CStone Pharmaceuticals

基石藥業

(Incorporated in the Cayman Islands with limited liability)

(**Stock Code: 2616**)

VOLUNTARY ANNOUNCEMENT
CSTONE PRESENTS PRELIMINARY RESULTS FROM A PHASE IB STUDY OF THE ANTI-CTLA-4 MONOCLONAL ANTIBODY (MAB) CS1002 IN COMBINATION WITH THE ANTI-PD-1 MAB CS1003 IN PATIENTS WITH ADVANCED SOLID TUMORS AT ESMO 2021

CStone Pharmaceuticals (the "**Company**" or "**CStone**") is pleased to announce the preliminary results from the phase Ib study of anti-CTLA-4 mAb CS1002 in combination with anti-PD-1 mAb CS1003 in patients with advanced solid tumors (Study CS1002-101; NCT03523819) at the 2021 European Society for Medical Oncology ("**ESMO**") Congress (Poster ID: 981P). Dual checkpoint blockade with CS1002 and CS1003 showed well tolerated safety profile and encouraging clinical activities in both anti-PD-(L)1 naïve high microsatellite instability ("**MSI-H**")/mismatch repair deficient ("**dMMR**") solid tumors and anti-PD-(L)1-refractory melanoma.

CS1002-101 is a multi-center, open-label, dose escalation, and dose expansion phase Ia/Ib study to evaluate the safety, tolerability, pharmacokinetics, and preliminary antitumor activity of CS1002 as monotherapy (phase Ia) and in combination with CS1003 (phase Ib).

In the dose escalation of the phase Ib study, patients with advanced solid tumors received CS1002 at 4 dose regimens in combination with CS1003. No dose limiting toxicities ("**DLT**") were observed and the maximum tolerated dose ("**MTD**") was not reached.

In the dose expansion of the phase Ib study, patients with advanced anti-PD-(L)1-naïve MSI-H/dMMR solid tumors, or anti-PD-(L)1-refractory melanoma were randomized to receive CS1002 at either a conventional dosing schedule (1 mg/kg Q3W, up to 4 doses, Arm B) or a lower intensity schedule (0.3 mg/kg Q6W, Arm A), both in combination with CS1003 (200 mg, flat dose, Q3W).

As of March 1, 2021, of the 16 evaluable patients with MSI-H/dMMR solid tumors in Arms A and B, the overall response rate ("**ORR**") was 50%. Four of nine (44.4%) patients in Arm A achieved a partial response ("**PR**"), whereas four of seven (57.1%) patients in Arm B achieved a response (1 complete

response ("**CR**") and 3 PRs). Among the 8 evaluable patients with melanoma in Arms A and B, the overall ORR was 50%, with 2 of 4 patients in each arm achieving a PR.

Of the 33 patients included in the safety analysis, 29 (87.9%) patients reported at least one adverse event ("**AE**"). Twenty-one (63.6%) patients reported treatment-related adverse events ("**TRAEs**"), of whom 5 (15.2%) reported Grade≥3 TRAEs (2 pts in Arm A, 3 pts in Arm B). The most common TRAEs were diarrhea, fatigue, and rash.

In summary, combination of the anti-CTLA-4 mAb CS1002 with the anti-PD-1 mAb CS1003 demonstrated encouraging and durable anti-tumor activities in both tumor types irrespective of the dosing regimen of CS1002. The lower dosing regimen of CS1002 (0.3 mg/kg, Q6W) appears to be associated with a better safety profile.

Dr. Archie Tse, Chief Scientific Officer of CStone, said, "Cytotoxic T-lymphocyte antigen-4 ("**CTLA-4**") is a key negative regulator of T-cell responses following T-cell stimulation. Currently there are multiple on-going clinical trials targeting CLTA-4. So far, only one anti-CTLA-4 mAb has been approved globally. We are encouraged by the clinical activities and safety of the combination of CS1002 and CS1003 in patients with advanced solid tumors, in particular, advanced anti-PD-(L)1-naïve MSI-H/dMMR solid tumors and anti-PD-(L)1-refractory melanoma; the data support further clinical development of this combination."

About CS1002 (anti-CTLA-4 antibody)

CS1002 is an investigational anti-CTLA-4 monoclonal antibody being developed by CStone. CTLA-4, also known as CD152, is a transmembrane protein encoded by the CTLA-4 gene that can down-regulate 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 immuno-therapeutic approach to a number of human cancers.

About CS1003 (Anti-PD-1 antibody)

CS1003 is a humanized recombinant IgG4 monoclonal antibody targeting human programmed cell death protein 1 ("**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.

About CStone

CStone is a biopharmaceutical company focused on researching, developing and commercializing innovative immuno-oncology and precision medicines to address the unmet medical needs of cancer patients in Mainland 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 three drug approvals in Greater China, including two in Mainland China and one in Taiwan, China. 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.

By Order of the Board
CStone Pharmaceuticals
Dr. Frank Ningjun Jiang
Chairman

Suzhou, the People's Republic of China, September 20, 2021

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. 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.