RNS Number : 1871G
Hutchmed (China) Limited
05 November 2025

Press Release

HUTCHMED Announces Enrollment Completed of SAFFRON Global Phase III Trial of ORPATHYS® and TAGRISSO® Combination for Certain Lung Cancer Patients with MET Overexpression and/or Amplification After Progression on TAGRISSO®

Hong Kong, Shanghai & Florham Park, NJ - Wednesday, November 5, 2025: HUTCHMED (China) Limited ("HUTCHMED") (Nasdaq/AIM:HCM; HKEX:13) today announces the completion of patient enrollment of SAFFRON, a global Phase III study of ORPATHYS® (savolitinib) and TAGRISSO® (osimertinib) for the treatment of patients with epidermal growth factor receptor ("EGFR")-mutated, MET-overexpressed and/or amplified, locally advanced or metastatic non-small cell lung cancer ("NSCLC") following progression on treatment with TAGRISSO®. The last patient was randomized on October 31, 2025.

This combination represents a promising, chemotherapy-free, all-oral treatment option following progression on an EGFR tyrosine kinase inhibitor ("TKI"), and was granted approval in China in June 2025 based on the results of the SACHI randomized Phase III trial. ORPATHYS® is an oral, potent and highly selective MET TKI being jointly developed by AstraZeneca and HUTCHMED and commercialized by AstraZeneca. TAGRISSO® is a third-generation, irreversible EGFR TKI.

SAFFRON is a global Phase III, open-label, randomized, multicenter study to investigate the efficacy and safety of ORPATHYS® administered orally in combination with TAGRISSO® versus platinum-based doublet chemotherapy in participants with EGFR-mutated, MET-overexpressed and/or amplified, locally advanced or metastatic NSCLC who have progressed on first- or second-line treatment with TAGRISSO® as the most recent therapy. The primary endpoint of the study is progression free survival (PFS) as assessed by blinded independent central review (BICR) according to RECIST 1.1 criteria. Other endpoints include overall survival (OS), objective response rate ("ORR"), duration of response (DoR), disease control rate (DCR), time to response (TTR), and safety. This study randomized 338 patients, screened from over 230 sites across 29 countries. Additional details may be found at clinicaltrials.gov, using identifier NCT05261399.

Topline results from the SAFFRON study are estimated to be reported in the first half of 2026, followed by submission of results for presentation at an appropriate medical congress. If favorable, the results could support global regulatory filings for the ORPATHYS® and TAGRISSO® combination.

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 up to 40-50% of patients in Asia have EGFR-mutated ("EGFRm") NSCLC.[3],[4],[5],[6],[7]

MET is a tyrosine kinase receptor that has an essential role in normal cell development. MET overexpression and/or amplification can lead to tumor growth and the metastatic progression of cancer cells, and is one of the mechanisms of *de novo* or acquired resistance to EGFR TKI for metastatic EGFRm NSCLC.[8],[9]

About ORPATHYS®

ORPATHYS® (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), gene amplification or protein

of mutations (such as exon 14 skipping alterations or other point mutations), gene amplification or protein overexpression.

ORPATHYS® is approved in China and is marketed by AstraZeneca for the treatment of adult patients with locally advanced or metastatic NSCLC with MET exon 14 skipping alterations, representing the first selective MET inhibitor approved in China. ORPATHYS® is also approved in China for the treatment of patients with locally advanced or metastatic EGFRm-positive non-squamous NSCLC with MET amplification after disease progression on EGFR tyrosine kinase inhibitor therapy, in combination with TAGRISSO®.

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.

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 more than one million 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® in EGFRm NSCLC, and it is the only targeted therapy shown to improve patient outcomes across all stages of the disease.

In late-stage disease, TAGRISSO® demonstrated improved outcomes as monotherapy in the FLAURA Phase III trial and in combination with chemotherapy in the FLAURA2 Phase III trial. TAGRISSO® is also being investigated in this setting in combination with ORPATHYS® (savolitinib) in the SAFFRON Phase III trial and in combination with DATROWAY® (datopotamab deruxtecan or Dato-DXd) in the TROPION-Lung14 and TROPION-Lung15 Phase III trials.

TAGRISSO® also showed improved outcomes in early-stage disease in the NeoADAURA and ADAURA Phase III trials and in locally advanced stages in the LAURA Phase III trial. As part of AstraZeneca's ongoing commitment to treating patients as early as possible in lung cancer, TAGRISSO® is also being investigated in the early-stage adjuvant resectable setting in the ADAURA2 Phase III trial.

About ORPATHYS® and TAGRISSO® Combination Development in EGFR-mutated NSCLC

This combination represents a promising chemotherapy-free oral treatment strategy to address mechanisms of resistance in this setting. Among patients who experience disease progression following treatment with a third-generation EGFR TKI, approximately 15-50% present with MET aberration, depending on the sample type, detection method and assay cut-off used. TAGRISSO® is a third-generation, irreversible EGFR-TKI with proven clinical activity in NSCLC, including against central nervous system metastases. Treatment with ORPATHYS® in combination with TAGRISSO® has been studied extensively in these patients in the TATTON study (NCT02143466) and the SAVANNAH single-arm Phase II study (NCT03778229). Strong data from SAVANNAH presented at the 2025 European Lung Cancer Congress (ELCC) demonstrated high, clinically meaningful and durable ORR, with consistent safety results. The encouraging results led to the initiation of several randomized Phase III trials in this setting including the SACHI trial in China (NCT05015608) and the global SAFFRON trial (NCT05261399), as well as the SANOVO trial in China (NCT05009836).

SACHI: This Phase III trial in China evaluated the combination of ORPATHYS® and TAGRISSO® compared to platinum-based doublet chemotherapy for the treatment of patients with EGFRm, MET-amplified locally advanced or metastatic NSCLC following progression on treatment with an EGFR TKI. Results were presented at the 2025 ASCO Annual Meeting. The treatment combination received approval in China in June 2025.

SAFFRON: This ongoing global Phase III trial is to evaluate the combination of ORPATHYS® and TAGRISSO® compared to platinum-based doublet chemotherapy in patients with EGFRm, MET-overexpressed and/or amplified, locally advanced or metastatic NSCLC following progression on treatment with TAGRISSO®. This received Fast Track Designation from the US Food and Drug Administration (FDA) and enrollment was completed in October 2025. We

look forward to completing this trial to support potential US and other global registration filings.

SANOVO: This ongoing Phase III trial in China is to evaluate the combination of ORPATHYS® and TAGRISSO® compared to TAGRISSO® monotherapy in previously untreated patients with locally advanced or metastatic NSCLC with EGFRm and MET overexpression. Enrollment was completed in August 2025.

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. Since inception it 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.hutchmed.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 US 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®, the further clinical development for ORPATHYS®, its expectations as to whether any studies on 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 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 ORPATHYS®, including as a combination therapy, to meet the primary or secondary endpoint of a study, to obtain regulatory approval in other jurisdictions and to gain commercial acceptance after obtaining regulatory approval; the potential market of ORPATHYS® for a targeted indication; and HUTCHMED and/or its partner's ability to fund, implement and complete its further clinical development and commercialization plans for ORPATHYS®, and the timing of these events. In addition, as certain studies rely on the use of other drug products such as TAGRISSO® as combination therapeutics with ORPATHYS®, 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 US 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 / Tim Stamper	+44 7771 913 902 (Mobile) / +44 7421 898 348 (Mobile)
Brunswick - Zhou Yi	+852 9783 6894 (Mobile) / HUTCHMED@brunswickgroup.com
Panmure Liberum	*Nominated Advisor and Joint Broker*
Atholl Tweedie / Emma Earl / Rupert Dearden	+44 20 7886 2500
Cavendish	*Joint Broker*
Geoff Nash / Nigel Birks	+44 20 7220 0500

Deutsche Numis *Joint Broker*
Freddie Barnfield / Jeffrey Wong / Duncan Monteith +44 20 7260 1000

---

[1] World Health Organization. International Agency for Research on Cancer. All cancers fact sheet. Available at: https://gco.iarc.fr/today/-data/factsheets/cancers/39-All-cancers-fact-sheet.pdf. Accessed November 2022.

[2] American Cancer Society. What is Lung Cancer? Available at: https://www.cancer.org/cancer/lung-cancer/about/what-is.html. Accessed November 2022.

[3] Knight SB, *et al.* Progress and prospects of early detection in lung cancer. *Open Biol.* 2017;7(9): 170070.

[4] Keedy VL, *et al.* American Society of Clinical Oncology Provisional Clinical Opinion: Epidermal Growth Factor Receptor (EGFR) Mutation Testing for Patients with Advanced Non-Small-Cell Lung Cancer Considering First-Line EGFR Tyrosine Kinase Inhibitor Therapy. *J Clin Oncol.* 2011:29;2121-27.

[5] Zhang Y, *et al.* The prevalence of EGFR mutation in patients with non-small cell lung cancer: a systematic review and meta-analysis. *Oncotarget*. 2016;7(48).

[6] Szumera-Ciećkiewicz A, *et al*. EGFR Mutation Testing on Cytological and Histological Samples in 11. Non-Small Cell Lung Cancer: a Polish, Single Institution Study and Systematic Review of European Incidence. *Int J Clin Exp Pathol*. 2013:6;2800-12.

[7] Gou LY, *et al.* Prevalence of driver mutations in non-small-cell lung cancers in the People's Republic of China. *Lung Cancer: Targets and Therapy.* 2014; 5; 1-9.

[8] Uchikawa E, *et al*. Structural basis of the activation of c-MET receptor. *Nat Commun.* 2021;12(4074).

[9] Wang Q, *et al.* MET inhibitors for targeted therapy of EGFR TKI-resistant lung cancer. *Journal of Hematology & Oncology.* 2019;63.

END

NRADZLFBEFLXFBF