**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's Marketing Authorization Application for Surufatinib Submitted and Validated by the European Medicines Agency

HUTCHMED (China) Limited ("HUTCHMED") today announces that the European Medicines Agency ("EMA") has validated and accepted its marketing authorization application ("MAA") for surufatinib for the treatment of pancreatic and extra-pancreatic (non-pancreatic) neuroendocrine tumors ("NETs"). The EMA's validation confirms that the submission is sufficiently complete and that it is ready to commence the formal review process.

The submission follows scientific advice from the EMA's Committee for Medicinal Products for Human Use ("CHMP"), from which it was concluded that the two positive Phase III studies of surufatinib in patients with pancreatic and extra-pancreatic NET in China (SANET-p[1] and SANET-ep[2], both previously reported in *The Lancet Oncology*), along with existing data from surufatinib in U.S. extra-pancreatic and pancreatic NET patients, could form the basis to support a MAA. The submission follows the acceptance of a new drug application ("NDA") with the U.S. Food and Drug Administration ("FDA"), as announced on July 1, 2021.

Dr. Marek Kania, Managing Director and Chief Medical Officer of HUTCHMED International Corporation, said, "HUTCHMED's novel oncology pipeline is making important progress globally and the EMA's validation of surufatinib's MAA, which we believe recognizes the scientific value of this submission package, follows the recent acceptance of the U.S. NDA by the FDA. With its launch earlier this year in China, surufatinib has given NET patients an important new therapeutic option and we now hope to soon be able to bring this important treatment to patients across the U.S. and Europe."

## About NETs

NETs form in cells that interact with the nervous system or in glands that produce hormones. They can originate in various parts of the body, most often in the gut or the lungs and can be benign or malignant. NETs are typically classified as pancreatic NET ("pNET") or extra-pancreatic (non-pancreatic) NET ("epNET").

According to Frost & Sullivan, there were 19,000 newly diagnosed cases of NET in the U.S. in 2020. Rates across the European Union (E.U.) appear largely similar to the U.S.. This is supported by an analysis of global epidemiologic trends, which also show growth in the incidence of NETs worldwide.[3] Importantly, NETs are associated with a relatively long duration of survival compared to other tumors. As a result, there were approximately 140,000 estimated patients living with NET in France, Germany, Italy, Spain, and the United Kingdom in 2020.[4]

## About Surufatinib

Surufatinib is a novel, oral angio-immuno kinase inhibitor that selectively inhibits the tyrosine kinase activity associated with vascular endothelial growth factor receptors (VEGFR) and fibroblast growth factor receptor (FGFR), which both inhibit angiogenesis, and colony stimulating factor-1 receptor (CSF-1R), which regulates tumor-associated macrophages, promoting the body's immune response against tumor cells. Its unique dual mechanism of action may be very suitable for possible combinations with other immunotherapies, where there may be synergistic anti-tumor effects.

HUTCHMED currently retains all rights to surufatinib worldwide.

## About Surufatinib Development

*NETs in the U.S. and Europe:* A U.S. FDA NDA submission was accepted in June 2021, followed by a MAA submission to the EMA in Europe validated in July 2021. The basis to support these filings includes the completed SANET-ep and SANET-p studies, along with existing data from surufatinib in U.S. epNET and pNET patients (clinicaltrials.gov identifier: NCT02549937). In the U.S., surufatinib was granted Fast Track Designations for development in pNET and epNET in April 2020, and Orphan Drug Designation for pNET in November 2019.

*epNETs in China:* On December 30, 2020, surufatinib was granted drug registration approval by the National Medical Products Administration of China ("NMPA") for the treatment of epNET. Surufatinib is marketed in China under the brand name Sulanda®. The approval was based on results from the SANET-ep study, a Phase III trial (clinicaltrials.gov identifier: NCT02588170) in patients with advanced epNETs conducted in China. The study met the pre-defined primary endpoint of progression-free survival ("PFS") at a preplanned interim analysis. The positive results of this trial were highlighted in an oral presentation at the 2019 ESMO Congress and published in *The Lancet Oncology* in September 2020.[5] Median PFS was significantly longer for patients treated with surufatinib at 9.2 months, compared to 3.8 months for patients in the placebo group (HR 0.334; 95% CI: 0.223-0.499; $p$<0.0001). Surufatinib had an acceptable safety profile, with the most common treatment-related adverse events of grade 3 or worse being hypertension (36% of surufatinib patients vs. 13% of placebo patients), proteinuria (19% vs. 0%) and anemia (5% vs. 3%).

*pNETs in China:* On June 18, 2021, surufatinib was granted drug registration approval by the NMPA for the treatment of pNET. The approval was based on results from the SANET-p study, a Phase III trial (clinicaltrials.gov identifier: NCT02589821) in patients with advanced pNET in China. The pre-defined primary endpoint of PFS was met at a preplanned interim analysis, leading to a second NDA accepted by the NMPA in September 2020. The positive results of this study were presented at the 2020 ESMO Virtual Congress and published simultaneously in *The Lancet Oncology*[6], demonstrating that surufatinib reduces the risk of disease progression or death by 51% in patients, with a median PFS of 10.9 months compared to 3.7 months on placebo (HR 0.491; 95% CI: 0.391-0.755; $p$=0.0011). The safety profile of surufatinib was manageable and consistent with observations in prior studies.

*Biliary tract cancer in China:* In March 2019, HUTCHMED initiated a Phase IIb/III study comparing surufatinib with capecitabine in patients with advanced biliary tract cancer whose disease progressed on first-line chemotherapy. The primary endpoint is overall survival (OS) (clinicaltrials.gov identifier: NCT03873532).

*Immunotherapy combinations:* HUTCHMED entered into collaboration agreements to evaluate the safety, tolerability and efficacy of surufatinib in combination with anti-PD-1 monoclonal antibodies, including with tislelizumab (BGB-A317), Tuoyi® (toripalimab) and Tyvyt® (sintilimab), which are approved as monotherapies in China.

## 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. A dedicated organization of over 1,300 personnel has advanced ten cancer drug candidates from in-house discovery into clinical studies around the world, with its first three oncology drugs now approved and marketed. 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 review of an MAA for surufatinib for the treatment of NET with the EMA and the timing of such review, the therapeutic potential of surufatinib for the treatment of patients with NET and the further clinical development of surufatinib in this and other indications. Forward-looking statements involve risks and uncertainties. Such risks and uncertainties include, among other things, assumptions regarding the sufficiency of clinical data to support NDA approval of surufatinib for the treatment of patients with NET in the U.S., China and other jurisdictions such as the E.U., its potential to gain expeditious approvals from regulatory authorities, the safety profile of surufatinib, HUTCHMED's ability to fund, implement and complete its further clinical development and commercialization plans for surufatinib, the timing of these events, and the impact of the COVID-19 pandemic on general economic, regulatory and political conditions. In addition, as certain studies rely on the use of capecitabine, tislelizumab, Tuoyi®, and Tyvyt® as combination therapeutics with surufatinib, such risks and uncertainties include assumptions regarding the safety, efficacy, supply and continued regulatory approval of these therapeutics. 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, on AIM and on The Stock Exchange of Hong Kong Limited. 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.*

[1] Surufatinib in advanced neuroendocrine tumors – pancreatic.
[2] Surufatinib in advanced neuroendocrine tumors – extra-pancreatic (non-pancreatic).
[3] Fraenkel M, Kim M, Faggiano A, de Herder WW, Valk GD; Knowledge NETwork. Incidence of gastroenteropancreatic neuroendocrine tumours: a systematic review of the literature. *Endocr Relat Cancer*. 2014;21(3):R153-R163. Published 2014 May 6. doi:10.1530/ERC-13-0125.
[4] According to Frost & Sullivan, in 2020, there were 19,000 newly diagnosed cases of NETs in the U.S. and an estimated 143,000 patients living with NETs.
[5] Xu J, Shen L, Zhou Z, et al. Surufatinib in advanced extrapancreatic neuroendocrine tumours (SANET-ep): a randomised, double-blind, placebo-controlled, phase 3 study [published online ahead of print, 2020 Sep 20]. *Lancet Oncol.* 2020; S1470-2045(20)30496-4. DOI: 10.1016/S1470-2045(20)30496-4.
[6] Xu J, Shen L, Bai C, et al. Surufatinib in advanced pancreatic neuroendocrine tumours (SANET-p): a randomised, double-blind, placebo-controlled, phase 3 study [published online ahead of print, 2020 Sep 20]. *Lancet Oncol.* 2020; S1470-2045(20)30493-9. DOI: 10.1016/S1470-2045(20)30493-9.

By Order of the Board

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

Hong Kong, July 16, 2021

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