HUTCHMED Provides Update on Fruquintinib for Second-Line Gastric Cancer in China

Hong Kong, Shanghai & Florham Park, NJ — Friday, August 30, 2024: HUTCHMED (China) Limited ("HUTCHMED") (Nasdaq/AIM:HCM; HKEX:13) today announces that it has voluntarily withdrawn its supplemental New Drug Application ("NDA") in China for fruquintinib in combination with paclitaxel for the treatment of second-line advanced gastric or gastroesophageal junction adenocarcinoma and will evaluate a new route forward. Following an additional internal review of the current data package, in light of recent discussions with the National Medical Products Administration of China ("NMPA"), HUTCHMED has determined that the submission is unlikely to support an approval in China at this time.

This supplemental NDA for fruquintinib was based on data from the Phase III FRUTIGA study, which was declared positive due to a statistically significant improvements in many clinically meaningful endpoints, including progression-free survival ("PFS"), which served as one of two primary endpoints. However, while an improvement was also observed in the second primary endpoint of median overall survival ("OS"), it was not statistically significant. Extensive subsequent analyses conducted indicate that, although the high and imbalanced proportion of patients receiving subsequent antitumor therapies confounded the OS effect, fruquintinib plus paclitaxel demonstrated meaningful clinical benefit and favorable OS trends through a variety of models. Furthermore, no new safety signals were observed, and fruquintinib plus paclitaxel showed a tolerable safety profile. However, it became clear from dialogue with the Centre for Drug Evaluation (CDE) of the NMPA and its external committee members that the current understanding and interpretation of the OS results could not serve as the basis of the supplemental NDA approval, and that further work needs to be undertaken.

Dr Weiguo Su, Chief Executive Officer and Chief Scientific Officer of HUTCHMED, commented, "Whilst disappointed by this outcome, we remain optimistic about the utility of fruquintinib in the treatment of gastric cancer. The data set from FRUTIGA demonstrates that fruquintinib plus paclitaxel could offer a promising new treatment option to certain patients in future, and we are driven to investigate this possibility thoroughly. We look forward to evaluating a path forward and would like to thank both the patients and principal investigators who took part in this study for contributing to a better understanding of this devastating disease."

Dr Rui-Hua Xu, Professor at the Department of Medical Oncology, Sun Yat-sen University Cancer Center, Guangzhou, added, "Gastric cancer is the fifth most common cancer worldwide and patients in China are currently underserved by available treatment options. Although the current data package would not support approval on this occasion, the Phase III study demonstrated clear benefits of this fruquintinib combination across many clinically meaningful endpoints and the team are committed to evaluating all options. Promising subgroup analyses are helping us to better understand how we can effectively combat this disease, and we remain hopeful that this study forms part of an important journey to a much-needed new therapy."

Fruquintinib is approved in China, the US and Europe for the treatment of previously-treated patients with metastatic colorectal cancer ("CRC"), and regulatory applications for this indication are progressing as expected in over a dozen jurisdictions. It works as an anti-cancer therapy by blocking tumor angiogenesis, a proliferation of blood vessels that is critical for cancer growth. It is a selective oral inhibitor of vascular endothelial growth factor receptors ("VEGFRs") 1, 2 and 3, and this pathway plays a key role in the pathogenesis of many solid tumors including gastric cancer.

An NDA in China for fruquintinib in combination with sintilimab in endometrial cancer was accepted with priority review status in April 2024, and a Phase III trial in China of fruquintinib in combination with sintilimab in renal cell carcinoma was fully enrolled in December 2023.

About the Phase III FRUTIGA Trial

FRUTIGA (NCT03223376) was a 1:1 randomized, double-blind, Phase III study conducted across 35 sites in China. 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.[1]

Results were published in *Nature Medicine* and presented at the ASCO 2024 Annual Meeting, concluding that fruquintinib plus paclitaxel could be a promising second-line treatment option for patients with advanced gastric or gastroesophageal adenocarcinoma, who have failed fluoropyrimidine- or platinum-containing chemotherapy.

About Gastric Cancer

Gastric cancer is a cancer that starts in the stomach. It is the fifth most common cancer worldwide in 2022. It was estimated to have caused approximately 660,000 deaths worldwide.[2] In China, it was estimated that over 359,000 people were diagnosed with gastric cancer, and approximately 260,000 people died from gastric cancer.[3]

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 the 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 for metastatic CRC in China

Fruquintinib is approved for marketing in China, where it is co-marketed by HUTCHMED and Lilly 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, fruquintinib has benefited over 100,000 patients in China.

About Takeda and Fruquintinib Approval for metastatic CRC outside China

Takeda has the exclusive worldwide license to further develop, commercialize, and manufacture fruquintinib outside of mainland China, Hong Kong and Macau. For the treatment of metastatic CRC, fruquintinib received approval in the US in November 2023 and in Europe in June 2024, where it is marketed by Takeda under the brand name FRUZAQLA®. The approvals were 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*, and the FRESCO trial conducted in China. The trials investigated fruquintinib plus best supportive care versus placebo plus best supportive care in patients with previously treated metastatic CRC. Both FRESCO and FRESCO-2 met their primary and key secondary efficacy endpoints and showed consistent benefit among a total of 734 patients treated with fruquintinib. Safety profiles were consistent across trials. Other regulatory applications for this indication are progressing as expected in Japan and in many other jurisdictions.

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 US and Europe. 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 US 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 US, 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. 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 US 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.

Inside Information

This announcement contains inside information for the purposes of Article 7 of Regulation (EU) No 596/2014 (as it forms part of retained EU law as defined in the European Union (Withdrawal) Act 2018).

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[1] 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.

[2] The Global Cancer Observatory, Stomach Cancer Fact Sheet. Accessed August 14, 2024.

[3] The Global Cancer Observatory, China Fact Sheet. Accessed August 14, 2024.