HUTCHMED (China) Limited
和黃醫藥（中國）有限公司
(Incorporated in the Cayman Islands with limited liability)
(Stock Code: 13)

INSIDE INFORMATION

HUTCHMED Announces that TAGRISSO® plus ORPATHYS® demonstrated high, clinically meaningful response rate in lung cancer patients with high levels of MET overexpression and/or amplification in SAVANNAH Phase II trial

— New data demonstrate efficacy for the oral treatment combination to address MET-driven resistance in EGFR-mutated lung cancer —

— MET is a common biomarker in this setting for patients who develop resistance to EGFR targeted therapies —

This announcement is made by HUTCHMED (China) Limited ("HUTCHMED") pursuant to Rule 13.09(2)(a) of the Rules Governing the Listing of Securities on The Stock Exchange of Hong Kong Limited and the Inside Information Provisions under Part XIVA of the Securities and Futures Ordinance (Cap. 571).

HUTCHMED today announces positive high-level results from the SAVANNAH Phase II trial that showed TAGRISSO® (osimertinib) plus ORPATHYS® (savolitinib) demonstrated a high, clinically meaningful and durable objective response rate ("ORR") for patients with epidermal growth factor receptor-mutated ("EGFRm") non-small cell lung cancer ("NSCLC") with high levels of MET overexpression and/or amplification, defined as IHC90+ and/or FISH10+, whose disease progressed on treatment with TAGRISSO®. These data will be presented at a forthcoming medical meeting and shared with global regulatory authorities. In 2023, TAGRISSO® plus ORPATHYS® received Fast Track designation from the US Food and Drug Administration (FDA) in this setting.

ORPATHYS® is an oral, potent, and highly selective MET tyrosine kinase inhibitor ("TKI") being jointly developed by AstraZeneca and HUTCHMED and commercialized by AstraZeneca. It is approved in China 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.

While EGFR-targeted therapy can provide a substantial survival benefit to patients with EGFRm NSCLC, most will eventually develop resistance to their treatment, with MET being a common resistance biomarker.[1] Among patients screened for enrollment in SAVANNAH, an estimated 62% had tumors with MET overexpression and/or amplification, and approximately 34% met the defined high MET level cut-off upon clinical progression.

Myung-Ju Ahn, MD, PhD, Professor of Hemato-Oncology at the Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea, and principal investigator in the SAVANNAH Phase II trial, said: "Osimertinib can provide patients with EGFR-mutated lung cancer unprecedented survival and has transformed the treatment landscape, but patients can develop resistance due to genes like MET – a common resistance biomarker. These results show that adding savolitinib, a selective MET-inhibitor, while continuing osimertinib treatment helped to deliver a meaningful response among patients whose disease progressed, providing a potential new treatment option following standard-of-care osimertinib."

Susan Galbraith, Executive Vice President, Oncology R&D, AstraZeneca, said: "These positive SAVANNAH results show the benefit of a targeted treatment approach in EGFR-mutated lung cancer patients who experience MET-driven resistance. The improved response rates from ORPATHYS® added to TAGRISSO®, which is the backbone EGFR-mutated lung cancer therapy, reinforce the importance of identifying MET aberration and validate our combination strategy to address resistance while allowing continued TAGRISSO® treatment."

Weiguo Su, Chief Executive Officer and Chief Scientific Officer, HUTCHMED, said: "Previous results from the SAVANNAH Phase II trial provided a novel biomarker approach for identifying patients with MET overexpression and/or amplification who are most likely to benefit from a MET-directed therapy, an existing unmet need. These new, positive results affirm our selective, patient-centric approach, which could allow us to deliver the first biomarker-driven targeted therapy combination option in this setting."

The safety and tolerability of TAGRISSO® plus ORPATHYS® was consistent with the known safety profiles of the combination and each treatment alone. No new safety signals were identified.

In August 2022, initial positive ORR results from the SAVANNAH trial were presented at the International Association for the Study of Lung Cancer 2022 World Conference on Lung Cancer (WCLC).

The global SAFFRON Phase III trial sponsored by AstraZeneca will further assess the TAGRISSO® plus ORPATHYS® combination versus platinum-based doublet chemotherapy in patients with EGFRm, MET-overexpressed and/or amplified, locally advanced or metastatic NSCLC following TAGRISSO®. Patients are being prospectively selected using the high MET level cut-off identified in SAVANNAH.

About NSCLC and MET aberrations

Lung cancer is the leading cause of cancer death among both men and women, accounting for about one-fifth of all cancer deaths.[2,3] Lung cancer is broadly split into NSCLC and small cell lung cancer.[4] Each year there are an estimated 2.4 million people diagnosed with lung cancer globally, with 80-85% of patients diagnosed with NSCLC, the most common form of lung cancer.[2,4,5] Approximately 10-15% of NSCLC patients in the US and Europe, and 30-40% of patients in Asia have EGFRm NSCLC.[6,7,8]

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 the primary mechanism of acquired resistance to EGFR TKIs for metastatic EGFRm NSCLC. Among patients who experience disease progression post-osimertinib treatment, approximately 15-50% present with MET aberration.[9,10,11,12,13] The prevalence of MET depends on the sample type, detection method and assay cut-off used.[14]

About SAVANNAH

SAVANNAH is an ongoing global, randomised, Phase II trial sponsored by AstraZeneca studying the efficacy of ORPATHYS® added to TAGRISSO® in patients with EGFRm, locally advanced or metastatic NSCLC with MET overexpression and/or amplification who progressed following treatment with TAGRISSO®. Based on the original single-arm trial design, patients were treated with ORPATHYS® 300 or 600 mg once-daily (QD) or 300 mg twice-daily, in combination with oral TAGRISSO® 80 mg QD. In 2022, a registrational component was added to the trial that compared ORPATHYS® 300 mg twice-daily and TAGRISSO® 80 mg QD to ORPATHYS® 300 mg twice-daily and placebo.

The trial enrolled over 360 patients in more than 80 centers globally, including in North America, Europe, South America and Asia. The primary endpoint is ORR and key secondary endpoints include progression-free survival and duration of response.

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 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 overexpression.

It is approved in China 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 the first selective MET inhibitor approved in China and the first in the National Reimbursement Drug List of China (NRDL).

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 addition to SAVANNAH and SAFFRON, in China the combination of savolitinib and osimertinib in lung cancer is also being studied in the SACHI and SANOVO Phase III trials.

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. It has approximately 5,000 personnel across all its companies, at the center of which is a team of about 1,800 in oncology/immunology. Since inception, HUTCHMED has focused on bringing cancer 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 announcement 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 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; and AstraZeneca's ability to successfully develop and commercialize savolitinib.. 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 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 announcement, whether as a result of new information, future events or circumstances or otherwise.

Medical Information

This announcement 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.

Inside Information

This announcement contains inside information for the purposes of Article 7 of Regulation (EU) No 596/2014 (as it forms part of retained EU law as defined in the European Union (Withdrawal) Act 2018).

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By Order of the Board

Edith Shih
Non-executive Director and Company Secretary

Hong Kong, October 16, 2024

As at the date of this announcement, the Directors of the Company are:

Chairman and Non-executive Director:
Dr Dan ELDAR

Executive Directors:
Dr Weiguo SU
(Chief Executive Officer and Chief Scientific Officer)
Mr CHENG Chig Fung, Johnny
(Chief Financial Officer)

Non-executive Directors:
Ms Edith SHIH
Ms Ling YANG

Independent Non-executive Directors:
Mr Paul Rutherford CARTER
(Senior Independent Director)
Dr Renu BHATIA
Mr Graeme Allan JACK
Professor MOK Shu Kam, Tony