CStone Pharmaceuticals

基石藥業

(Incorporated in the Cayman Islands with limited liability)

(**Stock Code: 2616**)

VOLUNTARY ANNOUNCEMENT

CSTONE RELEASES PRELIMINARY RESULTS FROM THE PHASE IA TRIAL OF CS1003 IN PATIENTS IN CHINA WITH ADVANCED TUMORS

Today, CStone Pharmaceuticals (the "**Company**" or "**CStone**") released the preliminary data from the Phase I bridging study of the Company's investigational anti-PD-1 monoclonal antibody CS1003 for the first time in an oral presentation at the 22nd Annual Meeting of the Chinese Society of Clinical Oncology ("**CSCO**").

CS1003-102 is a multi-center, open-label, dose-escalation and indication-expansion Phase I clinical trial being conducted in China. Initiated in November 2018, the trial is designed to evaluate the safety, pharmacokinetics, immunogenicity and preliminary anti-tumor efficacy of CS1003 in patients with advanced tumors.

Professor Lin Shen, Vice President of Beijing Cancer Hospital and the presenter of the results, commented: "Data from the dose escalation phase of the trial demonstrated CS1003's favorable safety and tolerability in Chinese patients with advanced tumors. Furthermore, preliminary yet noticeable anti-tumor activities were also observed in multiple tumor types."

Dr. Frank Ningjun Jiang, chairman, executive director and chief executive officer of CStone, commented: "CS1003 is one of CStone's three backbone immuno-oncology drug candidates. I am very pleased about the encouraging initial data from this Phase Ia trial, as it provides a solid foundation for the continued development of this asset. We will continue to vigorously advance the clinical development of CS1003 around the world. In addition to the on-going programs in China and Australia, we have received Investigational New Drug approval for CS1003 in the United States. With a robust pipeline and core strategy centering on combination

cancer immunotherapy, we will further utilise CS1003's unique advantages and its vast application potential in combination with multiple drugs."

Dr. Ngai Chiu Archie Tse, chief translational medicine officer of CStone, noted: "CS1003 is a high-affinity monoclonal antibody that potently blocks the binding of PD-1 to its ligands. It is worth noting that CS1003's ability to cross-react with both human PD-1 and mouse PD-1 will allow us to significantly accelerate the preclinical proof-of-concept of CS1003 in combination with new targeted drugs in syngeneic tumor models. Through clinical development, we will further explore the potential of CS1003 as cancer immunotherapy."

Overview of CS1003-102 study results

The CS1003-102 study data presented at this year's CSCO Annual Meeting was generated from 19 patients with advanced tumors, who were enrolled during the dose escalation phase of the study. As of June 15, 2019, 3 patients with gastric adenocarcinoma, 2 with esophageal squamous cell carcinoma, 2 with leiomyosarcoma and 12 with other advanced tumors were enrolled. 7 patients were administered with CS1003 once every three weeks, at a fixed dose of 60 mg; 12 patients were administered with CS1003 once every three weeks, at a fixed dose of 200 mg. The median treatment duration was 9.1 weeks (range, 3.0 to 29.3 weeks) and 9.0 weeks (range, 4.9 to 21.7 weeks) at 60 mg and 200 mg dose, respectively.

Preliminary safety data on CS1003

- No dose-limiting toxicity was observed at either 60 mg or 200 mg, and the maximum tolerated dose was not reached;

- Of the 18 patients (94.7%) who developed treatment-related adverse events ("**TRAEs**"), 3 reported Grade 3 or higher TRAEs, and the rest were all Grade 1 to 2 in severity. The common TRAEs included fatigue (26.3%), elevated serum bilirubin levels (15.8%), hypothyroidism (15.8%) and anemia (15.8%); and

- Nine patients reported at least one immune-related adverse event ("**irAE**"), and the most common irAEs included fatigue (15.8%), hypothyroidism (15.8%), hyperthyroidism (10.5%) and rash (10.5%).

The pharmacokinetic characteristics of CS1003

In the on-going Phase I trial in China, CS1003 demonstrated dose-proportional systemic exposure. Comparable pharmacokinetic characteristics were observed between patients in China and Australia.

The immunogenicity of CS1003

The preliminary analysis of anti-drug antibody ("**ADA**") data suggests CS1003 has relatively low immunogenicity. No treatment-induced and enhanced ADA responses (ADA-positive) were observed.

Preliminary efficacy data on CS1003

- Of the 16 efficacy-evaluable patients, 7 remained on the treatment, with a median treatment duration of 21.3 weeks (range, 5.6 to 29.3 weeks);

- At 60 mg, 1 patient with esophageal squamous cell carcinoma and 1 patient with uterine leiomyosarcoma had a confirmed partial response ("**PR**") per RECIST v1.1. At 200 mg, 1 patient with laryngeal squamous cell carcinoma was determined to be in PR awaiting confirmation; and

- One patient treated at 200 mg was evaluated as having disease progression per RECIST v1.1 during the first post-baseline tumor assessment and continued to receive CS1003 beyond progression. Noticeable tumor reduction compared to baseline was observed during the following tumor assessment, and the patient remained on treatment as of the data cut-off date.

About CS1003 and the PD-1/PD-L1 pathway

CS1003 is a humanized anti-PD-1 IgG4 monoclonal antibody developed by CStone using an internationally leading hybridoma platform. CS1003 has shown good tolerability and efficacy profile in preclinical in vivo studies. Unlike other anti-PD-1 antibodies, CS1003 recognizes both human and murine PD-1, providing a unique competitive advantage during efficacy testing in syngeneic mouse tumor models particularly for development of effective combination therapies.

PD-1, or programmed death-1, is an inhibitory checkpoint receptor expressed mainly on T cells. Under normal circumstances, it binds with its ligands, programmed death ligand-1 or ligand 2 (PD-L1/PD-L2), inhibiting T cell and cytokine activation and serving to dampen the immune response in order to prevent damage to healthy tissues. However, studies have shown that PD-L1 can be abundantly expressed on the surface of many solid tumors as well as hematological malignancies. Cancer cells can therefore make use of the PD-1/PD-L1 pathway to successfully avoid immune system recognition. Targeting of the PD-1/PD-L1 checkpoint by anti-tumor drugs can block the "tumor immune evasion mechanism" and restore anti-cancer immune ability in patients.

About CStone

CStone is a biopharmaceutical company focused on developing and commercializing innovative immuno-oncology and molecularly-targeted drugs to address unmet medical needs for cancer patients in China and worldwide. Since the Company's establishment in 2015, CStone has assembled a world-class management team that has a full spectrum of complementary skillsets from preclinical research to clinical development and commercialization. With combination therapies as a core strategy, the Company has built a rich oncology pipeline of 15 oncology drug candidates. Currently, five late-stage drug candidates are at or near 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 and differentiated 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 20, 2019

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.