HUTCHMED (China) Limited

和黃醫藥（中國）有限公司

(Incorporated in the Cayman Islands with limited liability)

(Stock Code: 13)

VOLUNTARY ANNOUNCEMENT
HUTCHMED and Takeda Announce Publication of Phase III FRESCO-2 Results in *The Lancet*

— Publication shows FRESCO-2 demonstrated treatment with fruquintinib reduced the risk of death by 34% in previously treated metastatic colorectal cancer (0.66 HR) —

— Data support regulatory submissions in the U.S., Europe and Japan during 2023 —

HUTCHMED (China) Limited ("HUTCHMED") and Takeda (TSE:4502, NYSE:TAK) today announced that results of the Phase III FRESCO-2 study evaluating fruquintinib in patients with previously treated metastatic colorectal cancer ("CRC") were published in *The Lancet*.

The publication provides details of the FRESCO-2 study results as of June 24, 2022. Summary results from this cut-off date were presented on September 12, 2022, at the European Society for Medical Oncology Congress 2022 ("ESMO22").

Fruquintinib is a highly selective and potent inhibitor of vascular endothelial growth factor receptors ("VEGFR") -1, -2 and -3. FRESCO-2 is a global Phase III multi-regional clinical trial (MRCT) conducted in the U.S., Europe, Japan and Australia investigating fruquintinib plus best supportive care ("BSC") vs placebo plus BSC in patients with previously treated metastatic CRC. The FRESCO-2 study met its primary and key secondary endpoints, demonstrating that treatment with fruquintinib resulted in a statistically significant and clinically meaningful improvement in overall survival ("OS") and progression-free survival ("PFS"), respectively. The safety profile of fruquintinib in FRESCO-2 was consistent with previously reported fruquintinib studies.

FRESCO-2 was a key study supporting regulatory submissions to the U.S. Food and Drug Administration ("FDA") for fruquintinib for the treatment of previously treated metastatic CRC, which was accepted for review and granted Priority Review in May 2023. Filing of a Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) and an NDA to the Japan Pharmaceuticals and Medical Devices Agency (PMDA) are planned in 2023.

In March 2023, HUTCHMED and Takeda closed an exclusive license agreement to further the global development, commercialization and manufacture of fruquintinib outside of China.

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., it is estimated that 153,000 patients will be diagnosed with CRC and 53,000 deaths from the disease will occur in 2023.[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 was 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. Some patients with metastatic CRC may benefit from personalized therapeutic strategies based on molecular characteristics; however, most patients have tumors that do not harbor actionable mutations.[3,4,5,6,7]

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 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). Approval in China is supported by the results of the FRESCO study, a Phase III pivotal registration trial of fruquintinib in 416 patients with metastatic CRC in China, published in *The Journal of the American Medical Association*, JAMA, in June 2018 (NCT02314819).[8]

HUTCHMED markets fruquintinib in China in partnership with Eli Lilly and Company.

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 of China

The FRESCO-2 study is a multi-regional clinical trial conducted in the U.S., Europe, Japan and Australia investigating fruquintinib plus BSC vs placebo plus BSC in patients with previously treated metastatic CRC (NCT04322539). The study met its primary and key secondary endpoints, demonstrating that treatment with fruquintinib resulted in a statistically significant and clinically meaningful improvement in OS and PFS, respectively. Results from the study were presented at ESMO22 in September 2022 and subsequently published in *The Lancet*.[9,10]

The median OS was 7.4 months for the 461 patients treated with fruquintinib compared with 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 with 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 56% in the fruquintinib group compared with 16% for patients in the placebo group (95% CI, 32.8-46.0; p<0.001). 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 higher adverse events occurred in 63% (286/456) of patients who received fruquintinib plus BSC, compared to 50% (116/230) of patients who received placebo plus BSC. Grade 3 or higher adverse events that occurred in ≥ 5% of patients who received fruquintinib were hypertension (14% vs 1% in the placebo group), asthenia (8% vs 4% in the placebo group) and hand-foot syndrome (6% vs 0% in the placebo group). Adverse events leading to discontinuation occurred in 20% of patients who received fruquintinib, compared to 21% 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 announced 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 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.

About Takeda

Takeda is focused on creating better health for people and a brighter future for the world. We aim to discover and deliver life-transforming treatments in our core therapeutic and business areas, including gastrointestinal and inflammation, rare diseases, plasma-derived therapies, oncology, neuroscience and vaccines. Together with our partners, we aim to improve the patient experience and advance a new frontier of treatment options through our dynamic and diverse pipeline. As a leading values-based, R&D-driven biopharmaceutical company headquartered in Japan, we are guided by our commitment to patients, our people and the planet. Our employees in approximately 80 countries and regions are driven by our purpose and are grounded in the values that have defined us for more than two centuries. For more information, visit https://www.takeda.com.

HUTCHMED 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 a New Drug Application ("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.

Takeda Important Notice

For the purposes of this notice, "announcement" means this document, any oral presentation, any question and answer session and any written or oral material discussed or distributed by Takeda Pharmaceutical Company Limited ("Takeda") regarding this release. This announcement (including any oral briefing and any question-and-answer in connection with it) is not intended to, and does not constitute, represent or form part of any offer, invitation or solicitation of any offer to purchase, otherwise acquire, subscribe for, exchange, sell or otherwise dispose of, any securities or the solicitation of any vote or approval in any jurisdiction. No shares or other securities are being offered to the public by means of this announcement. No offering of securities shall be made in the United States except pursuant to registration under the U.S. Securities Act of 1933, as amended, or an exemption therefrom. This announcement

is being given (together with any further information which may be provided to the recipient) on the condition that it is for use by the recipient for information purposes only (and not for the evaluation of any investment, acquisition, disposal or any other transaction). Any failure to comply with these restrictions may constitute a violation of applicable securities laws.

The companies in which Takeda directly and indirectly owns investments are separate entities. In this announcement, "Takeda" is sometimes used for convenience where references are made to Takeda and its subsidiaries in general. Likewise, the words "we", "us" and "our" are also used to refer to subsidiaries in general or to those who work for them. These expressions are also used where no useful purpose is served by identifying the particular company or companies.

Takeda Forward-Looking Statements

This announcement and any materials distributed in connection with this announcement may contain forward-looking statements, beliefs or opinions regarding Takeda's future business, future position and results of operations, including estimates, forecasts, targets and plans for Takeda. Without limitation, forward-looking statements often include words such as "targets", "plans", "believes", "hopes", "continues", "expects", "aims", "intends", "ensures", "will", "may", "should", "would", "could" "anticipates", "estimates", "projects" or similar expressions or the negative thereof. These forward-looking statements are based on assumptions about many important factors, including the following, which could cause actual results to differ materially from those expressed or implied by the forward-looking statements: the economic circumstances surrounding Takeda's global business, including general economic conditions in Japan and the United States; competitive pressures and developments; changes to applicable laws and regulations, including global health care reforms; challenges inherent in new product development, including uncertainty of clinical success and decisions of regulatory authorities and the timing thereof; uncertainty of commercial success for new and existing products; manufacturing difficulties or delays; fluctuations in interest and currency exchange rates; claims or concerns regarding the safety or efficacy of marketed products or product candidates; the impact of health crises, like the novel coronavirus pandemic, on Takeda and its customers and suppliers, including foreign governments in countries in which Takeda operates, or on other facets of its business; the timing and impact of post-merger integration efforts with acquired companies; the ability to divest assets that are not core to Takeda's operations and the timing of any such divestment(s); and other factors identified in Takeda's most recent Annual Report on Form 20-F and Takeda's other reports filed with the U.S. Securities and Exchange Commission, available on Takeda's website at: https://www.takeda.com/investors/sec-filings/ or at www.sec.gov. Takeda does not undertake to update any of the forward-looking statements contained in this announcement or any other forward-looking statements it may make, except as required by law or stock exchange rule. Past performance is not an indicator of future results and the results or statements of Takeda in this announcement may not be indicative of, and are not an estimate, forecast, guarantee or projection of Takeda's future results.

Takeda Medical Information

This announcement contains information about products that may not be available in all countries, or may be available under different trademarks, for different indications, in different dosages, or in different strengths. Nothing contained herein should be considered a solicitation, promotion or advertisement for any prescription drugs including the ones under development.

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By Order of the Board

Edith Shih
Non-executive Director and Company Secretary

Hong Kong, June 16, 2023

As at the date of this announcement, the Directors of the Company are:

Executive Directors:
Mr TO Chi Keung, Simon
(Chairman)
Dr Weiguo SU
(Chief Executive Officer and Chief Scientific Officer)
Mr CHENG Chig Fung, Johnny
(Chief Financial Officer)

Non-executive Directors:
Dr Dan ELDAR
Ms Edith SHIH
Mr Lefei SUN

Independent Non-executive Directors:
Mr Paul Rutherford CARTER
(Senior Independent Director)
Mr Graeme Allan JACK
Professor MOK Shu Kam, Tony