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 Global Clinical Development of ATTC Candidate HMPL-A251 in Patients with Solid Tumors

— First-in-human trial of candidate from the next-generation ATTC platform —

— Simultaneous China and global clinical development strategy to expedite development process —

HUTCHMED (China) Limited ("HUTCHMED") today announces the initiation of its global Phase I clinical development program for HMPL-A251, a first-in-class PI3K/PIKK-HER2 Antibody-Targeted Therapy Conjugate ("ATTC") comprising a highly selective and potent PI3K/PIKK inhibitor payload conjugated to a humanized anti-HER2 IgG1 antibody via a cleavable linker. Study sites are in the US and China. The first patient received the first dose on December 16, 2025, in China.

This first-in-human Phase I/IIa, open-label, multicenter clinical study evaluates HMPL-A251 monotherapy in adult patients with unresectable, advanced or metastatic HER2-expressing solid tumors. The study is divided into two parts, a Phase I dose escalation part and a Phase IIa dose expansion and optimization part. The primary outcome measures are to evaluate the safety and tolerability of HMPL-A251 and to determine the maximum tolerated dose (MTD) and/or recommended dose(s) for expansion ("RDE") in the Phase I part, and to further evaluate safety and preliminary efficacy at RDEs and to determine the recommended dose for Phase II (RP2D) or Phase III (RP3D) in the Phase IIa part. Secondary outcome measures include preliminary antitumor activity, pharmacokinetic profile, and the immunogenicity of HMPL-A251. Additional details may be found at clinicaltrials.gov, using identifier NCT07228247.

HMPL-A251 is the first clinical-stage candidate derived from HUTCHMED's next-generation ATTC platform. The first family of programs are based on a highly potent and selective PI3K/PIKK inhibitor payload. By conjugating this highly novel payload to an anti-HER2 antibody, the molecule is designed to deliver targeted pathway inhibition directly into HER2-expressing tumor cells, thereby potentially overcoming the systemic toxicity and narrow therapeutic index historically associated with PI3K/PIKK inhibitors. This approach aims to achieve deeper and more durable target inhibition while improving the overall tolerability profile.

Preclinical data for HMPL-A251 were presented at the 2025 AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics. This body of evidence supports the translational potential of the ATTC platform, the ongoing global clinical evaluation of HMPL-A251, and the broad potential of HUTCHMED's PI3K/PIKK inhibitor linker-payload to underpin a family of future ATTC drug candidates.

About the ATTC Platform

HUTCHMED's ATTC platform represents a next-generation approach to precision oncology, combining monoclonal antibodies with proprietary small-molecule inhibitor payloads to deliver dual mechanisms of action. Unlike traditional cytotoxin-based Antibody Drug Conjugates, ATTCs combine targeted therapies to achieve synergistic anti-tumor activity and durable responses in preclinical models, outperforming standalone antibody or small-molecule inhibitor components in efficacy and safety.

Built on over 20 years of targeted therapy expertise, the platform enables development of drug candidates for diverse cancer types. By leveraging antibody-guided delivery and tumor-specific payload release, ATTCs improve the accessibility to tumors and reduce off-tumor toxicity. This overcomes challenges of traditional small-molecule inhibitors, ensures safer long-term use, and supports combinations with chemotherapy and immunotherapy, unlocking potential for early-line treatments.

About the PAM Pathway and HMPL-A251

The PI3K/AKT/mTOR ("PAM") pathway is a critical intracellular network involved in cell growth, survival, and division. Alterations in the PAM pathway are frequently associated with poor prognosis and resistance to treatment across various cancers. However, existing PAM-targeted drugs face significant challenges, including on-target toxicities that restrict dosing, feedback loops that enable pathway reactivation, and insufficient tumor-specific delivery. HUTCHMED has designed a highly novel PI3K/PIKK inhibitor linker-payload to overcome these challenges with broad potential to lead to a family of antibody conjugate drug candidates.

HMPL-A251 is a first-in-class ATTC comprising of this highly selective and potent PI3K/PIKK inhibitor payload conjugated to a humanized anti-HER2 IgG1 antibody via a cleavable linker, designed to address challenges by enhancing targeted delivery directly to tumor cells, maximizing therapeutic benefit while minimizing systemic exposure. In preclinical studies, the HMPL-A251 payload exhibited high selectivity, potency, and robust anti-tumor activity. HMPL-A251 exhibited superior anti-tumor efficacy and tolerability compared to co-administration of the naked antibody and payload.

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. Since inception it has focused on bringing drug candidates from in-house discovery to patients around the world, with its first three medicines marketed in China, the first of which is also approved around the world including in the US, Europe and Japan. 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-A251 and other drug candidates from the ATTC platform and the further development of HMPL-A251 and other drug candidates from the ATTC platform 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 new drug application submission of HMPL-A251 and other drug candidates from the ATTC platform 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-A251 and other drug candidates from the ATTC platform, HUTCHMED's ability to fund, implement and complete its further clinical development and commercialization plans for HMPL-A251 and other drug candidates from the ATTC platform 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 US 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.

By Order of the Board

Edith Shih
Non-executive Director and Company Secretary

Hong Kong, December 17, 2025

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

Chairman and Non-executive Director:
Dr Dan ELDAR

Executive Directors:
Dr Weiguo SU
(Chief Executive Officer and Chief Scientific Officer)
Mr CHENG Chig Fung, Johnny
(Acting Chief Executive Officer and Chief Financial Officer)

Non-executive Directors:
Ms Edith SHIH
Ms Ling YANG

Independent Non-executive Directors:
Professor MOK Shu Kam, Tony
(Senior and Lead Independent Non-executive Director)
Dr Renu BHATIA
Dr Chaohong HU
Professor TAN Shao Weng, Daniel
Mr WONG Tak Wai