For more information about the PIONEER trial, please visit www.clinicaltrials.gov (ClinicalTrials.gov Identifier: NCT03731260).

About CStone

CStone is a biopharmaceutical company focused on research, development, and commercialization of 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 ten NDA approvals for its four drugs. Multiple late-stage drug candidates are now under pivotal clinical trials or registration. 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.

Forward Looking Statement

There is no assurance that any forward-looking statements regarding the business development of the Group in this announcement or any of the matters set out herein are attainable, will actually occur or will be realised or are complete or accurate. The financial and other data relating to the Group as disclosed in this announcement has also not been audited or reviewed by its auditors. Shareholders and/or potential investors of the Company are advised to exercise caution when dealing in the securities of the Company and not to place any excessive reliance on the information disclosed herein. Any shareholder or potential investor who is in doubt is advised to seek advice from professional advisors.

Trademarks

Blueprint Medicines, AYVAKIT, AYVAKYT and associated logos are trademarks of Blueprint Medicines Corporation.

By Order of the Board
CStone Pharmaceuticals
Dr. Wei Li
Chairman

Suzhou, the People's Republic of China, March 13, 2023

As at the date of this announcement, the board of directors of the Company comprises Dr. Wei Li as Chairman and non-executive director, Dr. Jianxin Yang as executive director, Mr. Kenneth Walton Hitchner III, 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.