**CStone Pharmaceuticals**

**基石藥業**

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

(**Stock Code: 2616**)

## VOLUNTARY ANNOUNCEMENT

# CSTONE ANNOUNCES PROMISING TRIAL DATA ON ITS ANTI-PD-L1 ANTIBODY IN RR-ENKTL PATIENTS WITH A COMPLETE RESPONSE RATE OF 31.8%

CStone Pharmaceuticals (the "**Company**" or "**CStone**") announced that an abstract on the CS1001-201 clinical trial (abstract number: 2833) was accepted by the 2019 American Society of Hematology ("**ASH**") Annual Meeting and has been published online yesterday on the meeting's official website. Additionally, the Company will release further updated data from the CS1001-201 trial in a poster presentation at the conference.

CS1001-201 is a single-arm, multicenter Phase II clinical study designed to evaluate CS1001 monotherapy in relapsed or refractory extranodal natural killer ("**NK**")/T-cell lymphoma ("**rr-ENKTL**"). The primary endpoint of the trial is objective response rate ("**ORR**") assessed by an independent radiological review committee ("**IRRC**"); the secondary endpoints include investigator-assessed ORR, IRRC-assessed complete and partial response rates, time to response, duration of response, progression-free survival, overall survival and safety.

Extranodal NK/T-cell lymphoma ("**ENKTL**") is a subtype of mature T cell and NK cell lymphoma, with a higher incidence rate in Asia than in Europe or North America. ENKTL is an aggressive malignancy characterized by its rapid progression and poor prognosis. Patients with rr-ENKTL lack effective standard treatment after failing an L-asparaginase-based combination chemotherapy regimen. Studies to date have shown that Epstein-Barr virus ("**EBV**") infection is linked to the pathogenic mechanisms of ENKTL, as

EBV infection induces immune tolerance by upgrading PD-L1 expression in tumor cells, thus promoting tumor growth.

Dr. Frank Ningjun Jiang, chairman, executive director and chief executive officer of CStone, commented: "In China, ENKTL accounts for approximately 6% of all lymphoma incidences, and those relapsed or refractory patients in particular have urgent unmet clinical needs. CS1001-201 is the first clinical trial worldwide investigating an anti-PD-L1 antibody in ENKTL patients, and promising initial antitumor activity has already been observed in the trial. I am glad that the preliminary results from this trial will be announced for the first time at the 2019 ASH Annual Meeting. CStone remains committed to addressing treatment gaps in China and around the world. We hope this trial will continue its rapid progress and soon produce more breakthroughs in the treatment of ENKTL."

CStone's chief medical officer, Dr. Jason Yang, noted: "The close association between ENKTL and the increased PD-L1 expression resulted by EBV infection suggests that blocking the PD-1/PD-L1 pathway could be an effective treatment for ENKTL patients. In the abstract published by ASH, CS1001 demonstrated an ORR of 40.9%, a complete and durable response rate of 31.8% and a benign safety profile. These results represent a major breakthrough in the treatment of rr-ENKTL and support the further development of CS1001 as a treatment for rr-ENKTL. We look forward to sharing encouraging additional data updates in the poster presentation at the 2019 ASH Annual Meeting."

**Results in the abstract on CS1001-201 published by ASH**

As of June 17, 2019, 29 patients were enrolled into the study. Among them, 22 (75.9%) patients had Stage IV of the disease at screening, 8 patients received 2 lines of prior treatments, and 6 patients received 3 or more lines of prior treatments. All of the patients received 1,200 mg CS1001 intravenously every 3 weeks for up to 2 years, until disease progression, intolerance, etc. The median duration of follow-up was 5.55 (ranging from 0.69 to 12.19) months.

**Demographics and baseline characteristics**

- 15 (51.7%) of the 29 enrolled patients remained on treatment, and 14 (48.3%) had discontinued from the study treatment.
- Reasons for discontinuations included disease progression (12 patients) and adverse events ("**AEs**", 2 patients).
- No discontinuations or deaths due to treatment-related AEs ("**TRAEs**").

**Preliminary efficacy data**

CS1001 demonstrated promising antitumor activity in rr-ENKTL patients.

- Among the 22 efficacy-evaluable patients, the investigator-assessed ORR was 40.9%. 7 patients (31.8%) achieved complete and durable response.
- 2 patients (9.1%) achieved partial response, and 1 additional patient achieved partial response after pseudo-progression.

- The duration of response ("**DoR**") ranged from 0.03+ to 8.61+ months, and the median DoR was not reached.

- The IRRC assessments have not been started at the time of data cut-off.

**Safety data**

CS1001 was well tolerated in patients with rr-ENKTL.

- The median duration of treatment was 11.7 weeks (ranging from 2.9 to 53.0 weeks).

- 25 patients (86.2%) reported treatment-emergent AEs ("**TEAEs**").

- 21 patients (72.4%) reported TRAEs, of which 3 (10.3%) had Grade ⩾3 TRAEs.

- Grade 5 AEs were reported in 2 patients (6.9%), and none was assessed as related to CS1001.

- Serious AEs were observed in 5 patients (17.2%), and 1 of them (sinus node dysfunction) was assessed as related to CS1001 by the investigator.

- Immune-related AEs ("**irAEs**") were reported in 5 patients (17.2%). Except 1 Grade 3 rash, all irAEs were Grade 1 in severity.

- TEAEs that led to permanent treatment discontinuation occurred in 2 patients (6.9%) but no permanent discontinuation or death due to AEs were assessed as related to CS1001.

After data cut-off date, 3 additional patients reached the response assessment time point, of which 2 patients achieved complete response, elevating the ORR to 44.0% (11/25) and complete response rate to 36.0% (9/25). More details of the updated data will be reported at the 2019 ASH Annual Meeting.

**About CS1001**

CS1001 is an investigational monoclonal antibody directed against PD-L1 being developed by CStone. Authorized by a company based in the United States, Ligand Pharmaceuticals Inc. (NASDAQ: LGND), CS1001 is developed by the OMT transgenic animal platform, which can generate fully human antibodies in one step. As a fully human, full-length anti-PD-L1 monoclonal antibody, CS1001 mirrors natural G-type immune globulin 4 (IgG4) human antibody, which can reduce the risk of immunogenicity and potential toxicities in patients, potentially representing a unique advantage over similar drugs.

CS1001 has completed a Phase I dose-escalation study in China, in which CS1001 showed good tolerability and produced sustained clinical benefits during Phase Ia and Ib stages of the study in multiple indications.

CS1001 is being investigated in a number of ongoing clinical trials, including one Phase I bridging study in the United States. In China, its clinical program includes one multi-arm Phase Ib study, two pivotal Phase II studies and three Phase III studies for several tumor types.

**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 inception 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, November 7, 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.*