CStone Pharmaceuticals

基石藥業

(Incorporated in the Cayman Islands with limited liability)

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VOLUNTARY ANNOUNCEMENT
CSTONE'S PARTNER SERVIER PRESENTS POSITIVE NEW TIBSOVO® (IVOSIDENIB TABLETS) DATA FOR IDH1-MUTATED ACUTE MYELOID LEUKEMIA AT ASCO

The partner of CStone Pharmaceuticals (the "**Company**" or "**CStone**"), Servier presented updated efficacy and safety data from the global Phase 3 AGILE study of TIBSOVO® (ivosidenib tablets) in combination with the chemotherapy azacitidine for newly-diagnosed acute myeloid leukemia (AML), and a new analysis of treatment response to TIBSOVO, an inhibitor of the mutated isocitrate dehydrogenase-1 (IDH1) enzyme at the 2023 Annual Meeting of the American Society of Clinical Oncology (ASCO). The new data further demonstrate the significant clinical and survival benefits of first-line treatment with TIBSOVO and azacitidine for patients with IDH1-mutated AML. As the first IDH1 mutation specific targeted therapy to demonstrate improved overall survival (OS) in combination with azacitidine compared to azacitidine plus placebo, TIBSOVO was also recently approved by the European Commission as the first IDH1 inhibitor in Europe.

Key Highlights

- Updated data from Phase 3 AGILE study show additional extension in median OS to 29.3 months with TIBSOVO® (ivosidenib tablets) in combination with azacitidine and confirm continued benefit of TIBSOVO as first-line treatment of newly-diagnosed acute myeloid leukemia (AML)

- Analysis of Phase 1 expansion study identifies clinical and molecular characteristics of AML patients with an exceptional response to TIBSOVO

The AGILE trial is a global, Phase 3, double blinded, placebo-controlled study of TIBSOVO in combination with azacitidine vs. azacitidine plus placebo in adults with previously untreated IDH1-mutated AML who were ineligible to receive intensive chemotherapy. TIBSOVO in combination with azacitidine demonstrated a three-fold improvement in median OS (24 months) compared to azacitidine plus placebo (7.9 months) as a first-line treatment for IDH1-mutated AML (HR: 0.44; p=0.0005). In long-

term follow-up data as of June 2022, at a median follow-up of 28.6 months, median OS was 29.3 months (95% CI 13.2, not reached) for TIBSOVO in combination with azacitidine vs. to 7.9 months (95% CI 4.1, 11.3) for placebo plus azacitidine (HR: 0.42 [0.27, 0.65]; 1-sided p<0.0001).

Additional updated results include:

- At 24 months, OS rates were 53.1% with TIBSOVO in combination with azacitidine, compared to 17.4% with azacitidine plus placebo. At 12 months, OS rates were 62.9% with TIBSOVO in combination with azacytidine, compared to 38.3% with azacitidine plus placebo.

- In the TIBSOVO in combination with azacitidine arm, hemoglobin levels steadily increased from baseline and then stabilized; mean platelet count recovered from baseline values as early as week 8 and remained stable through week 80; and mean neutrophil counts rapidly increased from baseline to weeks 3 and 4 and then stabilized to within the normal range.

- Conversion from baseline transfusion dependence (red blood cell and/or platelet transfusion dependence) to post-baseline transfusion independence was significantly higher with TIBSOVO in combination with azacytidine, compared with azacitidine plus placebo (53.8% v 17.1%, respectively; 1-sided p=0.0004).

TIBSOVO in combination with azacitidine demonstrated a safety profile consistent with previously published data. There were fewer neutropenic fever events (27.8% v 33.8%) and infections (34.7% v 51.4%) with TIBSOVO in combination with azacitidine than with azacitidine plus placebo. Treatment-emergent adverse events led to discontinuation of TIBSOVO in combination with azacitidine or azacitidine plus placebo in 26.4% and 25.7% of patients, respectively.

The Phase 3 AGILE study was the basis of the FDA approval for TIBSOVO in combination with azacitidine for newly diagnosed AML, and the original study results were published in the New England Journal of Medicine.

In addition, a Phase 1 dose escalation study was conducted to evaluate the clinical and molecular characteristics of patients with IDH1-mutated relapsed/refractory AML who achieved an exceptional response to treatment with TIBSOVO.

Of 179 patients with R/R AML who received TIBSOVO in the study, 57 (31.8%) achieved complete response (CR)/CR with partial hematologic recovery (CRh). Of these, 13 patients (22.8% of responders, 7.3% of cohort) achieved exceptional response, defined as a duration of CR/CRh response (DOCRCRh) without hematopoietic stem cell transplantation of more than 12 months, and eight (14.0% of responders, 4.5% of cohort) had a DOCRCRh of more than two years. The 13 exceptional responders all achieved a complete response, with a median DOCRCRh of 43 months. No patient with DOCRCRh > 32 months relapsed.

Clinical and molecular characteristics among patients who achieved an exceptional response included a low mutational burden, lack of receptor tyrosine kinase (RTK) pathway mutations and canonical AML drivers, and co-occurrence of mutations associated with clonal hematopoiesis appear to be associated with exceptional response.

TIBSOVO is currently approved in the U.S. as monotherapy for the treatment of adults with IDH1-mutant relapsed or refractory AML and in monotherapy or in combination with azacitidine for adults with newly diagnosed IDH1-mutant AML who are ≥75 years old or who have comorbidities that preclude the use of intensive induction chemotherapy. TIBSOVO is also approved as the first and only targeted therapy for patients with previously treated IDH1-mutated cholangiocarcinoma. TIBSOVO was recently approved by the European Commission as a targeted therapy in two indications: in combination with azacitidine for

the treatment of adult patients with newly diagnosed AML with an isocitrate dehydrogenase-1 (IDH1) R132 mutation who are not eligible to receive standard induction chemotherapy; as well as in monotherapy for the treatment of adult patients with locally advanced or metastatic cholangiocarcinoma with an IDH1 R132 mutation who were previously treated by at least one prior line of systemic therapy. TIBSOVO has also been approved in the U.S. and Australia for patients with previously treated IDH1-mutated cholangiocarcinoma. TIBSOVO is also approved in China for the treatment of adult patients with relapsed or refractory AML who have a susceptible IDH1 mutation. Servier has granted CStone a co-exclusive license for the development and an exclusive license agreement for the commercialization of TIBSOVO in Mainland China, Taiwan, Hong Kong, Macau and Singapore.

About the NCT03173248 AGILE Phase 3 AML Trial

The AGILE trial is a global, Phase 3, multicenter, double-blind, randomized, placebo-controlled clinical trial designed to evaluate the efficacy and safety of TIBSOVO in combination with azacitidine compared with placebo in combination with azacitidine, in adults with previously untreated IDH1-mutated acute myeloid leukemia (AML) who are not candidates for intensive chemotherapy (≥75 years old or who have comorbidities that preclude the use of intensive induction chemotherapy). The study's primary endpoint is event-free survival (EFS), defined as the time from randomization until treatment failure, relapse from remission, or death from any cause, whichever occurs first. Treatment failure is defined as failure to achieve complete remission (CR) by Week 24.

Key secondary endpoints included CR rate, defined as the proportion of participants who achieve a CR; overall survival (OS), defined as the time from date of randomization to the date of death due to any cause; CR and complete remission with partial hematologic recovery (CRh) rate, defined as the proportion of participants who achieve a CR or CRh; and objective response rate (ORR), defined as the rate of CR, CR with incomplete hematologic recovery (CRi) (including CR with incomplete platelet recovery [CRp]), partial remission (PR), and morphologic leukemia-free state (MLFS).

About Acute Myeloid Leukemia

Acute myeloid leukemia (AML) is the most common leukemia in the adult population, affecting 80% of adults with leukemia[1,2]AML is characterized by clonal expansion of immature blast cells in the peripheral blood and bone marrow resulting in ineffective erythropoiesis and bone marrow failure.[1,3,4] In the US, the incidence is over 20,000 cases per year, with the average age at diagnosis being 65 years.[1] The global incidence of AML increased by 87.3% from 1990 to 2017, with a higher incidence in males than females.[5] The overall prognosis for patients with AML is poor; the 5-year relative survival is 30.5% (2012-2015).[6] Untreated, death usually ensues within months of diagnosis secondary to infection or bleeding.[2] Even with current treatments, as many as 70% of patients aged ≥65 years will die within 1 year of diagnosis.[2]

About TIBSOVO® (ivosidenib tablets)

TIBSOVO is an oral targeted IDH1 inhibitor. The NMPA of China has approved the NDA of TIBSOVO for the treatment of adult patients with relapsed/refractory acute myeloid leukemia who have a susceptible IDH1 mutation.

TIBSOVO is approved in the U.S. for patients with a susceptible IDH1 mutation as detected by an FDA-

[1] Vakiti A, Mewawalla P, Wood SK. Acute Myeloid Leukemia. In: StatPearls. StatPearls Publishing; 2022. Accessed January 19, 2023. http://www.ncbi.nlm.nih.gov/books/NBK507875/.
[2] De Kouchkovsky I, Abdul-Hay M. Acute myeloid leukemia: a comprehensive review and 2016 update. Blood Cancer J. 2016;6(7):e441-e441. doi:10.1038/bcj.2016.50
[3] Döhner H, Weisdorf DJ, Bloomfield CD. Acute myeloid leukemia. Longo DL, ed. N Engl J Med. 2015;373(12):1136-1152. doi:10.1056/NEJMra1406184
[4] Licht JD, Sternberg DW. The molecular pathology of acute myeloid leukemia. Hematology. 2005;2005(1):137-142. doi:10.1182/asheducation-2005.1.137
[5] Yi M, Li A, Zhou L, Chu Q, Song Y, Wu K. The global burden and attributable risk factor analysis of acute myeloid leukemia in 195 countries and territories from 1990 to 2017: estimates based on the global burden of disease study 2017. J Hematol OncolJ Hematol Oncol. 2020;13(1):72. doi:10.1186/s13045-020-00908-z
[6] National Cancer Institute. Acute Myeloid Leukemia — Cancer Stat Facts. Accessed January 19, 2023. https://seer.cancer.gov/statfacts/html/amyl.html

approved test with:

- Newly Diagnosed Acute Myeloid Leukemia (AML): In combination with azacitidine or as monotherapy for the treatment of newly diagnosed AML in adults 75 years or older, or who have comorbidities that preclude the use of intensive induction chemotherapy

- Relapsed or Refractory AML: For the treatment of adult patients with relapsed or refractory AML

- Locally Advanced or Metastatic Cholangiocarcinoma: For the treatment of adult patients with locally advanced or metastatic cholangiocarcinoma who have been previously treated

TIBSOVO is also approved by the European Commission as a targeted therapy in two indications: in combination with azacitidine for the treatment of adult patients with newly diagnosed acute myeloid leukemia (AML) with an isocitrate dehydrogenase-1 (IDH1) R132 mutation who are not eligible to receive standard induction chemotherapy; as well as in monotherapy for the treatment of adult patients with locally advanced or metastatic cholangiocarcinoma with an IDH1 R132 mutation who were previously treated by at least one prior line of systemic therapy.

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 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 seven NDA approvals for four drugs. CStone's vision is to bring 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 realized 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.

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

Suzhou, the People's Republic of China, June 7, 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.