**CStone Pharmaceuticals**

**基石藥業**

*(Incorporated in the Cayman Islands with limited liability)*

**(Stock Code: 2616)**

# VOLUNTARY ANNOUNCEMENT
# CSTONE PRESENTS RESEARCH DATA OF CS5001 (ROR1 ADC) AT THE 33RD AACR-NCI-EORTC INTERNATIONAL CONFERENCE ON MOLECULAR TARGETS AND CANCER THERAPEUTICS 2021

CStone Pharmaceuticals (the "**Company**" or "**CStone**") is pleased to announce that the data on the preclinical characterization of the potentially global best-in-class drug CS5001(receptor tyrosine kinase-like orphan receptor 1 ("**ROR1**") antibody drug conjugate ("**ADC**")) was accepted in a late-breaking abstract ("**LBA**") session as a virtual poster presentation at the 33rd AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics 2021(Poster ID: LBA008). The results showed that CS5001 exhibited potent and selective cytotoxicity to a variety of ROR1-expressing cell lines and demonstrated remarkable in vivo antitumor activity in xenograft mouse models. ROR1 expression appears to predict sensitivity to CS5001 in a panel of cancer cell lines. Our data indicated that CS5001 is a promising therapeutic candidate for the treatment of ROR1-expressing hematological and solid malignancies with precision medicine potential.

**Summary of the Presentation:**

- Presentation session: Multiple solid and hematological malignancies
- Date: October 7-10, 2021
- Format: LBA
- Title: CS5001, a novel ROR1-targeting ADC armed with tumor-cleavable β-glucuronide linkers and pyrrolobenzodiazepine ("**PBD**") prodrugs for hematological and solid malignancies
- Speakers/Leading Principal Investigator: Dr. Archie N. Tse, Chief Scientific Officer of CStone

CS5001 is an ADC composed of a human monoclonal antibody targeting ROR1, site-specifically conjugated with a proprietary cleavable β-glucuronide linker to a prodrug of PBD dimer. Both linker and prodrug are selectively cleaved by the lysosomal β-glucuronidase, which is overexpressed in many cancerous cells, to allow tumor-selective release of the DNA-crosslinking PBD prodrug.

CS5001 bound specifically to human ROR1, but not ROR2. CS5001 has cross reactivity against mouse, rat and cynomolgus ROR1 at similar affinities. Upon binding, CS5001 was rapidly internalized by ROR1-expressing cancer cells. CS5001 demonstrated potent cytotoxicity towards ROR1 high expressing cell lines such as Jeko-1 (mantle cell lymphoma) and MDA-MB-231 (triple-negative breast cancer), with sub-nanomolar IC50 values. The growth inhibition activity of CS5001 was significantly correlated with ROR1 density in a panel of cancer cell lines.

CS5001 exhibited prominent antitumor activity in both Jeko-1 and MDA-MB-231 xenograft models in a dose-dependent manner. In addition, CS5001 demonstrated superior efficacy compared to an MMAE-based ROR1 ADC at equitoxic doses in the Jeko-1 model.

Dr. Archie N. Tse, Chief Scientific Officer of CStone, said: "ROR1 is a very promising target as it is differentially expressed in a variety of solid and hematological malignancies but not in normal adult tissues. This means that ROR1 has the potential to be an oncological target like PD-1/L1 for a broad spectrum of cancers. The preclinical pharmacology and biomarker data presented at the conference were encouraging and demonstrated the precision medicine potential of CS5001 for the treatment of multiple hematological and solid malignancies. We expect Investigational New Drug ("**IND**") filing by year end and clinical testing shortly thereafter."

CS5001 is a pre-clinical ADC completing IND enabling studies. CS5001 has a uniquely design tumor-cleavable linker that is conjugated to a LCB's proprietary PBD prodrug playload. Only after reaching the tumor, the linker and PBD 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 addressing the toxicity problem associated with traditional PBD payloads, leading to a better safety profile. Additionally, CS5001 utilizes site-specific conjugation for a precise drug antibody ratio ("**DAR**") which enables homogeneous production and large-scale manufacturing.

In October 2020, CStone signed a licensing agreement with LegoChem Biosciences, Inc. ("**LCB**") for the development and commercialization of CS5001. Under the agreement, CStone obtains the exclusive global right to lead development and commercialization of CS5001 outside the Republic of Korea.

The work was collaboratively accomplished by CStone, LCB, and ABL Bio (a company incorporated in the Republic of Korea).

**About CStone**

CStone is a biopharmaceutical company focused on researching, developing and commercializing innovative immuno-oncology and precision medicines to address the unmet medical needs of cancer patients in Mainland China and worldwide. Established in 2015, CStone has assembled a world-class management team with extensive experience in innovative drug development, clinical research, and commercialization. The Company has built an oncology-focused pipeline of 15 drug candidates with a strategic emphasis on immuno-oncology combination therapies. Currently, CStone has received three drug approvals in Greater China, including two in Mainland China and one in Taiwan, China. CStone's vision is to become globally recognized as a world-renowned biopharmaceutical company by bringing innovative oncology therapies to cancer patients worldwide.

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

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

Suzhou, the People's Republic of China, October 8, 2021

*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. 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.*