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 ITS TUMOR IMMUNE MICROENVIRONMENT MODULATOR CS3005 TO ENABLE STUDY INITIATION IN AUSTRALIA

CStone Pharmaceuticals (the "**Company**" or "**CStone**") announces that the Company has recently received the approval from the Human Research Ethics Committee in Australia, and the acknowledgement from Australia's Therapeutic Goods Administration on the Phase I clinical trial of CS3005. This Phase I trial is an open-label, multicenter, dose-escalation study designed to evaluate the safety, tolerability, pharmacokinetics, and preliminary antitumor activity of CS3005 in patients with advanced solid tumors.

The tumor microenvironment ("**TME**") is a cellular space in which the tumor dynamically interacts with the surrounding blood vessels, immune cells, stromal components, signaling molecules, and the extracellular matrix. Studies showed that multiple compensatory immunosuppressive mechanisms exist in the TME not only contribute to the development of tumors but also affect the response to immunotherapies. The adenosine signaling pathway plays a critical role in immune modulation and is an important compensatory resistance mechanism against immune checkpoint inhibitors.

Discovered by CStone, CS3005 is an adenosine A2a receptor antagonist that modulates the tumor immune microenvironment. CS3005 could potentially activate antitumor immunity and improve the response to immune checkpoint inhibitors by blocking the binding of adenosine with adenosine A2a receptors and thereby reversing the immunosuppressive mechanism. At present, no adenosine A2a receptor antagonist has been approved for cancer treatment anywhere in the world.

Dr. Frank Ningjun Jiang, chairman, executive director and chief executive officer of CStone, commented: "I am pleased that the clinical trial of CS3005 has been approved in Australia. This drug candidate is the Company's first tumor immune microenvironment modulator entering clinical development as we have begun to roll out CStone's Pipeline 2.0. Immuno-oncology therapy has brought new hope to cancer patients in recent years, yet many patients fail to respond to those treatments. We are hopeful that the research and development of tumor microenvironment modulators will allow immunotherapies to benefit more patients."

CStone's chief scientific officer, Dr. Jon Wang, noted: "Early studies on adenosine A2a receptor antagonists have shown good safety profiles and antitumor activities, either as monotherapies or in combination with immune checkpoint inhibitors, in patients with advanced solid tumors. Interestingly, adenosine A2a receptor antagonists have also demonstrated antitumor activities in patients with low PD-L1 expressing tumors or who are resistant/refractory to anti-PD-(L)1. These observations implicate possible benefits to patients with solid tumors. CS3005 also adds to the depth and flexibility of CStone's strategy in immuno-oncology combination therapy."

About CS3005

CS3005 is a highly selective adenosine A2a receptor antagonist discovered by CStone.

Immunotherapy has achieved great success in the treatment of advanced tumors, but the response to immunotherapy remains suboptimal due to the existence of multiple compensatory immunosuppressive mechanisms in the TME. Among those mechanisms, the adenosine signaling pathway plays a key role in down-regulating anticancer immunity. Hypoxia in the TME results in strained energy supply to tumor cells and cell death, and the subsequent release of a large amount of adenosine triphosphate ("**ATP**") into the TME. ATP is then metabolized into adenosine by CD39 and CD73, thereby causing the accumulation of extracellular adenosine in the TME. The level of adenosine in the TME is much higher than that in normal tissues. Upon binding with adenosine A2a receptors, adenosine suppresses the innate and adaptive immune function of immune cells. The adenosine A2a receptor is expressed in a host of immune cells such as the T-cells, natural killer (NK) cells, monocytes, and dendritic cells. Early clinical studies of adenosine A2a receptor antagonists, as monotherapies or in combination with immune checkpoint inhibitors, have shown good safety profiles and antitumor activities in patients with advanced tumors, including those with low PD-L1 expressing tumors or who are resistant/refractory to anti-PD-(L)1. These observations implicate potentially broad clinical applications of adenosine A2a receptor antagonists to the treatment of solid tumors and in immuno-oncology combination 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, December 11, 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.