**CStone Pharmaceuticals**

**基石藥業**

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

(**Stock Code: 2616**)

## VOLUNTARY ANNOUNCEMENT

# CSTONE COMPLETES REGISTRATION FILING FOR THE PHASE I TRIAL OF CDK4/6 INHIBITOR CS3002 IN AUSTRALIA AND WILL SOON INITIATE THE STUDY

CStone Pharmaceuticals (the "**Company**" or "**CStone**") announces that the Company has recently received ethics approval from the Human Research Ethics Committee in Australia for the Phase I clinical trial of CS3002. On August 14, 2019, Australia's Therapeutic Goods Administration (TGA) acknowledged the electronic Clinical Trial Notification (eCTN) the Company submitted for the trial. This clinical trial is an open-label, multi-dose, dose-escalation and dose-expansion Phase I clinical study designed to evaluate the safety, tolerability, pharmacokinetics, and anti-tumor efficacy of CS3002 in patients with advanced solid tumors.

Being developed by CStone, CS3002 is a selective inhibitor of the cyclin-dependent kinases 4 and 6 ("**CDK4/6**"). Inducing cell cycle arrest of tumor cells through the selective inhibition of CDK4/6, CS3002 has demonstrated high therapeutic potential for combination with endocrine therapy or immune checkpoint inhibitor therapy in various solid tumors. At present, three CDK4/6 inhibitors have been approved by the United States Food and Drug Administration (FDA). However, in China, palbociclib is the only approved CDK4/6 inhibitor, indicated for the treatment of hormone receptor-positive (HR+), human epidermal growth factor receptor 2 negative (HER2-) advanced or metastatic breast cancer in combination with an aromatase inhibitor as initial endocrine-based therapy in postmenopausal women.

Preclinical studies have revealed that CS3002's in vivo and in vitro activities are comparable to that of palbociclib's. In mouse models, CS3002 combined with PD-1 monoclonal antibody therapy or endocrine

therapy has shown improved tumor suppressing activities compared to monotherapies. In addition, CS3002 has also demonstrated potentially favorable safety and tolerability profiles.

Dr. Frank Ningjun Jiang, chairman, executive director and chief executive officer of CStone, commented: "Currently, there are several CDK4/6 inhibitors that are either approved or in clinical development in the world. However, options in this class of therapies available to Chinese patients remain very limited and no domestically developed CDK4/6 inhibitor has been approved. I am pleased that we are about to initiate the Phase I trial on CS3002 in Australia. We will accelerate our work in obtaining its clinical trial approval in China and actively explore CS3002's application in the treatment of various tumor types and different combination therapies. We hope CS3002 will become a new effective treatment option benefiting Chinese patients."

Dr. Jon Wang, CStone's chief scientific officer, noted: "The aberrant activation CDK4/6 was observed across various tumor types, suggesting CS3002's potential utility in the treatment of breast cancer and a variety of other solid tumors. Recent studies have shown that, in addition to inducing cell cycle arrests of tumor cells, CDK4/6 inhibitors also have the effects of strengthening anti-tumor immunity and modulating the tumor microenvironment. These discoveries provide the foundation for a new approach in cancer treatment, which is the combination of CDK4/6 inhibitors and immunotherapies. We are hopeful that the clinical trial on CS3002 in Australia will be carried out successfully."

**About CS3002**

CS3002 is a new generation of well-tolerated and highly selective CDK4/6 inhibitor developed by CStone.

CDK4/6 inhibitors are the cyclin-dependent kinases that play a crucial role in the regulation of cell cycle progression from the first Growth phase ("**G1 phase**") to the Synthesis phase ("**S phase**"). Upon activation of the cell proliferation signal, cyclin D protein binds to CDK4/6. The cyclin D–CDK4/6 complex then phosphorylates downstream retinoblastoma (Rb) protein, resulting in the aberrant proliferative signaling in the CDK4/6 pathway that drives the cell cycle progression from the G1 phase to the S phase. Aberrant CDK4/6 activity is a common feature of most cancer types. CDK4/6 inhibitors could suppress the activities of CDK4/6 and the phosphorylation of Rb protein, thereby achieving the suppression of tumor cell growth by interrupting the cell cycle transition from the G1 phase to the S phase. The commonality of aberrant cyclin D–CDK4/6–INK4–Rb pathway signaling in a tumor cells suggests CDK4/6 inhibitors' potential application in strengthening anti-tumor immunity, and CDK4/6 inhibitors' promising potential for the treatment of various solid tumors and synergistic combination with immuno-oncology therapies.

**About CStone**

CStone is a biopharmaceutical company focused on developing and commercializing innovative immuno-oncology and molecularly-targeted drugs to address unmet medical needs for cancer patients in China and worldwide. Since the Company's establishment in 2015, CStone has assembled a world-class management team that has a full spectrum of complementary skillsets from preclinical research to clinical development and commercialization. With combination therapies as a core strategy, the Company has built a rich oncology pipeline of 15 oncology drug candidates. Currently, five late-stage drug candidates are at or near pivotal trials. With an experienced team, a rich pipeline, a robust clinical development-driven business model, and

substantial funding, CStone's vision is to become globally recognized as a leading Chinese biopharmaceutical company by bringing innovative and differentiated 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, People's Republic of China, August 22, 2019

*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. Guobin Zhang and Dr. Lian Yong Chen as non-executive Directors, and Dr. Paul Herbert Chew, Mr. Ting Yuk Anthony Wu and Mr. Hongbin Sun as independent non-executive Directors.*