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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 PROMISING ANTITUMOR ACTIVITY AND SAFETY ON ITS ANTI-PD-L1 ANTIBODY IN RR-ENKTL PATIENTS WITH A COMPLETE RESPONSE RATE OF 33.3%**

CStone Pharmaceuticals (the “**Company**” or “**CStone**”) updated results from the CS1001-201 trial in a poster presentation at the 2019 American Society of Hematology (“**ASH**”) Annual Meeting. CS1001-201 trial 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**”).

Extranodal NK/T-cell lymphoma (“**ENKTL**”) is a subtype of mature T cell and NK cell lymphoma. It has a higher incidence rate in Asia than in Europe or North America. ENKTL is characterized by its rapid progression and poor prognosis. Currently, patients with rr-ENKTL lack effective standard treatment after failing an L-asparaginase-based combination chemotherapy regimen and targeted monotherapy only produces a complete response (“**CR**”) rate of below 10%.

Dr. Frank Ningjun Jiang, chairman, executive director and chief executive officer of CStone, commented: “ENKTL accounts for approximately 6% of all lymphoma incidences in China, and there are vast unmet medical needs in this patient population that has failed the first-line treatment. Our latest data demonstrated that CS1001 is the first anti-PD-L1 antibody shown to be well-tolerated with preliminary antitumor efficacy and survival benefit in rr-ENKTL patients. We will continue to advance this development program and hope that CS1001 will soon become a new treatment option for rr-ENKTL patients.”

CStone's chief medical officer, Dr. Jason Yang, noted: "The CS1001-201 trial is the first clinical study of an anti-PD-L1 antibody in ENKTL worldwide. CR is a critical outcome measure for the treatment of ENKTL. Studies have shown that patients who achieve CR can significantly prolong survival and improve prognosis compared with patients who achieved partial response ("PR") before autotransplantation. These latest results of CS1001 demonstrated a CR rate of 33.3% with durable response, an objective response rate ("ORR") of 43.3%, and a 1-year overall survival rate of 72.4%. These results represent a major breakthrough compared to current treatment options and support CS1001 as a potential conditioning regimen for hematopoietic stem cell transplantations."

### **Overview of the CS1001-201 trial**

CS1001-201 is a single-arm, multicenter Phase II clinical study designed to evaluate CS1001 monotherapy in rr-ENKTL.

- The primary endpoint of the trial is ORR assessed by an independent radiological review committee ("IRRC");
- Secondary endpoints include investigator-assessed ORR, IRRC-assessed CR and PR rates, time to response, duration of response, progression-free survival, overall survival and safety.

### **Results reported in the poster at the 2019 ASH Annual Meeting**

As of October 8, 2019, 32 patients were enrolled in the study. Among them, 24 patients (75.0%) had Stage IV ENKTL at screening, 9 patients (28.1%) received 2 lines of prior treatments, and 7 patients (21.9%) received 3 or more lines of prior treatments. All 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 6.54 months (ranging from 0.72 to 15.64).

- 13 patients (40.6%) of the 32 enrolled patients remained on treatment, and 19 patients (59.4%) had discontinued from the study treatment.
- Reasons for discontinuations included radiographic disease progression (12 patients), adverse events ("AEs", 4 patients), and non-radiographic symptomatic progression (3 patients).
- No deaths due to treatment-related AEs ("TRAEs").

### **Preliminary efficacy data**

CS1001 demonstrated promising antitumor activity and a favorable CR rate with durable response and survival benefit in rr-ENKTL patients.

- Among the 30 efficacy-evaluable patients, the investigator-assessed ORR was 43.3%.
- 10 patients (33.3%) achieved CR and were still in remission.
- 3 patients (10.0%) achieved PR, and 1 additional patient achieved PR after pseudo-progression. The median duration of response ("DoR") was not reached, and the maximum DoR was 10.9+ months.

- The 1-year overall survival was 72.4% (95% CI: 52.0% to 85.2%).
- The IRRC assessments were not available at the time of data cut-off.

### **Safety data**

CS1001 was well tolerated in patients with rr-ENKTL.

- The median duration of treatment was 12.6 weeks (ranging from 3.0 to 69.1 weeks).
- 30 patients (93.8%) reported treatment-emergent AEs (“TEAEs”).
- 24 patients (75.0%) reported TRAEs, of which 3 (9.4%) had Grade  $\geq 3$  TRAEs.
- Grade 5 AEs were reported in 3 patients (9.4%), and none was assessed as related to CS1001.
- 7 patients (21.9%) reported serious AEs (“SAEs”). 1 case of Grade 4 sinus node dysfunction and 1 case of Grade 1 myositis were assessed as related to CS1001 by the investigator. Both patients later recovered from the SAEs.
- Immune-related AEs (“irAEs”) were reported in 5 patients (15.6%). Except for 1 Grade 3 rash, all irAEs were Grade 1 in severity.
- TEAEs that led to permanent treatment discontinuation occurred in 4 patients (12.5%).
- No deaths due to AEs were assessed as related to CS1001.

### **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](http://www.cstonepharma.com).

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

Suzhou, People's Republic of China, December 9, 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.*