CStone Pharmaceuticals

基石藥業

(Incorporated in the Cayman Islands with limited liability)

(**Stock Code: 2616**)

INSIDE INFORMATION ANNOUNCEMENT
CSTONE ANNOUNCES EUROPEAN COMMISSION APPROVAL OF SUGEMALIMAB (CEJEMLY®) AS FIRST-LINE TREATMENT FOR NON-SMALL CELL LUNG CANCER

This announcement is issued pursuant to Rule 13.09 of the Rules Governing the Listing of the Securities on The Stock Exchange of Hong Kong Limited (the "**Listing Rules**") and the inside information provision (as defined in the Listing Rules) under Part XIVA of the Securities and Futures Ordinance (Cap. 571 of the Laws of Hong Kong).

CStone Pharmaceuticals (the "**Company**" or "**CStone**") is pleased to announce that the European Commission (EC) has approved sugemalimab (Brand name: Cejemly®) in combination with platinum-based chemotherapy is indicated for the first-line treatment of adults patients with metastatic non-small-cell lung cancer (NSCLC) with no sensitizing EGFR mutations, or ALK, ROS1 or RET genomic tumor aberrations. Sugemalimab has become the first anti-PD-L1 monoclonal antibody (mAb) approved in Europe in combination with chemotherapy as first-line treatment for both squamous and non-squamous NSCLC, making CStone the first innovative biopharmaceutical company to successfully bring a China domestic anti-PD-L1 mAb to the international market.

Key Highlights

- Sugemalimab becomes the world's first anti-PD-L1 monoclonal antibody (mAb) approved in Europe for first-line treatment of both squamous and non-squamous non-small cell lung cancer (NSCLC), also marking the first successful international approval of a China domestic anti-PD-L1 mAb.
- The European Commission (EC) approval is based on the results of GEMSTONE-302 Phase III trial, which demonstrated that sugemalimab in combination with chemotherapy significantly prolongs progression-free survival and overall survival in treatment-naive patients with metastatic NSCLC.

- CStone has entered into a strategic commercialization partnership with Ewopharma for sugemalimab in Central & Eastern Europe and Switzerland.
- Discussions for commercial partnerships in including Western Europe, Latin America, the Middle East, Southeast Asia, etc., are progressing well and are expected to conclude soon.
- CStone is actively preparing to submit additional Marketing Authorization Applications (MAAs) to European Medicines Agency (EMA) for new indications, including Stage III NSCLC, first-line Gastric Cancer, first-line Esophageal Cancer, and relapsed/refractory extranodal natural killer/T-cell lymphoma (r/r ENKTL).

The EC approval is primarily based on the results of the GEMSTONE-302, a multicenter, randomized, double-blind phase 3 study. The study demonstrated that sugemalimab in combination with chemotherapy significantly prolongs progression-free survival and overall survival compared to placebo combined with chemotherapy in treatment-naïve patients with metastatic NSCLC. The study results have been published in The Lancet Oncology and Nature Cancer, and have been presented at multiple international academic conferences. Additionally, long-term treatment and survival data from the GEMSTONE-302 study will be presented in a poster session (#1318P) at the 2024 European Society of Medical Oncology (ESMO) Annual Meeting.

Dr. Jason Yang ("**Dr. Yang**"), CEO, President of R&D and Executive Director of the Board at CStone, said, "We are extremely excited by EC's approval, which represents a major milestone in CStone's journey towards becoming a leading global company dedicated to eradicating cancer. Sugemalimab has not only become CStone's first independently-developed product to receive overseas marketing authorization but it is also the world's first anti-PD-L1 mAb to receive regulatory approval in Europe in combination with chemotherapy as first-line treatment for both squamous and non-squamous NSCLC. This achievement reflects the international regulatory authorities' recognition of our high-quality R&D and manufacturing standards, and it infuses new momentum into our globalization strategy. We are humbled by level of interest in sugemalimab commercial partnership from companies around the world which only signifies the large unmet need in this class for newer and better drugs. We are actively engaging with potential partners in Western Europe, Latin America, the Middle East and Africa, Southeast Asia, and Canada and we expect to announce the completion of these deals soon."

Dr. Yang recalled, " In early May 2023, CStone regained the development and commercialization rights for sugemalimab outside Greater China. Since then, the entire company acted swiftly, with all departments working in coordination to thoroughly review regulatory and submission documents, assess their completeness, perform gap analyses, screened and replaced numerous suppliers, and completed the applicant transfer and submission dossier updates. Within just over a month of fully taking over the MAA, the EMA issued a critical Day 120 List containing 194 outstanding questions. After analyzing a vast amount of data, our team submitted a detailed response to the EMA within the required timeframe. By Day 180, nearly 90% of the responses had been accepted by EMA's Reviewers, and the remaining ones were further clarified and eventually agreed by the Reviewers. During the review period, we also successfully passed the EMA's routine Good Manufacturing Practice of Medical Products (GMP) inspection of the manufacturing plant, and Good Clinical Practice (GCP) inspections of two study centers and a Contract Research Organization (CRO), which lasted a total of three weeks. Subsequently, at the end of May this year, we received a positive opinion from the EMA's Committee for Medicinal Products for Human Use (CHMP) recommending approval of sugemalimab. I truly believe that this journey, marked by numerous challenges, reflects the CStone team's resilience and innovative spirit."

Dr. Yang emphasized, "The international approval and commercialization of sugemalimab mark a significant milestone in CStone's Pipeline 1.0 strategy, demonstrating our success in developing best-in-class immuno-oncology drugs for monotherapy and as a foundation for combination therapies. In Pipeline 2.0, we have global rights for a range of highly promising candidates, either in international multicenter clinical trials or approaching the clinical stage, with the potential to be first-in-class or best-in-class.

Additionally, we are actively exploring the combination of sugemalimab with other treatment modalities, such as antibody-drug conjugates (ADCs) and bi-/tri-specific antibodies, to enhance its clinical value as a backbone of cancer immunotherapy."

Dr. Yang added, "The seven-year journey of sugemalimab to becoming a first-line treatment for NSCLC in Europe and other cancers in China is a testament to the extensive expertise of numerous Chinese oncology specialists. It also reflects the dedication of patients who participated in sugemalimab clinical trials and the relentless efforts of our R&D team over the years. The remarkable results of the GEMSTONE-302 study provide definitive scientific evidence supporting the use of sugemalimab in combination with chemotherapy as a first-line standard therapy for Stage IV NSCLC. We are honored and humbled that this 'Chinese innovative solution' may significantly improve outcomes for lung cancer patients worldwide, offering both longer survival and a better quality of life."

Meanwhile, CStone is actively preparing to submit additional Marketing Authorization Applications (MAAs) to EMA for additional indications, including Stage III NSCLC, first-line Gastric Cancer, first-line Esophageal Cancer, and relapsed/refractory extranodal natural killer/T-cell lymphoma (r/r ENKTL).

About Lung Cancer

In 2020, lung cancer was the third most diagnosed cancer in Europe and the leading cause of cancer-related mortality, accounting for one fifth of cancer deaths. Approximately fifty to seventy percent of lung cancer cases in Europe are diagnosed in Stage IV. Globally, it is estimated that NSCLC accounts for approximately 85% of all lung cancers.

About Sugemalimab

The anti-PD-L1 monoclonal antibody sugemalimab was developed by CStone using OmniRat® transgenic animal platform, which allows creation of fully human antibodies in one step. Sugemalimab is a fully human, full-length anti-PD-L1 immunoglobulin G4 (IgG4) monoclonal antibody, which may reduce the risk of immunogenicity and toxicity for patients, a unique advantage over similar drugs. Sugemalimab's unique molecular design enables a dual mechanism of action that not only blocks PD-1/PD-L1 interaction, but also induces antibody dependent cellular phagocytosis (ADCP) by cross-linking PD-L1 expressing tumor cells with tumor associated macrophages (TAMs) without harming Effector T-cells. This differentiation has resulted in potentially best-in-class efficacy/safety across a variety of tumor types.

The National Medical Products Administration (NMPA) of China has approved sugemalimab for five indications:

- In combination with chemotherapy as first-line treatment of patients with metastatic squamous and non-squamous NSCLC;
- For the treatment of patients with unresectable Stage III NSCLC whose disease has not progressed following concurrent or sequential platinum-based chemoradiotherapy;
- For the treatment of patients with relapsed or refractory extranodal NK/T-cell lymphoma;
- In combination with fluorouracil and platinum-based chemotherapy as first-line treatment of patients with unresectable locally advanced, recurrent or metastatic ESCC; and
- In combination with fluoropyrimidine- and platinum-containing chemotherapy as first-line treatment for unresectable locally advanced or metastatic gastric or gastroesophageal junction (G/GEJ) adenocarcinoma with a PD-L1 expression (Combined Positive Score [CPS] ≥5).

The European Commission (EC) has approved sugemalimab (brand name: Cejemly®) in combination with chemotherapy for the first-line treatment of patients with metastatic NSCLC.

The Medicines and Healthcare products Regulatory Agency (MHRA) in the United Kingdom has accepted the marketing authorization application for sugemalimab in combination with chemotherapy for first-line treatment of metastatic NSCLC. The application is currently under review

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 worldwide, the company has made significant strides since its inception. To date, the company has successfully launched 4 innovative drugs and secured approvals for 15 New Drug Applications (NDAs) covering 9 indications. The company's pipeline is balanced by 12 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 researches 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 SUGEMALIMAB 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, July 26, 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.