Press Release

HUTCHMED and AstraZeneca Initiate SAMETA Global Phase III Trial of Savolitinib in Combination with PD-L1 Inhibitor IMFINZI® in Patients with MET-Driven Advanced Papillary Renal Cell Carcinoma

— Follows multiple global studies of savolitinib in papillary renal cell carcinoma patients including SAVOIR and CALYPSO —

— In CALYPSO, savolitinib and IMFINZI® combination demonstrated a 57% confirmed response rate in PRCC patients with tumors harboring MET-driven alterations —

Hong Kong, Shanghai & Florham Park, NJ — Monday, November 1, 2021: HUTCHMED (China) Limited ("HUTCHMED") (Nasdaq/AIM:HCM; HKEX:13) and AstraZeneca PLC ("AstraZeneca") (LSE/STO/Nasdaq: AZN) have initiated SAMETA, a global Phase III study of savolitinib (ORPATHYS® in China), an oral, potent, and highly selective small molecule inhibitor of MET, a receptor tyrosine kinase, in combination with AstraZeneca's PD-L1 inhibitor IMFINZI® (durvalumab) in patients with MET-driven advanced papillary renal cell carcinoma ("PRCC"). The first patient received their first dose on October 28, 2021.

The Phase III trial is an open-label, randomized, controlled study in treatment-naïve patients with MET-driven, unresectable and locally advanced or metastatic PRCC, to evaluate the efficacy and safety of savolitinib in combination with IMFINZI®, compared to single agent IMFINZI® or single agent SUTENT® (sunitinib), an oral multi-kinase inhibitor considered the standard-of-care treatment option in PRCC. The primary endpoint of the study is median progression free survival ("PFS"). Other endpoints include median overall survival ("OS"), objective response rate ("ORR"), duration of response ("DoR"), 6-months and 12-months disease control rate ("DCR"), time to second progression (PFS2), safety, pharmacokinetics ("PK") and quality of life. Additional details may be found at clinicaltrials.gov, using identifier NCT05043090.

About PRCC

PRCC is a subtype of kidney cancer that is unusually difficult to treat, with low response rates from current treatment options and no treatments approved for patients with tumors that harbor MET-driven alterations. Worldwide, about 430,000 new patients were diagnosed with kidney cancer in 2020.[1] In the US, an estimated 76,000 people will be diagnosed with kidney cancer in 2021[2]. Approximately 90% of kidney tumors are renal cell carcinoma ("RCC"), which consist of several heterogeneous subtypes with highly variable clinical courses and outcomes[3,4]. PRCC accounts for up to 15% of RCC[4,5]. The *MET* gene has been found to be a major chromosome-level alteration in 81% of type-1 PRCC and 46% of type-2 PRCC, or 63% of PRCC[6].

About Savolitinib (ORPATHYS® in China)

Savolitinib is an oral, potent, and highly selective MET tyrosine kinase inhibitor ("TKI") that has demonstrated clinical activity in advanced solid tumors. It blocks atypical activation of the MET receptor tyrosine kinase pathway that occurs because of mutations (such as exon 14 skipping alterations or other point mutations) or gene amplification.

Savolitinib is marketed in China under the brand name ORPATHYS® for the treatment of patients with non-small cell lung cancer ("NSCLC") with MET exon 14 skipping alterations who have progressed following prior systemic therapy or are unable to receive chemotherapy. It is currently under clinical development for multiple tumor types, including lung, kidney, and gastric cancers, as a single treatment and in combination with other medicines.

In 2011, following its discovery and initial development by HUTCHMED, AstraZeneca and HUTCHMED entered a global licensing agreement to jointly develop and commercialize savolitinib. Joint development in China is led by HUTCHMED, while AstraZeneca leads development outside of China. HUTCHMED is responsible for the marketing authorization, manufacturing and supply of savolitinib in China. AstraZeneca is responsible for the commercialization of savolitinib in China and worldwide. Sales of savolitinib are recognized by AstraZeneca.

Savolitinib development in NSCLC

Phase II study of savolitinib monotherapy in MET Exon 14 skipping alteration NSCLC (NCT02897479) – In June 2021, savolitinib was granted drug registration conditional approval by the National Medical Products Administration of China (NMPA) for MET Exon 14 skipping alteration NSCLC. The approval was based on the results of a Phase II study in China; results of this study were published in *The Lancet Respiratory Medicine*[7]. At a median follow up of 17.6 months, savolitinib demonstrated an ORR of 42.9% (95% confidence interval [CI] 31.1-55.3) and median PFS of 6.8 months (95% CI 4.2-9.6) in the overall trial population. DCR in the overall trial population was 82.9% (95% CI 72.0-90.8). The safety and tolerability profile of savolitinib was consistent with previous trials, and no new safety signals were identified. Continued approval is contingent upon the successful completion of a confirmatory trial in this patient population (NCT04923945).

TATTON Phase Ib/II expansion studies of savolitinib in combination with TAGRISSO® in patients who have progressed following EGFR TKI treatment due to MET amplification (NCT02143466) – This global exploratory study in over 220 EGFR mutation positive NSCLC patients with MET amplified tumors following progression after treatment with any EGFR TKI. Results were published in *Lancet Oncology*[8] and final analysis was presented at the World Conference on Lung Cancer[9]. Three cohorts with patients treated following progression on first- or second-generation EGFR TKI demonstrated an ORR of 64.7-66.7% and a median PFS of 9.0-11.1 months. The cohort of patients treated following progression on a third-generation EGFR TKI demonstrated an ORR of 33.3% (95% CI 22.4-45.7), with a median PFS of 5.5 months (95% CI 4.1-7.7). The combination demonstrated encouraging anti-tumor activity and an acceptable risk-benefit profile.

SAVANNAH Phase II study of savolitinib in combination with TAGRISSO® in patients who have progressed following TAGRISSO® due to MET amplification or overexpression (NCT03778229) – This is a single-arm, open-label, global study in epidermal growth factor receptor ("EGFR") mutation positive NSCLC patients with MET amplified/overexpressed tumors following progression after treatment with TAGRISSO®, an EGFR TKI owned by AstraZeneca.

SACHI Phase III study of savolitinib in combination with TAGRISSO® in patients who have progressed following EGFR TKI treatment due to MET amplification (NCT05015608) – This is a randomized, open-label study in China in EGFR mutation positive NSCLC patients with MET amplified tumors following progression after treatment with any EGFR TKI.

SANOVO Phase III study of savolitinib in combination with TAGRISSO® in treatment-naïve patients with EGFR mutant positive NSCLC with MET overexpression (NCT05009836) – This is a randomized, blinded study in China in untreated, unresectable or metastatic patients with EGFR mutation positive NSCLC with MET positive tumors.

Savolitinib development in kidney cancer

SAVOIR randomized, controlled study of savolitinib monotherapy in MET-driven PRCC (NCT03091192) – In May 2020, data from 60 patients in this global study of savolitinib monotherapy compared with sunitinib monotherapy in MET-driven papillary RCC was presented at the ASCO 2020 Program and published simultaneously in *JAMA Oncology*[10]. Savolitinib demonstrated encouraging activity, including an ORR of 27% versus 7% for sunitinib, with no savolitinib responding patients experiencing disease progression at data cut-off, and an encouraging OS hazard ratio of 0.51 (95% CI: 0.21–1.17; *p*=0.110) with median not reached at data cut-off.

CALYPSO Phase I/II study of savolitinib in combination with IMFINZI® PD-L1 inhibitor in RCC (NCT02819596) – The CALYPSO study is an investigator initiated open-label Phase I/II study of savolitinib in combination with IMFINZI®, a PD-L1 antibody owned by AstraZeneca. The study is evaluating the safety and efficacy of the savolitinib/IMFINZI® combination in patients with papillary RCC and clear cell RCC. An analysis of 41 patients enrolled in the PRCC cohort of in this study was presented at the 2021 *ASCO Annual Meeting*[11], showing a confirmed response rate in 8 out of the 14 MET-driven patients, or 57%, with a median DoR of 9.4 months, median PFS of 10.5 months and median OS of 27.4 months. No new safety signals were seen.

SAMETA Phase III study in combination with IMFINZI® PD-L1 inhibitor in MET-driven, unresectable and locally advanced or metastatic PRCC (NCT05043090) – Based on the encouraging results of the SAVOIR and CALYPSO studies, we have initiated SAMETA, a global Phase III, open-label, randomized, controlled study of savolitinib plus IMFINZI® versus sunitinib monotherapy versus IMFINZI® monotherapy in patients with MET-driven, unresectable and locally advanced or metastatic papillary RCC.

Savolitinib development in gastric cancer

Phase II study of savolitinib monotherapy in advanced or metastatic MET amplified gastric cancer ("GC") or adenocarcinoma of the gastroesophageal junction ("GEJ") (*NCT04923932*) – This is an open-label, two-cohort, multi-center study to evaluate the efficacy, safety and PK of savolitinib in locally advanced or metastatic GC or GEJ patients whose disease progressed after at least one line of standard therapy.

This trial follows multiple Phase II studies that have been conducted in Asia to study savolitinib in MET-driven GC patients, including VIKTORY.[12] VIKTORY is an investigator initiated Phase II umbrella study in GC in South Korea in which a total of 715 patients were successfully sequenced into molecular-driven patient groups, including those with MET amplified GC. Patients whose tumors harbor MET amplification were treated with savolitinib monotherapy, reporting an ORR of 50% (10/20, 95% CI: 28.0, 71.9).

Savolitinib development in other cancer indications

Savolitinib opportunities are also continuing to be explored in multiple other MET-driven tumor settings via investigator-initiated studies including colorectal cancer.

About IMFINZI®

IMFINZI® (durvalumab) is a human monoclonal antibody that binds to the PD-L1 protein and blocks the interaction of PD-L1 with PD-1 and CD80 proteins, countering the tumor's immune-evading tactics and releasing the inhibition of immune responses.

IMFINZI® is the only approved immunotherapy in the curative-intent setting of unresectable, Stage III NSCLC in patients whose disease has not progressed after chemoradiation therapy and is the global standard of care in this setting based on the PACIFIC Phase III trial.

IMFINZI® is also approved in the US, EU, Japan, China and many other countries around the world for the treatment of extensive-stage small cell lung cancer ("SCLC") based on the CASPIAN Phase III trial.

IMFINZI® is also approved for previously treated patients with advanced bladder cancer in several countries. Since the first approval in May 2017, more than 100,000 patients have been treated with IMFINZI®.

As part of a broad development program, IMFINZI® is being tested as a single treatment and in combinations with other anti-cancer treatments for patients with NSCLC, SCLC, bladder cancer, liver cancer, biliary tract cancer, esophageal cancer, gastric and gastroesophageal cancer, cervical cancer, ovarian cancer, endometrial cancer, and other solid tumors.

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 more than 4,500 personnel across all its companies, at the center of which is a team of over 1,400 in oncology/immunology. Since inception it 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. These forward-looking statements reflect HUTCHMED's current expectations regarding future events, including its expectations regarding the therapeutic potential of savolitinib for the treatment of patients with kidney cancer, the further clinical development of savolitinib in this and other indications, its expectations as to whether clinical studies of savolitinib would meet their primary or secondary endpoints, and its expectations as to the timing of the completion and the release of results from such studies. Forward-looking statements involve risks and uncertainties. Such risks and uncertainties include, among other things, assumptions regarding the sufficiency of its data to support New Drug Application approval of savolitinib for the treatment of patients with kidney cancer, its potential to gain expeditious approvals for savolitinib in other jurisdictions such as China E.U. or Japan, the safety profile of savolitinib the potential for savolitinib to become a new standard of care for kidney cancer patients, its ability to implement and complete its further clinical development plans for savolitinib its potential commercial launch in the U.S., E.U., Japan, China and other jurisdictions, the timing of these events, and the impact of the COVID-19 pandemic on general economic, regulatory and political conditions. In addition, as certain studies rely on the use of TAGRISSO® and IMFINZI® as combination therapeutics with savolitinib, such risks and uncertainties include assumptions regarding the safety, efficacy, supply and continued regulatory approval of TAGRISSO® and IMFINZI®. 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 with 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.

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