Press Release

HUTCHMED Initiates International Phase I Trials of IDH1/2 Dual Inhibitor in Patients with Advanced Solid Tumors or Hematological Malignancies

— HMPL-306 is the sixth innovative oncology drug candidate discovered in house by HUTCHMED to enter into global development —

Hong Kong, Shanghai & Florham Park, NJ — Monday, March 29, 2021: Hutchison China MediTech Limited ("HUTCHMED") (Nasdaq/AIM: HCM) has initiated two international Phase I studies of HMPL-306, its novel selective small molecule dual inhibitor of isocitrate dehydrogenase ("IDH") 1 and 2 mutations. One trial is in patients with advanced solid tumors and one trial is in patients with hematological malignancies. Both trials have sites in the US and Europe. The first international patient was dosed on March 25, 2021, following a Phase I trial that was initiated in China in the second half of 2020. This new program is a demonstration of HUTCHMED's accelerating and expanding global clinical development presence.

These two trials are multi-center studies to evaluate the safety, tolerability pharmacokinetics, pharmacodynamics and preliminary efficacy of HMPL-306. The first trial is in solid tumors (including but not limited to gliomas, chondrosarcomas, or cholangiocarcinomas), while a second trial is in advanced relapsed, refractory or resistant hematological malignancies that harbor IDH1 or IDH2 mutations. The first stage of each study is a dose escalation phase where cohorts of patients will receive ascending oral doses of HMPL-306 to determine the maximum tolerated dose and/or the recommended Phase II dose ("RP2D"). The second stage is a dose expansion phase where patients will receive HMPL-306 to further evaluate the safety, tolerability, and clinical activity at the RP2D. Additional details may be found at clinicaltrials.gov, using identifiers NCT04762602 and NCT04764474, respectively.

The MD Anderson Cancer Center ("MDACC") is the lead institution on both studies. The lead investigator for the hematological malignancies study is Dr. Farhad Ravandi, the Janiece and Stephen A. Lasher Professor of Medicine and Chief of Section of Developmental Therapeutics in the Department of Leukemia at The University of Texas MDACC. The lead investigator for the solid tumor study is Dr. Filip Janku, Associate Professor, Department of Investigational Cancer Therapeutics at The University of Texas MDACC.

A Phase I study of HMPL-306 is underway in China, with the first patient dosed in July 2020. Additional details of that study may be found at clinicaltrials.gov, using identifier NCT04272957.

HMPL-306 is HUTCHMED's ninth innovative oncology drug candidate that it has discovered that has entered clinical development and the sixth to enter global clinical development. Cytoplasmic mutant IDH1 and mitochondrial mutant IDH2 have been known to switch to the other form when targeted by an inhibitor of IDH1 mutant alone or IDH2 mutant alone. By targeting both IDH1 and IDH2 mutations, HMPL-306 could potentially provide therapeutic benefits in cancer patients harboring either IDH mutation, and may address acquired resistance to IDH inhibition through isoform switching.

About IDH and Malignancies

IDHs are critical metabolic enzymes that help to break down nutrients and generate energy for cells. When mutated, IDH creates a molecule that alters the cell's genetic programming and prevents cells from maturing, 2-hydroxyglutarate ("2-HG"). Reduction in 2-HG levels can be used as a marker of target engagement by an IDH inhibitor. IDH1 or IDH2 mutations are common genetic alterations in various types of blood and solid tumors, including acute myeloid leukemia ("AML") with approximately 20% of patients having mutant IDH genes, myelodysplastic syndrome (MDS), myeloproliferative neoplasms (MPNs), low-grade glioma and intrahepatic cholangiocarcinoma ("IHCC"). Mutant IDH isoform switching, either from cytoplasmic mutant IDH1 to mitochondrial mutant IDH2, or vice versa, is a mechanism of acquired resistance to IDH inhibition in AML and cholangiocarcinoma.[1,2,3] Currently, the U.S. Food and Drug Administration (FDA) has approved one drug for IDH1 mutation and one drug for IDH2 mutation, but no dual inhibitor targeting both IDH1 and IDH2 mutants has been approved.

In the US, it is estimated that there were approximately 20,000 new cases of AML in 2020 and the five-year relative survival rate is 28.7%.[4]

IDH mutations are present in a number of solid tumors, including malignant glioma and IHCC. In the US, the annual incidence of malignant glioma is estimated to be 20,000, 50-70% of which are glioblastoma.[5,6] Approximately 60-80% of Grade 2 or 3 glioma and secondary glioblastoma harbor IDH mutations.[7] IHCC accounts for 10-20% of primary liver cancer, which was estimated to be diagnosed in 42,810 US patients in 2020.[8,9] Approximately 20-30% of IHCC harbors IDH mutations.[10]

About HUTCHMED

HUTCHMED (Nasdaq/AIM: HCM) is an innovative, commercial-stage, biopharmaceutical company committed, over the past twenty years, to the discovery and global development of targeted therapies and immunotherapies for the treatment of cancer and immunological diseases. It has advanced ten cancer drug candidates from discovery into clinical studies around the world and has extensive commercial infrastructure in its home market of China. For more information, please visit: www.hutch-med.com.

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 for the initiation of clinical development of HMPL-306 and the potential benefits of HMPL-306 in patients harboring IDH mutations. Forward-looking statements involve risks and uncertainties. Such risks and uncertainties include, among other things, assumptions regarding clinical trial enrollment rates, 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 drug candidate HMPL-306 as a monotherapy or in combinations 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 HMPL-306 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 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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