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**CStone Pharmaceuticals**
**基石藥業**
*(Incorporated in the Cayman Islands with limited liability)*
**(Stock Code: 2616)**

# VOLUNTARY ANNOUNCEMENT
# ESMO 2025: CSTONE DISCLOSES PHASE I DATA FOR CS2009 (PD-1/VEGF/CTLA-4 TRISPECIFIC ANTIBODY)

This announcement is made by CStone Pharmaceuticals (the "**Company**," together with its subsidiaries, collectively referred to as the "**Group**" or "**CStone**") on a voluntary basis for the purpose of keeping the shareholders of the Company and potential investors abreast of the latest business development of the Group.

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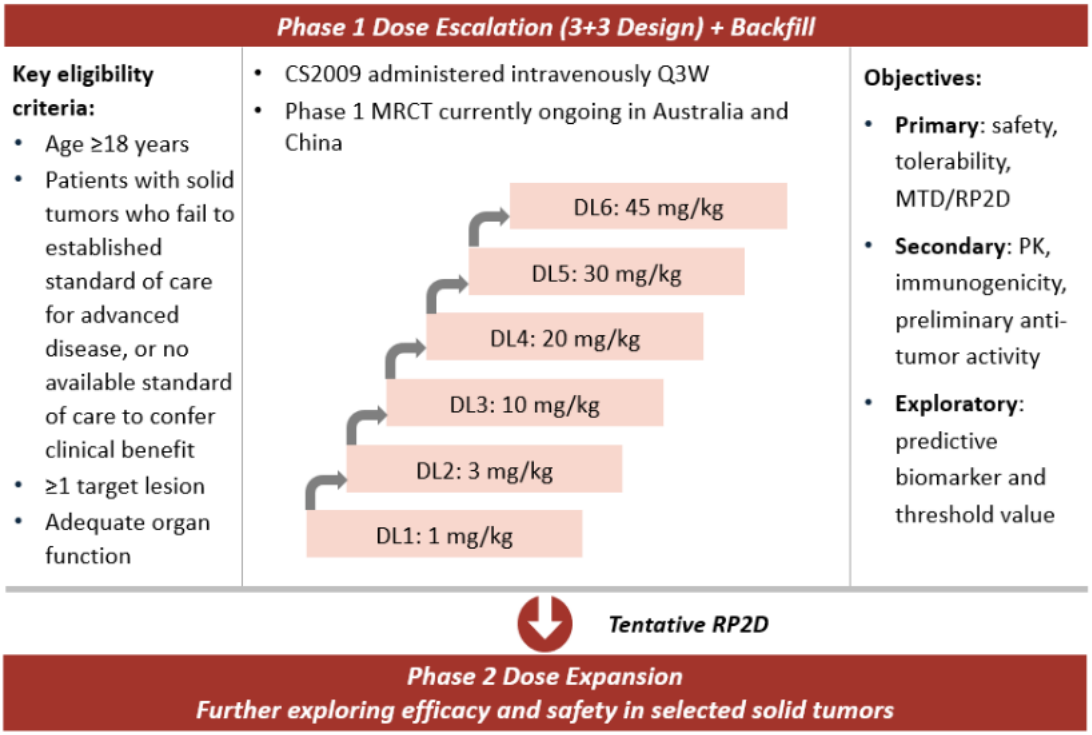
CStone today announced the first disclosure of preliminary Phase I data for CS2009 (a PD-1/VEGF/CTLA-4 trispecific antibody) and the Phase Ib study design for CS5001 (a ROR1-targeted Antibody-Drug Conjugate [ADC]) at the 2025 European Society for Medical Oncology (ESMO) Annual Congress.

**Key Highlights of CS2009 Poster Presentation:**

This also represents the first known clinical data publication of a PD-1/VEGF/CTLA-4 trispecific antibody to date.

CS2009-101 is a multi-regional Phase I study currently ongoing in Australia and China. The study evaluates the safety, tolerability, pharmacokinetics (PK)/ pharmacodynamics (PD), and antitumor activity of CS2009 in patients with advanced solid tumors.




DL=dose level; MRCT=multi-regional clinical trial; MTD=maximum tolerated dose; PK=pharmacokinetics; Q3W=every 3 weeks; RP2D=recommended phase 2 dose.

**Patients baseline characteristics:**

1. As of the data cutoff date, 72 patients with advanced solid tumors treated across 6 dose levels (DL1-6, 1-45 mg/kg); 72.2% remain on treatment.

2. Heavily pretreated population: over 51% received prior immuno-oncology (IO) therapies. Median follow-up: only 1.9 months (range 0.1-6.7 months) at data cutoff.

**Table 1. Baseline Characteristics (Safety Analysis Set)**

| Characteristics | Total (N=72) | Characteristics | Total (N=72) |
|---|---|---|---|
| **Age, years** | | **Prior IO therapy, n (%)** | 37 (51.4) |
| Median (range) | 60.5 (19-80) | **Prior anti-angiogenic therapy, n (%)** | 30 (41.7) |
| **Sex, n (%)** | | **Tumor type, n (%)** | |
| Female | 36 (50.0) | Non-small cell lung cancer (NSCLC) | 33 (45.8) |
| Male | 36 (50.0) | Ovarian carcinoma (OC) | 10 (13.9) |
| **Race, n (%)** | | Soft tissue sarcoma (STS) | 9 (12.5) |
| Black or African American | 1 (1.4) | Renal cell carcinoma (RCC) | 4 (5.6) |
| Asian | 31 (43.1) | Triple negative breast carcinoma (TNBC) | 4 (5.6) |
| White | 39 (54.2) | Adrenocortical carcinoma (ACC) | 2 (2.8) |
| Other | 1 (1.4) | Cervical carcinoma (CC) | 2 (2.8) |
| **ECOG PS, n (%)** | | Gastric carcinoma (GC) | 2 (2.8) |
| 0 | 32 (44.4) | Prostate carcinoma (PCa) | 2 (2.8) |
| 1 | 40 (55.6) | Biliary tract carcinoma (BTC) | 1 (1.4) |
| **Prior therapy, n (%)** | | Bladder mucinous adenocarcinoma | 1 (1.4) |
| 1 | 24 (33.3) | Hepatocellular carcinoma (HCC) | 1 (1.4) |
| 2 | 17 (23.6) | Head and neck squamous cell carcinoma (HNSCC) | 1 (1.4) |
| ≥3 | 27 (37.5) | | |

ECOG PS=Eastern Cooperative Oncology Group performance status; IO=immuno-oncology.

**Favorable safety and tolerability:**

1. Dose escalation completed with no dose-limiting toxicity (DLT) reported; maximum tolerated dose (MTD) not reached.

2. No Grade 4 or 5 treatment-related adverse event (TRAE) observed. Incidence of Grade ≥3 TRAEs, immune-related AEs (irAEs), and VEGF-related TRAEs was 13.9%, 4.2%, and 2.8%, respectively.

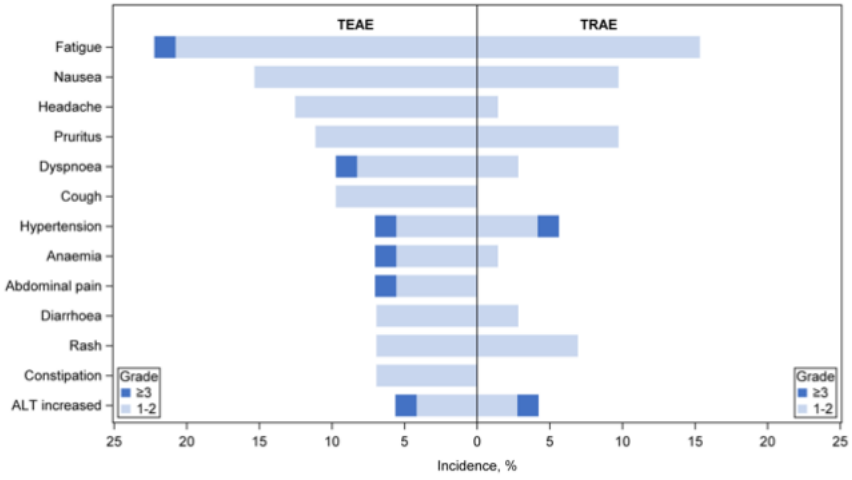
3. Only 1 treatment-emergent adverse event (TEAE) leading to drug permanent discontinuation observed (at DL4 [20 mg/kg]; 1.4% incidence).

**Table 2. Safety Summary (Safety Analysis Set)**

| n (%) | DL1-3 1-10 mg/kg, Q3W (N=21) | DL4 20 mg/kg, Q3W (N=21) | DL5 30 mg/kg, Q3W (N=27) | DL6 45 mg/kg, Q3W (N=3) | All DLs (N=72) |
|---|---|---|---|---|---|
| No. of patients with ≥1 | | | | | |
| TEAE | 21 (100.0) | 19 (90.5) | 13 (48.1) | 3 (100.0) | 56 (77.8) |
| Grade ≥3 TEAE | 8 (38.1) | 6 (28.6) | 6 (22.2) | 1 (33.3) | 21 (29.2) |
| Treatment-related TEAE (TRAE) | 18 (85.7) | 16 (76.2) | 8 (29.6) | 3 (100.0) | 45 (62.5) |
| Grade ≥3 TRAE | 5 (23.8) | 2 (9.5) | 2 (7.4) | 1 (33.3) | 10 (13.9) |
| Serious TEAE | 7 (33.3) | 6 (28.6) | 4 (14.8) | 0 | 17 (23.6) |
| Treatment-related serious TEAE | 2 (9.5) | 4 (19.0) | 0 | 0 | 6 (8.3) |
| Immune-related TEAE | 8 (38.1) | 2 (9.5) | 2 (7.4) | 0 | 12 (16.7) |
| Grade ≥3 immune-related TEAE | 2 (9.5) | 1 (4.8) | 0 | 0 | 3 (4.2) |
| Infusion-related reaction | 0 | 1 (4.8) | 0 | 1 (33.3) | 2 (2.8) |
| TEAE leading to drug permanent discontinuation | 0 | 1 (4.8) | 0 | 0 | 1 (1.4) |

DL=dose level; TEAE=treatment-emergent adverse event.

**Figure 2. Most Frequent TEAEs and TRAEs* (Safety Analysis Set)**




*TEAEs with incidence rate ≥5% and the corresponding TRAEs.
AEs were graded according to National Cancer Institute Common Terminology Criteria for AE (NCI-CTCAE) v5.0.
ALT=alanine aminotransferase; TEAE=treatment-emergent adverse event; TRAE=treatment-related adverse event.

**Promising antitumor activity and high disease control rate (DCR):**

CS2009 demonstrated encouraging anti-tumor activities across tumor types. As of the cutoff date, the overall follow-up duration remained limited, particularly in higher-dose cohorts where the majority patients had yet to reach the protocol-specified time point of post-baseline tumor assessment:

1. 49/72 patients underwent at least one post-baseline tumor assessment by data cutoff.

2. Despite limited follow-up duration, anti-tumor activity was observed across all dose levels with dose-dependent uptrend:

   - Among all 49 evaluable patients, overall response rate (ORR) was 12.2%; DCR was 71.4%. Efficacy data remains immature; with additional follow-up beyond the poster data cutoff, ORR was further improved to 14.3%.

   - Higher ORR (25.0%) at tentative recommended Phase 2 dose (RP2D, 30 mg/kg) and higher dose.

3. Promising efficacy signals were observed across multiple tumor types within the short follow-up period:

- Non-Small Cell Lung Cancer (NSCLC): ORR: 11.8%, DCR: 82.4%; Post-ESMO update: stable disease (SD)-to-partial response (PR) conversion observed, ORR further elevated to 17.6%; In AGA-negative subgroup, ORR reached **25%;**
- Ovarian Cancer (OC): ORR: 16.7%, DCR: 66.7%;
- Triple-Negative Breast Cancer (TNBC): ORR: 25.0%, DCR: 75.0%;
- Non–Clear Cell Renal Cell Carcinoma (nccRCC): ORR: 33.3%, DCR: 100.0%;
- Soft Tissue Sarcoma (STS): ORR: 11.1%, DCR: 66.7%.

**Table 3. BoR in All Evaluable Patients and in Specific Tumor Types (Efficacy Analysis Set)**

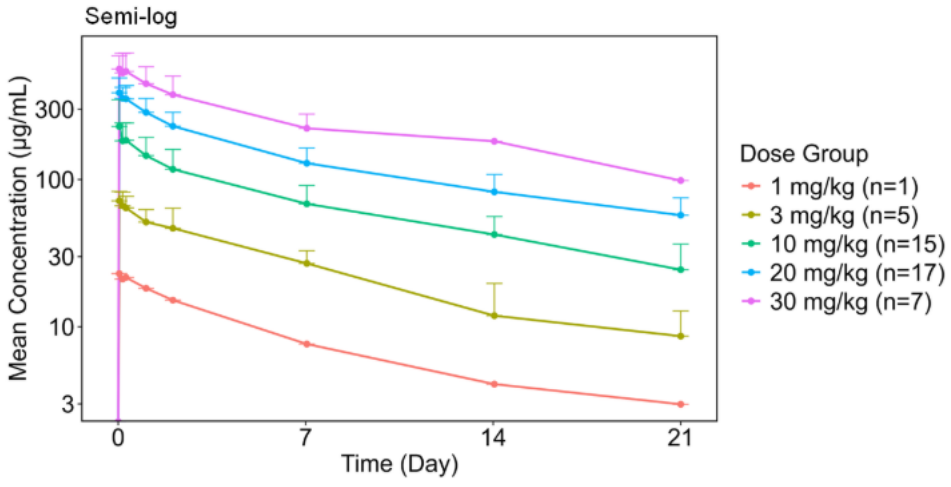
| All Evaluable Patients, n (%) | DL1-3 1-10 mg/kg, Q3W (N=20) | DL4 20 mg/kg, Q3W (N=17) | DL5 30 mg/kg, Q3W (N=9) | DL6 45 mg/kg, Q3W (N=3) | All DLs (N=49) |
|---|---|---|---|---|---|
| **Overall response rate** | **2 (10.0)** | **1 (5.9)** | **2 (22.2)** | **1 (33.3)** | **6 (12.2)** |
| Partial Response (PR) | 2 (10.0) | 1 (5.9) | 2 (22.2) | 1 (33.3) | 6 (12.2)* |
| Stable Disease (SD) | 11 (55.0) | 12 (70.6) | 4 (44.4) | 2 (66.7) | 29 (59.2) |
| Progressive Disease (PD) | 7 (35.0) | 4 (23.5) | 3 (33.3) | 0 | 14 (28.6) |
| **Disease control rate** | **13 (65.0)** | **13 (76.5)** | **6 (66.7)** | **3 (100.0)** | **35 (71.4)** |
| **Tumor Type, n (%)** | **NSCLC# (N=17)** | **OC (N=6)** | **TNBC (N=4)** | **nccRCC (N=3)** | **STS (N=9)** |
| Prior IO Therapy | 17 (100.0) | 1 (16.7) | 2 (50.0) | 2 (66.7) | 2 (22.2) |
| Prior Anti-angiogenic Therapy | 7 (41.2) | 4 (66.7) | 1 (25.0) | 3 (100.0) | 4 (44.4) |
| **Overall response rate** | **2 (11.8)** | **1 (16.7)** | **1 (25.0)** | **1 (33.3)** | **1 (11.1)** |
| Partial Response (PR) | 2 (11.8) | 1 (16.7) | 1 (25.0) | 1 (33.3) | 1 (11.1) |
| Stable Disease (SD) | 12 (70.6) | 3 (50.0) | 2 (50.0) | 2 (66.7) | 5 (55.6) |
| Progressive Disease (PD) | 3 (17.6) | 2 (33.3) | 1 (25.0) | 0 | 3 (33.3) |
| **Disease control rate** | **14 (82.4)** | **4 (66.7)** | **3 (75.0)** | **3 (100.0)** | **6 (66.7)** |

#For NSCLC, 10 mg/kg (n=5), 20 mg/kg (n=8), 30 mg/kg (n=4), responders were observed at 10 and 30 mg/kg

**Favorable PK and PD profiles:**

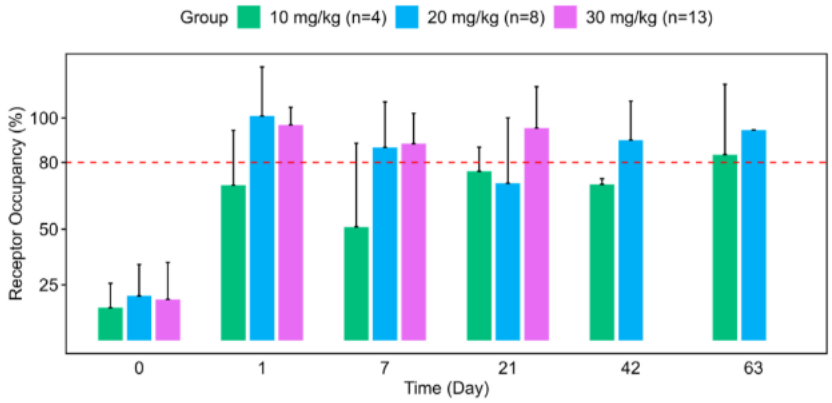
1. Linear PK with half-life of 6-8 days supported every-three-week (Q3W) dosing, with no significant accumulation observed at cycle 3.

**Figure 5. Mean Serum Concentration Profile of CS2009 at Cycle 1**




2. PD profile demonstrated saturated receptor occupancy and robust T-cell activation/proliferation confirming PD-1/CTLA-4 blockade and deep and sustained VEGFA neutralization.
   - Receptor occupancy of PD-1/CTLA-4 on peripheral T cells reached saturation throughout dosing interval at doses ≥20 mg/kg.

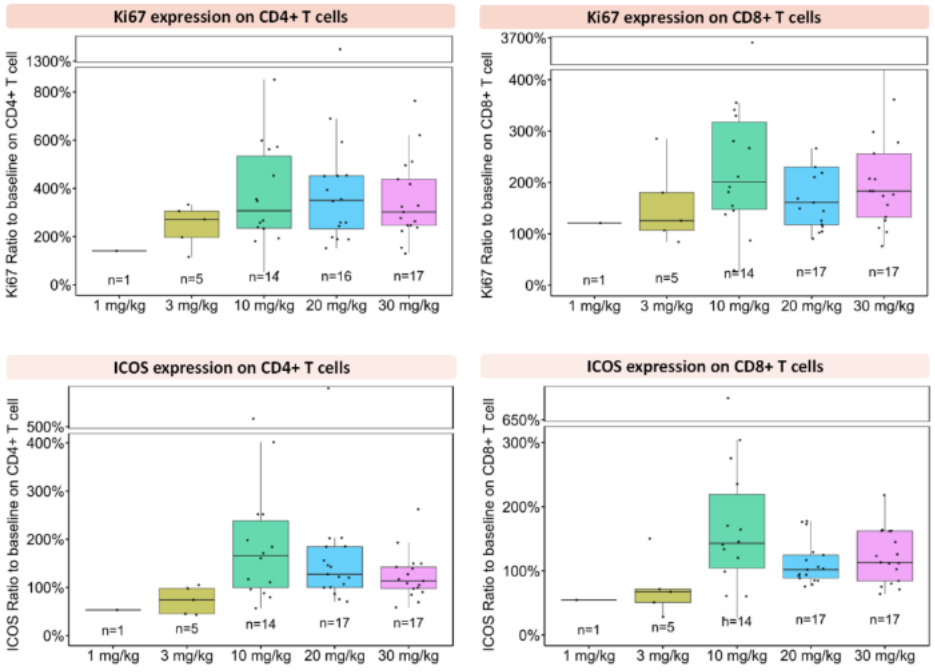
**Figure 6. Receptor Occupancy of PD-1/CTLA-4**




Flow cytometry. As of 23 September 2025, the 42-day and 63-day samples for the 30 mg/kg dose group have not yet been collected.

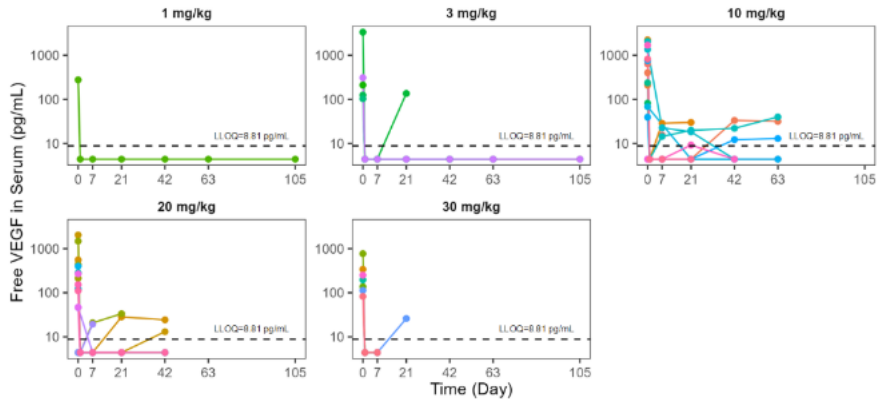
- On cycle 1 day 8, CS2009 induced notable, dose-dependent upregulation of Ki67 (proliferation due to PD-1 and CTLA-4 blockade) and ICOS (activation due to CTLA-4 blockade) expression on both CD4+ and CD8+ T cells, collectively demonstrating effective PD-1 and CTLA-4 inhibition.

**Figure 7. Ki67 and ICOS Change on CD4+ and CD8+ T Cells on Cycle 1 Day 8**




- Serum-free VEGFA reduced deeply and rapidly across all dose levels, and the effect sustained throughout dose intervals.

**Figure 8. Serum-free VEGFA Concentrations by Dose Level**




Validated Electrochemiluminescence (ECL). Concentrations below the lower limit of quantification (LLOQ, 8.81 pg/mL) were imputed as one-half of the LLOQ.

CStone has initiated Phase II dose expansion study in first-line patients with selected tumor types for dose optimization and to generate data supporting registration trials in first-line NSCLC and other tumours as monotherapy or in combination therapies.

**CS2009 Data Review Conference Call:**

CStone will host an investor meeting to discuss presented data and future clinical development plan. The Company cordially invites all investors to attend this conference call.

**Chinese-language session:**

- **Date & Time**: Monday, October 20, 2025, at 14:00 (Beijing Time)/2:00 (US Eastern Time)
- **Registration Link**: Registration is required, please sign up via the link: https://s.comein.cn/iq2y9krs

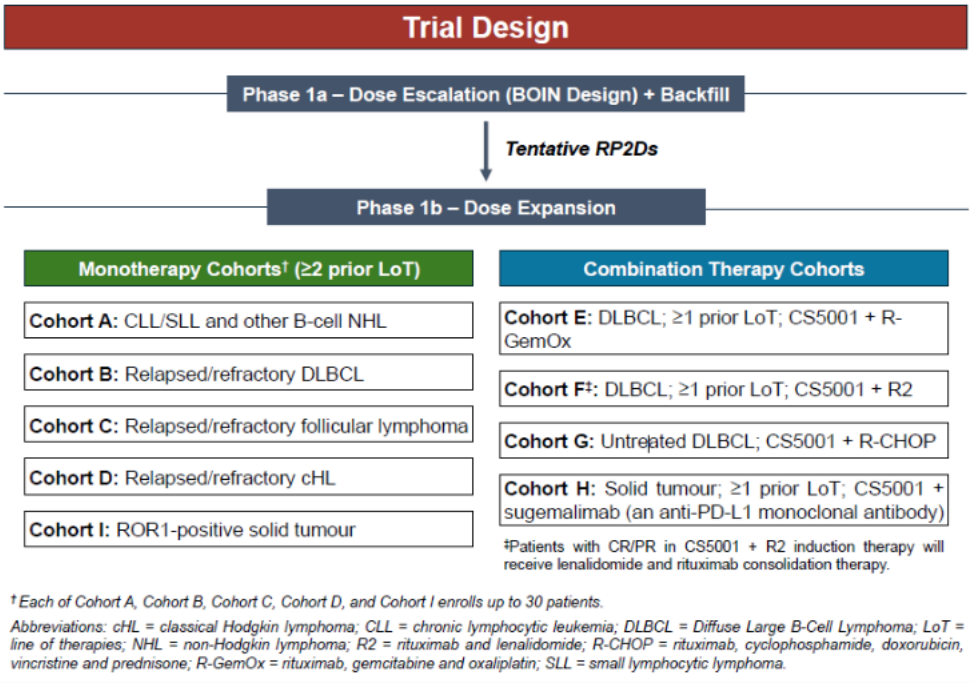
**English-language session:**

- **Date & Time**: Monday, October 20, 2025, at 21:00 (Beijing Time)/9:00 (US Eastern Time)
- **Registration Link**: The Zoom meeting link will be sent to you by email after registration via the below link. You may join the meeting by clicking the link in email: https://us06web.zoom.us/webinar/register/WN_PO-SYEhNScyOdlU1p75MdQ

**Key Highlights of CS5001 ePoster Presentation:**

1. CS5001 Phase Ib study aims to determine the RP2D and further evaluate the safety, tolerability, PK, and efficacy of CS5001 as a monotherapy and in combination with systemic therapies in selected tumour types.

2. In monotherapy cohorts, Cohorts A-D enroll patients with chronic lymphocytic leukemia and other B-cell lymphomas, and Cohort I enrolls patients with ROR1-positive solid tumors. In combination therapy cohorts (E-H), CS5001 will be administered with standard systemic therapies (R-GemOx, R2 or R-CHOP) or with sugemalimab (an anti-PD-L1 monoclonal antibody).




3. Patient enrollment for CS5001 Phase Ib study commenced in December 2024 and is currently advancing smoothly at 30 sites across Australia, the United States, and China.

**About CStone**

CStone (HKEX: 2616), established in late 2015, is an innovation-driven biopharmaceutical company focused on the research and development of therapies for oncology, autoimmune/inflammation, and other key disease areas. 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 covering 9 indications. The company's pipeline is balanced by 16 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 Rules Governing the Listing of Securities on The Stock Exchange of Hong Kong Limited:** THE COMPANY CANNOT GUARANTEE THAT WE MAY BE ABLE TO ULTIMATELY DEVELOP AND MARKET CS2009 AND 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, October 20, 2025

*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 and Mr. Edward Hu as non-executive directors, and Mr. Ting Yuk Anthony Wu, Ms. Yip Betty Ho and Mr. Kenneth Howard Jarrett as independent non-executive directors.*