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 Receives Breakthrough Therapy Designation in China for Fruquintinib Combination with Sintilimab for Treatment of Advanced Endometrial Cancer, and Completes Enrollment of Registration Study

HUTCHMED (China) Limited ("HUTCHMED") today announces that the Center for Drug Evaluation of China's National Medical Products Administration ("NMPA") has granted Breakthrough Therapy Designation ("BTD") to the combination of fruquintinib and sintilimab (a PD-1 antibody) for the treatment of patients with advanced endometrial cancer ("EMC") with pMMR[1] tumors that have failed at least one line of platinum-based therapy. A study for potential registration of this combination in patients with previously treated advanced EMC in China has recently completed enrollment.

It is a multi-center, open-label clinical study to evaluate the efficacy and safety of fruquintinib in combination with sintilimab. Entry criteria include those EMC patients who experienced disease recurrence, disease progression or grade 3 or higher serious adverse events with treatment on platinum-based chemotherapy. The primary endpoint is independent review committee (IRC) assessed objective response rate ("ORR"), with secondary endpoints including disease control rate ("DCR"), progression free survival ("PFS"), overall survival ("OS"), as well as pharmacokinetic (PK) assessments. A total of 142 previously treated, advanced EMC patients were enrolled. Additional details may be found at clinicaltrials.gov, using identifier NCT03903705.

Favorable results from this trial could lead to submission to the NMPA in the first half of 2024 for regulatory approval in this treatment setting.

About Breakthrough Therapy Designation in China

NMPA grants BTD to new drugs that treat life-threatening diseases or serious conditions for which there are no effective treatment options, and where clinical evidence demonstrates significant advantages over existing therapies. Drug candidates with BTD may be considered for conditional approval and priority review when submitting a New Drug Application ("NDA"). This indicates that the development and review of the therapy for this disease indication may be expedited, to address patients' unmet needs more quickly.

About EMC

EMC is a type of cancer that begins in the uterus. Globally, an estimated 417,000 people were diagnosed with EMC and it caused approximately 97,000 deaths in 2020.[2] In China, an estimated 82,000 people were diagnosed with EMC and it caused approximately 17,000 deaths in 2020.[3] Although early-stage EMC can be surgically resected, recurrent and/or metastatic EMC remains an area of high unmet need with poor outcomes and limited treatment options.[4,5,6]

About Fruquintinib

Fruquintinib is a highly selective and potent oral inhibitor of vascular endothelial growth factor receptor ("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.

Fruquintinib was approved for marketing by the NMPA in September 2018 and commercially launched in China in November 2018 under the brand name ELUNATE® for the treatment of patients with metastatic colorectal cancer ("CRC") who have been previously treated with fluoropyrimidine, oxaliplatin and irinotecan, including those who have previously received anti-VEGF therapy and/or anti-epidermal growth factor receptor (EGFR) therapy (RAS wild type). It has been included in the National Reimbursement Drug List ("NRDL") since January 2020.

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.

Filing of a rolling submission of NDA to the U.S. Food and Drug Administration ("FDA") was accepted and granted priority review in May 2023 with a Prescription Drug User Fee Act (PDUFA) date of November 30, 2023. Submission to the European Medicines Agency (EMA) was validated in June 2023, and submission to the Japan Pharmaceuticals and Medical Devices Agency (PMDA) is expected to be completed in 2023. The submissions to the FDA and the EMA include results from the Phase III FRESCO-2 trial along with data from the Phase III FRESCO trial conducted in China. 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 trial met its primary and key secondary endpoints, showing a significant and clinically meaningful improvement in OS and PFS, respectively. Fruquintinib has been generally well tolerated in patients to date (NCT04322539).[7]

An NDA to the NMPA was accepted in April 2023 for fruquintinib in combination with paclitaxel for the treatment of second-line advanced gastric or gastroesophageal junction adenocarcinoma. The NDA includes results from the Phase III FRUTIGA trial, a study in China to evaluate fruquintinib combined with paclitaxel compared with paclitaxel monotherapy in this patient population. Its dual-primary endpoints were PFS and OS. The trial met the PFS endpoint at a statistically and clinically meaningful level, and while there was an improvement in median OS, the OS endpoint was not statistically significant. Statistically significant improvements were also shown in secondary endpoints including ORR, DCR and duration of response (DoR). The safety profile was consistent with previously reported studies (NCT03223376).

HUTCHMED is also developing fruquintinib in China for the treatment of multiple other solid tumor cancers in combination with anti-PD-1 monoclonal antibodies. Fruquintinib is licensed to Takeda Pharmaceutical Company Limited outside of China. HUTCHMED markets fruquintinib in China in partnership with Eli Lilly and Company.

About Sintilimab

Sintilimab, marketed as TYVYT® (sintilimab injection) in China, is a PD-1 immunoglobulin G4 monoclonal antibody co-developed by Innovent Biologics, Inc. and Eli Lilly and Company. Sintilimab is a type of immunoglobulin G4 monoclonal antibody, which binds to PD-1 molecules on the surface of T-cells, blocks the PD-1 / PD-Ligand 1 (PD-L1) pathway, and reactivates T-cells to kill cancer cells.[8] Innovent is currently conducting more than 20 clinical studies of sintilimab to evaluate its safety and efficacy in a wide variety of cancer indications, including more than 10 registrational or pivotal clinical trials.

In China, sintilimab has been approved for seven indications and included in the NRDL for six indications.

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 therapeutic potential of fruquintinib in combination with sintilimab for the treatment of patients with advanced EMC 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 sufficiency of clinical data to support NDA approval of fruquintinib in combination with sintilimab for the treatment of patients with advanced EMC in China, the U.S., Europe, Japan, Australia or other jurisdictions, its potential to gain expeditious approvals from regulatory authorities, 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 COVID-19 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.

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[1] pMMR = Mismatch Repair proficient

[2] The Global Cancer Observatory, World Fact Sheet. Accessed June 12, 2023.

[3] The Global Cancer Observatory, China Fact Sheet. Accessed June 12, 2023.

[4] Yi A, et al. Real-world characteristics and treatment pattern of patients with newly diagnosed endometrial cancer in China. *J Clin Oncol.* 2023;41, no. 16_suppl (June 01, 2023) e17613-e17613. DOI: 10.1200/JCO.2023.41.16_suppl.e17613.

[5] Koppikar S, et al. Pan-Asian adapted ESMO Clinical Practice Guidelines for the diagnosis, treatment and follow-up of patients with endometrial cancer. *ESMO Open*. 2023;8(1):100774. DOI:10.1016/j.esmoop.2022.100774.

[6] Siegel RL, et al. Cancer statistics, 2023. *CA Cancer J Clin*. 2023;73(1):17-48. DOI:10.3322/caac.21763.

[7] Dasari NA, et al. Fruquintinib versus placebo in patients with refractory metastatic colorectal cancer (FRESCO-2): an international, multicentre, randomised, double-blind, phase 3 study [published online ahead of print, 2023 Jun 15]. *Lancet*. 2023. DOI: 10.1016/S0140-6736(23)00772-9.

[8] Wang J, Fei K, Jing H, et al. Durable blockade of PD-1 signaling links preclinical efficacy of sintilimab to its clinical benefit. mAbs 2019;11(8): 1443-1451. DOI: 10.1080/19420862.2019.1654303.

By Order of the Board

Edith Shih
Non-executive Director and Company Secretary

Hong Kong, July 20, 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
Ms Ling YANG

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