Press Release

HUTCHMED Initiates a Phase II/III Trial of Fruquintinib in Combination with Sintilimab for Advanced Renal Cell Carcinoma in China

Hong Kong, Shanghai & Florham Park, NJ — Thursday, October 27, 2022: HUTCHMED (China) Limited ("HUTCHMED") (Nasdaq/AIM:HCM; HKEX:13) today announces that it has initiated a Phase II/III trial of fruquintinib in combination with sintilimab as second-line treatment for locally advanced or metastatic renal cell carcinoma ("RCC") in China. The first patient in China received the first dose on October 27, 2022.

The study is a randomized, open-label, active-controlled study to evaluate the efficacy and safety of fruquintinib in combination with sintilimab versus axitinib or everolimus monotherapy for the second-line treatment of advanced RCC. The primary endpoint is progression free survival ("PFS") per RECIST 1.1 as assessed by blinded independent central review (BICR). The secondary endpoints include safety, quality of life, disease control rate ("DCR"), duration of response, time to response and overall survival ("OS"). Approximately 260 patients will be enrolled in the study. The leading principal investigators are Dr Dingwei Ye of Fudan University Shanghai Cancer Center and Dr Zhisong He of Peking University First Hospital. Additional details may be found at clinicaltrials.gov, using identifier NCT05522231.

About Kidney Cancer and RCC

It is estimated that approximately 430,000 new patients were diagnosed with kidney cancer worldwide in 2020.[1] In China, an estimated 74,000 new patients were diagnosed with kidney cancer in 2020.[2] Approximately 90% of kidney tumors are RCC.

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:

About Fruquintinib and Second-line treatment of RCC

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.

The U.S. Food and Drug Administration ("FDA") has approved five immune-oncology combination therapies for first-line treatment of advanced RCC, however, no immune-oncology combination therapies have been approved in China, indicating an unmet medical need in these settings. As presented at the 2021 Chinese Society of Clinical Oncology Annual Meeting (CSCO), a Phase Ib/II study of fruquintinib in combination with sintilimab for the second-line treatment of RCC demonstrated promising efficacy and tolerable safety profile in this setting.

As of the data cutoff date of August 31, 2021, all 20 enrolled patients in such Phase Ib/II study were efficacy evaluable. 19 patients previously received VEGFR inhibitors, and one received interferon. The confirmed objective response rate (ORR) was 55.0% (95% CI: 31.5-76.9) and DCR was 85.0% (95% CI: 62.1-96.8). PFS rate at 9 months was 63.6% (95% CI: 38.1-80.9). Both median PFS and OS were not reached. Median treatment time was 38.6 weeks, with the longest being over 50 weeks and ongoing.

About Fruquintinib Development In CRC Monotherapy

Metastatic colorectal cancers ("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 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 (NCT02314819).

Metastatic CRC outside China: 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.

About Other Fruquintinib Development

Gastric Cancer 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 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 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, kidney cancer fact sheet. https://gco.iarc.fr/today/data/factsheets/cancers/29-Kidney-fact-sheet.pdf. Accessed September 28, 2022.
[2] The Global Cancer Observatory, China fact sheet. https://gco.iarc.fr/today/data/factsheets/populations/160-china-fact-sheets.pdf. Accessed September 30, 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.

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 RCC 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 RCC, CRC, gastric cancer, TNBC, endometrial cancer 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.

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