HUTCHMED (China) Limited

和黃醫藥（中國）有限公司

(Incorporated in the Cayman Islands with limited liability)

(Stock Code: 13)

VOLUNTARY ANNOUNCEMENT

HUTCHMED Highlights Publication of Phase III FRUTIGA Results in Nature Medicine

Updated subgroup efficacy and quality of life data were also presented on June 1 at ASCO 2024

HUTCHMED (China) Limited ("HUTCHMED") today announces that results from FRUTIGA, HUTCHMED's Phase III trial of fruquintinib in combination with paclitaxel for the treatment of second-line advanced gastric cancer in China, were published in *Nature Medicine*. Updated efficacy data in key subgroups and data on quality of life (QoL) within this publication were also presented on June 1 at the American Society of Clinical Oncology ("ASCO") 2024 Annual Meeting.

Fruquintinib is a selective oral inhibitor of vascular endothelial growth factor receptors ("VEGFRs") 1, 2 and 3. It works as an anti-cancer therapy by blocking tumor angiogenesis, a proliferation of blood vessels that is critical for cancer growth. The VEGFR pathway plays a key role in the pathogenesis of gastric cancer, which is the fifth most common malignant cancer worldwide, with 1.1 million new cases per year[1]. The FRUTIGA trial results published by *Nature Medicine* suggest that fruquintinib could be another effective treatment option for gastric cancer patients.

FRUTIGA was a 1:1 randomized, double-blind, Phase III study conducted across 35 sites in China (NCT03223376). It evaluated fruquintinib in combination with paclitaxel chemotherapy, compared with paclitaxel monotherapy, for second-line treatment in 703 patients with advanced gastric or gastroesophageal junction adenocarcinoma. The study was declared positive due to a statistically significant improvement in progression-free survival ("PFS"), one of two dual primary endpoints. Median PFS for patients who received fruquintinib plus paclitaxel was 5.6 months, compared to 2.7 months for those who received paclitaxel monotherapy (stratified hazard ratio ["HR"] = 0.569; $p < 0.0001$). An improvement was also observed in the dual primary endpoint of median overall survival ("OS"), (9.6 months vs. 8.4 months) but this was not statistically significant. Fruquintinib plus paclitaxel demonstrated statistically significant improvements in multiple other endpoints including objective response rate ("ORR"), disease control rate (DCR) and duration of response (DoR). It was well tolerated, with a safety profile consistent with expectations and previously reported studies.[2]

In further analysis of key subgroups presented at ASCO, PFS and OS results were consistent with the primary analysis compared to the intention-to-treat (ITT) population. There was a clear PFS benefit observed for fruquintinib plus paclitaxel in the majority of subgroups, with particular benefit in both PFS and OS in the intestinal-type and lymph node metastasis subgroups. An exploratory post-hoc analysis for patients with lymph node metastasis revealed superior benefits of fruquintinib versus placebo in PFS, OS, ORR, disease control rate and duration of response. A possible mechanism for this effect is fruquintinib's potent inhibition of VEGFR-3, which is closely linked to lymph node metastasis and tumor invasion. Further analysis of patient-reported quality of life ("QoL") revealed no adverse impact on QoL at end of treatment compared to current standard of care. Together, these additional findings, alongside previously reported results, support fruquintinib plus paclitaxel as another treatment option in this indication.

Key results from FRUTIGA were previously disclosed at the American Society of Clinical Oncology (ASCO) Plenary Series Session on February 6, 2024, with the full presentation available here.[3]

Fruquintinib is approved in China and the United States for the treatment of certain patients with metastatic colorectal cancer ("CRC"). A New Drug Application ("NDA") for fruquintinib in combination with paclitaxel for the treatment of second-line advanced gastric or gastroesophageal junction adenocarcinoma in China was accepted for review by the China National Medical Products Administration (NMPA) in April 2023.

About Gastric Cancer

Gastric cancer is a cancer that starts in the stomach. It is the fifth most common cancer worldwide in 2020. It was estimated to have caused approximately 770,000 deaths worldwide.[4] In China, it was estimated that over 478,000 people were diagnosed with gastric cancer, and approximately 374,000 people died from gastric cancer.[5]

About Fruquintinib

Fruquintinib is a selective oral inhibitor of VEGFR-1, -2 and -3. VEGFR inhibitors play a pivotal role in inhibiting tumor angiogenesis. Fruquintinib was designed to have enhanced selectivity that limits off-target kinase activity, allowing for high drug exposure, sustained target inhibition, and flexibility for its potential use as part of combination therapy. Fruquintinib has demonstrated a manageable safety profile and is being investigated in combinations with other anti-cancer therapies.

About Fruquintinib Approval in China

In China, fruquintinib is co-developed and co-marketed by HUTCHMED and Eli Lilly and Company under the brand name ELUNATE®. It was included in the China National Reimbursement Drug List (NRDL) in January 2020. The approval was based on data from the FRESCO study, a Phase III pivotal registration trial of fruquintinib in 416 patients with metastatic CRC in China, which were published in the Journal of the American Medical Association, *JAMA*. Since its launch in China and as of mid-2023, more than 80,000 colorectal cancer patients have been treated with fruquintinib.

About Fruquintinib Approval in the U.S.

Takeda has the exclusive worldwide license to further develop, commercialize, and manufacture fruquintinib outside of mainland China, Hong Kong and Macau. Fruquintinib received approval in the U.S. in November 2023, where it is marketed by Takeda under the brand name FRUZAQLA®. The approval was based on data from two large, randomized, controlled Phase III trials: the multi-regional FRESCO-2 trial, data from which were published in *The Lancet*, along with the FRESCO trial conducted in China, showing consistent benefit among a total of 734 patients treated with fruquintinib. Safety profiles were consistent across trials. Please see FRUZAQLA® full Prescribing Information here.

About HUTCHMED

HUTCHMED (Nasdaq/AIM:HCM; HKEX:13) is an innovative, commercial-stage, biopharmaceutical company. It is committed to the discovery and global development and commercialization of targeted therapies and immunotherapies for the treatment of cancer and immunological diseases. It has approximately 5,000 personnel across all its companies, at the center of which is a team of about 1,800 in oncology/immunology. Since inception it has focused on bringing cancer drug candidates from in-house discovery to patients around the world, with its first three medicines marketed in China, the first of which is also marketed in the U.S. For more information, please visit: www.hutch-med.com or follow us on LinkedIn.

Forward-Looking Statements

This announcement contains forward-looking statements within the meaning of the "safe harbor" provisions of the U.S. Private Securities Litigation Reform Act of 1995. These forward-looking statements reflect HUTCHMED's current expectations regarding future events, including its expectations regarding the therapeutic potential of fruquintinib for the treatment of patients with advanced gastric cancer and the further clinical development of fruquintinib in this and other indications. Forward-looking statements involve risks and uncertainties. Such risks and uncertainties include, among other things, assumptions regarding the sufficiency of clinical data to support NDA approval of fruquintinib for the treatment of patients with advanced gastric cancer in China, the U.S., Europe, Japan, Australia or other jurisdictions, its potential to gain expeditious approvals from regulatory authorities, the safety profile of fruquintinib, HUTCHMED's ability to fund, implement and complete its further clinical development and commercialization plans for fruquintinib, and the timing of these events. In addition, as certain studies rely on the use of other drug products such as paclitaxel, tislelizumab and sintilimab as combination therapeutics with fruquintinib, such risks and uncertainties include assumptions regarding the safety, efficacy, supply and continued regulatory approval of these therapeutics. Existing and prospective investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. For further discussion of these and other risks, see HUTCHMED's filings with the U.S. Securities and Exchange Commission, on AIM and on The Stock Exchange of Hong Kong Limited. HUTCHMED undertakes no obligation to update or revise the information contained in this announcement, whether as a result of new information, future events or circumstances or otherwise.

Medical Information

This announcement contains information about products that may not be available in all countries, or may be available under different trademarks, for different indications, in different dosages, or in different strengths. Nothing contained herein should be considered a solicitation, promotion or advertisement for any prescription drugs including the ones under development.

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[1] World Health Organization. GLOBOCAN 2020. Population fact sheets. China, https://gco.iarc.fr/today/data/factsheets/populations/160-china-fact-sheets.pdf (2020).

[2] Wang F, et al. Fruquintinib plus paclitaxel versus placebo plus paclitaxel as second-line therapy for advanced gastric or gastro-esophageal junction adenocarcinoma (FRUTIGA): a randomized, multicenter, double-blind, placebo-controlled, phase 3 study [published online ahead of print, 2024 Jun 1]. *Nat Med*. 2024. DOI: 10.1038/s41591-024-02989-6.

[3] Xu RH, et al., Fruquintinib plus paclitaxel versus paclitaxel as second-line therapy for patients with advanced gastric or gastroesophageal junction adenocarcinoma (FRUTIGA): A randomized, multicenter, double-blind, placebo-controlled, phase 3 study. *J Clin Oncol*. 2024;42, 438780-438780. DOI: 10.1200/JCO.2024.42.36_suppl.438780.

[4] The Global Cancer Observatory, Stomach Cancer Fact Sheet. Accessed April 6, 2023.

[5] The Global Cancer Observatory, China Fact Sheet. Accessed April 6, 2023.

By Order of the Board

Edith Shih
Non-executive Director and Company Secretary

Hong Kong, June 3, 2024

As at the date of this announcement, the Directors of the Company are:

Chairman and Non-executive Director:
Dr Dan ELDAR

Executive Directors:
Dr Weiguo SU
(Chief Executive Officer and Chief Scientific Officer)
Mr CHENG Chig Fung, Johnny
(Chief Financial Officer)

Non-executive Directors:
Ms Edith SHIH
Ms Ling YANG

Independent Non-executive Directors:
Mr Paul Rutherford CARTER
(Senior Independent Director)
Dr Renu BHATIA
Mr Graeme Allan JACK
Professor MOK Shu Kam, Tony