Press Release

HUTCHMED and Innovent Jointly Announce NMPA Conditional Approval for ELUNATE® (Fruquintinib) in Combination with TYVYT® (Sintilimab Injection) for the Treatment of Advanced Endometrial Cancer

— First regulatory approval for fruquintinib combination therapy with an immune checkpoint inhibitor —

Hong Kong, Shanghai & Florham Park, NJ — Tuesday, December 3, 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 ELUNATE® (fruquintinib) and TYVYT® (sintilimab injection) has been granted conditional approval in China for the treatment of patients with advanced endometrial cancer with Mismatch Repair proficient ("pMMR") tumors that have failed prior systemic therapy and are not candidates for curative surgery or radiation. This approval follows the priority review status and breakthrough therapy designation by the National Medical Products Administration ("NMPA") of China and marks the first regulatory approval for the combination of fruquintinib with a leading immune checkpoint inhibitor.

The conditional approval by the NMPA was supported by registration stage 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 have experienced disease recurrence, disease progression or intolerable toxicity with treatment on platinum-based doublet chemotherapy. Results from FRUSICA-1 were presented at the American Society of Clinical Oncology annual meeting in June 2024.[1] The study results showed that IRC-assessed objective response rate (ORR) and disease control rate (DCR) was 35.6% and 88.5% respectively. The combination treatment showed rapid on-set efficacy, with a median time to response (TTR) of only 1.6 months. The median progression free survival (PFS) and overall survival (OS) reached 9.5 months and 21.3 months respectively. Adverse events are consistent with those reported for similar immunotherapy and antiangiogenic agents combination treatments. Additional details can be found at clinicaltrials.gov, using identifier NCT03903705.

"This approval of fruquintinib plus sintilimab could represent a paradigm shift in managing this challenging disease. This innovative combination not only leverages the synergistic effects of targeted therapy and immunotherapy, but also addresses a critical gap in treatments available for patients with limited responses to traditional therapies," said **Prof. Xiaohua Wu, Director of the Department of Gynecologic Oncology at Fudan University Affiliated Cancer Hospital and Principal Investigator of the FRUSICA-1 study**. "With the promising efficacy and manageable safety profile observed in clinical trials, we are eager to have this treatment option available to patients. It brings us closer to our goal of improving survival and enhancing quality of life for patients living with advanced endometrial cancer."

"This NMPA approval of fruquintinib in combination with sintilimab represents a significant advancement for patients with advanced endometrial cancer who have long await more effective treatments. It underscores the potential of fruquintinib to be used with other therapeutic agents to improve patient outcomes," said **Dr. Michael Shi, Head of R&D and Chief Medical Officer of HUTCHMED.** "It is also a testament to our ongoing efforts to extend the clinical benefit of fruquintinib to a broader patient population. We are eager to make this innovative treatment available to advanced endometrial cancer patients as soon as we can and will continue to explore further opportunities to bring hope to more patients battling cancer."

Dr. Hui Zhou, Senior Vice President of Innovent, stated: "This approval of sintilimab and fruquintinib combination therapy marks a meaningful advancement in the treatment landscape for advanced endometrial cancer. Together with HUTCHMED, we aim to provide a novel treatment option that improves survival rates and quality of life for patients facing limited treatment options against this aggressive cancer. TYVYT® (sintilimab injection), as a cornerstone in immuno-therapy, continues to be evaluated in clinical trials in combination with novel modalities. We remain steadfast in our commitment to reinforcing the leadership position of TYVYT® (sintilimab injection) in immuno-therapy and driving forward treatment solutions through innovation and cooperation."

In July 2023, the NMPA granted Breakthrough Therapy Designation to the combination of fruquintinib and sintilimab for this potential indication. This designation recognizes the potential of a therapy to address a severe condition with no effective treatment options, and where clinical evidence demonstrates substantial advantages over existing therapies.

A Phase III confirmatory study of the fruquintinib and sintilimab combination in this setting has been planned (NCT06584032).

About Endometrial Cancer

Endometrial cancer originates in the uterus and remains a significant global health challenge. In 2020, approximately 417,000 people were diagnosed with endometrial cancer, resulting in around 97,000 deaths.[2] In China alone, an estimated 82,000 new cases and 17,000 were reported in 2020.[3] While early-stage endometrial cancer can often be surgically resected, recurrent and/or metastatic endometrial cancer remains an area of high unmet need with poor outcomes and limited treatment options.[4,5,6]

About Fruquintinib

Fruquintinib is a selective oral inhibitor of all three vascular endothelial growth factor ("VEGF") receptors (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 drug exposure that achieves sustained target inhibition and flexibility for potential use as part of a combination therapy.

About Fruquintinib Approvals

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-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. Since its launch in China, over 100,000 patients with colorectal cancer have been treated with fruquintinib.

Takeda has the exclusive worldwide license to further develop, commercialize, and manufacture fruquintinib outside of mainland China, Hong Kong and Macau, and markets under the FRUZAQLA® brand name. Fruquintinib received approval in the US in November 2023, in the EU in June 2024, in Switzerland in August 2024, in Canada, Japan and the United Kingdom in September 2024 and in Argentina, Australia and Singapore in October 2024. Regulatory applications are progressing in many other jurisdictions.

The global regulatory submissions are based on data from two large, randomized, controlled Phase III trials, the global, multi-regional FRESCO-2 trial and the FRESCO trial conducted in China, showing consistent benefit among a total of 734 patients treated with fruquintinib. Safety profiles were consistent across trials. Results from the FRESCO-2 trial were published in *The Lancet* in June 2023,[7] while results from the FRESCO trial were published in The Journal of the American Medical Association, *JAMA*.[8]

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.[9]

In China, sintilimab has been approved and included in the updated 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.

Furthermore, sintilimab's eighth indication, in combination with fruquintinib for the treatment of patients with advanced endometrial cancer with pMMR tumors that have failed prior systemic therapy and are not candidates for curative surgery or radiation, has been approved by the NMPA in December 2024.

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 non-small cell lung cancer 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 approved in the US, Europe and Japan. 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 empower patients worldwide with affordable, high-quality biopharmaceuticals. The company discovers, develops, manufactures and commercializes innovative medicines that target some of the most intractable diseases. Its pioneering therapies treat cancer, cardiovascular and metabolic, autoimmune and eye diseases. Innovent has launched 11 products in the market. It has 5 new drug applications under regulatory review, 3 assets in Phase III or pivotal clinical trials and 17 more molecules in early clinical stage. Innovent partners with over 30 global healthcare companies, including Eli Lilly, Sanofi, Incyte, Adimab, LG Chem 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 and other jurisdictions, the safety profile of the fruquintinib and sintilimab combination, HUTCHMED's ability to fund, implement and complete its further clinical development and commercialization plans for fruquintinib, 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, The Stock Exchange of Hong Kong Limited and on AIM. 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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