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

VOLUNTARY ANNOUNCEMENT
CSTONE PRESENTS PRECLINICAL DATA ON CS2009 AT THE 2024 SITC ANNUAL MEETING

CStone Pharmaceuticals (the "**Company**" or "**CStone**") is pleased to announce the presentation of preclinical data on CS2009, a leading asset from the Company's Pipeline 2.0, at the 39th Annual Meeting of the Society for Immunotherapy of Cancer (SITC Annual Meeting). CS2009 is a trispecific antibody that simultaneously targets PD-1, CTLA-4, and VEGFA.

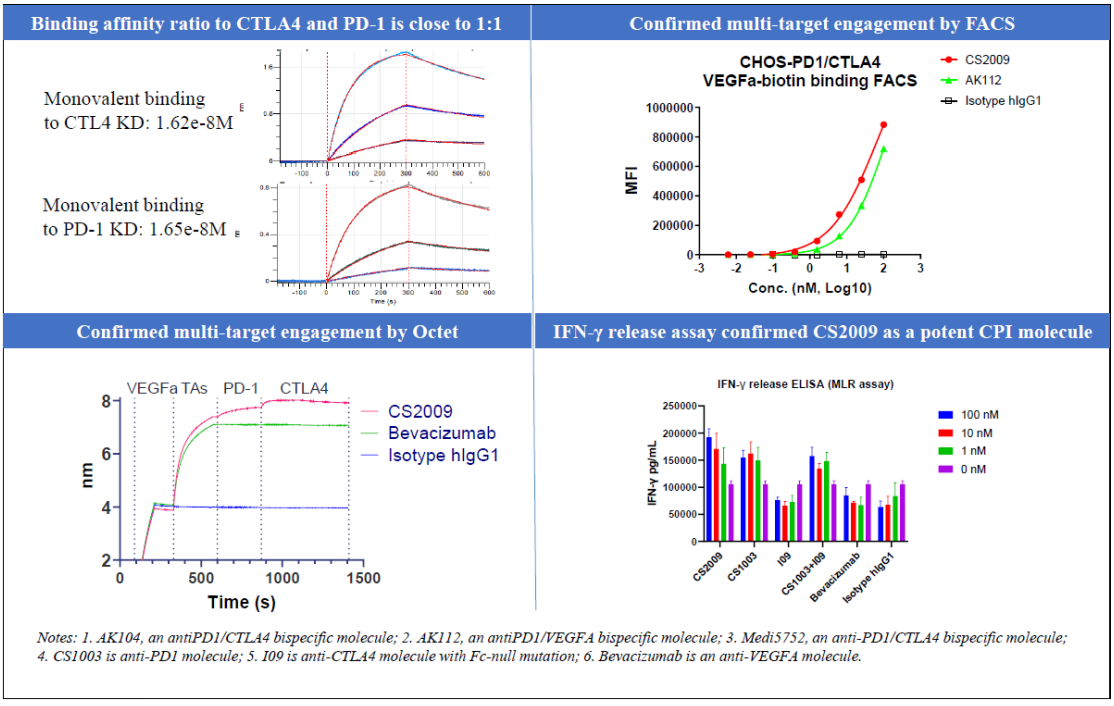
Key Highlight

- CS2009 is a trispecific antibody targeting PD-1, CTLA-4, and VEGFA.
- Preclinical results show CS2009 has superior anti-tumor activity compared to potential competitors.
- CS2009 holds potential for broad application across multiple tumor types and aims to become a first- or best-in-class, next-generation cancer immunotherapy.
- CStone plans to submit an Investigational New Drug (IND) application for CS2009 by late 2024 or early 2025, with first-in-human trial expected to be initiated in early 2025.

Dr. Jason Yang, CEO, President of R&D, and Executive Director at CStone, commented, "We are excited to present the latest preclinical data on CS2009 at SITC Annual Meeting, marking its debut on the international stage. As a pivotal asset in CStone's Pipeline 2.0, CS2009 holds the potential to become a next-generation, first- or best-in-class immunotherapy backbone to replace the current anti-PD-(L)1 therapies. These compelling preclinical results strengthen our confidence in advancing its clinical development. We look forward to seeing CS2009 to benefit patients with various cancers, including non-small cell lung cancer, ovarian cancer, renal cell carcinoma, cervical cancer, hepatocellular carcinoma, and gastric cancer, particularly those with low or negative PD-L1 expression who respond poorly to PD-(L)1 therapies."

Key Findings

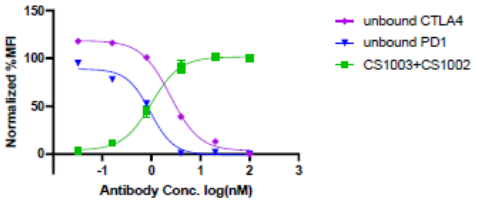
- **Innovative Design**: CS2009 features balanced affinities for PD-1 and CTLA-4, validated through protein and cellular assays to bind PD-1, CTLA-4, and VEGFA simultaneously.

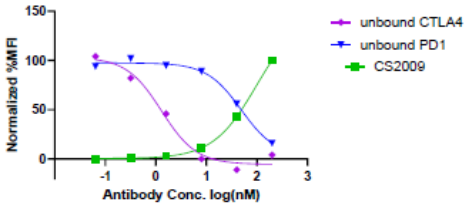


Notes: 1. AK104, an antiPD1/CTLA4 bispecific molecule; 2. AK112, an antiPD1/VEGFA bispecific molecule; 3. Medi5752, an anti-PD1/CTLA4 bispecific molecule; 4. CS1003 is anti-PD1 molecule; 5. I09 is anti-CTLA4 molecule with Fc-null mutation; 6. Bevacizumab is an anti-VEGFA molecule.

- **Targeted Engagement**: CS2009 preferentially blocks PD-1 and CTLA-4 on double-positive tumor-infiltrating T cells, without interfering CTLA-4 regulation on peripheral T cells, thereby enhancing safety without compromising efficacy. CS2009 also induces rapid internalization of PD-1 and CTLA-4 on double-positive T cells, reducing the levels of these two immune checkpoint molecules.

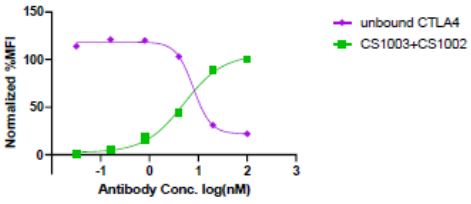
CHOs-PD-1/CTLA4

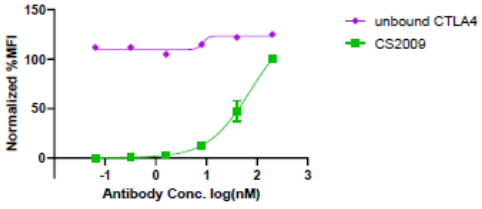




- PD-1/CTLA4≈40:1, similar to the ratio on TILs
- Blocked B7/CTLA4 more effectively than combo regimen
- Monovalent anti-PD-1 arm of CS2009 remains functional

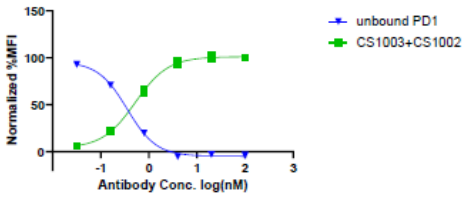
CHOK1-CTLA4

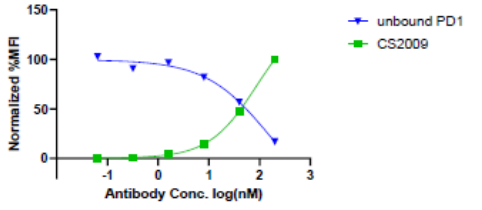




- CTLA4 single positive
- Monovalent anti-CTLA4 arm of CS2009 unable to block CTLA4/B7 interaction

NK92-PD-1

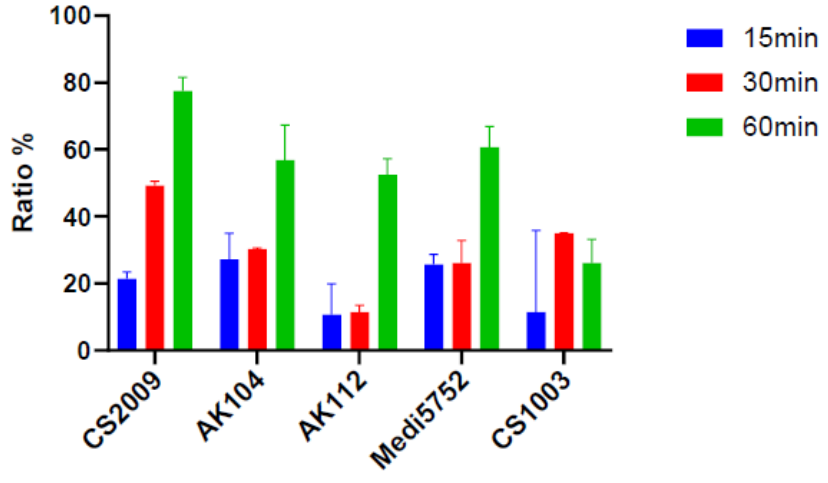




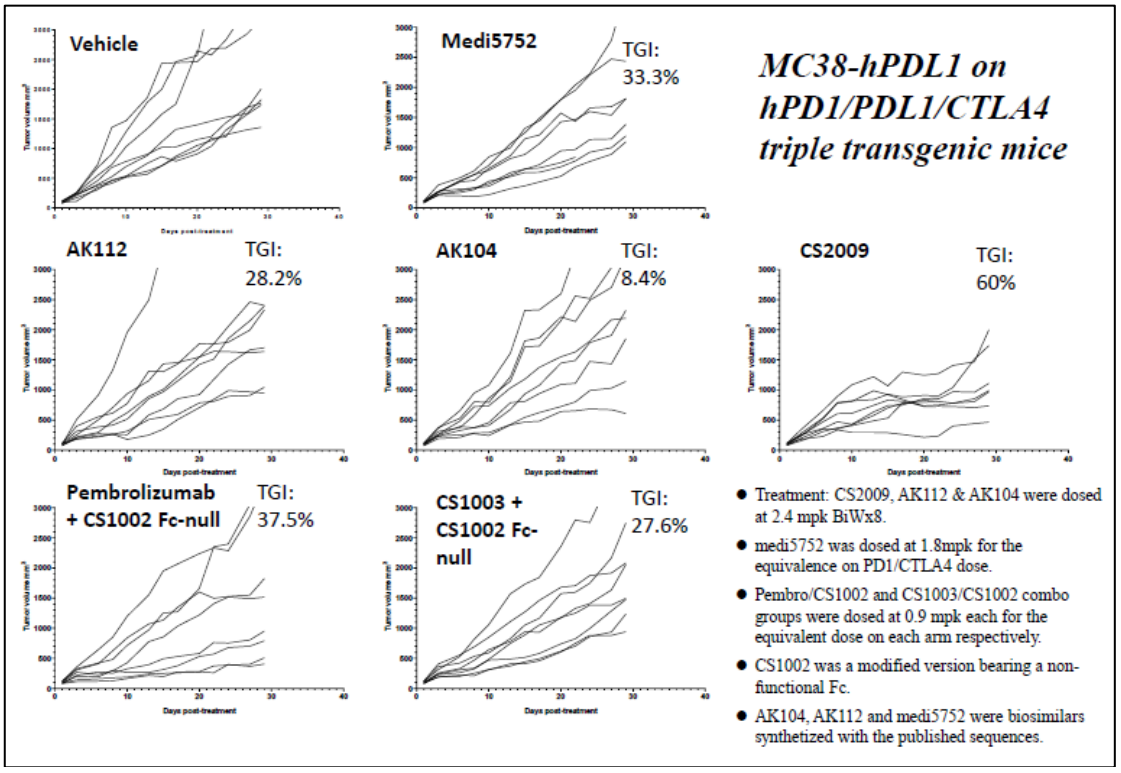
- PD-1 single positive
- Monovalent anti-PD-1 arm of CS2009 remains functional

Notes:CS1002 is anti-CTLA4 molecule.

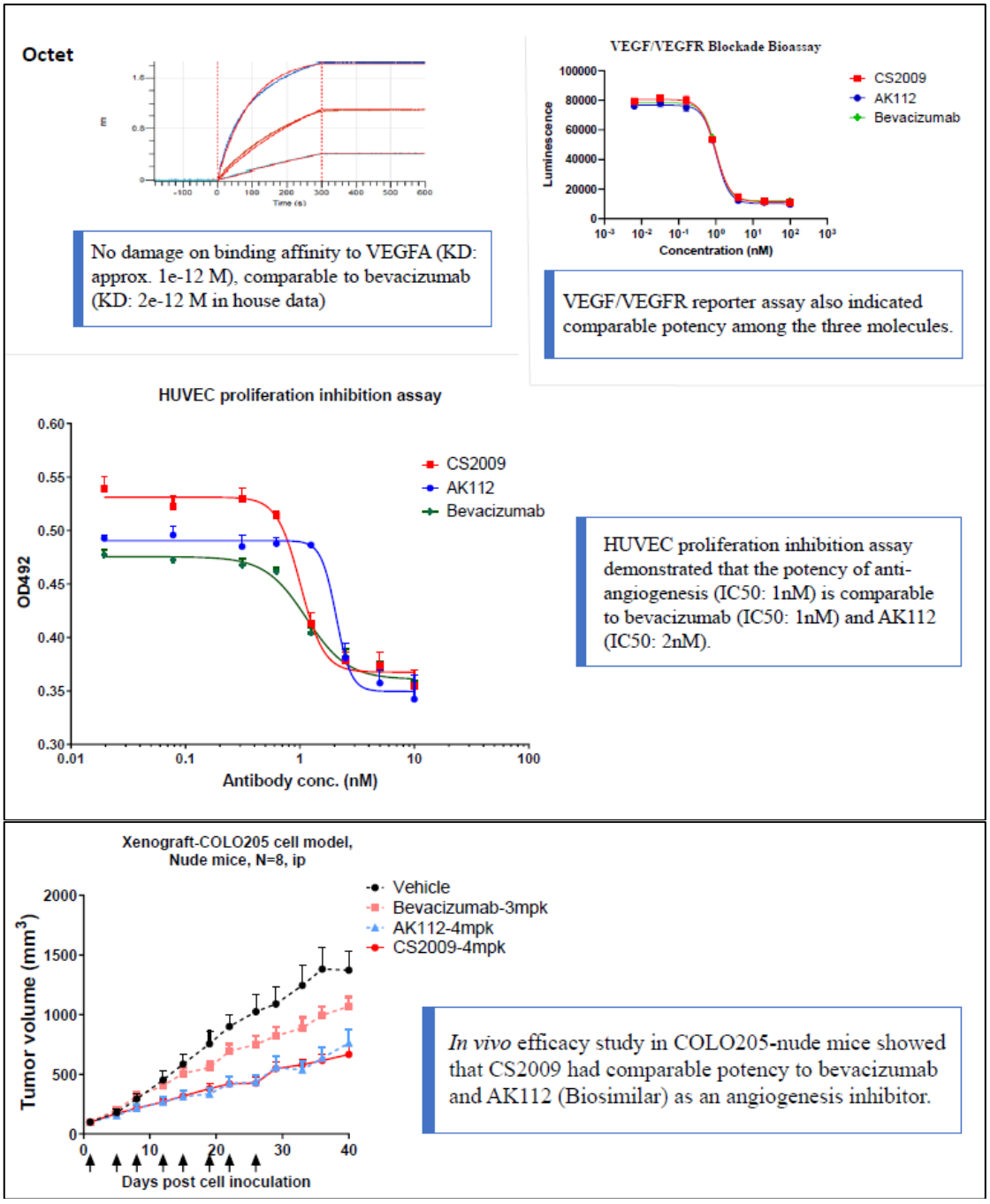
Internalization on CHOS-PD1/CTLA4



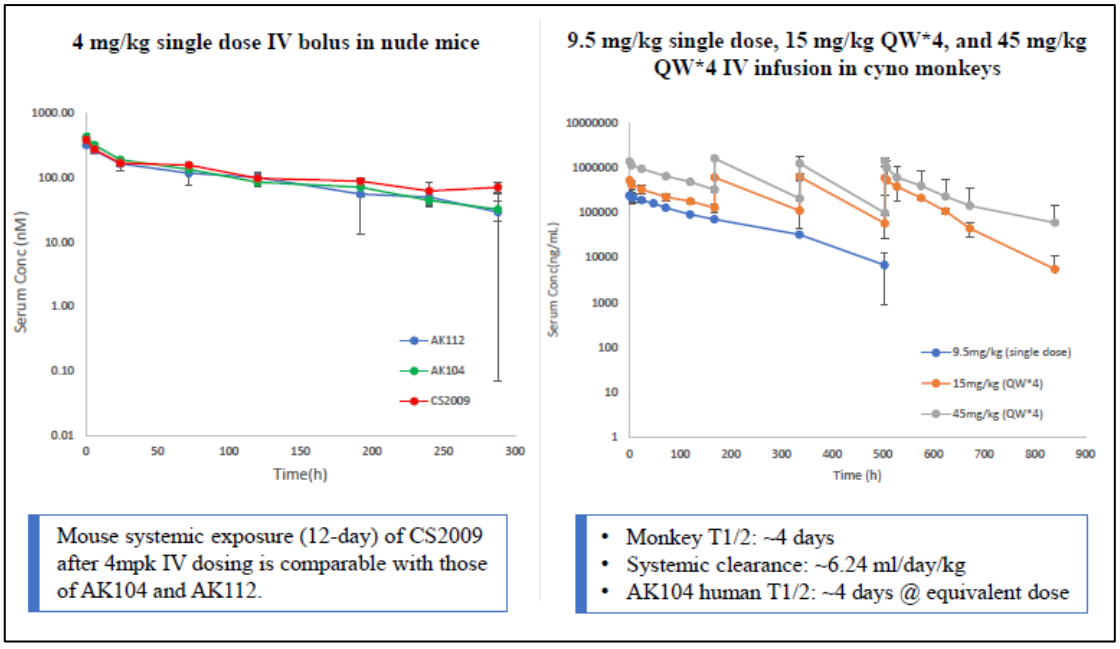
- **Enhanced Anti-Tumor Activity**: In immunocompetent mouse models, CS2009 demonstrated superior anti-tumor activity compared to potential competitors, including PD-1/CTLA-4 bispecific antibody, PD-1/VEGFA bispecific antibody, and PD-1/CTLA-4 combination therapies.



- **VEGFA Inhibition**: CS2009's unattenuated VEGFA blockade capabilities led to comparable efficacy to benchmark agents in vivo mouse studies, including bevacizumab.



- **Pharmacokinetics (PK)**: CS2009 demonstrated PK profiles in both mice and cynomolgus monkeys similar to most monoclonal antibodies



CS2009 is currently in preparation for an IND submission, with filing anticipated by late 2024 or early 2025 and first-in-human trial to be initiated in early 2025.

About CS2009 (PD-1/CTLA4/VEGFA Trispecific Antibody)

CS2009 is a trispecific antibody targeting PD-1, CTLA-4, and VEGFA, with the potential to be first- or best-in-class for major tumor types. CS2009 has a differentiated molecular design that combines three clinically validated targets, preferentially invigorating exhausted TILs and demonstrating VEGFA neutralization comparable to existing anti-VEGFA antibodies. It covers a wide range of cancers, including non-small cell lung cancer, ovarian cancer, renal cell carcinoma, cervical cancer, hepatocellular carcinoma, and gastric cancer.

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 18 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, November 11, 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.