

Press Release

Chi-Med Initiates a Phase I Trial of IDH1/2 Dual Inhibitor in Patients with Hematological Malignancies in China

— *HMPL-306 is the ninth innovative oncology drug candidate discovered in house by Chi-Med —*

Hong Kong, Shanghai & Florham Park, NJ: Friday, July 24, 2020: Hutchison China MediTech Limited (“[Chi-Med](#)”) (Nasdaq/AIM: HCM) has initiated a Phase I study of HMPL-306, its novel selective small molecule dual inhibitor of isocitrate dehydrogenase (“IDH”) 1 and 2 mutations, in patients with hematological malignancies in China. The first patient was dosed today.

This is a multi-center study to evaluate the safety, pharmacokinetics, pharmacodynamics and efficacy of HMPL-306 in patients of relapsed or refractory hematological malignancies with an IDH1 and/or IDH2 mutation. The first stage of the 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 of the study is a dose expansion phase where three cohorts of 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 identifier [NCT04272957](#).

HMPL-306 is Chi-Med’s ninth innovative oncology asset discovered in house. 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, this drug candidate may provide therapeutic benefits in cancer patients harboring IDH mutations, and may address acquired resistance to IDH inhibition through isoform switching.

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 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. 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}

According to the National Cancer Institute (NCI), there will be approximately 20,000 new cases of AML in the U.S. in 2020 and the five-year relative survival rate is 28.7%⁴. 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. There were an estimated 19,700 new cases of AML in China in 2018 and is estimated to reach 24,200 in China in 2030.⁵ In China no IDH inhibitor has been approved.

About Chi-Med

Chi-Med (Nasdaq/AIM: HCM) is an innovative 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 a portfolio of nine cancer drug candidates currently in clinical studies around the world and extensive commercial infrastructure in its home market of China. For more information, please visit: [www.chi-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 Chi-Med’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 Chi-Med's filings with the U.S. Securities and Exchange Commission and on AIM. Chi-Med 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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¹ S Choe S et al. *Blood* 2019;134(Supplement_1):545. doi:[10.1182/blood-2019-122671](https://doi.org/10.1182/blood-2019-122671).

² Harding JJ et al. Isoform Switching as a Mechanism of Acquired Resistance to Mutant Isocitrate Dehydrogenase Inhibition. *Cancer Discov.* 2018;8(12):1540-1547. doi:[10.1158/2159-8290.CD-18-0877](https://doi.org/10.1158/2159-8290.CD-18-0877).

³ Delahousse J et al. Circulating oncometabolite D-2-hydroxyglutarate enantiomer is a surrogate marker of isocitrate dehydrogenase-mutated intrahepatic cholangiocarcinomas. *Eur J Cancer.* 2018;90:83-91. doi:[10.1016/j.ejca.2017.11.024](https://doi.org/10.1016/j.ejca.2017.11.024).

⁴ Source: National Cancer Institute – seer.cancer.gov/statfacts/html/amyl.html.

⁵ Lin J et al. IDH1 and IDH2 mutation analysis in Chinese patients with acute myeloid leukemia and myelodysplastic syndrome. *Ann Hematol.* 2012;91(4):519-525. doi:[10.1007/s00277-011-1352-7](https://doi.org/10.1007/s00277-011-1352-7).