

## Press Release

### **HUTCHMED and AstraZeneca Initiate Phase II Trial of ORPATHYS® in Patients with MET Amplified Gastric Cancer**

*— Follows multiple Phase II studies of ORPATHYS® in Asia including VIKTORY, which reported an 50% objective response rate (ORR) in gastric cancer patients whose tumors harbor MET amplification —*

**Hong Kong, Shanghai & Florham Park, NJ — Wednesday, July 28, 2021:** HUTCHMED (China) Limited ("[HUTCHMED](#)") (Nasdaq/AIM:HCM; HKEX:13) and AstraZeneca PLC ("AstraZeneca") (LSE/STO/Nasdaq: AZN) have initiated a Phase II study of ORPATHYS® (savolitinib), an oral, potent, and highly selective small molecule inhibitor of MET, a receptor tyrosine kinase, in patients with advanced or metastatic MET amplified gastric cancer ("GC") or adenocarcinoma of the gastroesophageal junction ("GEJ"). The first patient was dosed on July 27, 2021.

The Phase II trial 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. The primary endpoint is objective response rate ("ORR") as assessed by an independent review committee. Other endpoints include 12-week and 6-month progression-free survival ("PFS") rates, median PFS, duration of response ("DoR"), disease control rate ("DCR"), median overall survival ("OS"), safety, PK and quality of life.

The Beijing Cancer Hospital is the lead institution of this study. The lead investigator is Dr Shen Lin. For more information, please see [clinicaltrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT04923932) identifier: [NCT04923932](https://clinicaltrials.gov/ct2/show/study/NCT04923932).

MET-driven gastric cancer has a very poor prognosis.<sup>1</sup> This trial follows multiple Phase II studies that have been conducted in Asia to study ORPATHYS® in MET-driven gastric cancer patients, including VIKTORY.<sup>2</sup> VIKTORY is an investigator initiated Phase II umbrella study in gastric cancer in South Korea in which a total of 715 patients were successfully sequenced into molecular-driven patient groups, including those with MET amplified gastric cancer. Patients whose tumors harbor MET amplification were treated with ORPATHYS® monotherapy, reporting an ORR of 50% (10/20, 95% CI: 28.0, 71.9).

It is estimated that MET amplification accounts for approximately 4-6% of GC patients.<sup>2,3</sup> The annual incidence of MET amplification GC is estimated to be approximately 24,000 in China.<sup>4</sup>

#### **About ORPATHYS®**

ORPATHYS® is an oral, potent, and highly selective MET tyrosine kinase inhibitor ("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.

ORPATHYS® is [marketed](#) in China for the treatment of patients with non-small cell lung cancer ("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 ORPATHYS®. 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 ORPATHYS® in China. AstraZeneca is responsible for the commercialization of ORPATHYS® in China and worldwide. Sales of ORPATHYS® will be recognized by AstraZeneca.

## **ORPATHYS® development in NSCLC**

Phase II study of ORPATHYS® monotherapy in MET Exon 14 skipping alteration NSCLC (NCT02897479) – In June 2021, ORPATHYS® 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 presented during the American Society of Clinical Oncology ASCO20 Virtual Scientific Program in May 2020, and updated results were published in *The Lancet Respiratory Medicine*<sup>5</sup> in June 2021. At a median follow up of 17.6 months, ORPATHYS® 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. PFS was clinically meaningful across subgroups, and ORR results were consistent regardless of prior treatment or tumor histology, including in patients with the pulmonary sarcomatoid carcinoma (PSC) subtype (40.0%, 95% CI 21.1-61.3) and patients with other NSCLC subtypes (44.4%, 95% CI 29.6-60.0). Disease control rate (“DCR”) in the overall trial population was 82.9% (95% CI 72.0-90.8). The safety and tolerability profile of ORPATHYS® 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](#)).

SAVANNAH Phase II study of ORPATHYS® 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.

Phase III study of ORPATHYS® in combination with TAGRISSO® in patients who have progressed following EGFR TKI treatment due to MET amplification (in planning) – 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.

Phase III study of ORPATHYS® in combination with TAGRISSO® in treatment naïve patients with EGFR mutant positive NSCLC with MET overexpression (in planning) – This is a randomized, blinded study in China in untreated, unresectable or metastatic patients with EGFR mutation positive NSCLC with MET positive tumors.

## **ORPATHYS® 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 ORPATHYS® monotherapy compared with sunitinib monotherapy in MET-driven papillary RCC was presented at the ASCO 2020 Program and published simultaneously in *JAMA Oncology*<sup>6</sup>. ORPATHYS® demonstrated encouraging activity, including an ORR of 27% versus 7% for sunitinib, with no ORPATHYS® responding patients experiencing disease progression at data cut-off, and an encouraging overall survival (“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 ORPATHYS® in combination with IMFINZI® PD-L1 inhibitor in RCC (NCT02819596) – The CALYPSO study is an investigator initiated open-label Phase I/II study of ORPATHYS® in combination with IMFINZI®, a PD-L1 antibody owned by AstraZeneca. The study is evaluating the safety and efficacy of the ORPATHYS®/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<sup>7</sup>, showing a confirmed response rate in 14 MET-driven patients of 57%, with a median duration of response (“DoR”) of 9.4 months, median PFS of 10.5 months and median OS of 27.4 months. No new safety signals were seen.

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 intend to initiate a global Phase III, open-label, randomized, controlled study of ORPATHYS® plus IMFINZI® versus sunitinib monotherapy versus IMFINZI® monotherapy in patients with MET-driven, unresectable and locally advanced or metastatic PRCC.

## **ORPATHYS® development in other cancer indications**

ORPATHYS® opportunities are also continuing to be explored in multiple other MET-driven tumor settings via investigator-initiated studies including non-small cell lung cancer, gastric cancer and 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. A dedicated organization of over 1,300 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](http://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 gastric cancer, 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 gastric cancer 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 gastric cancer 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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<sup>3</sup> Van Cutsem E, Karaszewska B, Kang YK, et al. A Multicenter Phase II Study of AMG 337 in Patients with MET-Amplified Gastric/Gastroesophageal Junction/Esophageal Adenocarcinoma and Other MET-Amplified Solid Tumors. *Clin Cancer Res*. 2019;25(8):2414-2423. doi:10.1158/1078-0432.CCR-18-1337

<sup>4</sup> Global Cancer Observatory. China Fact Sheet. [gco.iarc.fr/today/data/factsheets/populations/160-china-fact-sheets.pdf](http://gco.iarc.fr/today/data/factsheets/populations/160-china-fact-sheets.pdf).

<sup>5</sup> Lu S, et al. Once-daily savolitinib in Chinese patients with pulmonary sarcomatoid carcinomas and other non-small-cell lung cancers harbouring MET exon 14 skipping alterations: a multicentre, single-arm, open-label, phase 2 study. *Lancet Respir Med*. 2021 Jun 21:S2213-2600(21)00084-9. doi: [10.1016/S2213-2600\(21\)00084-9](https://doi.org/10.1016/S2213-2600(21)00084-9).

<sup>6</sup> Choueiri TK, et al. Efficacy of Savolitinib vs Sunitinib in Patients With MET-Driven Papillary Renal Cell Carcinoma: The SAVOIR Phase 3 Randomized Clinical Trial. *JAMA Oncol*. 2020 Aug 1;6(8):1247-1255. doi: [10.1001/jamaoncol.2020.2218](https://doi.org/10.1001/jamaoncol.2020.2218).

<sup>7</sup> Powles T, et al. A phase II study investigating the safety and efficacy of savolitinib and durvalumab in metastatic papillary renal cancer (CALYPSO). *J Clin Oncol* 37, 2019 (suppl 7S; abstr 545). doi: [10.1200/JCO.2019.37.7\\_suppl.545](https://doi.org/10.1200/JCO.2019.37.7_suppl.545).