**Press Release**

# HUTCHMED Receives a US$15 million Milestone from AstraZeneca for Initiating Start-up Activities for a Global Phase III Study of ORPATHYS® in Lung Cancer

**Hong Kong, Shanghai & Florham Park, NJ — Monday, March 7, 2022:** ("HUTCHMED") (Nasdaq/AIM:HCM; HKEX:13) today announces that it has received a US$15 million milestone payment from AstraZeneca PLC ("AstraZeneca") (LSE/STO/Nasdaq:AZN).

This milestone has been triggered by the initiation of start-up activities for SAFFRON, the first global Phase III study for ORPATHYS® in combination with TAGRISSO® in epidermal growth factor receptor ("EGFR")-mutated non-small cell lung cancer ("NSCLC") patients with mesenchymal epithelial transition receptor ("MET") driven tumors following progression after TAGRISSO®. SAFFRON, which is expected to commence enrolling patients in mid-2022, follows important lessons learned from the SAVANNAH study, which is targeted to be presented at an upcoming scientific conference in the second half of 2022.

To date, AstraZeneca has now paid HUTCHMED US$85 million of the total US$140 million in upfront payments, development and first-sale milestones due under the license and collaboration agreement between HUTCHMED and AstraZeneca.

## 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 U.S. 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 tyrosine kinase inhibitor ("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] Approximately 2-3% of NSCLC patients have tumors with MET exon 14 skipping alterations, a targetable mutation in the MET gene.[14]

## 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 and collaboration agreement to jointly develop and commercialize savolitinib. Under the current terms of the agreement, a US$15 million milestone payment is triggered by the initiation of start-up activities for the SAFFRON study. Joint development of savolitinib 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)* – The conditional approval in China for MET Exon 14 skipping alteration NSCLC was based on the results of a Phase II study that were published in *The Lancet Respiratory Medicine*[15]. At a median follow up of 17.6 months, savolitinib demonstrated an objective response rate ("ORR") of 42.9% (95% confidence interval [CI] 31.1-55.3) and median progression-free survival ("PFS") of 6.8 months (95% CI 4.2-9.6) in the overall trial population. Disease control rate ("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).

Based on results of the TATTON and SAVANNAH studies below, several Phase III studies of savolitinib in combination with TAGRISSO® have been initiated, including SACHI, and SANOVO and SAFFRON.

*SACHI Phase III study of savolitinib in combination with TAGRISSO® in patients who have progressed following EGFR TKI treatment due to MET amplification (NCT05015608)* – Initiated in the second half of 2021, 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)* – Initiated in the second half of 2021, this is a randomized, blinded study in China in untreated, unresectable or metastatic patients with EGFR mutation positive NSCLC with MET positive tumors.

TATTON Phase Ib/II 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[16] and final analysis was presented at the World Conference on Lung Cancer[17]. 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 EGFR mutated NSCLC patients with MET amplified/overexpressed tumors following progression after treatment with TAGRISSO®, an EGFR TKI owned by AstraZeneca. We plan to submit results for presentation at an upcoming scientific conference.

**Savolitinib development in kidney cancer**

*SAMETA Phase III study in combination with IMFINZI® PD-L1 inhibitor in MET-driven, unresectable and locally advanced or metastatic papillary renal cell carcinoma ("RCC") (NCT05043090)* – Based on the encouraging results of the SAVOIR monotherapy and CALYPSO combination therapy studies below, we 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.

*SAVOIR randomized, controlled study of savolitinib monotherapy in MET-driven PRCC (NCT03091192)* – 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*[18]. 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 study of savolitinib in combination with IMFINZI® PD-L1 inhibitor in RCC (NCT02819596)* – This investigator initiated open-label Phase I/II study of savolitinib in combination with IMFINZI®, a PD-L1 antibody owned by AstraZeneca, evaluated the safety and efficacy of the savolitinib/IMFINZI® combination in patients with RCC. An analysis of 41 papillary RCC patients was presented at the 2021 American Society of Clinical Oncology (*ASCO) Annual Meeting*[19], 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.

**Savolitinib development in gastric cancer and other cancer indications**

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

**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 4,600 personnel across all its companies, at the center of which is a team of over 1,500 in oncology/immunology. Since inception it has advanced 12 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 NSCLC, 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 NSCLC in China, its potential to gain expeditious approvals for savolitinib in other jurisdictions such as E.U. or Japan, the safety profile of savolitinib, the potential for savolitinib to become a new standard of care for NSCLC 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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