Press Release

HUTCHMED Announces NDA Acceptance in China with Priority Review Status for ORPATHYS® and TAGRISSO® Combination in Lung Cancer Patients with MET amplification After Progression on First-Line EGFR Inhibitor Therapy

Hong Kong, Shanghai & Florham Park, NJ — Thursday, January 2, 2025: HUTCHMED (China) Limited ("HUTCHMED") (Nasdaq/AIM:HCM; HKEX:13) today announces that the New Drug Application ("NDA") for the combination of ORPATHYS® (savolitinib) and TAGRISSO® (osimertinib) for the treatment of patients with locally advanced or metastatic epidermal growth factor receptor ("EGFR") mutation-positive non-small cell lung cancer ("NSCLC") with MET amplification after disease progression on first-line EGFR inhibitor therapy has been accepted and granted priority review by the China National Medical Products Administration ("NMPA"). ORPATHYS® is an oral, potent and highly selective MET tyrosine kinase inhibitor ("TKI"). TAGRISSO® is a third-generation, irreversible EGFR TKI. This acceptance also triggers a milestone payment from AstraZeneca.

The NDA is supported by data from SACHI, a multi-center, open-label, randomized, controlled, Phase III trial which evaluated the efficacy and safety of a combination of ORPATHYS® and TAGRISSO® compared to platinum-based doublet-chemotherapy (pemetrexed plus cisplatin or carboplatin), the standard-of-care treatment option in this setting. The primary endpoint of the study was progression free survival ("PFS") as assessed by investigators. Other endpoints include PFS assessed by an independent review committee, overall survival (OS), objective response rate (ORR), duration of response (DoR), disease control rate (DCR), time to response (TTR), and safety. The Independent Data Monitoring Committee ("IDMC") of SACHI has considered that the study has met the pre-defined primary endpoint of PFS in a planned interim analysis and as a result, enrollment into the study has concluded. Results from SACHI will be submitted for presentation at an upcoming scientific conference (clinicaltrials.gov identifier NCT05015608).

"This marks the first regulatory filing for the ORPATHYS® and TAGRISSO® combination. The combination has demonstrated clear evidence to address MET-driven EGFR-inhibitor resistance and offers a continued path for oral treatment." said **Dr Michael Shi, Head of R&D and Chief Medical Officer of HUTCHMED**. "With our biomarker-specific approach, we are hopeful to enhance treatment continuity and quality of life for NSCLC patients navigating this challenging journey. We and our partner AstraZeneca have been exploring this combination globally, through an array of late-stage clinical trials including the TATTON, SAVANNAH, SAFFRON and ORCHARD studies, and we hope to bring this all-oral, chemotherapy-free treatment option to patients with MET-driven lung cancer in the near future."

The NMPA granted Breakthrough Therapy designation to the combination of ORPATHYS® and TAGRISSO® for this potential indication in December 2024. The NMPA granted this designation to this combination as a new treatment that could target a serious condition where clinical evidence demonstrates substantial advantages over existing therapies.

About NSCLC and MET aberrations

Lung cancer is the leading cause of cancer death, accounting for about one-fifth of all cancer deaths.[1] Lung cancer is broadly split into NSCLC and small cell lung cancer, with 80-85% classified as NSCLC.[2] The majority of NSCLC patients (approximately 75%) are diagnosed with advanced disease, and approximately 10-15% of NSCLC patients in the US and Europe and 30-40% of patients in Asia have EGFR-mutated ("EGFRm") NSCLC.[3,4,5,6]

MET is a tyrosine kinase receptor that has an essential role in normal cell development.[7] MET overexpression and/or amplification can lead to tumor growth and the metastatic progression of cancer cells, and is one of the mechanisms of acquired resistance to EGFR TKI for metastatic EGFR-mutated NSCLC.[7,8] Approximately 2-3% of NSCLC patients have tumors with MET exon 14 skipping alterations, a targetable mutation in the MET gene.[9] MET aberration is a major mechanism for acquired resistance to both first/second-generation EGFR TKIs as well as third-generation EGFR TKIs like osimertinib. Among patients who experience disease progression post-osimertinib treatment, approximately 15-50% present with MET aberration.[10,11,12,13,14] The prevalence of MET aberration depends on the sample type, detection method and assay thresholds used.[15]

About ORPATHYS® and TAGRISSO® Combination Development in EGFR mutation-positive NSCLC

The combination of ORPATHYS® and TAGRISSO® has been studied extensively in patients with EGFR mutation-positive NSCLC, including the TATTON (NCT02143466) and SAVANNAH (NCT03778229) studies. The encouraging results from these studies led to the initiation of three Phase III trials with this combination: SACHI (NCT05015608) and SANOVO (NCT05009836) were initiated in China in 2021, and the global, pivotal Phase III SAFFRON (NCT05261399) study started enrollment in 2022. In comparison to other treatment options, this combination treatment is chemotherapy-free, biomarker-specific and orally administered, aiming for a balanced efficacy, safety and quality-of-life profile for lung cancer patients.

SAVANNAH is a global Phase II study in patients who have progressed following osimertinib due to MET amplification or overexpression, and recruitment completed earlier in 2024. The evaluation of savolitinib in combination with osimertinib was designated as a Fast Track development program by the US Food and Drug Administration (FDA) in 2023.

SAFFRON is a multi-center, randomized, controlled, open-label, global Phase III trial in patients with EGFR mutation-positive NSCLC with MET overexpression and/or amplification after disease progression on osimertinib.

SACHI is a multi-center, randomized, controlled, open-label, China Phase III trial in patients with EGFR mutation-positive NSCLC with MET amplification after disease progression on any EGFR inhibitor therapy, including third-generation EGFR-TKIs such as osimertinib.

SANOVO is a multi-center, randomized, controlled, blinded, China Phase III trial in treatment-naïve patients with EGFR mutation-positive NSCLC with MET-positive tumors.

About ORPATHYS® Approval in China

ORPATHYS® was granted conditional approval in China for the treatment of patients with locally advanced or metastatic NSCLC with MET exon 14 skipping alterations who have progressed following prior systemic therapy or are unable to receive chemotherapy. ORPATHYS® is the first selective MET inhibitor approved in China. It has been included in the National Reimbursement Drug List of China (NRDL) since March 2023. A supplementary NDA is under review which, if approved, could expand this indication to include treatment-naïve adult patients in China. More than a third of the world's lung cancer patients are in China and, among those with NSCLC globally, approximately 2-3% have tumors with MET exon 14 skipping alterations.

About ORPATHYS® (savolitinib)

ORPATHYS® 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), gene amplification or protein overexpression.

ORPATHYS® is marketed in China and 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, AstraZeneca and HUTCHMED entered a global licensing and collaboration agreement to jointly develop and commercialize ORPATHYS®. Joint development of ORPATHYS® in China is led by HUTCHMED, while AstraZeneca leads development outside of China. HUTCHMED is responsible for the marketing authorization, manufacturing and supply of ORPATHYS® in China. AstraZeneca is responsible for the commercialization of ORPATHYS® in China and worldwide. Sales of ORPATHYS® are recognized by AstraZeneca.

About TAGRISSO®

TAGRISSO® (osimertinib) is a third-generation, irreversible EGFR-TKI with proven clinical activity in NSCLC, including against central nervous system (CNS) metastases. TAGRISSO® (40mg and 80mg once-daily oral tablets) has been used to treat nearly 800,000 patients across its indications worldwide and AstraZeneca continues to explore TAGRISSO® as a treatment for patients across multiple stages of EGFRm NSCLC.

There is an extensive body of evidence supporting the use of TAGRISSO® as standard of care in EGFRm NSCLC. TAGRISSO® improved patient outcomes in early-stage disease in the ADAURA Phase III trial, locally advanced disease in the LAURA Phase III trial, late-stage disease in the FLAURA Phase III trial, and with chemotherapy in the FLAURA2 Phase III trial.

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 in the US, Europe and Japan. 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, the further clinical development for savolitinib, its expectations as to whether any studies on 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 enrollment rates and the timing and availability of subjects meeting a study's inclusion and exclusion criteria; changes to clinical protocols or regulatory requirements; unexpected adverse events or safety issues; the ability of savolitinib, including as a combination therapy, to meet the primary or secondary endpoint of a study, to obtain regulatory approval in different jurisdictions and to gain commercial acceptance after obtaining regulatory approval; the potential market of savolitinib for a targeted indication; and the sufficiency of funding. In addition, as certain studies rely on the use of other drug products such as osimertinib as combination therapeutics with savolitinib, 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.

CONTACTS

Investor Enquiries	+852 2121 8200 / ir@hutch-med.com
Media Enquiries	
FTI Consulting –	+44 20 3727 1030 / HUTCHMED@fticonsulting.com
Ben Atwell / Alex Shaw	+44 7771 913 902 (Mobile) / +44 7779 545 055 (Mobile)
Brunswick – Zhou Yi	+852 9783 6894 (Mobile) / HUTCHMED@brunswickgroup.com
Panmure Liberum	*Nominated Advisor and Joint Broker*
Atholl Tweedie / Freddy Crossley / Rupert Dearden	+44 20 7886 2500
HSBC	*Joint Broker*
Simon Alexander / Alina Vaskina / Arnav Kapoor	+44 20 7991 8888
Cavendish	*Joint Broker*
Geoff Nash / Nigel Birks	+44 20 7220 0500

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