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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 PRELIMINARY RESULTS FROM PHASE I TRIAL OF CS1002

DEMONSTRATING CHARACTERISTICS COMPARABLE TO IPILIMUMAB

CStone Pharmaceuticals (the “**Company**” or “**CStone**”) announced preliminary results from the Phase Ia trial of CS1002, the Company’s investigational anti-CTLA-4 antibody, in an oral presentation at the 22nd Annual Meeting of the Chinese Society of Clinical Oncology (“**CSCO**”). This presentation marks the first data release on CS1002’s clinical development at a scientific meeting.

CS1002-101 is an open-label, multi-dose, dose-escalation, and dose-expansion study conducted in Australia that aims to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics, and preliminary anti-tumor activity of CS1002 in patients with advanced solid tumors. The study has completed dose-escalation of CS1002 as a single agent.

The data were presented by Dr. Rasha Cosman, medical oncologist from the Oncology Department at St Vincent Hospital’s Kinghorn Cancer Center in Australia. “Data from this study demonstrate that CS1002 has a favorable tolerability profile. As of data cut-off date, dose-limiting toxicity was not observed up to 10 mg/kg of CS1002, and the maximum tolerated dose was not reached,” said Dr. Cosman. “Additionally, these initial results of the safety, preliminary efficacy, pharmacokinetics and pharmacodynamics of CS1002 are comparable to those of ipilimumab.”

Dr. Frank Ningjun Jiang, chairman, executive director and chief executive officer of CStone, commented: “Ipilimumab is currently the only approved CTLA-4 inhibitor globally, and the product has not been

launched in China. We are encouraged by the promising preliminary data from this Phase Ia study of CS1002. We are planning to initiate a dose-escalation study of CS1002 combined with CS1003 (an anti-PD-1 antibody) and a dose-expansion study of the combination therapy in selected tumor types. We hope these two of CStone's backbone immunotherapy drug candidates in combination will produce favorable clinical results, and soon benefit tumor patients in need."

Dr. Ngai Chiu Archie Tse, chief translational medicine officer of CStone, noted: "In terms of mechanism of action, anti-CTLA-4 monoclonal antibodies stimulate the proliferation of immune cells by blocking the down-regulating immune effect of CTLA-4, thereby inducing or strengthening the anti-tumor immune responses. This mechanism of action suggests the wide-ranging potential of this class of therapies in cancer treatments. CS1002 is a fully human, full-length monoclonal immunoglobulin G1 (IgG1) that shares the same amino acid sequence with ipilimumab. We expect that CS1002 can potentially become another outstanding CTLA-4 inhibitor after ipilimumab."

Overview of results from CS1002-101 study

As of data cut off on April 25, 2019, 13 patients with advanced solid tumors were enrolled in the dose-escalation phase of the CS1002-101 study, of which 4 had colorectal cancer, 2 had metastatic adenocarcinoma, and 7 had other solid tumors. Among those patients, 6 patients were administered CS1002 once every three weeks at 1mg/kg, 3 patients at 3mg/kg and 4 patients at 10mg/kg. At data cut off, 2 patients remained on treatment.

Safety data on CS1002

- No dose-limiting toxicity (DLT) was observed at 1mg/kg, 3mg/kg, and 10mg/kg, and the maximum tolerated dose (MTD) was not reached.
- 4 patients (30.8%) reported at least one 1 treatment-emergent adverse events ("TEAEs") that included diarrhea (15.4%), fatigue (15.4%), elevated alanine aminotransferase (ALT) level (7.7%) and elevated aspartate aminotransferase (AST) level (7.7%). 2 of those patients (15.4%) developed TEAEs that were Grade 3 or higher and the rest had TEAEs between Grade 1 to 2.
- 2 patients reported immune-related adverse events (irAEs) that included diarrhea (7.7%) and fatigue (7.7%).
- No serious TEAE was observed.
- There was no death related to the treatment.
- There was no discontinuation due to TEAEs.

Pharmacokinetics of CS1002

CS1002 has been shown in all three dose cohorts to have dose-proportional pharmacokinetic characteristics. The terminal half-life ranged from 12 to 15 days.

Pharmacodynamics of CS1002

Across all three dose cohorts, increase in absolute lymphocyte count (ALC) in peripheral blood were observed early during the initial stage of CS1002 treatment, indicating that the pharmacodynamics of CS1002 was comparable to that of the historical data of ipilimumab.

Preliminary efficacy data on CS1002

- Of the 9 patients with evaluable efficacy, no patient has achieved complete response (CR) or partial response (PR);
- 2 patients were assessed as stable disease (“SD”).
- One cholangiocarcinoma patient is still on treatment with SD for 11 months.

About CS1002 and the CTLA-4 pathway

CS1002 is an investigational anti-CTLA-4 monoclonal antibody being developed by CStone.

Cytotoxic T lymphocyte associated antigen 4 (CTLA-4), also known as CD152, is a transmembrane protein encoded by the CTLA-4 gene that can downregulate the activity of T cells when binding with its ligand, B7.1/B7.2, a pathway also used by tumor cells to avoid T lymphocyte attack. Consequently, blockade of the CTLA-4 pathway can stimulate T cell activation and proliferation to induce or enhance anti-tumor immune responses. CTLA-4 provides a new immunotherapeutic approach to a number of diseases, including tumors.

Presently, ipilimumab of Bristol-Myers Squibb Company's (NYSE: BMY) is the only CTLA-4 inhibitor to gain a market approval worldwide, although ipilimumab has not yet been approved in China. Preclinical tests have shown that CS1002 has a relatively strong affinity to CTLA-4 and is expected to match ipilimumab in terms of efficacy.

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 22, 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.