Press Release

HUTCHMED Initiates a Phase Ib/II Trial of Fruquintinib in Combination with Tislelizumab in Advanced Triple Negative Breast Cancer or Advanced Endometrial Cancer

Hong Kong, Shanghai & Florham Park, NJ — Thursday, August 26, 2021: HUTCHMED (China) Limited ("HUTCHMED") (Nasdaq/AIM: HCM; HKEX:13) has initiated a Phase Ib/II study of fruquintinib in combination with BeiGene's tislelizumab in patients with advanced triple negative breast cancer ("TNBC") or advanced endometrial cancer ("EC") in the U.S. The first patient was dosed on August 24, 2021. This trial is to explore the potential for the addition of a highly selective vascular endothelial growth factor receptor ("VEGFR") inhibitor, fruquintinib, to anti-programmed death-1 ("PD-1") antibody tislelizumab in inducing activity to immune checkpoint inhibitors.

This is an open-label, multi-center, non-randomized study to assess the safety and efficacy of fruquintinib in combination with tislelizumab in patients with locally advanced or metastatic TNBC or advanced EC. This study will be conducted in two parts; a safety lead-in phase (Part 1) and a dose expansion phase (Part 2). The safety lead-in phase will determine safety and tolerability and the recommended Phase II dose ("RP2D") of the combination. In the dose expansion phase, the RP2D will be administered to two cohorts of patients: Cohort A – Patients with TNBC who have received prior therapy with an immune checkpoint inhibitor; and Cohort B – Patients with TNBC who have not received prior therapy with an immune checkpoint inhibitor. A cohort evaluating the combination in second line advanced EC is anticipated to open in 3Q2021. Additional details may be found at clinicaltrials.gov, using identifier NCT04577963.

About TNBC and EC

Breast cancer is a common type of cancer in the U.S., estimated to be diagnosed in over 281,000 women during 2021.[1] TNBC is one of several subtypes of breast cancer, accounting for approximately 10% of newly diagnosed breast cancer cases.[2] The number of women living with TNBC in the U.S. was estimated to be over 150,000 in 2018.[3] PD-L1 expression is estimated to be present in approximately 20% of TNBC.[4] TNBC is distinguished from the other subtypes of breast cancer in that the cancer cells do not have receptors for the hormones estrogen or progesterone (hormone receptor negative) and do not make excessive amount of the protein human epidermal growth factor receptor 2 (HER2). TNBC is more aggressive and has a worse prognosis compared to other types of breast cancer.

EC is the fourth most common type of cancer among women in the U.S., estimated to be diagnosed in over 66,000 women during 2021.[5] The number of women living with EC in the U.S. was estimated to be over 800,000 in 2018. Options are limited beyond front line chemotherapy treatment for the 20-30% of women who are diagnosed at an advanced stage of the disease, as well as those who develop advanced disease that are not curable with surgery. Among patients with EC, an estimated 14% of advanced stage tumors express PD-L1, and approximately 20-30% of EC are microsatellite instability-high (MSI-H).[6,7,8,9]

Immune checkpoint inhibitors ("ICIs") have improved clinical outcomes in TNBC and EC, but a large proportion of patients do not respond to ICIs and initial responders eventually develop resistance. Combination therapy including VEGFR inhibition may improve the clinical efficacy of ICIs by promoting inhibition of angiogenesis in the tumor region, which can suppress tumor growth and reduce metastasis.

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.

HUTCHMED retains all rights to fruquintinib outside of China. In China, HUTCHMED is partnered with Eli Lilly and Company and is responsible for development and execution of all on-the-ground medical detailing, promotion and local and regional marketing.

About Fruquintinib Development

Metastatic colorectal cancer in China: Fruquintinib was approved for marketing by the China National Medical Products Administration ("NMPA") in September 2018 and commercially launched in China in late November 2018 under the brand name Elunate®. It was included in the China National Reimbursement Drug List (NRDL) in January 2020. Elunate® is 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-EGFR therapy (RAS wild type). Results of the FRESCO study, 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 (clinicaltrials.gov identifier: NCT02314819).

Metastatic CRC in the U.S., Europe, and Japan: The U.S. Food and Drug Administration ("FDA") granted Fast Track Designation for the development of fruquintinib for the treatment of patients with metastatic CRC in June 2020. A Phase III registration study of fruquintinib for the treatment of patients with metastatic CRC, FRESCO-2, is currently underway in the U.S., Europe, Japan and Australia. Additional details of the study may be found at clinicaltrials.gov, using identifier NCT04322539. The U.S. FDA has acknowledged that the totality of the fruquintinib clinical data, including the FRESCO-2 study (if positive), the prior positive Phase III FRESCO study demonstrating improvement in overall survival that led to fruquintinib approval for metastatic CRC in China in 2018, and additional completed and ongoing supporting studies in metastatic CRC, could potentially support a New Drug Application (NDA) for the treatment of patients with advanced metastatic CRC (third-line and above). The FRESCO-2 study design was also reviewed and endorsed by The European Medicines Agency (EMA) and Japanese Pharmaceuticals and Medical Devices Agency (PMDA).

Gastric Cancer in China: In October 2017, HUTCHMED initiated the FRUTIGA study, a randomized, double-blind, Phase III trial evaluating the efficacy and safety of fruquintinib combined with paclitaxel for second-line treatment of advanced gastric or esophagogastric junction ("GEJ") adenocarcinoma. The trial is designed to enroll patients who did not respond to first-line standard chemotherapy. Subjects receive either fruquintinib combined with paclitaxel or placebo combined with paclitaxel. Patients are randomized at a 1:1 ratio and stratified according to factors such as stomach vs. GEJ tumor type and performance status. The primary efficacy endpoint is overall survival. Secondary efficacy endpoints include progression-free survival (as defined by RECIST 1.1), objective response rate, disease control rate, duration of response, and quality-of-life score (EORTC QLQ-C30, version 3.0). Biomarkers related to the antitumor activity of fruquintinib will also be explored (clinicaltrials.gov identifier: NCT03223376). In June 2020, HUTCHMED completed a planned interim data review. Based on the preset criteria, the Independent Data Monitoring Committee (IDMC) recommended that the trial continue.

Metastatic breast cancer: HUTCHMED initiated this open-label, multi-center, non-randomized, Phase Ib/II study in the U.S. to assess the safety and efficacy of fruquintinib in combination with tislelizumab in patients with advanced, refractory TNBC. This study is being conducted to investigate if the addition of fruquintinib can potentially induce activity to ICIs therapy in TNBC. Additional details of the study may be found at clinicaltrials.gov, using identifier NCT04577963. Safety and preliminary efficacy of fruquintinib were demonstrated in advanced solid tumors, including TNBC, in a phase I study conducted in China (NCT01645215) and a phase 1/1b study is ongoing in the United States (NCT03251378).

Other Immunotherapy combinations: HUTCHMED has entered into other collaboration agreements to evaluate the safety, tolerability and efficacy of fruquintinib in combination with PD-1 monoclonal antibodies, including with Tyvyt® (sintilimab, IBI308, developed by Innovent Biologics, Inc.).

About Tislelizumab

Tislelizumab (BGB-A317) is a humanized IgG4 anti-PD-1 monoclonal antibody specifically designed to minimize binding to FcγR on macrophages. In pre-clinical studies, binding to FcγR on macrophages has been shown to compromise the anti-tumor activity of PD-1 antibodies through activation of antibody-dependent macrophage-mediated killing of T effector cells. Tislelizumab is the first drug from BeiGene's immuno-oncology biologics program and is being developed internationally as a monotherapy and in combination with other therapies for the treatment of a broad array of both solid tumor and hematologic cancers.

The NMPA has granted tislelizumab approval in five indications, including full approval for first-line treatment of patients with advanced squamous non-small cell lung cancer ("NSCLC") in combination with chemotherapy and for first-line treatment of patients with advanced non-squamous NSCLC in combination with chemotherapy; and conditional approval for the treatment of patients with classical Hodgkin's lymphoma (cHL) who received at least two prior therapies, for the treatment of patients with locally advanced or metastatic urothelial carcinoma

(UC) with PD-L1 high expression whose disease progressed during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy, and for the treatment of patients with hepatocellular carcinoma (HCC) who have received at least one systemic therapy. Full approval for these indications is contingent upon results from ongoing randomized, controlled confirmatory clinical trials.

In addition, four supplemental Biologics License Applications for tislelizumab have been accepted by the Center for Drug Evaluation (CDE) of the NMPA and are under review for second- or third-line treatment of patients with locally advanced or metastatic NSCLC who progressed on prior platinum-based chemotherapy, for patients with previously treated, locally advanced unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair-deficient (dMMR) solid tumors, for the treatment of patients with locally advanced or metastatic esophageal squamous cell carcinoma (ESCC) who have disease progression following or are intolerant to first-line standard chemotherapy, and for first-line treatment of patients with recurrent or metastatic nasopharyngeal cancer (NPC).

BeiGene has initiated or completed 17 potentially registration-enabling clinical trials in China and globally, including 13 Phase III trials and four pivotal Phase II trials.

In January 2021, BeiGene and Novartis entered into a collaboration and license agreement granting Novartis rights to develop, manufacture, and commercialize tislelizumab in North America, Europe, and Japan.

Tislelizumab is not approved for use outside of China.

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. A dedicated organization of over 1,400 personnel has advanced eleven cancer drug candidates from in-house discovery into clinical studies around the world, with its first three oncology drugs now approved and marketed. For more information, please visit: www.hutch-med.com or follow us on LinkedIn.

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 and other federal securities laws, including statements regarding the clinical development of fruquintinib in combination with tislelizumab, HUTCHMED's and BeiGene's roles and responsibilities in the collaboration, the opportunity and potential benefits of their product candidates both as monotherapies and in combination, and other information that is not historical information. Actual results may differ materially from those indicated in the forward-looking statements as a result of various important factors, including the ability of HUTCHMED and BeiGene to develop and receive regulatory approvals for the combination therapies in the collaboration; the risk that the potential benefits of the collaboration do not materialize or do not outweigh the costs; the ability of HUTCHMED and BeiGene to demonstrate the efficacy and safety of their respective drug candidates as monotherapies or in combination; the clinical results for such drug candidates, which may not support further development or marketing approval; actions of regulatory agencies, which may affect the initiation, timing and progress of clinical trials and marketing approval; HUTCHMED's and BeiGene's ability to achieve commercial success for their marketed products and drug candidates, if approved; HUTCHMED's and BeiGene's ability to obtain and maintain protection of intellectual property for their respective technology and drugs; HUTCHMED's and BeiGene's reliance on third parties to conduct drug development, manufacturing and other services; HUTCHMED's and BeiGene's limited experience in obtaining regulatory approvals and commercializing pharmaceutical products and HUTCHMED's and BeiGene's ability to obtain additional funding for operations and to complete the development and commercialization of their drug candidates; and the impact of the COVID-19 pandemic on general economic regulatory and political conditions and on HUTCHMED's and BeiGene's clinical development, regulatory, commercial and other operations. 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 or BeiGene's filings with the U.S. Securities and Exchange Commission, The Stock Exchange of Hong Kong Limited and, in the case of HUTCHMED, on AIM. All information in this press release is as of the date of this press release, and neither HUTCHMED nor BeiGene undertakes a duty to update such information unless required by law.

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