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**CStone Pharmaceuticals**

**基石藥業**

*(Incorporated in the Cayman Islands with limited liability)*

(**Stock Code: 2616**)

# VOLUNTARY ANNOUNCEMENT

# CSTONE ANNOUNCES RESULTS FROM TWO STUDIES OF ANTI-PD-1 MONOCLONAL ANTIBODY CS1003 AT THE 2020 ESMO ANNUAL MEETING

CStone Pharmaceuticals (the "**Company**" or "**CStone**") presented the results from two Phase 1 studies of CS1003 at the 2020 European Society for Medical Oncology ("**ESMO**") meeting held from September 19th to September 21st, 2020. These two studies are 1) the Phrase Ib CS1003-101 study, which is designed to evaluate the safety, pharmacokinetics ("**PK")**, immunogenicity and preliminary anti-tumor activity of CS1003 in patients with advanced cancer, and 2) the Phrase Ib CS1003-102 clinical study, which is designed to evaluate CS1003 in combination with lenvatinib as a first-line treatment for Chinese patients with unresectable hepatocellular carcinoma ("**uHCC**"). In both studies, CS1003, an anti-programmed cell death protein 1 ("**PD-1**") monoclonal antibody used either as monotherapy or in combination with standard of care ("**SoC**"), was safe and well tolerated, and demonstrated promising anti-tumor activity, supporting future clinical development of this molecule as an immune-oncology backbone agent.

CS1003 is a full-length, humanized immunoglobulin G4 ("**IgG4**") monoclonal antibody against PD-1 developed by CStone using a state-of-the-art hybridoma platform. CS1003 has shown good tolerability and efficacy profile in preclinical in vivo studies. Unlike other anti-PD-1 antibodies, CS1003 developed by CStone has comparable binding affinity against both human and mouse PD-1, which allows rapid evaluation of anti-tumor effect in syneneic mouse tumor models, including the combination with lenvatinib described herein.

**About CS1003-101 Study**

The Phase 1b part of the first-in-human study of CS1003 aimed to evaluate the efficacy, safety and pharmacokinetics of two dosing schedules of CS1003, at 200 mg Q3W and at 400 mg Q6W. The primary endpoint was objective response rate ("**ORR**") per RECIST V1.1 by investigators, and secondary endpoints included progression-free survival ("**PFS**"), disease control rate ("**DCR**"), duration of response ("**DOR**"), overall survival ("**OS**"), safety, tolerability, pharmacokinetics, and immunogenicity.

In patients with advanced solid tumors, the average plasma concentration at steady state of 400mg Q6W was comparable to that of 200 mg Q3W. Both dosing regimens are well tolerated and showed promising antitumor activity with an ORR of above 20%.

- As of July 15th, 2020, Cohort A (200 mg Q3W) enrolled 29 patients and Cohort B (400 mg Q6W) enrolled 31 patients;
- 15 patients from Cohort A and four patients from Cohort B were included in the steady-state PK analysis. The average plasma concentration of the two dosing regimens were comparable to each other;
- A total of 29 patients from Cohort A and 31 patients from Cohort B were included in the Efficacy Analysis Set. The ORRs in Cohort A and in Cohort B were 24.1% and 32.3%, respectively (confirmed ORRs in Cohort A and in Cohort B were 20.7% and 25.8% respectively); the median DoR in both Cohort A and Cohort B had not been reached;
- A total of 29 patients from Cohort A and 31 patients from Cohort B were included in the Safety Analysis Set. At least one treatment-emergent adverse event ("**TEAE**") was reported in 96.6% and 96.8% of the patients from Cohort A and B, respectively. Most treatment related TEAEs were of Grade 1-2; the incidence of Grade 3-4 treatment related TEAEs in Cohort A and Cohort B were 0% and 9.7%, respectively; no treatment-related deaths were observed; and the incidence of immune-related AEs were comparable between Cohort A (34.5%) and Cohort B ( 32.3%);
- CS 1003 dosing regimen at 400 mg Q6W offers a more flexible and convenient dosing option.

**About CS1003-102 Study**

CS1003-102 is a multi-center, open-label Phase I dose escalation, and indication expansion study conducted in China, Arm 5 of Phase Ib part of which aimed to evaluate the safety and efficacy of CS1003 in combination with lenvatinib as a first-line treatment for Chinese patients with uHCC. The primary endpoint was ORR per RECIST V1.1 by investigators, and secondary endpoints included PFS, DCR, DOR, OS, safety and tolerability, pharmacokinetics, and immunogenicity.

- As of June 22nd, 2020, a total of 20 patients were enrolled and received treatment. The majority of patients were male (90%), had a ECOG score of 1 (75%), had BCLC stage C HCC (90%), and had HBV infection (65%)
- CS1003 in combination with lenvatinib as a first-line treatment of Chinese patients with uHCC demonstrated promising efficacy and was well tolerated:
- A total of 20 patients were included for efficacy analysis set, of which 6 patients achieved a confirmed partial response ("**PR**") , and 2 other patients had their PR confirmed after the data cut-off. The ORR was 40% (8/20)
- Median follow-up duration was 6.2 months, and median PFS was 8.4 months. By the data cut-off date, median OS and DoR had not been reached

- A total of 20 patients were included in the safety analysis set. The most common treatment related TEAEs of any grade were elevated bilirubin, urine protein present and proteinuria. Five patients each had a Grade 3 treatment related TEAE, including hypertension, elevated conjugated bilirubin, diarrhea, diabetes, and hypophosphatemia. No patients had Grade 4/5 treatment related TEAE.

**Dr. Archie Tse, Chief Translational Medicine Officer of CStone, said**, "We are very pleased to see the excellent efficacy and safety demonstrated by CS1003 monotherapy alone or in combination with standard treatment so far. CS1003 is a monoclonal antibody with high-affinity to disrupt the interaction of PD-1 with its ligands. CS1003 has demonstrated good safety and anti-tumor activity in patients with advanced solid tumors. The 400mg Q6W dosing regimen offers a more flexible and convenient dosing option for patients. In addition, as a novel anti-PD-1, CS1003 in combination with lenvatinib has resulted in an ORR of 40%, indicating a potential clinical advantage for treating advanced uHCC. All of these preliminary results support further development of CS1003 as an immune-oncology backbone agent."

**About CS1003**

CS1003 is a humanized recombinant IgG4 monoclonal antibody targeting human PD-1 being developed for immunotherapy of various tumors. Compared to most of the monoclonal antibodies that bind human and monkey PD-1(either already approved or in clinical stage) , CS1003 demonstrates comparable high binding affinities across species against human, cynomolgus monkey and mouse PD-1, and is developed to disrupt the interaction of PD-1 with its ligands PD-L1 and PD-L2 . CS1003 is also unique in that it can simultaneously recognize human and mouse PD-1, which allows fast pre-clinical proof of concept for CS1003 in combination with novel targeted therapies using syngeneic mouse tumor models.

**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.

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, September 25, 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.*