Press Release

HUTCHMED and Innovent Jointly Announce NDA Acceptance in China for Fruquintinib Combination with Sintilimab for the Treatment of Advanced Endometrial Cancer with Priority Review Status

— NDA accepted and both fruquintinib and sintilimab granted Priority Review, following Breakthrough Therapy designation in July 2023 —

— First regulatory filing for fruquintinib for use in combination with a leading immune checkpoint inhibitor —

Hong Kong, Shanghai & Florham Park, NJ — Tuesday, April 2, 2024: HUTCHMED (China) Limited ("HUTCHMED") (Nasdaq/AIM:HCM; HKEX:13) and Innovent Biologics, Inc. ("Innovent") (HKEX:1801) today jointly announce that the New Drug Application ("NDA") for the combination of fruquintinib and sintilimab for the treatment of patients with advanced endometrial cancer with pMMR[1] or non-MSI-H[2] tumors that have failed prior systemic therapy but are not candidates for curative surgery or radiation has been accepted and granted priority review by the China National Medical Products Administration ("NMPA").

The NDA is supported by data from FRUSICA-1, the endometrial cancer registration cohort of a multi-center, open-label Phase II study investigating fruquintinib in combination with sintilimab in endometrial cancer patients who experienced disease recurrence, disease progression or intolerable toxicity with treatment on platinum-based doublet chemotherapy. The primary endpoint was independent review committee (IRC) assessed objective response rate (ORR), with secondary endpoints including disease control rate (DCR), duration of response (DoR), progression free survival (PFS), overall survival (OS), as well as pharmacokinetic (PK) assessments. Data from FRUSICA-1 will be submitted for presentation at an upcoming medical conference. Additional details may be found at clinicaltrials.gov, using identifier NCT03903705.

"This is the first regulatory filing for the combination of fruquintinib and the immune checkpoint inhibitor sintilimab. It also represents an important step closer to reshaping the treatment landscape for this challenging disease in China," said **Dr. Michael Shi, Head of R&D and Chief Medical Officer of HUTCHMED**. "Endometrial cancer remains one of the most common gynecological malignancies. We look forward to bringing this much-awaited treatment advancement to endometrial cancer patients to improve their treatment outcome."

"TYVYT® (sintilimab injection), as a backbone therapy in immuno-oncology, in combination with an anti-angiogenetic drug, may improve the prognosis for endometrial cancer patients in China," said **Dr. Hui Zhou, Senior Vice President of Innovent.** "We are excited about the NDA acceptance and priority review designation, which increases our potential to bring a new treatment option to endometrial cancer patients, and concurrently strengthens the leadership position of TYVYT® in China."

The NMPA granted Breakthrough Therapy designation to the combination of fruquintinib and sintilimab for this potential indication in July 2023. The NMPA granted this designation to this combination as a new treatment that could target a serious condition for which there are no effective treatment options, and where clinical evidence demonstrates substantial advantages over existing therapies.

About Endometrial Cancer

Endometrial cancer is a type of cancer that begins in the uterus. Globally, an estimated 417,000 people were diagnosed with endometrial cancer and it caused approximately 97,000 deaths in 2020.[3] In China, an estimated 82,000 people were diagnosed with endometrial cancer, causing approximately 17,000 deaths in 2020.[4] Although early-stage endometrial cancer can be surgically resected, recurrent and/or metastatic endometrial cancer remains an area of high unmet need with poor outcomes and limited treatment options.[5,6,7]

About Fruquintinib

Fruquintinib is a selective oral inhibitor of vascular endothelial growth factor receptor ("VEGFR")-1, -2 and -3. VEGFR inhibitors play a pivotal role in inhibiting tumor angiogenesis. Fruquintinib was designed to have enhanced selectivity that limits off-target kinase activity, allowing for high drug exposure, sustained target inhibition, and flexibility for its potential use as part of a combination therapy. Fruquintinib has demonstrated a manageable safety profile and is being investigated in combinations with other anti-cancer therapies.

About Fruquintinib Approval in China

Fruquintinib is approved for marketing for the treatment of patients with metastatic colorectal cancer who have previously received fluoropyrimidine, oxaliplatin and irinotecan-based chemotherapy, and those who have previously received or are not suitable for receiving anti-vascular endothelial growth factor ("VEGF") therapy or anti-epidermal growth factor receptor ("EGFR") therapy (RAS wild-type) in China, where it is co-developed and co-marketed by HUTCHMED and Eli Lilly and Company under the brand name ELUNATE®. It was included in the China National Reimbursement Drug List ("NRDL") in January 2020. The approval was based on data from the FRESCO study, a Phase III pivotal registration trial of fruquintinib in 416 patients with metastatic colorectal cancer in China, which were published in The Journal of the American Medical Association, *JAMA*. Since its launch in China and as of mid-2023, fruquintinib has benefited more than 80,000 colorectal cancer patients.

About Fruquintinib Approval in the United States

Fruquintinib received approval for the treatment of adult patients with metastatic colorectal cancer who have been previously treated with fluoropyrimidine, oxaliplatin, and irinotecan-based chemotherapy, an anti-VEGF therapy, and, if RAS wild-type and medically appropriate, an anti-EGFR therapy in the United States in November 2023, where it is marketed by Takeda under the brand name FRUZAQLA™. The approval was based on data from two large Phase III trials: the multi-regional FRESCO-2 trial, data from which were published in *The Lancet*, along with the FRESCO trial conducted in China. The trials investigated fruquintinib plus best supportive care versus placebo plus best supportive care in patients with previously treated metastatic colorectal cancer. Both FRESCO and FRESCO-2 met their primary and key secondary efficacy endpoints and showed consistent benefit among a total of 734 patients treated with fruquintinib. Safety profiles were consistent across trials. Takeda has the exclusive worldwide license to further develop, commercialize, and manufacture fruquintinib outside of mainland China, Hong Kong and Macau.

About Sintilimab

Sintilimab, marketed as TYVYT® (sintilimab injection) in China, is a PD-1 immunoglobulin G4 monoclonal antibody co-developed by Innovent 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]

In China, sintilimab has been approved and included in the NRDL for seven indications. The updated NRDL reimbursement scope for TYVYT® (sintilimab injection) includes:

- For the treatment of relapsed or refractory classic Hodgkin's lymphoma after two lines or later of systemic chemotherapy;
- For the first-line treatment of unresectable locally advanced or metastatic non-squamous non-small cell lung cancer lacking EGFR or ALK driver gene mutations;
- For the treatment of patients with EGFR-mutated locally advanced or metastatic non-squamous non-small cell lung cancer who progressed after EGFR-TKI therapy;
- For the first-line treatment of unresectable locally advanced or metastatic squamous non-small cell lung cancer;
- For the first-line treatment of unresectable or metastatic hepatocellular carcinoma with no prior systematic treatment;
- For the first-line treatment of unresectable locally advanced, recurrent or metastatic esophageal squamous cell carcinoma;
- For the first-line treatment of unresectable locally advanced, recurrent or metastatic gastric or gastroesophageal junction adenocarcinoma.

Besides, the combination of sintilimab and fruquintinib for the treatment of patients with advanced endometrial cancer with pMMR or non-MSI-H tumors that have failed prior systemic therapy but are not candidates for curative surgery or radiation has been accepted and granted priority review by the NMPA.

In addition, two clinical studies of sintilimab have met their primary endpoints:

- Phase II study of sintilimab monotherapy as second-line treatment of esophageal squamous cell carcinoma;
- Phase III study of sintilimab monotherapy as second-line treatment for squamous NSCLC with disease progression following platinum-based chemotherapy.

Statement: Innovent does not recommend the use of any unapproved drug(s)/indication(s).

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 medicines marketed in China, the first of which is also marketed in the U.S. For more information, please visit: www.hutch-med.com or follow us on LinkedIn.

About Innovent

Innovent is a leading biopharmaceutical company founded in 2011 with the mission to provide high-quality biologics that are affordable to all. The company discovers, develops, manufactures and commercializes innovative medicines that treat some of the most intractable diseases. Its pioneering therapies treat cancer, cardiovascular and metabolic, autoimmune and eye diseases. Innovent has launched 10 products in the market, 3 new drug applications under NMPA review, 5 assets in Phase III or pivotal clinical trials and 18 more molecules in early clinical stage. Innovent partners with over 30 global healthcare leaders, including Eli Lilly, Roche, Sanofi, Adimab, Incyte and MD Anderson Cancer Center.

Guided by the motto, “Start with Integrity, Succeed through Action,” Innovent maintains the highest standard of industry practices and works collaboratively to advance the biopharmaceutical industry so that first-rate pharmaceutical drugs can become widely accessible. For more information, visit www.innoventbio.com, or follow Innovent on Facebook and 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. These forward-looking statements reflect HUTCHMED’s current expectations regarding future events, including its expectations regarding the therapeutic potential of the fruquintinib and sintilimab combination for the treatment of patients with advanced endometrial cancer and the further clinical development of the fruquintinib and sintilimab combination 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 the fruquintinib and sintilimab combination for the treatment of patients with advanced endometrial cancer in China, 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 the fruquintinib and sintilimab combination, and the timing of these events. In addition, as certain studies rely on the use of other drug products such as 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.

Medical Information

This press release 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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References

[1] pMMR = Mismatch Repair proficient.
[2] MSI-H = Microsatellite instability-high.
[3] The Global Cancer Observatory, World Fact Sheet. Accessed June 12, 2023.
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[5] 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.

[6] 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.

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[8] Wang J, 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.