

HUTCHMED Announces Positive Topline Result in Fruquintinib Phase III FRUTIGA Study in Second-Line Gastric Cancer in China

- Results of dual primary endpoint study showed statistically significant and clinically meaningful benefit in progression-free survival, a primary endpoint —
- Overall survival, the other primary endpoint, was not statistically significant —
- Safety findings consistent with fruquintinib known profile —

Hong Kong, Shanghai & Florham Park, NJ — Monday, November 14, 2022: HUTCHMED (China) Limited (“[HUTCHMED](#)”) (Nasdaq/AIM: HCM, HKEX: 13) today announces initial results from FRUTIGA, a Phase III study of fruquintinib combined with paclitaxel in 703 Chinese patients with advanced gastric or gastroesophageal junction (“GEJ”) adenocarcinoma.

The trial was positive, having met one of the primary endpoints of statistically significant improvement in progression-free survival (“PFS”), which is clinically meaningful. The other primary endpoint of overall survival (“OS”) was not statistically significant per the pre-specified statistical plan, although there was an improvement in median OS. Fruquintinib also demonstrated a statistically significant improvement in secondary endpoints including objective response rate (ORR), disease control rate (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 National Medical Products Administration (“NMPA”).

“The combination of fruquintinib and paclitaxel demonstrated significant clinical benefits for these patients in controlling this disease. Our team will continue to analyze the data and discuss these findings with the NMPA for possible NDA filing,” said Dr Weiguo Su, Chief Executive Officer and Chief Scientific Officer of HUTCHMED.

Professor Rui-Hua Xu, MD, President of the Sun Yat-Sen University Cancer Center, who served as the FRUTIGA lead principal investigator and Steering Committee Chairman, said: “By meeting the primary endpoint of PFS, fruquintinib demonstrated consistent efficacy and safety in gastric cancer indication in addition to its approved colorectal cancer indication. I am extremely excited that fruquintinib may provide a potential new oral treatment option for second line gastric cancer patients based on the FRUTIGA trial.”

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. HUTCHMED 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 FRUTIGA and Gastric Cancer

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:

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. The trial enrolled patients who did not respond to first-line standard chemotherapy. Patients were randomized at a 1:1 ratio and stratified according to factors such as stomach vs. GEJ tumor type and performance status. Additional details about this study can be found at clinicaltrials.gov, using identifier [NCT03223376](#).

Gastric cancer is the fourth leading cause of cancer death worldwide. Over one million new cases of gastric cancer and approximately 769,000 deaths were estimated in 2020 worldwide, with the highest incidence rates

in several Eastern Asian countries. In 2020, there were 478,500 new gastric cancer cases and 331,600 deaths estimated in China.¹ Due to late-onset symptoms, gastric cancer is often diagnosed at an advanced stage with poor prognosis and limited treatment options.

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 colorectal cancer ("CRC") in China: Fruquintinib was approved for marketing by the NMPA in September 2018 and commercially launched in China in 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 study², 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 Development

Metastatic CRC in the U.S., Europe, Japan and Australia: The FRESCO-2 study is a multi-regional clinical trial ("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 CRC. The results were recently [presented](#) at the European Society for Medical Oncology Congress 2022. The MRCT FRESCO-2 study demonstrated that treatment with fruquintinib resulted in a statistically significant and clinically meaningful increase in the primary OS endpoint and key secondary PFS endpoint compared to treatment with placebo. The safety profile of fruquintinib in FRESCO-2 was consistent with previously reported fruquintinib studies. We plan to complete new drug application filings in the U.S., Europe and Japan in 2023 ([NCT04322539](#)). The U.S. FDA granted Fast Track Designation for the development of fruquintinib for the treatment of patients with metastatic CRC in [June 2020](#).

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 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 ([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 gastric cancer, 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, gastric cancer, 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](#).

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 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 timing and outcome of clinical studies and the sufficiency of clinical data to support NDA approval of fruquintinib for the treatment of patients with gastric cancer or other indications in China 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 Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin.* 2021; 71(3):209-49.

² 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).