HUTCHMED Announces License to Takeda to Develop and Commercialize Fruquintinib Outside China

— HUTCHMED to receive US$400 million upfront on deal closing and up to US$730 million in potential future milestone payments, totaling up to US$1.13 billion, plus royalties on net sales —

— Marketing authorization submissions in the U.S., Europe and Japan planned to complete in 2023 —

— Partnership approach aligned with HUTCHMED's path to profitability and strategy to bring its innovative medicines to patients worldwide —

— HUTCHMED to host a conference call and webcast at 8:30 a.m. EST (1:30 p.m. GMT / 9:30 p.m. HKT) on Monday, January 23, 2023 —

Hong Kong, Shanghai & Florham Park, NJ — Monday, January 23, 2023: HUTCHMED (China) Limited ("HUTCHMED") (Nasdaq/AIM:HCM, HKEX:13) today announces that its subsidiary, HUTCHMED Limited, has entered into an exclusive license agreement with a subsidiary of Takeda Pharmaceutical Company Limited (TSE:4502, NYSE:TAK) to further the global development, commercialization and manufacture of fruquintinib outside of mainland China, Hong Kong and Macau, where it is marketed by HUTCHMED. HUTCHMED Limited will receive up to US$1.13 billion including US$400 million upfront on closing as well as potential regulatory, development and commercial sales milestone payments, plus royalties on net sales.

Fruquintinib is a highly selective and potent inhibitor of vascular endothelial growth factor receptors ("VEGFR") -1, -2 and -3. Fruquintinib is orally administered and has the potential to be used across subtypes of metastatic colorectal cancer ("CRC"), regardless of biomarker status. Positive results of FRESCO-2, the global Phase III multi-regional clinical trial of fruquintinib in refractory metastatic colorectal cancer ("CRC"), were presented at the European Society for Medical Oncology Congress ("ESMO") in September 2022. FRESCO-2 met its primary endpoint of improving overall survival ("OS") in patients with metastatic CRC and was generally well tolerated.

"We are pleased to be partnering with a company that shares our mission to improve treatment outcomes for cancer patients and has the scale and expertise in global drug development and commercialization to advance fruquintinib globally outside of China," said **Dr. Weiguo Su, Executive Director, Chief Executive Officer and Chief Scientific Officer of HUTCHMED**.

"For HUTCHMED, this transaction is consistent with our strategic shift that we announced in November 2022 to accelerate our path to profitability. We stated that we would focus on the innovative medicines in our pipeline such as fruquintinib and others that are most likely to generate near-term value, and that we would be uncompromising in our commitment to bringing our medicines to patients worldwide. Not only does the license with Takeda accelerate this global ambition, but it provides us with more bandwidth and extended cash runway to advance other opportunities. We are very excited about the future for HUTCHMED."

"Fruquintinib has the potential to change the treatment landscape for patients with refractory metastatic CRC who are in need of additional treatment options. We look forward to utilizing our development and commercial capabilities to expand the potential of this innovative medicine to patients beyond China," said **Teresa Bitetti, President of the Global Oncology Business Unit at Takeda**. "We have a strong track record of working with companies that share our focus on bringing transformative medicines to patients around the globe who need them. Working with HUTCHMED will enable us to expand our oncology portfolio, bringing us one step closer to achieving our aspiration to cure cancer."

Under the terms of the agreement, Takeda will receive an exclusive worldwide license to develop and commercialize fruquintinib from HUTCHMED Limited in all indications and territories outside of mainland China, Hong Kong and Macau. Subject to the terms of the agreement, HUTCHMED Limited will be eligible to receive up to US$1.13 billion, including US$400 million upfront on closing of the agreement, and up to US$730 million in additional potential payments relating to regulatory, development and commercial sales milestones, as well as royalties on net sales.

The deal is subject to customary closing conditions, including completion of antitrust regulatory reviews. Following these clearances, Takeda will become solely responsible for the development and commercialization of fruquintinib in all included territories worldwide excluding mainland China, Hong Kong and Macau. As previously announced, marketing authorization submissions in the U.S., Europe and Japan are planned to complete in 2023, with the rolling submission to the U.S. Food and Drug Administration ("FDA") planned to complete in the first half of 2023.

HUTCHMED will continue to focus on progressing late-stage clinical trials and the commercialization of fruquintinib in mainland China in collaboration with Eli Lilly and Company, where it is approved 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-vascular endothelial growth factor therapy and/or anti-epidermal growth factor receptor ("EGFR") therapy (RAS wild type). ELUNATE® has been included in the China National Reimbursement Drug List ("NRDL") since January 2020.

Management of HUTCHMED will host a conference call and webcast for investors and analysts on Monday, January 23, 2023, at 8:30 a.m. New York time (1:30 p.m. London time, 9:30 p.m. Hong Kong Time). 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.

Evercore Group LLC is acting as exclusive financial advisor to HUTCHMED and Ropes & Gray LLP is serving as its legal advisor.

About CRC

CRC is a cancer that starts in either the colon or rectum. According to the International Agency for Research on Cancer, CRC is the third most prevalent cancer worldwide, associated with more than 935,000 deaths in 2020.[1] In the U.S., an estimated 155,000 patients were diagnosed with CRC and there were 54,000 deaths from the disease.[2] In Europe, CRC was the second most common cancer in 2020, with approximately 520,000 new cases and 245,000 deaths. In Japan, CRC is the most common cancer, with an estimated 148,000 new cases and 60,000 deaths in 2020.[1] Although early stage CRC can be surgically resected, metastatic CRC remains an area of high unmet need with poor outcomes 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 with the intention of minimizing off-target toxicities, improving tolerability and providing more consistent target coverage. Fruquintinib has been generally well tolerated in patients to date, and is being investigated in combinations with other anti-cancer therapies.

About Fruquintinib Approval in 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).

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 the FRESCO-2 Phase III Trial in CRC Outside China

The FRESCO-2 study is 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 refractory metastatic CRC (NCT04322539). The results were presented at ESMO in September 2022.[4] 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 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). 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. 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). 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.

About Other Fruquintinib Developments

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 gastroesophageal junction 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.

HUTCHMED is also developing fruquintinib for the treatment of multiple solid tumor cancers in combination with PD-1 monoclonal antibodies for the treatment of endometrial and other solid tumors.

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 approximately 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 to patients 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 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 Europe or Japan, its potential to gain approvals from regulatory authorities on an expedited basis or at all; the efficacy and 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; each party's ability to satisfy the terms and conditions under the license agreement; actions of regulatory agencies, which may affect the initiation, timing and progress of clinical trials or the regulatory pathway for fruquintinib; Takeda's ability to successfully develop and commercialize fruquintinib; 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 as combination therapeutics with fruquintinib, such risks and uncertainties include assumptions regarding the safety, efficacy, supply and continued regulatory approval of these therapeutics. Such forward-looking statements include, without limitation, statements regarding the plan to develop and commercialize fruquintinib under the license agreement; potential payments under the license agreement, including the upfront payment and any milestone or royalty payments; potential benefits of the license agreement; and HUTCHMED's strategy, goals and anticipated milestones, business plans and focus. 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 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.
[4] Dasari NA, Lonardi S, et al. LBA25 – FRESCO-2: A global phase III multiregional clinical trial (MRCT) evaluating the efficacy and safety of fruquintinib in patients with refractory metastatic colorectal cancer. *Ann Oncol*. 2022 Sep;33(suppl_7): S808-S869. 10.1016/annonc/annonc1089.