CStone Pharmaceuticals
基石藥業
(Incorporated in the Cayman Islands with limited liability)
(Stock Code: 2616)

VOLUNTARY ANNOUNCEMENT
CSTONE ANNOUNCES THE ACCEPTANCE OF RET INHIBITOR GAVRETO® (PRALSETINIB) MANUFACTURING LOCALIZATION APPLICATION BY CENTER FOR DRUG EVALUATION OF CHINA NMPA

CStone Pharmaceuticals (the "**Company**" or "**CStone**") is pleased to announce the acceptance of the manufacturing localization application for the RET inhibitor GAVRETO® (pralsetinib) by the Center for Drug Evaluation of China National Medical Products Administration (NMPA). It is also worth noting that the manufacturing localization application for the precision therapy – AYVAKIT® (avapritinib) was accepted in June 2023 and is currently under review, with CStone anticipating domestic supply in 2024.

Dr. Jason Yang, CEO and executive director of CStone, said, "The acceptance of the manufacturing localization applications for both GAVRETO and AYVAKIT signifies a pivotal moment for CStone towards the goal of domestic manufacturing. We are committed to expediting the domestic manufacturing processes of both products with urgency. This endeavor holds the promise of not only over 50% reductions in drug manufacturing cost but also significantly enhances product supply availability and flexibility, thereby more effectively catering to the demand of the domestic market and extending the benefits to more patients in China. These endeavors will also amplify the competitiveness of GAVRETO and AYVAKIT within the Chinese marketplace.

Recently, the government has implemented a range of supportive measures to encourage domestic drug manufacturing, including simplifying application procedures, providing clarity on regulatory pathways, and reducing the complexity of documentation requirements. The NMPA's recent draft regulation suggests that applications for localized manufacturing may receive priority review. As a pioneer in this field, we anticipate that these regulatory changes will expedite the approval and launch of domestically manufactured drugs allowing CStone to quickly expand into additional indication for GAVRETO and AYVAKIT."

The manufacturing localization application of GAVRETO is the result of collaborative efforts between

CStone, the foreign Marketing Authorization Holder (MAH), commercial partners, and domestic contract manufacturing organizations. These efforts facilitated expedited technical transfer, including process optimizations, and commercial scale validation for both active pharmaceutical ingredient (API) and formulations of pralsetinib. Consistent manufacturing processes and quality standards have been applied to the domestically manufactured products as compared to the imported products, with human bioequivalence has been confirmed through a clinical study. From a company system perspective, CStone, as the MAH, has established commercial manufacturing capability by implementing a quality management system compliant with the latest national laws and regulations, meeting the requirements for MAH contract manufacturing and Good Manufacturing Practice (GMP).

GAVRETO was the first targeted RET inhibitor approved by the China NMPA and was initially approved in March 2021 for the treatment of locally advanced or metastatic RET fusion-positive non-small cell lung cancer (NSCLC) after platinum-based chemotherapy. It was also granted approval by the China NMPA as the first selective RET inhibitor for the treatment of advanced RET-altered thyroid cancer in March 2022. In June 2023, the China NMPA approved the supplemental new drug application (sNDA) of GAVRETO for the first-line treatment of adults with locally advanced or metastatic RET fusion-positive NSCLC. To date, GAVRETO has obtained full approvals for first- and second-line indications in RET fusion-positive NSCLC in both the United States and Mainland China, also covering RET-altered thyroid cancer.

Data from the global phase 1/2 ARROW study showed that GAVRETO exhibited potent and durable anti-tumor activity in patients with advanced RET fusion-positive NSCLC, RET-mutant medullary thyroid cancer (MTC) and RET fusion-positive thyroid cancer. Overall safety was generally manageable, with no new safety signals detected. Additionally, GAVRETO demonstrated broad and persistent antitumor activity with manageable safety profiles in patients with various RET fusion-positive solid tumors, including pancreatic cancer and cholangiocarcinoma. These results have been published in top-tier international medical journals such as Lancet Oncology, Lancet Diabetes & Endocrinology, Nature Medicine, Annals of Oncology, and Thyroid.

In addition, the efficacy and safety results of GAVRETO in Chinese patients with RET-mutant MTC were published in the highly cited endocrine and oncology journal Endocrine-Related Cancer in February 2024. Following the prior publication of GAVRETO data in RET fusion-positive NSCLC in Chinese patients in June 2023 in Cancer, this publication marks another recognition from the international academic society, highlighting the significant academic and clinical value of GAVRETO.

GAVRETO and AYVAKIT were discovered by CStone's partner, Blueprint Medicines. CStone has an exclusive collaboration and license agreement with Blueprint Medicines for the development and commercialization of GAVRETO and AYVAKIT in Greater China, which encompasses Mainland China, Hong Kong, Macau and Taiwan. In November 2023, CStone announced an exclusive agreement with Shanghai Allist Pharmaceuticals Co., Ltd.to commercialize GAVRETO in Mainland China.

About GAVRETO (pralsetinib)

GAVRETO is a once-daily oral targeted therapy approved by the China NMPA for the treatment of adults with locally advanced or metastatic RET fusion-positive NSCLC, adult and pediatric patients 12 years of age and older with advanced or metastatic RET-mutant MTC who requires systemic therapy, and adult and pediatric patients 12 years of age and older with advanced or metastatic RET fusion-positive thyroid cancer who requires systemic therapy and radioactive iodine-refractory (if radioactive iodine treatment is appropriate).

GAVRETO has been approved in Hong Kong and Mainland China for the treatment of adult patients with RET fusion-positive metastatic NSCLC, and in Taiwan and Mainland China for the treatment of adult

patients with locally advanced or metastatic RET fusion-positive NSCLC, advanced or metastatic RET-mutant MTC who require systemic therapy, and advanced or metastatic RET fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate).

GAVRETO is approved by the U.S. Food and Drug Administration (FDA) for the treatment of:

- Adult patients with metastatic RET fusion-positive NSCLC as detected by an FDA approved test
- Adult and pediatric patients 12 years of age and older with advanced or metastatic RET fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate). *

This indication is approved under accelerated approval based on objective response rate (ORR) and duration of response (DOR). Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

About AYVAKIT (avapritinib)

AYVAKIT is a precision therapy approved by the China NMPA for the treatment of adults with unresectable or metastatic gastrointestinal stromal tumor (GIST) harboring the PDGFRA exon 18 mutation, including PDGFRA D842V mutations. AYVAKIT was approved by the Department of Health (DOH), Hong Kong, Mainland China, and Taiwan Food and Drug Administration (TFDA) for the treatment of adults with unresectable or metastatic GIST harboring a PDGFRA D842V mutation.

AYVAKIT is approved by the U.S. Food and Drug Administration (FDA) for the treatment of three indications: adults with indolent systemic mastocytosis (ISM), adults with advanced systemic mastocytosis (advanced SM), including aggressive SM (ASM), SM with an associated hematological neoplasm (SM-AHN) and mast cell leukemia (MCL), and adults with unresectable or metastatic GIST harboring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations.

About CStone

CStone (HKEX: 2616) is a biopharmaceutical company focused on research, development, and commercialization of 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 management team with extensive experience in innovative drug development, clinical research, and commercialization. The company has built an oncology-focused pipeline of 12 drug candidates with a strategic emphasis on immuno-oncology combination therapies. Since inception, CStone has obtained 14 NDA approvals for various drugs (including ivosidenib). Multiple late-stage drug candidates are now under pivotal clinical trials or registration. CStone's vision is to bring innovative oncology therapies to cancer patients worldwide.

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 GAVRETO AND AYVAKIT 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, April 9th, 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.