Press Release

HUTCHMED Initiates the RAPHAEL Registrational Phase III Trial of HMPL-306 for Patients with IDH1- and/or IDH2-Mutated Relapsed/Refractory Acute Myeloid Leukemia in China

Hong Kong, Shanghai & Florham Park, NJ — Tuesday, May 14, 2024: HUTCHMED (China) Limited ("HUTCHMED") (Nasdaq/AIM:HCM; HKEX:13) today announces that it has initiated a registrational Phase III clinical trial of HMPL-306 in patients with mutated isocitrate dehydrogenase ("IDH") 1 or 2 relapsed / refractory acute myeloid leukemia ("AML") in China. The first patient received their first dose on May 11, 2024.

HMPL-306 is a novel dual-inhibitor of IDH1 and IDH2 enzymes. Mutations of IDH1 and IDH2 have been implicated as drivers of certain hematological malignancies, gliomas and solid tumors, particularly among AML patients. Although some IDH inhibitors have been approved in certain markets for AML, isoform switching between the cytoplasmic mutant IDH1 and mitochondrial mutant IDH2 often leads to acquired resistance to single inhibitors of IDH1 or IDH2. Targeting both IDH1 and IDH2 mutations may provide therapeutic benefits in cancer patients by overcoming this acquired resistance.

RAPHAEL is a multicenter, randomized, open-label, registrational Phase III clinical trial designed to evaluate the safety and efficacy of HMPL-306 as a monotherapy in patients with relapsed or refractory AML harboring IDH1 and/or IDH2 mutations. The primary endpoint of overall survival (OS) and the secondary endpoints, including event-free survival (EFS) and complete remission ("CR") rate, will be tested in comparison with current salvage chemotherapy regimens. The Company is looking to enroll approximately 320 patients for this registrational study, which is being led by principal investigator Prof Xiaojun Huang of Peking University People's Hospital. Additional details may be found at clinicaltrials.gov, using identifier NCT06387069.

The study follows positive data from a two-stage, open-label Phase I study evaluating the safety, pharmacokinetics, pharmacodynamics and efficacy of HMPL-306 in this indication (NCT04272957). The first-in-human dose-escalation stage data was presented at the European Hematology Association Congress ("EHA") in June 2023.[1] Results of the dose expansion stage of the study in over 50 patients demonstrated promising CR rates at the recommended Phase II dose are expected to be presented at the EHA Congress in June 2024.

About IDH and Hematological 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. IDH1 or IDH2 mutations are common genetic alterations in various types of blood and solid tumors, including AML with approximately 14-20% of patients having mutant IDH genes, myelodysplastic syndrome (MDS), myeloproliferative neoplasms (MPNs), low-grade glioma and intrahepatic cholangiocarcinoma. 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.[2,3,4]

According to the National Cancer Institute (NCI), there will be approximately 20,380 new cases of AML in the U.S. in 2023 and the five-year relative survival rate is 31.7%[5]. Currently, the U.S. Food and Drug Administration (FDA) has approved two drugs for IDH1 mutation and one drug for IDH2 mutation, but no dual inhibitor targeting both IDH1 and IDH2 mutants has been approved. There were an estimated 19,700 new cases of AML in China in 2018 and is estimated to reach 24,200 in China in 2030.[6] In China one IDH1 inhibitor was approved in 2022.

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 now marketed in China, the first of which is also marketed in the U.S. 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, including its expectations regarding the therapeutic potential of HMPL-306 for the treatment of patients with relapsed or refractory AML and the further development of HMPL-306 in this and other indications. Forward-looking statements involve risks and uncertainties. Such risks and uncertainties include, among other things, assumptions regarding the timing and outcome of clinical studies and the sufficiency of clinical data to support an NDA submission of HMPL-306 for the treatment of patients with relapsed or refractory AML or other indications in China or other jurisdictions, its potential to gain approvals from regulatory authorities on an expedited basis or at all, the efficacy and safety profile of HMPL-306, HUTCHMED's ability to fund, implement and complete its further clinical development and commercialization plans for HMPL-306 and the timing of these events. 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.

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.

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