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Press Release

HUTCHMED Highlights Presentations at American Association for Cancer Research Annual Meeting 2023

Hong Kong, Shanghai & Florham Park, NJ - Wednesday, April 12, 2023: HUTCHMED (China) Limited ("HUTCHMED") (Nasdaq/AIM: HCM, HKEX: 13) today announces that new and updated clinical and non-clinical data related to five HUTCHMED investigational drug candidates will be presented during the American Association for Cancer Research Annual Meeting 2023 (AACR 2023), which will take place from April 14 to 19, 2023 in Orlando, Florida.

Savolitinib

Title:	**A multicenter Phase II study of savolitinib in patients with MET-amplified gastroesophageal junction adenocarcinomas or gastric cancer**
Lead Author:	Lin Shen, MD, Peking University Cancer Hospital & Institute
Type:	Poster presentation
Session Number:	PO.CT02.01 - Phase II Clinical Trials 1
Abstract Link:	https://www.abstractsonline.com/pp8/#!/10828/presentation/10376

Title:	**Baseline and on-treatment plasma-based genomics as a predictor of outcome in SAVANNAH: Savolitinib + osimertinib in EGFRm MET overexpressed/amplified NSCLC post-osimertinib**
Lead Author:	Ryan J Hartmaier, Ph.D, AstraZeneca
Type:	Poster presentation
Session Number:	LB294/7
Abstract Link:	https://www.abstractsonline.com/pp8/#!/10828/presentation/9996

Mesenchymal epithelial transition factor ("MET") gene amplification is associated with poor prognosis in gastric cancer ("GC") and gastroesophageal junction adenocarcinomas ("GEJ"). Savolitinib is a potent and highly selective oral MET tyrosine-kinase inhibitor.

Here we reported the preliminary efficacy and safety data from a Phase II trial of savolitinib monotherapy in patients with MET-amplified advanced or metastatic GC/GEJ (NCT04923932). Additionally, utility of plasma-based genomics was investigated in the SAVANNAH Phase II trial of savolitinib in addition to osimertinib in epidermal growth factor receptor (EGFR) mutated, MET overexpressed/amplified non-small cell lung cancer ("NSCLC") post osimertinib. First presentation of the SAVANNAH results occurred at the International Association for the Study of Lung Cancer (IASLC) 2022 World Conference on Lung Cancer (WCLC) in August 2022.

Surufatinib

Title:	**Surufatinib plus toripalimab for first-line treatment of advanced non-small cell lung cancer (NSCLC) with PD-L1 positive expression: A multicenter, single-arm phase 2 study**
Lead Author:	Ying Cheng, MD, Jilin Cancer Hospital
Type:	Poster presentation
Session Number:	PO.CT02.02 - Phase II Clinical Trials 2
Abstract Link:	https://www.abstractsonline.com/pp8/#!/10828/presentation/10405

Surufatinib (a small-molecule inhibitor of vascular endothelial growth factor receptor ("VEGFR") 1-3, fibroblast growth factor receptor ("FGFR") 1 and colony-stimulating factor 1 receptor ("CSF-1R")) plus toripalimab (an anti-programmed cell death protein-1 ("PD-1") antibody) showed encouraging antitumor activity in solid tumors. Programmed death ligand 1 ("PD-L1") expression is the established biomarker for first-line immune checkpoint inhibitors therapy in advanced NSCLC. We conducted an open-label, multi-cohort, single-arm Phase II study to evaluate the safety and efficacy of surufatinib plus toripalimab in patients with advanced solid tumors. Here, we reported the results of advanced NSCLC with PD-L1 positive expression cohort (NCT04169672).

HMPL-760

Title:	**HMPL-760 is a highly potent and selective reversible BTK inhibitor, targeting BTK and BTK^{C481S} in B-cell malignancies**
Lead Author:	Linfang Wang, HUTCHMED
Type:	Poster presentation
Session Number:	PO.ET09.07 - Tyrosine Kinase and Phosphatase Inhibitors 1
Abstract Link:	https://www.abstractsonline.com/pp8/#!/10828/presentation/6728

Bruton's tyrosine kinase ("BTK"), a member of the Tec family, plays a crucial role in signaling through B-cell receptor ("BCR"). BTK inhibition blocks BCR signals and prevents B-cell activation and growth. First-generation BTK inhibitors such as ibrutinib covalently binds to a cysteine residue ("C481") of BTK. Their most frequent acquired resistance is the development of a serine mutation in the binding site ("C481S"). Next generation BTK inhibitors such as HMPL-760 aim to overcome this resistance to first-generation inhibitors.

The poster outlined preclinical data showing HMPL-760 is a reversible, selective, highly potent BTK inhibitor targeting both BTK^{WT} and BTK^{C481S}. The first-in-human Phase I clinical trials of HMPL-760 are under way in patients with relapsed/refractory B-Cell Non-Hodgkin's Lymphoma (NCT05190068).

HMPL-306

Title:	**Preclinical characteristic of HMPL-306, a CNS-penetrable dual inhibitor of mutant IDH1 and IDH2**
Lead Author:	Na Yang, HUTCHMED
Type:	Poster presentation
Session Number:	PO.ET01.01 - Oncogenes and Tumor Suppressor Genes as Targets for Therapy 1
Abstract Link:	https://www.abstractsonline.com/pp8/#!/10828/presentation/8579

Mutations in isocitrate dehydrogenase ("IDH") 1/2 are frequently identified in various cancers, such as acute myeloid leukemia ("AML"), cholangiocarcinoma, chondrosarcoma and glioma. Mutant IDHs ("mIDHs") cause accumulated 2-hydroxyglutarate, leading to blockage of cell differentiation, thereby inducing malignant transformation. Rare cases were identified carrying co-existing mutations in IDH1 and IDH2. mIDH isoform switching, from mutant IDH1 to mutant IDH2 and vice versa, have been reported as a mechanism of acquired resistance to IDH inhibition in AML and cholangiocarcinoma. Thus, simultaneous inhibition on both mIDH1 and mIDH2 may be a promising strategy to overcome resistance and improve clinical efficacy. HMPL-306, a dual inhibitor of mIDH1/mIDH2, developed by HUTCHMED, is being evaluated in clinical trials (NCT04272957, NCT04762602, NCT04764474).

The poster outlines preclinical data that shows that HMPL-306 is a potent, durable, dual inhibitor of IDH1/2 mutation that crosses the blood brain barrier and demonstrated effect on pharmacodynamic markers that lead to the differentiation of immature malignant cells to mature normal cells. The strong activity and favorable pharmacokinetics profiles support further clinical evaluation.

HMPL-453

Title:	**HMPL-453, a highly selective inhibitor of fibroblast growth factor receptors 1, 2, and 3, displays potent activity in FGFR-altered tumor models**
Lead Author:	Jia Hu, HUTCHMED
Type:	Poster presentation
Session Number:	PO.ET01.07 - Growth Factor Receptors as Therapeutic Targets
Abstract Link:	https://www.abstractsonline.com/pp8/#!/10828/presentation/8706

Fibroblast growth factors ("FGFs") and their receptors ("FGFRs") regulate numerous cellular processes. Dysregulation of FGFR signaling due to receptor fusion, mutation or amplification is observed across multiple cancer types, making activated FGFRs an important therapeutic target. Herein, we presented the preclinical characterization of HMPL-453, a highly potent and selective inhibitor of FGFR1, 2, and 3, discovered and being currently developed in Phase II clinical trial (NCT04353375) by HUTCHMED.

The presentation outlines preclinical data that shows that HMPL-453 is a highly potent and selective inhibitor of FGFR 1, 2, and 3 with strong activity against FGFR-deregulated tumors in preclinical models, supporting continued investigation in patients with FGFR alterations (such as fusion and mutation) either as a single agent or in combination with PD-1 blockade.

About Savolitinib (ORPATHYS® in China)

Savolitinib is an oral, potent and highly selective MET tyrosine kinase inhibitor 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.

In 2011, AstraZeneca and HUTCHMED entered a global licensing and collaboration agreement to jointly develop and commercialize savolitinib. 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.

About Surufatinib (SULANDA® in China)

Surufatinib is a novel, oral angio-immuno kinase inhibitor that selectively inhibits the tyrosine kinase activity associated with VEGFR and FGFR, which both inhibit angiogenesis, and CSF-1R, which regulates tumor-associated macrophages, promoting the body's immune response against tumor cells. Its unique dual mechanism of action may be very suitable for possible combinations with other immunotherapies, where there may be synergistic anti-tumor effects.

HUTCHMED currently retains all rights to surufatinib worldwide.

About HMPL-760

HMPL-760 is an investigational, non-covalent, third-generation BTK inhibitor. It is a highly potent, selective, and reversible inhibitor against both wild-type and C481S-mutated BTK.

HUTCHMED currently retains all rights to HMPL-760 worldwide.

About HMPL-306

HMPL-306 is a novel dual-inhibitor of □DH1 and □DH2 enzymes. □DH1 and □DH2 mutations have been implicated as drivers of certain hematological malignancies, gliomas and solid tumors, particularly among acute myeloid leukemia patients.

HUTCHMED currently retains all rights to HMPL-306 worldwide.

About HMPL-453

HMPL 453 is a novel, highly selective and potent inhibitor targeting FGFR 1, 2 and 3. Aberrant FGFR signaling has been found to be a driving force in tumor growth (through tissue growth and repair), promotion of angiogenesis and resistance to anti-tumor therapies. Abnormal FGFR gene alterations are believed to be the drivers of tumor cell proliferation in several solid tumor settings.

HUTCHMED currently retains all rights to HMPL-453 worldwide.

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 5,000 personnel across all its companies, at the center of which is a team of about 1,800 in oncology/immunology. Since inception it has focused on bringing cancer drug candidates from in-house discovery to patients around the world, with its first three oncology drugs now approved and marketed in China. 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, includ-ing its expectations regarding the thera-peutic potential of savolitinib, surufatinib, HMPL-760, HMPL-306 and HMPL-453, the further clinical develop-ment for savolitinib, surufatinib, HMPL-760, HMPL-306 and HMPL-453, its expectations as to whether any studies on savolitinib and HMPL-453 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, surufatinib, HMPL-760, HMPL-306 and HMPL-453, 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, surufatinib, HMPL-760, HMPL-306 and HMPL-453 for a targeted indication; the sufficiency of funding; and the impact of the COVID-19 pandemic on general economic, regulatory and political conditions. 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.

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