**HUTCHMED (China) Limited**

**和黃醫藥（中國）有限公司**

*(Incorporated in the Cayman Islands with limited liability)*

**(Stock Code: 13)**

## VOLUNTARY ANNOUNCEMENT

# HUTCHMED Initiates Phase I Study of BTK Inhibitor HMPL-760 in Patients with Previously Treated B-Cell Non-Hodgkin Lymphoma in China

*— HMPL-760 is the eleventh innovative potential oncology drug candidate discovered in-house by HUTCHMED —*

*— HMPL-760 is HUTCHMED's fifth candidate in clinical development for hematological malignancies, including amdizalisib and HMPL-523 that also target the B-cell receptor ("BCR") signaling pathway, and tazemetostat and HMPL-306 —*

HUTCHMED (China) Limited ("HUTCHMED") has initiated a Phase I study in China of HMPL-760, a highly potent, selective, and reversible inhibitor with long target engagement against Bruton's tyrosine kinase ("BTK"), including wild-type and C481S-mutated BTK. The first patient received their first dose on January 4, 2022.

The clinical study is a multi-center, open-label study to evaluate the safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD) and preliminary efficacy profile of HMPL-760. The study is enrolling patients with previously treated chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) or other types of Non-Hodgkin Lymphoma ("NHL"), including patients treated with a prior regimen containing a BTK inhibitor, whose disease carries either wild-type BTK or acquired resistance to first generation BTK inhibitors due to additional mutations to BTK.

An initial dose escalation stage to determine the maximum tolerated dose (MTD) and/or the recommended Phase II dose ("RP2D") is planned, to be followed by a dose expansion phase where patients will receive HMPL-760 to further evaluate the safety, tolerability, and clinical activity at the RP2D. Approximately 100 patients are expected to be enrolled.

HMPL-760 is HUTCHMED's fifth investigational drug candidate targeting hematological malignancies in clinical development. Amdizalisib (HMPL-689, targeting the delta isoform of phosphoinositide 3-kinase or PI3K delta) and HMPL-523 (targeting spleen tyrosine kinase or Syk) are also being studied in several Phase II trials against B-cell dominant malignancies. Phase II registration studies are underway in China for amdizalisib in patients with follicular lymphoma (FL), for which it has been granted Breakthrough Therapy Designation in China, and marginal zone lymphoma (MZL).

In addition to the three BCR inhibitors, for hematological malignancies HUTCHMED is also developing its in-house discovered drug candidate HMPL-306, a dual-inhibitor of mutant isocitrate dehydrogenase 1 and 2, and tazemetostat, a methyltransferase inhibitor of EZH2 (being developed in Greater China by HUTCHMED pursuant to a strategic collaboration with Epizyme).

## About BTK and Non-Hodgkin Lymphoma

BTK is a key component of the B-cell receptor signaling pathway and is an important regulator of cell proliferation and cell survival in various lymphomas. The abnormal activation of B-cell receptor signaling is closely related to the development of B-cell type hematological cancers, which represent approximately 85% of all NHL cases.[1] BTK is considered a validated target for drugs that aim to treat certain hematological cancers, however C481S mutation of BTK is a known resistance mechanism for first and second generation BTK inhibitors. In 2020, approximately 93,000 new cases of NHL are estimated to have been diagnosed in China.[2]

## About HMPL-760

HMPL-760 is an investigational, highly selective, non-covalent, third-generation inhibitor of BTK, both wild-type and C481S mutant enzymes, with pre-clinical data suggesting high target specificity and higher potency versus first generation BTK inhibitors. BTK C481S mutation plays an important role in resistance to certain BTK inhibitors.[3,4]

HMPL-760 is HUTCHMED's eleventh innovative potential oncology drug candidate to enter clinical development. HUTCHMED currently retains all rights to HMPL-760 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 4,500 personnel across all its companies, at the center of which is a team of over 1,400 in oncology/immunology. Since inception it has advanced 11 cancer drug candidates from in-house discovery into clinical studies 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 announcement 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-760, amdizalisib, HMPL-523, HMPL-306 and tazemetostat for patients, its expectations as to whether any studies on HMPL-760, amdizalisib, HMPL-523, HMPL-306 and tazemetostat 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 HMPL-760, amdizalisib, HMPL-523, HMPL-306 and tazemetostat, 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 HMPL-760, amdizalisib, HMPL-523, HMPL-306 and tazemetostat 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 announcement, whether as a result of new information, future events or circumstances or otherwise.*

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[1] American Cancer Society (2019, January 29). *Types of B-cell Lymphoma.* https://www.cancer.org/cancer/non-hodgkin-lymphoma/about/b-cell-lymphoma.html. Accessed January 5, 2022.

[2] The Global Cancer Observatory, China fact sheet. https://gco.iarc.fr/today/data/factsheets/populations/160-china-fact-sheets.pdf. Accessed November 17, 2021.

[3] Woyach JA, Ruppert AS, Guinn D, et al. BTK$^{C481S}$-Mediated Resistance to Ibrutinib in Chronic Lymphocytic Leukemia. *J Clin Oncol.* 2017;35(13):1437-1443. doi:10.1200/JCO.2016.70.2282.

[4] Woyach JA, Huang Y, Rogers K, et al. Resistance to Acalabrutinib in CLL is Mediated Primarily by BTK Mutations. *Blood.* 2019;134 (Supplement_1): 504. doi:10.1182/blood-2019-127674.

By Order of the Board

**Edith Shih**
*Non-executive Director and Company Secretary*

Hong Kong, January 10, 2022

As at the date of this announcement, the Directors of the Company are:

**Executive Directors:**
Mr TO Chi Keung, Simon
*(Chairman)*
Mr Christian Lawrence HOGG
*(Chief Executive Officer)*
Mr CHENG Chig Fung, Johnny
*(Chief Financial Officer)*
Dr Weiguo SU
*(Chief Scientific Officer)*

**Non-executive Directors:**
Dr Dan ELDAR
Ms Edith SHIH

**Independent Non-executive Directors:**
Mr Paul Rutherford CARTER
*(Senior Independent Director)*
Dr Karen Jean FERRANTE
Mr Graeme Allan JACK
Professor MOK Shu Kam, Tony