Press Release

HUTCHMED and AstraZeneca Initiate SANOVO Phase III Trial of ORPATHYS® and TAGRISSO® Combination as a First-Line Therapy for Certain Lung Cancer Patients in China

— Follows important findings from the SAVANNAH study of this combination in lung cancer patients whose tumors harbor mutations or aberrations of EGFR and MET —

Hong Kong, Shanghai & Florham Park, NJ — Wednesday, September 8, 2021: HUTCHMED (China) Limited ("HUTCHMED") (Nasdaq/AIM:HCM; HKEX:13) and AstraZeneca PLC ("AstraZeneca") (LSE/STO/Nasdaq:AZN) have initiated SANOVO, a China Phase III study of ORPATHYS® (savolitinib), an oral, potent, and highly selective MET tyrosine kinase inhibitor ("TKI"), in combination with AstraZeneca's third-generation, irreversible epidermal growth factor receptor ("EGFR") TKI, TAGRISSO® (osimertinib) as a first-line treatment in certain non-small cell lung cancer ("NSCLC") patients whose tumors harbor EGFR mutation and overexpress MET. The first patient was dosed on September 7, 2021.

The Phase III trial is a blinded, randomized, controlled study in previously untreated patients with locally advanced or metastatic NSCLC with activating EGFR mutations and MET overexpression. The study will evaluate the efficacy and safety of TAGRISSO® in combination with ORPATHYS® comparing to TAGRISSO® alone, a standard-of-care treatment option for these patients. The primary endpoint of the study is median progression free survival ("PFS") as assessed by investigators. Other endpoints include median PFS assessed by an independent review committee, median overall survival ("OS"), objective response rate ("ORR"), duration of response ("DoR"), disease control rate ("DCR"), time to response (TTR), and safety. Additional details may be found at clinicaltrials.gov, using identifier NCT05009836.

About NSCLC, EGFR and MET Aberrations

Lung cancer is the leading cause of cancer death among men and women, accounting for about one-fifth of all cancer deaths.[1] More than a third of the world's lung cancer patients are in China.[2] Lung cancer is broadly split into NSCLC and small cell lung cancer, with 80-85% classified as NSCLC.[3] The majority of NSCLC patients are diagnosed with advanced disease while approximately 25-30% present with resectable disease at diagnosis.[4,5] For patients with resectable tumors, the majority of patients eventually develop recurrence despite complete tumor resection and adjuvant chemotherapy.[6]

Approximately 10-25% of NSCLC patients in the US and Europe, and 30-40% of patients in Asia have EGFR-mutated NSCLC.[7,8,9] These patients are particularly sensitive to treatment with an EGFR TKI which blocks the cell-signaling pathways that drive the growth of tumor cells.[10]

MET is a tyrosine kinase receptor.[11] Aberration of MET (amplification or overexpression) is present in both treatment naïve patients as well as being one of the primary mechanisms of acquired resistance to EGFR TKIs for metastatic EGFR-mutated NSCLC. [12,13]

About Savolitinib (ORPATHYS® in China)

Savolitinib is an oral, potent, and highly selective MET 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 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*[14]. 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*[15] and final analysis was presented at the World Conference on Lung Cancer[16]. 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 ORPATHYS® monotherapy in MET-driven papillary renal cell carcinoma ("RCC") (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*[17]. 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*[18], showing a confirmed response rate in 8 out of 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 (in planning) – Based on the encouraging results of the SAVOIR and CALYPSO studies, we are planning to initiate 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 PRCC.

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 pharmacokinetics (PK) of ORPATHYS® in locally advanced or metastatic GC or GEJ patients whose disease progressed after at least one line of standard therapy.

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 TAGRISSO®

TAGRISSO® is a third-generation, irreversible EGFR TKI with clinical activity against central nervous system metastases. TAGRISSO® (40mg and 80mg once-daily oral tablets) has been used to treat more than 325,000 patients across indications worldwide and AstraZeneca continues to explore TAGRISSO® as a treatment for patients across multiple stages of EGFR-mutated NSCLC.

In Phase III trials, TAGRISSO® is being tested in the neoadjuvant resectable setting (NeoADAURA), in the Stage III locally advanced unresectable setting (LAURA) and, in combination with chemotherapy, in the Stage III locally advanced or Stage IV metastatic settings (FLAURA2). AstraZeneca is also researching ways to address tumor mechanisms of resistance through the SACHI and SANOVO Phase III trials, as well as the SAVANNAH and ORCHARD Phase II trials, which test TAGRISSO® given concomitantly with savolitinib, as well as other potential new medicines.

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. These forward-looking statements reflect HUTCHMED's current expectations regarding future events, including its expectations regarding the therapeutic potential of ORPATHYS® for the treatment of patients with NSCLC, the further clinical development of ORPATHYS® in this and other indications, its expectations as to whether clinical studies of ORPATHYS® 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 ORPATHYS® for the treatment of patients with NSCLC in China, its potential to gain expeditious approvals for ORPATHYS® in other jurisdictions such as the U.S., E.U. or Japan, the safety profile of ORPATHYS®, the potential for ORPATHYS® to become a new standard of care for NSCLC patients, its ability to implement and complete its further clinical development plans for ORPATHYS®, its potential commercial launch of ORPATHYS® in 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 ORPATHYS®, 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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