CStone Pharmaceuticals

基石藥業

(Incorporated in the Cayman Islands with limited liability)

(**Stock Code: 2616**)

VOLUNTARY ANNOUNCEMENT
CSTONE ANNOUNCES FIRST PATIENT DOSED IN GLOBAL MULTICENTER PHASE I CLINICAL TRIAL OF CS2009, A PD-1/VEGF/CTLA-4 TRISPECIFIC ANTIBODY

CStone Pharmaceuticals (the "**Company**" or "**CStone**") is pleased to announce that the first patient has been successfully dosed in the global multicenter Phase I clinical trial of its independently developed PD-1/VEGF/CTLA-4 trispecific antibody, CS2009, with no infusion reactions or other adverse events observed.

This trial will thoroughly evaluate the clinical potential of CS2009 in a wide range of advanced solid tumors, including but not limited to non-small cell lung cancer, hepatocellular carcinoma, gastric adenocarcinoma, endometrial cancer, ovarian cancer, renal cell carcinoma, and cervical cancer, in efforts to advance the development of innovative tumor immunotherapies.

CS2009, an innovative trispecific antibody designed and developed by CStone, combines three clinically validated targets: PD-1, VEGFA, and CTLA-4, and exerts multidimensional anti-tumor effects through synergistic actions. Specifically, anti-PD-1 activity reverses T-cell exhaustion and anti-CTLA-4 activity promotes T-cell activation and proliferation, while anti-VEGFA activity blocks tumor angiogenesis and improves the tumor micro-environment (TME). In the TME, anti-PD-1 and anti-CTLA-4 activities are significantly enhanced by crosslinking with VEGFA. Meanwhile, CS2009 preferentially blocks PD-1 and CTLA-4 on double-positive tumor-infiltrating T cells while minimizing interference with CTLA-4 regulation in peripheral T cells, thus potentially offering enhanced efficacy with lower systemic toxicity.

CS2009 demonstrated superior anti-tumor activity compared to potential competitors in preclinical studies. By combining CTLA-4 inhibition with PD-1 and VEGFA blockade, CS2009 may further enhance benefits for patients with low or negative PD-L1 expression, who respond poorly to PD-(L)1 therapies. This well positions CS2009 as a next-generation, first- or best-in-class immunotherapy backbone product, with the potential to replace current anti-PD-(L)1-based therapies.

Dr. Jason Yang, CEO, President of R&D, and Executive Director at CStone, stated, "The initiation of the

first-in-human study for CS2009 marks a breakthrough in our clinical development. Our robust preclinical data have confirmed CS2009's potential in a wide range of solid tumor indications. In in vitro studies, CS2009 demonstrated its ability to effectively and specifically activate tumor-infiltrating T cells, as well as robust synergistic effect with anti-VEGF activity; in immunocompetent mouse models, CS2009 showed stronger anti-tumor effects than both PD-1/CTLA-4 and PD-1/VEGF bispecific antibodies; and in toxicology studies, CS2009 exhibited a safety margin which was greater than the PD-1/CTLA-4 bispecific antibody and comparable to the PD-1/VEGF bispecific antibody. These results have given us confidence in CS2009's clinical potential. We look forward to sharing additional clinical data that will further validate its safety and anti-tumor activity, paving the way for a new era in cancer immunotherapy."

Dr. Qingmei Shi, Chief Medical Officer of CStone, added, "We are pleased to have achieved CS2009's first-patient-dosed milestone for CS2009, an innovative trispecific antibody which can potentially offer balanced efficacy and safety while addressing the unmet medical needs in patients with low or negative PD-L1 expression. We expect to see rapid and encouraging progress in this study and are committed to bringing improved treatment options for patients with solid tumors worldwide. We appreciate the exceptional efforts of our clinical team, who completed the entire process—from submitting the clinical trial application in Australia to dosing the first patient—in just two months despite multiple holidays in China and abroad. This is another testament to CStone's outstanding clinical development efficiency and unwavering commitment to serving patients."

Currently, the multicenter Phase I clinical trial of CS2009 is being conducted in Australia, with plans to expand into China and the United States in the near future.

About CS2009 (PD-1/VEGF/CTLA-4 Trispecific Antibody)

CS2009 is a trispecific antibody targeting PD-1, VEGFA, and CTLA-4, with the potential to be first- or best-in-class for major tumor types. Its differentiated molecular design combines three clinically validated targets, preferentially invigorating exhausted tumor infiltrating lymphocytes (TILs) while demonstrating VEGF neutralization comparable to existing anti-VEGF antibodies. CS2009 covers a wide range of cancers, including but not limited to non-small cell lung cancer, hepatocellular carcinoma, gastric adenocarcinoma, endometrial cancer, ovarian cancer, renal cell carcinoma, and cervical cancer.

In November 2024, CStone presented preclinical data for CS2009 at the 39th Annual Meeting of the Society for Immunotherapy of Cancer (SITC). These results show that CS2009 exhibits superior anti-tumor activity compared to potential competitors, including PD-1/CTLA-4 bispecific antibodies, PD-1/VEGF bispecific antibodies, and PD-1/CTLA-4 combination therapies.

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 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 Listing Rules: THE COMPANY CANNOT GUARANTEE THAT WE MAY BE ABLE TO ULTIMATELY DEVELOP AND MARKET CS2009 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, March 4, 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, Mr. Xianghong Lin and Mr. Edward Hu as non-executive directors, and Dr. Paul Herbert Chew, Mr. Ting Yuk Anthony Wu, Mr. Hongbin Sun and Ms. Yip Betty Ho as independent non-executive directors.