Press Release

HUTCHMED Initiates Rolling Submission of NDA to U.S. FDA for Fruquintinib for the Treatment of Refractory Colorectal Cancer

— Company plans to complete rolling submission to the U.S. in the first half of 2023, followed by filings in Europe and Japan —

— NDA is supported by global Phase III FRESCO-2 study conducted in the U.S., Europe, Japan and Australia —

— FRESCO-2 showed fruquintinib treatment reduced the risk of death by 34% in metastatic colorectal cancer (0.66 HR) —

Hong Kong, Shanghai & Florham Park, NJ — Monday, December 19, 2022: HUTCHMED (China) Limited ("HUTCHMED") (Nasdaq/AIM:HCM, HKEX:13) today announces that it has initiated the filing of a rolling submission of a New Drug Application ("NDA") to the U.S. Food and Drug Administration ("FDA") for fruquintinib, a highly selective and potent oral inhibitor of VEGFR-1, -2 and -3, for the treatment of refractory metastatic colorectal cancer ("CRC"). HUTCHMED plans to complete the NDA submission in the first half of 2023, to be followed by filing of a Marketing Authorization Application ("MAA") to the European Medicines Agency ("EMA") and an NDA to the Japan Pharmaceuticals and Medical Devices Agency ("PMDA").

The U.S. FDA granted Fast Track Designation for the development of fruquintinib for the treatment of patients with metastatic CRC in June 2020, enabling the company to submit sections of the NDA on a rolling basis. The NDA is supported by the global Phase III multi-regional clinical trial (MRCT) FRESCO-2 study conducted in the U.S., Europe, Japan and Australia that investigated fruquintinib plus best supportive care ("BSC") vs placebo plus BSC in patients with refractory metastatic CRC.

The FRESCO-2 results were recently presented at the European Society for Medical Oncology Congress 2022. The study demonstrated that treatment with fruquintinib resulted in a statistically significant and clinically meaningful increase in the primary endpoint of overall survival ("OS") and the key secondary endpoint of progression free survival ("PFS") compared to treatment with placebo. Specifically, the median OS was 7.4 months for the 461 patients treated with fruquintinib compared to 4.8 months for the 230 patients in the placebo group (hazard ratio ["HR"] 0.66; 95% confidence interval ["CI"] 0.55–0.80; p<0.001). The median PFS was 3.7 months for patients treated with fruquintinib compared to 1.8 months for patients in the placebo group (HR 0.32; 95% CI 0.27–0.39; p<0.001). The disease control rate ("DCR") was 55.5% in the fruquintinib group compared to 16.1% for patients in the placebo group. The safety profile of fruquintinib in FRESCO-2 was consistent with previously reported fruquintinib studies. Treatment related adverse events leading to discontinuation occurred in 20.4% of patients who received fruquintinib, compared to 21.1% of patients who received placebo.

"We are dedicated to executing on the next strategic steps in bringing fruquintinib to patients outside of China," said Dr. Weiguo Su, Executive Director, Chief Executive Officer and Chief Scientific Officer of HUTCHMED. "Colorectal cancer is one of the most common cancers worldwide, and over 50,000 people in the U.S. are estimated to die of colorectal cancer each year. Our U.S. NDA submission includes the successful multi-regional clinical trial, FRESCO-2, designed in consultation with the FDA, the EMA and the PMDA. The study showed a meaningful survival benefit and anti-tumor effect in patients treated with fruquintinib across patient populations, consistent with the pivotal Phase III FRESCO study supporting approval of fruquintinib for CRC in China. We look forward to submitting additional new drug applications in Europe and Japan next year."

Fruquintinib is approved in China under the brand name ELUNATE® for the treatment of patients with metastatic CRC who have been previously treated with fluoropyrimidine, oxaliplatin and irinotecan, including those who have previously received anti-VEGF therapy and/or anti-EGFR therapy (RAS wild type). It has been included in the China National Reimbursement Drug List ("NRDL") since January 2020. Approval in China is supported by the results of the FRESCO study, a Phase III pivotal trial of fruquintinib in 416 patients with metastatic CRC in China.

HUTCHMED retains all commercial rights to fruquintinib outside of China. In China, ELUNATE® is partnered with Eli Lilly and Company.

About CRC

CRC is a cancer that starts in either the colon or rectum. CRC is the third most common cancer worldwide, estimated to have caused more than 915,000 deaths in 2020.[1] In the U.S., an estimated 151,000 people will have been diagnosed with CRC and 53,000 people will have died from CRC in 2022.[2] In Europe, CRC is the second most common cancer, with an estimated 507,000 new cases and 240,000 deaths in 2020.[1] In Japan, CRC is the most common cancer, with an estimated 147,000 new cases and 59,000 deaths in 2020.[1]

About Fruquintinib

Fruquintinib is a highly selective and potent oral inhibitor of VEGFR-1, -2 and -3. VEGFR inhibitors play a pivotal role in blocking tumor angiogenesis. Fruquintinib was designed to improve kinase selectivity to minimize off-target toxicities, improve tolerability and provide more consistent target coverage. The generally good tolerability in patients to date, along with fruquintinib's low potential for drug-drug interaction based on preclinical assessment, suggests that it may also be highly suitable for combinations with other anti-cancer therapies.

About Fruquintinib Approval in China

CRC in China: Fruquintinib was approved for marketing by the China National Medical Products Administration ("NMPA") in September 2018 and commercially launched in China in November 2018 under the brand name ELUNATE®. It has been included in the NRDL since January 2020. ELUNATE® is indicated for the treatment of patients with metastatic CRC who have been previously treated with fluoropyrimidine, oxaliplatin and irinotecan, including those who have previously received anti-VEGF therapy and/or anti-EGFR therapy (RAS wild type). Results of the FRESCO study[3], a Phase III pivotal registration trial of fruquintinib in 416 patients with metastatic CRC in China, were published in *The Journal of the American Medical Association*, JAMA, in June 2018 (NCT02314819).

About Other Fruquintinib Developments

The safety and efficacy of fruquintinib for the following investigational uses have not been established and there is no guarantee that it will receive health authority approval or become commercially available in any country for the uses being investigated.

Gastric Cancer in China: The FRUTIGA study is a randomized, double-blind, Phase III study in China to evaluate fruquintinib combined with paclitaxel compared with paclitaxel monotherapy, for second-line treatment of advanced gastric cancer or GEJ adenocarcinoma (NCT03223376). Topline results were reported in November 2022. The trial met one of the primary endpoints of statistically significant improvement in PFS, which is clinically meaningful. The other primary endpoint of OS was not statistically significant per the pre-specified statistical plan, although there was a numerical improvement in median OS. Fruquintinib also demonstrated a statistically significant improvement in secondary endpoints including objective response rate (ORR), DCR, and improved duration of response (DoR). The safety profile of fruquintinib in FRUTIGA was consistent with previously reported studies. Full detailed results are subject to ongoing analysis and are expected to be disclosed at an upcoming scientific meeting. These results as well as further analyses will be shared with the China NMPA.

HUTCHMED is also developing fruquintinib for the treatment of multiple solid tumor cancers in combination with immunotherapies. Fruquintinib is being evaluated in combination with PD-1 monoclonal antibodies including tislelizumab (developed by BeiGene, Ltd) and sintilimab (developed by Innovent Biologics, Inc.) for the treatment of metastatic breast, endometrial and CRC in the U.S. (NCT04577963); gastric, CRC and NSCLC in China and Korea (initiated by BeiGene) (NCT04716634); and endometrial and other solid tumors in China (NCT03903705).

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 more than 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 into clinical studies around the world, with its first three oncology drugs now approved and marketed in China. For more information, please visit: www.hutch-med.com or follow us on LinkedIn.

Forward-Looking Statements

This press release 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 submission of an NDA for fruquintinib for the treatment of CRC with the FDA and the timing of such submission, the therapeutic potential of fruquintinib for the treatment of patients with CRC 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 timing and outcome of clinical studies and the sufficiency of clinical data to support NDA approval of fruquintinib for the treatment of patients with CRC or other indications in the U.S. or other jurisdictions such as the E.U. or Japan, its potential to gain approvals from regulatory authorities on an expedited basis or at all, the safety profile of fruquintinib, HUTCHMED's ability to fund, implement and complete its further clinical development and commercialization plans for fruquintinib, the timing of these events, and the impact of the COVID-19 pandemic on general economic, regulatory and political conditions. 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 press release, whether as a result of new information, future events or circumstances or otherwise.

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[1] The Global Cancer Observatory. Accessed December 12, 2022.
[2] SEER. Cancer Stat Facts: Colorectal Cancer. National Cancer Institute. https://seer.cancer.gov/statfacts/html/colorect.html. Accessed December 12, 2022.
[3] Li J, Qin S, Xu RH, et al. Effect of Fruquintinib vs Placebo on Overall Survival in Patients With Previously Treated Metastatic Colorectal Cancer: The FRESCO Randomized Clinical Trial. *JAMA*. 2018;319(24):2486-2496. doi:10.1001/jama.2018.7855.