HUTCHMED Announces that Fruquintinib Global Phase III FRESCO-2 Study Has Met Its Primary Endpoint in Metastatic Colorectal Cancer

— Trial met primary endpoint of overall survival and all secondary endpoints —

— Overall safety consistent with fruquintinib known profile —

— Plans for regulatory submissions underway in the U.S., Europe and Japan —

— Results to be submitted to an upcoming medical meeting —

Hong Kong, Shanghai & Florham Park, NJ — Monday, August 8, 2022: HUTCHMED (China) Limited ("HUTCHMED") (Nasdaq/AIM: HCM, HKEX: 13) today announces that the pivotal global Phase 3 FRESCO-2 trial evaluating the investigational use of fruquintinib met its primary endpoint of overall survival ("OS") in patients with advanced, refractory metastatic colorectal cancer ("CRC").

The FRESCO-2 study was a multi-regional clinical trial conducted in the U.S., Europe, Japan and Australia that investigated fruquintinib plus best supportive care ("BSC") vs placebo plus BSC in patients with metastatic CRC who had progressed on standard chemotherapy and relevant biologic agents and who had progressed on, or were intolerant to, TAS-102 and/or regorafenib. In addition to OS, a statistically-significant improvement in progression-free survival ("PFS"), a key secondary endpoint, was observed. The safety profile of fruquintinib in FRESCO-2 was consistent with previously reported studies. Full results will be submitted for presentation at an upcoming medical meeting.

HUTCHMED has been in communication with regulatory agencies globally regarding the FRESCO-2 trial design and conduct and will discuss these data with the agencies in the U.S., Europe and Japan with the intent to submit marketing authorization applications as soon as possible. The U.S. FDA granted Fast Track Designation for the development of fruquintinib for the treatment of patients with metastatic CRC in June 2020.

"We are very happy to see the positive outcomes of the FRESCO-2 study which offers a potential new treatment for patients with advanced metastatic colorectal cancer, where the unmet need is very high and patients have limited treatment options," said Dr Marek Kania, Executive Vice President, Managing Director and Chief Medical Officer of HUTCHMED International. "Results from the global FRESCO-2 study supplement findings from the original FRESCO study that led to the marketing approval and commercialization of fruquintinib in China. We would like to thank the patients, their families, and the healthcare professionals who participated in this study and helped achieve this important milestone."

Professor Cathy Eng, MD, FACP, FASCO, David H. Johnson Endowed Chair in Surgical and Medical Oncology and Co-Leader, Gastrointestinal Cancer Research Program, at the Vanderbilt-Ingram Cancer Center, who served as the FRESCO2 co-PI and Steering Committee member said: "Completion of the international FRESCO-2 phase III trial in a timely fashion during the era of COVID-19 isolation demonstrates the unmet need for new therapeutic agents in metastatic colorectal cancer. By meeting the primary endpoint of OS with a secondary endpoint of PFS, fruquintinib provides a significant potential new option for our refractory colorectal cancer patients. As an oral agent, fruquintinib also provides added convenience for our patients. Based on fruquintinib's profile, we will likely see further exploration in future clinical trials in different settings. This is extremely encouraging, and I look forward to seeing the final results."

Dr Weiguo Su, Chief Executive Officer and Chief Scientific Officer of HUTCHMED, said: "We are pleased to have successfully completed our first multi-regional clinical trial, FRESCO-2, to support the global registration of fruquintinib. It has already benefited patients with advanced CRC in China since its launch in 2018. It is also being evaluated alone and in combination with other agents in various tumor types in ongoing studies around the world."

HUTCHMED retains all commercial rights to fruquintinib outside of China. In China, where fruquintinib is marketed under the brand name ELUNATE®, HUTCHMED is partnered with Eli Lilly and Company and is responsible for development and execution of all on-the-ground medical detailing, promotion and local and regional marketing. Fruquintinib is not approved for use outside of China.

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

Metastatic 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 late November 2018 under the brand name ELUNATE®. It has been included in the China National Reimbursement Drug List (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 (clinicaltrials.gov identifier: NCT02314819).

About Fruquintinib Development Beyond CRC Monotherapy

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 ("GC") in China: The FRUTIGA study is a randomized, double-blind, Phase III trial evaluating the efficacy and safety of fruquintinib combined with paclitaxel for the treatment of patients with advanced gastric or esophagogastric junction ("GEJ") adenocarcinoma who did not respond to first-line standard chemotherapy. Approximately 700 patients have received either fruquintinib combined with paclitaxel or placebo combined with paclitaxel. The co-primary efficacy endpoints are OS and PFS (clinicaltrials.gov identifier: NCT03223376).

Immunotherapy combinations: HUTCHMED has entered into collaboration agreements to evaluate the safety, tolerability and efficacy of fruquintinib in combination with PD-1 monoclonal antibodies, including with tislelizumab (BGB-A317, developed by BeiGene, Ltd) and sintilimab (IBI308, developed by Innovent Biologics, Inc. and marketed as TYVYT® in China).

- *Metastatic breast, endometrial, and colorectal cancers in the U.S.:* HUTCHMED initiated this open-label, multi-center, non-randomized, Phase Ib/II study in the U.S. to investigate if the addition of fruquintinib can potentially induce activity to immune checkpoint inhibitor therapy in advanced, refractory triple negative breast cancer ("TNBC"), endometrial cancer, and CRC. Additional details of the study may be found at clinicaltrials.gov, using identifier NCT04577963. Safety and preliminary efficacy of fruquintinib as a single agent were demonstrated in advanced solid tumors, including TNBC, in a Phase I study conducted in China (NCT01645215) and a Phase I/Ib study is ongoing in the U.S. (NCT03251378).

- *Gastric, colorectal and non-small cell lung cancers in China & Korea:* BeiGene, Ltd. initiated this open-label, multi-center, Phase II study to assess the safety and efficacy of fruquintinib in combination with tislelizumab in patients with advanced or metastatic, unresectable GC, CRC or non-small cell lung cancer ("NSCLC"). Additional details of the study may be found at clinicaltrials.gov, using identifier NCT04716634.

- *Endometrial cancer and other solid tumors in China:* HUTCHMED initiated this open-label, multi-center, non-randomized, Phase II study to assess the safety and efficacy of fruquintinib in combination with

sintilimab in patients with advanced cervical cancer, endometrial cancer, GC, hepatocellular carcinoma (HCC), NSCLC or renal cell carcinoma (RCC). Preliminary results of certain cohorts were presented at the 2021 American Society of Clinical Oncology Annual Meeting (ASCO) and the Chinese Society of Clinical Oncology Annual Meeting (CSCO). Following encouraging data in the advanced endometrial cancer cohort, it has been expanded into a single-arm registrational Phase II study of over 130 patients. Additional details of the study may be found at clinicaltrials.gov, using identifier 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 4,900 personnel across all its companies, at the center of which is a team of about 1,800 in oncology/ immunology. Since inception it has advanced 13 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 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 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 advanced CRC or other indications in the U.S., Europe, Japan, Australia or other jurisdictions, 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 announcement, whether as a result of new information, future events or circumstances or otherwise.

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] The Global Cancer Observatory. Accessed September 21, 2021.
[2] SEER. Cancer Stat Facts: Colorectal Cancer. National Cancer Institute. https://seer.cancer.gov/statfacts/html/colorect.html. Accessed June 27, 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.

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