CStone Pharmaceuticals

基石藥業

(Incorporated in the Cayman Islands with limited liability)

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VOLUNTARY ANNOUNCEMENT

CSTONE AND BLUEPRINT MEDICINES INITIATE PHASE 1B/2 CLINICAL TRIAL OF FISOGATINIB IN COMBINATION WITH CS1001 FOR PATIENTS WITH HEPATOCELLULAR CARCINOMA

CStone Pharmaceuticals (the "**Company**" or "**CStone**") and Blueprint Medicines Corporation (NASDAQ: BPMC) ("**Blueprint Medicines**"), a precision therapy company focused on genomically-defined cancers, rare diseases and cancer immunotherapy, jointly announce the dosing of the first patient in a Phase 1b/2 trial evaluating fisogatinib in combination with CS1001 for the treatment of locally advanced or metastatic hepatocellular carcinoma ("**HCC**"). The study will be conducted across multiple clinical sites in China.

This trial will assess the potential for two complementary treatment approaches – precision therapy and immuno-oncology therapy – to enhance anti-tumor activity in locally advanced or metastatic HCC. Developed by Blueprint Medicines, fisogatinib is an investigational, potent and highly selective inhibitor of fibroblast growth factor receptor 4 ("**FGFR4**") in the treatment of advanced FGFR4-driven HCC. CS1001 is an investigational anti-PD-L1 monoclonal antibody being developed by CStone for multiple types of tumors. Preclinical studies have shown that treatment with fisogatinib stimulated T-cell to be infiltrated into the tumor microenvironment, suggesting that combining fisogatinib with an anti-PD-L1 inhibitor may enhance anti-tumor activity in patients with FGFR4-driven HCC.

Blueprint Medicines and CStone have entered into an exclusive collaboration and license agreement for the development and commercialization of three drug candidates, including fisogatinib, in Mainland China, Hong Kong, Macau and Taiwan. Blueprint Medicines retains the rights to develop and commercialize these three drug candidates in the rest of the world.

Dr. Andy Boral, chief medical officer of Blueprint Medicines, commented: "Collaboration with CStone has rapidly expanded our global development activities into the Asia-Pacific region, where CStone has rich experience in working with local academic institutions and regulatory authorities. We look forward to advancing our fisogatinib clinical program by conducting a Phase 1b/2 trial in China, where the incidence of HCC is disproportionately high. Because fisogatinib has exquisite selectivity against an oncogenic driver, we believe this investigational treatment is well-positioned for combination therapy. Also, fisogatinib and CStone's anti-PD-L1 inhibitor CS1001 have complementary mechanisms of action that may offer better clinical effects in patients with HCC."

Dr. Archie Tse, chief translational medicine officer of CStone, commented: "Advanced HCC is a particularly aggressive disease and China is currently faced with enormous challenges in the treatment of advanced HCC due to limited effective treatment options and poor prognosis in HCC patients at advanced stages. CStone is committed to addressing unmet clinical needs through exploring the possibility of combination regimens against complex cancers such as HCC. We are pleased that we have successfully achieved the dosing of the first patient in the Phase 1b/2 trial of fisogatinib in combination with CS1001, which hopefully will benefit advanced HCC patients. CS1001 is one of CStone's backbone immuno-oncology assets, and multiple combination therapy trials with CS1001 have been carried out."

A Phase 1 dose-escalation study of CS1001 has been completed in China. Phase 1 data published at the 22nd Annual Meeting of the Chinese Society of Clinical Oncology have demonstrated sustained clinical effects from CS1001 in multiple types of tumors, including gastric cancer, esophageal cancer and microsatellite instability high/deficient mismatch repair solid tumors. Pooled safety data of CS1001 released at the European Society of Medical Oncology 2019 Congress showed that CS1001 had an overall promising safety and tolerability profile. These data indicate CS1001's therapeutic potential in multiple types of tumors, including HCC.

About HCC

Liver cancer is the second largest leading cause of cancer-related deaths worldwide, with HCC accounting for the largest proportion. The highest incidence of HCC occurs in regions with endemic hepatitis B virus, including Southeast Asia and sub-Saharan Africa. Nearly half of the world's new HCC cases are diagnosed in China. Treatment options for patients with advanced HCC are limited, with currently approved therapies providing time to progression of three to seven months and an overall survival of nine to 13 months. FGF19 is the ligand that activates FGFR4, a receptor that promotes hepatocyte proliferation and regulates bile acid homeostasis in the liver. Blueprint Medicines estimates that approximately 30 percent of patients with HCC have tumors with aberrantly activated FGF19/FGFR4 signaling.

About the Phase 1b/2 Clinical Trial of Fisogatinib in Combination with CS1001

The Phase 1b/2 clinical trial is an open-label study of fisogatinib in combination with CS1001 for the treatment of patients with locally advanced or metastatic HCC. The trial consists of two parts: a dose-escalation phase and a dose-expansion phase. The dose-escalation phase was designed to evaluate two doses of fisogatinib in combination with a fixed dose of CS1001. The objective of the dose-escalation phase is to identify the recommended Phase 2 dose that will be used in the dose-expansion phase.

Objectives of the trial include evaluating the safety, tolerability, pharmacokinetics and anti-tumor activity of the combination regimen. FGF19 expression will be determined at a central laboratory. The trial is designed

to enroll approximately 50 patients across multiple sites in China. For additional information on the trial, please visit clinicaltrials.gov.

About Fisogatinib

Fisogatinib is an orally available, potent, irreversible inhibitor of FGFR4. Fisogatinib was specifically designed by Blueprint Medicines to inhibit FGFR4 with exquisite selectivity, thereby sparing the paralogs FGFR1, FGFR2 and FGFR3. Preclinical data has validated FGFR4 as an oncogenic driver for a subset of patients with advanced HCC.

Blueprint Medicines is developing fisogatinib, an investigational medicine, for the treatment of patients with FGFR4-activated HCC. The United States Food and Drug Administration has granted orphan drug designation to fisogatinib for the treatment of HCC.

About CS1001

CS1001 is an investigational monoclonal antibody directed against PD-L1 being developed by CStone. Authorized by a company based in the United States, Ligand Pharmaceuticals Inc. (NASDAQ: LGND), CS1001 is developed by the OMT transgenic animal platform, which can generate fully human antibodies in one step. As a fully human, full-length anti-PD-L1 monoclonal antibody, CS1001 mirrors natural G-type immune globulin 4 (IgG4) human antibody, which can reduce the risk of immunogenicity and potential toxicities in patients, potentially representing a unique advantage over similar drugs.

CS1001 has completed a Phase I dose-escalation study in China, in which CS1001 showed good tolerability and produced sustained clinical benefits during Phase Ia and Ib stages of the study in multiple indications.

CS1001 is being investigated in a number of ongoing clinical trials, including one Phase I bridging study in the United States. In China, its clinical program includes one multi-arm Phase Ib study, two pivotal Phase II studies and three Phase III studies for several types of tumors.

About Blueprint Medicines

Blueprint Medicines is a precision therapy company with a focus on genomically-defined cancers, rare diseases and cancer immunotherapy. Blueprint Medicines is currently advancing three investigational medicines in clinical development, along with multiple research programs.

About CStone

CStone is a biopharmaceutical company focused on developing and commercializing innovative immuno-oncology and precision medicines to address the unmet medical needs of cancer patients in 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, five late-stage candidates are at 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 oncology therapies to cancer patients worldwide.

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

Blueprint Medicines - Cautionary Note Regarding Forward-Looking Statements

This announcement contains forward-looking statements within the meaning of the *Private Securities Litigation Reform Act* of 1995, as amended, including, without limitation, statements regarding plans and timelines for the development of fisogatinib, including the timing, design, implementation, enrollment, plans and announcement of results regarding Blueprint Medicines' ongoing and planned clinical trials for fisogatinib; the potential benefits of fisogatinib and CS1001 in treating patients with locally advanced or metastatic HCC either as monotherapy or combination therapy; and Blueprint Medicines' strategy, goals and anticipated milestones, business plans and focus. The words "may," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "project," "potential," "continue," "target" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements in this announcement are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this announcement, including, without limitation, risks and uncertainties related to the delay of any current or planned clinical trials or the development of Blueprint Medicines' drug candidates; Blueprint Medicines' ability to successfully demonstrate the safety and efficacy of its drug candidates and gain approval of its drug candidates on a timely basis, if at all; the preclinical and clinical results for Blueprint Medicines' drug candidates, which may not support further development of such drug candidates; actions of regulatory agencies, which may affect the initiation, timing and progress of clinical trials; Blueprint Medicines' ability to develop and commercialize companion diagnostic tests for its current and future drug candidates; and the success of Blueprint Medicines' current and future collaborations and licensing arrangement, including its collaboration with CStone Pharmaceuticals. These and other risks and uncertainties are described in greater detail in the section entitled "Risk Factors" in Blueprint Medicines' filings with the Securities and Exchange Commission ("**SEC**"), including Blueprint Medicines' most recent Quarterly Report on Form 10-Q and any other filings that Blueprint Medicines has made or may make with the SEC in the future. Any forward-looking statements contained in this announcement represent our views only as of the date hereof and should not be relied upon as representing its views as of any subsequent date. Except as required by law, we explicitly disclaim any obligation to update any forward-looking statements.

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

Suzhou, People's Republic of China, January 6, 2020

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.