Press Release

HUTCHMED and Innovent Jointly Announce NDA Acceptance in China for Fruquintinib Combination with Sintilimab for the Treatment of Advanced Renal Cell Carcinoma

Hong Kong, Shanghai & Florham Park, NJ — Thursday, June 5, 2025: HUTCHMED (China) Limited ("HUTCHMED") (Nasdaq/AIM:HCM; HKEX:13) and Innovent Biologics, Inc. ("Innovent") (HKEX: 01801) today jointly announce that the New Drug Application ("NDA") for the combination of fruquintinib and sintilimab for the treatment of patients with locally advanced or metastatic renal cell carcinoma who have failed prior treatment with one tyrosine kinase inhibitor ("TKI") has been accepted for review by the China National Medical Products Administration ("NMPA").

The NDA is supported by data from FRUSICA-2, a randomized, open-label, active-controlled registration study evaluating the efficacy and safety of fruquintinib in combination with sintilimab versus axitinib or everolimus monotherapy for the second-line treatment of advanced renal cell carcinoma. The study has met its primary endpoint of progression free survival ("PFS"), as assessed by blinded independent central review (BICR) according to RECIST 1.1 criteria. The combination also demonstrated improvements in secondary endpoints including objective response rate ("ORR") and duration of response ("DoR"). The safety profile was tolerable and no new safety signals were observed. Data from FRUSICA-2 will be submitted for presentation at an upcoming scientific conference. Additional details may be found at clinicaltrials.gov, using identifier NCT05522231.

"Kidney cancer continues to pose significant challenges in China, with limited treatment options for patients who fail first-line therapies. Submitting this NDA for the fruquintinib and sintilimab combination for advanced renal cell carcinoma marks an important step in our efforts to address this unmet need," said **Dr Michael Shi, Head of R&D and Chief Medical Officer of HUTCHMED**. "We are dedicated to making this combination therapy available to patients with renal cell carcinoma. At the same time, through ongoing research, we remain focused on exploring the full potential of this combination, as well as advancing our broader pipeline across multiple cancer types, to provide more patients with new and effective treatment options."

"The NDA acceptance of sintilimab and fruquintinib combination represents a significant step toward providing a more effective second line treatment option for patients with advanced renal cell carcinoma in China," said **Dr Hui Zhou, Senior Vice President of Innovent.** "Our PD-1 inhibitor, sintilimab (TYVYT®), has solidified its position as a cornerstone of immuno-oncology (IO) therapy with this NDA as its 10th indication, marking a meaningful milestone in lifecycle management and clinical value optimization."

In December 2024, the combination of fruquintinib and sintilimab received conditional approval from the China NMPA for the treatment of patients with advanced mismatch repair proficient ("pMMR") endometrial cancer who have failed prior systemic therapy and are not candidates for curative surgery or radiation, based on data from the FRUSICA-1 study (NCT03903705).

About Kidney Cancer and Renal Cell Carcinoma

It is estimated that approximately 435,000 new patients were diagnosed with kidney cancer worldwide in 2022.[1] In China, an estimated 74,000 new patients were diagnosed with kidney cancer in 2022.[2] Approximately 90% of kidney tumors are renal cell carcinoma.

About Fruquintinib

Fruquintinib is a selective oral inhibitor of all three vascular endothelial growth factor 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.[3]

About Fruquintinib Approvals

Fruquintinib is co-developed and co-commercialized in China by HUTCHMED and Eli Lilly and Company under the brand name ELUNATE®. It is approved 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 to receive anti-VEGF therapy or anti-epidermal growth factor receptor (EGFR) therapy (RAS wild-type) in China. 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.

The combination of ELUNATE® (fruquintinib) and TYVYT® (sintilimab injection) has conditional approval in China for the treatment of patients with advanced pMMR endometrial cancer who have failed prior systemic therapy and are not candidates for curative surgery or radiation.

Takeda holds the exclusive worldwide license to further develop, commercialize, and manufacture fruquintinib outside mainland China, Hong Kong and Macau, marketing it under the brand name FRUZAQLA®. Fruquintinib received approval for the treatment of previously treated metastatic colorectal cancer in the US, Europe, Japan and many other countries around the world.

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 Fruquintinib for Second-line Treatment of Renal Cell Carcinoma

Single-agent targeted therapy continues to be one of the primary choices for first-line treatment of advanced renal cell carcinoma in China. Notably, advanced renal cell carcinoma patients who have experienced failure with single-agent targeted therapy previously still indicate an unmet medical need.

Results from a proof-of-concept Phase Ib/II study of fruquintinib plus sintilimab were published in *Targeted Oncology* in January 2025. The combination showed promising efficacy and a tolerable safety profile in this setting. At the data cutoff of October 9, 2024, all 20 enrolled previously treated patients were evaluable for efficacy, with a median follow-up duration of 45.7 months. The confirmed ORR was 60.0% and DCR was 85.0%. Median DoR was 13.9 months and median PFS was 15.9 months. Overall survival ("OS") was not reached, and the 36-month OS rate was 58.3%.[4]

About Sintilimab

Sintilimab, marketed as TYVYT® (sintilimab injection) in China, is a PD-1 immunoglobulin G4 monoclonal antibody co-developed and co-commercialized by Innovent and Eli Lilly and Company, 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. [5]

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, was conditional approved by the NMPA in December 2024.

Two NDAs for sintilimab are currently under the NMPA review, including:

- In combination with ipilimumab as neoadjuvant treatment for resectable MSI-H/dMMR colon cancer is under the NMPA review and has been granted Priority Review designation;

- In combination with fruquintinib for the treatment of patients with locally advanced or metastatic renal cell carcinoma who failed prior treatment with a TKI.

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

- Phase 2 study of sintilimab monotherapy as second-line treatment of esophageal squamous cell carcinoma;
- Phase 3 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, global development and commercialization of targeted therapies and immunotherapies for the treatment of cancer and immunological diseases. Since inception, HUTCHMED has focused on bringing 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 around the world including 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 15 products in the market. It has 3 new drug applications under regulatory review, 4 assets in Phase III or pivotal clinical trials and 15 more molecules in early clinical stage. Innovent partners with over 30 global healthcare companies, including Lilly, Sanofi, Incyte, 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.

Statement:
(1) Innovent does not recommend the use of any unapproved drug (s)/indication(s).
(2) Ramucirumab (Cyramza®) and Selpercatinib (Retsevmo®) and Pirtobrutinib (Jaypirca®) were developed by Eli Lilly and Company.

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 renal cell carcinoma 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 renal cell carcinoma 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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[1] The Global Cancer Observatory, kidney cancer fact sheet. https://gco.iarc.who.int/media/globocan/factsheets/cancers/29-kidney-fact-sheet.pdf. Accessed February 19, 2025.

[2] The Global Cancer Observatory, China fact sheet. https://gco.iarc.who.int/media/globocan/factsheets/populations/160-china-fact-sheet.pdf. Accessed February 19, 2025.

[3] Sun Q, et al. Discovery of fruquintinib, a potent and highly selective small molecule inhibitor of VEGFR 1, 2, 3 tyrosine kinases for cancer therapy. *Cancer Biol Ther*. 2014;15(12):1635-45. doi: 10.4161/15384047.2014.964087.

[4] Xu H, *et al.* Fruquintinib Plus Sintilimab in Patients with Treatment-Naïve and Previously Treated Advanced Renal Cell Carcinoma: Results from a Phase Ib/II Clinical Trial. *Targeted Oncology.* 2025; 20:113–125. doi.org/10.1007/s11523-024-01120-6.

[5] 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.