

Press Release

HUTCHMED Highlights Phase III FRESCO-2 MRCT Data Summary of Fruquintinib in Refractory Metastatic Colorectal Cancer from the Upcoming ESMO 2022 Presentation

— *Fruquintinib treatment reduced the risk of death by 34% in metastatic colorectal cancer (0.66 HR)* —

— *Increased disease control with risk of disease progression or death reduced by 68% (0.32 HR)* —

— *Results to be presented in a late-breaking, proffered paper presentation at ESMO* —

— *Conference call and webcast to be held on Monday, September 12 at 2:00 pm Paris time to discuss the full trial results and the unmet medical need in colorectal cancer* —

Hong Kong, Shanghai & Florham Park, NJ — Thursday, September 8, 2022: HUTCHMED (China) Limited ("[HUTCHMED](#)") (Nasdaq/AIM: HCM; HKEX: 13) today announces summary results of the 691-patient, multi-regional clinical trial ("MRCT") of fruquintinib. These results have been shared in an abstract of the upcoming presentation at the European Society for Medical Oncology Congress 2022 ("ESMO22") on September 12, 2022. ESMO22 will be held at the Paris Expo Porte de Versailles.

Dr Arvind Dasari, Associate Professor, Department of Gastrointestinal Medical Oncology, The University of Texas MD Anderson Cancer Center, will present the FRESCO-2 results at ESMO22. Dr Dasari commented, "These results are exciting and encouraging for patients and healthcare providers alike since they address a huge unmet need in refractory metastatic colorectal cancer. Fruquintinib provides a possible new treatment option with a meaningful survival benefit and manageable toxicity profile. These results also offer opportunities for further development of fruquintinib in other settings and combinations."

The MRCT FRESCO-2 study demonstrated that treatment with fruquintinib resulted in a statistically significant and clinically meaningful increase in the primary overall survival ("OS") endpoint and key secondary progression-free survival ("PFS") endpoint 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; $p < 0.001$). 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. Median duration of follow-up was approximately 11 months for patients in both groups.

The safety profile of fruquintinib in FRESCO-2 was consistent with previously reported fruquintinib studies. Grade 3 or above adverse events occurred in 62.7% of patients who received fruquintinib, compared to 50.4% of patients who received placebo. Grade 3 or above adverse events that occurred in more than 5% of patients who received fruquintinib were hypertension (13.6% vs 0.9% in the placebo group), asthenia (7.7% vs 3.9% in the placebo group) and hand-foot syndrome (6.4% vs 0% in the placebo group).

Further details of the FRESCO-2 presentation at ESMO22 are as follows:

Title: FRESCO-2: A global Phase 3 multi-regional clinical trial (MRCT) evaluating the efficacy and safety of fruquintinib in patients with refractory metastatic colorectal cancer
Session: Proffered Paper session 2: GI, lower digestive
Abstract No.: [LBA25](#)
Date & Time: Monday, September 12, 2022, 11:00–11:10 am Paris time
Location: 7.2.F – Fécamp Auditorium

Investor audio webcast and conference call is scheduled on Monday, September 12 at 2:00 pm Paris Time (1:00 pm London time, 8:00 am New York time, and 8:00 pm Hong Kong time).

Participating on the webcast will be members of the HUTCHMED management team, Dr Dasari and other co-Principal Investigators from the study:

- *Dr Cathy Eng*, David H. Johnson Endowed Chair in Surgical and Medical Oncology and Co-Leader, Gastrointestinal Cancer Research Program, at the Vanderbilt-Ingram Cancer Center;
- *Dr Josep Tabernero*, Head of the Medical Oncology Department of Vall d'Hebron University Hospital, Barcelona, Spain; Director of Clinical Research at Vall d'Hebron Institute of Oncology; Head of the Gastrointestinal and Endocrine Tumors Group; Past President, the European Society for Medical Oncology;
- *Dr James Yao*, Professor, Ellen F. Knisely Distinguished Chair in Colon Cancer Research, Department of GI Medical Oncology, Division of Cancer Medicine, MD Anderson Cancer Center, Houston, TX; and
- *Dr Takayuki Yoshino*, Professor, Director Department of Gastrointestinal Medical Oncology, National Cancer Hospital East, Chiba, Japan.

Details of the conference call dial-in and the webcast link will be provided on the company website at www.hutch-med.com/event/. A replay will also be available on the website shortly after the event.

About FRESCO-2

The FRESCO-2 study is a MRCT conducted in the U.S., Europe, Japan and Australia that investigated fruquintinib plus best supportive care (“BSC”) vs placebo plus BSC in patients with advanced, refractory metastatic colorectal cancer (“CRC”). As [previously disclosed](#), the 691-patient study met its primary endpoint of OS 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. Additional details of the study may be found at clinicaltrials.gov, using identifier [NCT04322539](https://clinicaltrials.gov/ct2/show/study/NCT04322539).

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 FRESCO and 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 study³, 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](https://clinicaltrials.gov/ct2/show/study/NCT02314819)). The study demonstrated that fruquintinib provided a statistically significant and clinically meaningful benefit in third-line metastatic CRC patients in China. Median OS was 9.3 months for patients treated with fruquintinib, as compared to 6.6 months for patients in the placebo group (HR 0.65; 95% CI 0.51–0.83; p<0.001). Median PFS was 3.7 months for patients treated with fruquintinib, as compared to 1.8 months for patients in the placebo group (HR 0.26; 95% CI 0.21–0.34; p<0.001). DCR was 62.2% vs. 12.3% for placebo. In terms of safety, results showed that fruquintinib had a manageable safety profile. The most frequently reported fruquintinib-related grade 3 and above adverse events included hypertension (21.2%) and hand-foot skin reaction (10.8%).

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 ([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 (developed by BeiGene, Ltd) and sintilimab (developed by Innovent Biologics, Inc.).

- **Metastatic breast, endometrial, and CRC 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 ([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 (“NSCLC”) 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 NSCLC ([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 ([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](#).

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](https://doi.org/10.1001/jama.2018.7855).

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 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 press release, whether as a result of new information, future events or circumstances or otherwise.

CONTACTS

Investor Enquiries

Mark Lee, Senior Vice President +852 2121 8200
Annie Cheng, Vice President +1 (973) 567 3786

Media Enquiries

Americas – Brad Miles, Solebury +1 (917) 570 7340 (Mobile) | bmiles@soleburystrat.com
Europe – Ben Atwell / Alex Shaw, FTI +44 20 3727 1030 / +44 7771 913 902 (Mobile) / +44 7779 545 055 (Mobile) | HUTCHMED@fticonsulting.com
Asia – Zhou Yi, Brunswick +852 9783 6894 (Mobile) | HUTCHMED@brunswickgroup.com

Nominated Advisor

Atholl Tweedie / Freddy Crossley, +44 (20) 7886 2500
Panmure Gordon (UK) Limited