CStone Pharmaceuticals

基石藥業

(Incorporated in the Cayman Islands with limited liability)

(**Stock Code: 2616**)

VOLUNTARY ANNOUNCEMENT
CSTONE PRESENTS LATEST CLINICAL DATA ON CS5001 FOR ADVANCED LYMPHOMA AT THE 66TH ASH ANNUAL MEETING

CStone Pharmaceuticals (the "**Company**" or "**CStone**") is pleased to announce the presentation of the latest clinical data for CS5001, an anti-ROR1 ADC and one of the leading assets in CStone pipeline 2.0, at the 66th American Society of Hematology (ASH) Annual Meeting. These data highlight the compound's potential as a treatment for lymphoma.

Key Highlight

- CS5001 is so far the first anti-ROR1 ADC known to show clinical anti-tumor activity in both solid tumors and lymphomas. The data presented at ASH Annual Meeting highlighted the latest safety and efficacy of CS5001 as a monotherapy for patients with advanced lymphomas.
- CS5001 is well tolerated in heavily pre-treated patients with advanced B-cell lymphoma. So far, no dose-limiting toxicity (DLT) has been reported up to dose level 10 (DL10).
- Starting from the effective dose, anti-tumor activity with high objective response rate (ORR) was observed regardless of ROR1 expression levels, in advanced Hodgkin lymphomas (HLs) (ORR=60.0%) and non-Hodgkin lymphomas (NHLs) (ORR=56.3%). At the preliminary recommended Phase II dose (RP2D) of DL8 (125 μg/kg), a notably higher ORR of 76.9% was observed in advanced B-cell lymphoma, including 3 evaluable HL cases with complete or partial response, and an ORR of 70% in NHL.
- The global multicenter Phase I trials of CS5001 are currently in progress in the USA, Australia, and China. Dose escalation has been completed with ongoing backfilling of patients for selective DLs. A Phase Ib dose-expansion study across multiple tumor types with registration potential is expected to be initiated soon.

Receptor tyrosine kinase-like orphan receptor 1 (ROR1) is an embryonic tyrosine kinase-like molecule implicated in multiple pathways promoting oncogenic signaling. ROR1 is overexpressed at high frequency in hematological malignancies and in a broad spectrum of solid tumors while lower or absent in normal tissues, which makes ROR1 an attractive anti-cancer therapy target. CS5001 is so far the first anti-ROR1

ADC known to show clinical anti-tumor activity in both solid tumors and lymphomas.

Dr. Jason Yang, CEO, President of R&D, and Executive Director at CStone, commented, "We are very encouraged that CS5001 continues to demonstrate potent anti-tumor activity and manageable safety and tolerability in the ongoing clinical study. The data presented at ASH Annual Meeting further validate CS5001's potential, particularly as a monotherapy for patients with advanced lymphomas, most of whom had failed at least 3 prior lines of therapy. We observe encouraging anti-tumor activity in both HLs and NHLs, especially the ORR of 76.9% among the 13 evaluable patients with advanced B-cell lymphoma at DL8 (125 μg/kg). As we move forward with our Phase Ib study, we will further evaluate and optimize the dose. Given CS5001's initial efficacy in both aggressive and indolent lymphomas, we are confident in its broad clinical potential and significant market competitiveness. We remain committed to accelerate the clinical development of CS5001 in bringing this novel therapy to lymphoma patients as soon as possible."

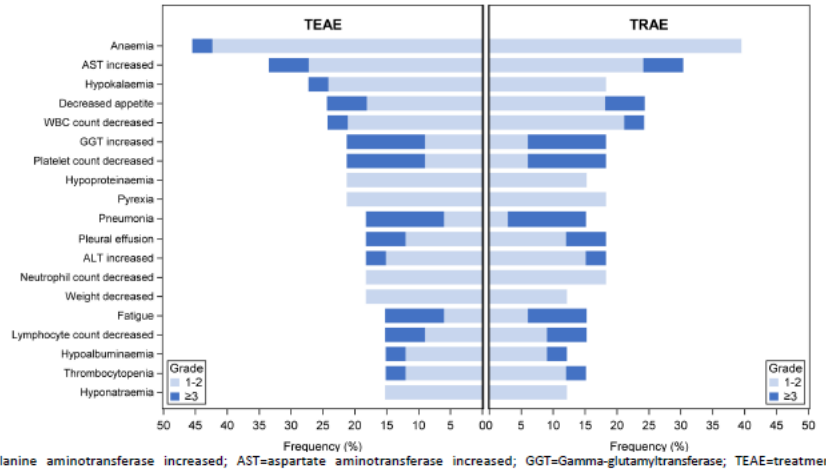
- **Patient baseline characteristics**

A total of 33 patients with advanced B-cell lymphoma were enrolled, including 17 diffuse large B-cell lymphoma (DLBCL), 11 HLs, 2 follicular lymphoma (FL), 1 mantle cell lymphoma (MCL), 1 marginal zone lymphoma (MZL), and 1 high-grade B-cell lymphoma (HGBCL). Among them, 84.8% were Asian, and the rest were non-Asian. 81.8% of the patients had received at least 3 prior lines of systemic anti-tumor therapy. In the DL8 cohort, patients who had previously received CART and hematopoietic stem cell transplantation therapy each accounted for over 20%.

- **Safety and tolerability**

Dose escalation has been completed and no DLT has been reported up to DL10 so far.

Figure 1： TEAEs and TRAEs* (Safety Analysis Set)



ALT=alanine aminotransferase increased; AST=aspartate aminotransferase increased; GGT=Gamma-glutamyltransferase; TEAE=treatment-emergent adverse event; TRAE=treatment-related adverse event; WBC=white blood cell.

* TEAEs with incidence rate ≥15% and the corresponding TRAEs.

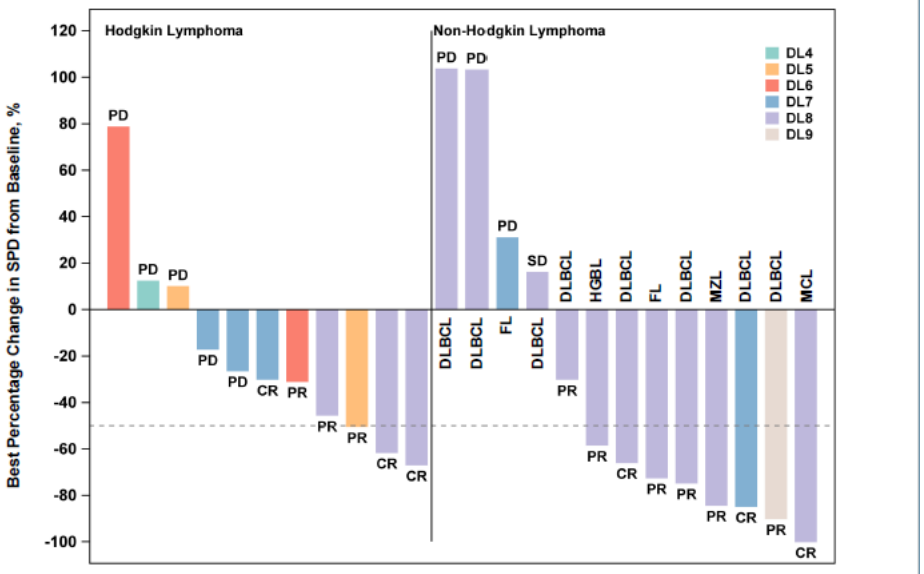
AEs were graded according to National Cancer Institute Common Terminology Criteria for AE (NCI-CTCAE) v5.0.

- **Efficacy data**

CS5001 demonstrated encouraging anti-tumor activity in B-cell lymphomas, with an ORR of 48.4% across all dose levels; a notably higher ORR of 76.9% was observed at DL8 (125 μg/kg) among 13 evaluable patients.

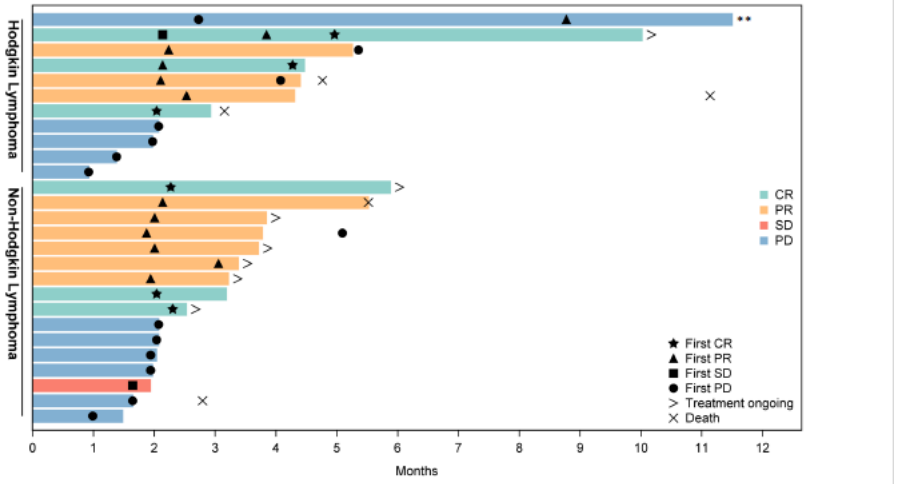
- Hodgkin Lymphoma (HL): objective responses were observed from effective dose of DL5 (50 μg/kg) and above, including 3 complete responses (CRs) and 3 partial responses (PRs) among 10 evaluable patients at DLs 5-9 (ORR: 60.0%). 2 CRs and 1 PR were observed at DL8 (125 μg/kg) among 3 evaluable patients.
- Non-Hodgkin Lymphoma (NHL): objective responses were observed from effective dose of DL7 (100 μg/kg) and above, including 3 CRs (2 DLBCL and 1 MCL) and 6 PRs (3 DLBCL, 1 MZL, 1 HGBC and 1 FL) among 16 evaluable patients at DLs 7-9 (ORR: 56.3%). A notably higher ORR of 70.0% was observed at DL8 (125 μg/kg) among 10 evaluable patients.

Figure 2. Best Percent Change from Baseline in Tumor Size (HL: n=11; NHL: n=13*)



CR=complete response; DLBCL= diffuse large B-cell lymphoma; FL=follicular lymphoma; HGBL=high-grade B-cell lymphoma; MCL=mantle cell lymphoma; MZL=marginal zone lymphoma; PD=progressive disease; PR=partial response; SD=stable disease, SPD=sum of the product of the diameters.
Include patients with target lesion at baseline and have post-baseline tumor assessments.
Overall tumor response is assessed based on CT/MRI, FDG-PET and pathology per Lugano 2014 by investigators.
* For patients with non-Hodgkin lymphoma, the waterfall plot only shows the patients in the group with doses ≥ the initial effective dose (DL7 100 μg/kg).

Figure 3. Time to Response and Response Duration (Efficacy Analysis Set) (HL: n=11; NHL: n=16*)



* For patients with non-Hodgkin lymphoma, the swimmer plot only shows the patients in the group with doses ≥ the initial effective dose (DL7 100 μg/kg).
** Mixed response(coexistence of responding and non-responding lesions) was observed for this patient in the first tumor assessment (First PD). The patient continued to received CS5001 after PD as a potential clinical benefit was derived. This patient had two intra-subject dose escalation with DL6 as the highest dose.

The global multicenter Phase I trial of CS5001 are currently in progress in the United States, Australia, and China. Dose escalation has been completed. Backfilling at DL8 (125 μg/kg) or DL9 (156 μg/kg) is still ongoing. A Phase Ib dose-expansion study with potential for registration across multiple tumor types is expected to be initiated soon.

Conference Call and Webcast

CStone will host a conference call and webcast to discuss this announcement on December 9, 2024, at 10:00 AM Beijing Time.

The conference call can be accessed via this link: https://s.comein.cn/sttbgkam

About CS5001

CS5001 is a clinical-stage antibody-drug conjugate ("ADC") targeting ROR1 (receptor tyrosine kinase-like orphan receptor 1). CS5001 has been uniquely designed with proprietary tumor-cleavable linker and pyrrolobenzodiazepine ("PBD") prodrug. Only after reaching the tumor, the linker and prodrug are cleaved to release the PBD toxin, resulting in lethal DNA cross-links in cancer cells. The use of the linker plus PBD prodrug effectively helps address toxicity associated with traditional PBD payloads, leading to a better safety profile. CS5001 has demonstrated complete tumor suppression in several preclinical cancer models and demonstrated favorable serum half-life and pharmacokinetic characteristics. CS5001 is a promising candidate drug with precision treatment potential in both hematologic tumors and malignant solid tumors. Additionally, CS5001 utilizes site-specific conjugation for a precise drug antibody ratio of which enables homogeneous production and large-scale manufacturing.

In October 2020, CStone entered into a licensing agreement with LigaChem Biosciences, Inc. (LCB) for the development and commercialization of CS5001. CS5001 was initially generated by collaboration of LCB and ABL Bio, both South Korea-based leading biotech companies. Pursuant to the agreement, CStone obtains the exclusive global right to develop and commercialize CS5001 outside the Republic of Korea.

Preliminary data from the first-in-human study presented at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting demonstrated that CS5001 is well-tolerated and exhibits encouraging anti-tumor activity across various dose levels in patients with heavily pre-treated advanced solid tumors and lymphomas.

About CStone

CStone (HKEX: 2616), established in late 2015, is an innovation-driven biopharmaceutical company focused on the research and development of anti-cancer therapies. Dedicated to addressing patients' unmet medical needs in China and globally, the Company has made significant strides since its inception. To date, the Company has successfully launched 4 innovative drugs and secured approvals for 16 new drug applications (NDAs) covering 9 indications. The Company's pipeline is balanced by 17 promising candidates, featuring potentially first-in-class or best-in-class antibody-drug conjugates (ADCs), multispecific antibodies, immunotherapies and precision medicines. CStone also prides itself on a management team with comprehensive experiences and capabilities that span the entire drug development spectrum, from preclinical and translational research to clinical development, drug manufacturing, business development, and commercialization.

For more information about CStone, please visit: www.cstonepharma.com.

Cautionary Statement required by Rule 18A.05 of the Listing Rules: THE COMPANY CANNOT GUARANTEE THAT WE MAY BE ABLE TO ULTIMATELY DEVELOP AND MARKET CS5001 SUCCESSFULLY. Shareholders of the Company and potential investors are advised to exercise due care when dealing in the shares of the Company.

Forward Looking Statement

There is no assurance that any forward-looking statements regarding the business development of the Group in this announcement or any of the matters set out herein are attainable, will actually occur or will be realized or are complete or accurate. The financial and other data relating to the Group as disclosed in this announcement has also not been audited or reviewed by its auditors. Shareholders and/or potential investors of the Company are advised to exercise caution when dealing in the securities of the Company and not to place any excessive reliance on the information disclosed herein. Any shareholder or potential investor who is in doubt is advised to seek advice from professional advisors.

By Order of the Board
CStone Pharmaceuticals
Dr. Wei Li
Chairman

Suzhou, the People's Republic of China, December 9, 2024

As at the date of this announcement, the board of directors of the Company comprises Dr. Wei Li as Chairman and non-executive director, Dr. Jianxin Yang as executive director, Mr. Kenneth Walton Hitchner III, 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.