

## Press Release

### **HUTCHMED Initiates SURTORI-01, a Phase III Trial of SULANDA® in Combination with TUOYI® in the Treatment of Advanced Neuroendocrine Carcinoma in China**

**Hong Kong, Shanghai & Florham Park, NJ — Tuesday, September 21, 2021:** HUTCHMED (China) Limited ("[HUTCHMED](#)") (Nasdaq/AIM: HCM; HKEX: 13) today announces that it has initiated **SURTORI-01**, a Phase III study to evaluate the efficacy and safety of **surufatinib** (SULANDA® in China) in combination with **toripalimab** compared with FOLFIRI to treat patients with advanced neuroendocrine carcinoma ("NEC") who have progression of disease or intolerable toxicity after previous first-line chemotherapy. The first patient was dosed on September 18, 2021 in China. Toripalimab is marketed as TUOYI® in China by Shanghai Junshi Biosciences Co., Ltd. ("Junshi Biosciences").

Professor Shen Lin, the lead principal investigator of the study and Vice President of Peking University Hospital and Cancer Institute, said: "There is a large unmet clinical need for patients with NEC, many of whom have a bleak prognosis. Following the encouraging preliminary data from the Phase II trial, we are excited to move into the next stage of development in combining the novel, oral angio-immuno kinase inhibitor surufatinib with the anti-PD-1 antibody toripalimab. We look forward to further testing the synergistic anti-tumor effects of this combination that could benefit NEC patients who have limited treatment options."

At the American Society of Clinical Oncology (ASCO) 2021 Annual Meeting, encouraging preliminary data from the Phase II trial were disclosed for the surufatinib and toripalimab combination<sup>1</sup>. For the 20 patients in the NEC cohort as of December 31, 2020, who received an average of 5 cycles of treatments and are efficacy evaluable, objective response rate ("ORR") was 20% and disease control rate ("DCR") was 70%. Median progression-free survival ("PFS") was 3.9 months (95% CI: 1.3 – not reached). Grade 3 or higher treatment-related adverse events occurred in 33% of patients. Treatment related adverse events ("TRAEs") were manageable, with surufatinib or toripalimab interruption occurred in 6 (28.6%) and 4 (19%) patients respectively. There were neither serious adverse events ("AEs") nor AEs inducing treatment discontinuations or deaths. Updated data will be presented at the Chinese Society of Clinical Oncology (CSCO) 2021 Annual Meeting in late September.

The SURTORI-01 Phase III study is a randomized, controlled, open-label, multi-center study where approximately 200 patients are expected to be enrolled. For the study group, all patients will receive study treatment in 21-day cycle and the treatment will continue until there is a progression of disease, death, intolerable toxicity, or the end of study treatment (as other criteria specified in the protocol are met), whichever occurs first. The primary outcome measure is OS. The secondary outcome measures include PFS, ORR, duration of response (DoR), and DCR. Additional details may be found at [clinicaltrials.gov](https://clinicaltrials.gov), using identifier [NCT05015621](#).

HUTCHMED is the sponsor of SURTORI-01 and responsible for all clinical and regulatory execution of the Phase III study. HUTCHMED and Junshi Biosciences are jointly funding the study.

Surufatinib is marketed in China under the brand name SULANDA® for treating advanced neuroendocrine tumors ("NETs").

#### **About NEC**

Neuroendocrine neoplasms ("NEN") occur almost everywhere in the body but are most common in the gastrointestinal tract, pancreas, and lungs. NEC is one of the two common phenotypes of NEN. NECs are poorly differentiated, highly proliferating NENs, while NETs are well-differentiated, low-proliferating NENs. NECs are aggressive, fast-growing neoplasms that usually fail to express hormones or produce hormonal syndromes, and are not associated with hereditary tumor diseases.<sup>2</sup>

## 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

*Extra-pancreatic NETs (“epNETs”) in China:* On December 29, 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 PFS at a preplanned interim analysis, and was [published](#) in *The Lancet Oncology*<sup>3</sup>. 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%).

*Pancreatic NETs (“pNETs”) in China:* On June 16, 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 and was [published](#) in *The Lancet Oncology*<sup>4</sup>, 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.

*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.

*NETs in the U.S. and Europe:* A U.S. Food and Drug Administration (“FDA”) New Drug Application (“NDA”) submission was [accepted in June 2021](#), followed by a Marketing Authorisation Application (“MAA”) submission to the European Medicines Agency (“EMA”) 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.

HUTCHMED has initiated an [Expanded Access Protocol](#) (EAP) in the U.S. to ensure patients with NET with limited therapeutic options have access to this treatment. Regulatory clearance of this protocol has been granted by the FDA and this program is open for site activation (clinicaltrials.gov identifier: [NCT04814732](#)).

## About Toripalimab

Toripalimab is the first domestic anti-PD-1 monoclonal antibody to obtain marketing approval in China. So far, more than thirty company-sponsored clinical studies covering more than fifteen indications have been conducted globally including in China and the United States. On December 17, 2018, toripalimab was granted conditional approval from the NMPA for the second-line treatment of patients with unresectable or metastatic melanoma. In December 2020, toripalimab was successfully included in the updated National Reimbursement Drug List. In February 2021, toripalimab received NMPA's conditional approval for the treatment of patients with recurrent or metastatic nasopharyngeal carcinoma (“NPC”) after failure of at least two lines of systemic therapy. In April 2021, toripalimab received NMPA's conditional approval for the treatment of patients with locally advanced or metastatic urothelial carcinoma who failed platinum-containing chemotherapy or progressed within 12 months of neoadjuvant or adjuvant platinum-containing chemotherapy. In addition, toripalimab has been included in the Guidelines of the Chinese Society of Clinical Oncology (CSCO) for the Diagnosis and Treatment of Melanoma, Head and Neck Tumors, Urothelial Carcinoma and other indications.

In February 2021, the supplemental new drug application (the “sNDA”) of toripalimab in combination with cisplatin and gemcitabine as the first-line treatment for patients with locally recurrent or metastatic NPC was accepted for review by the NMPA. In March 2021, toripalimab received Breakthrough Therapy Designation for the first-line treatment of advanced mucosal melanoma by the NMPA. In July 2021, the sNDA for toripalimab in combination with platinum-containing chemotherapy as the first-line treatment for patients with locally advanced or metastatic esophageal squamous cell carcinoma was accepted for review by the NMPA.

In terms of international development, the first toripalimab Biological License Application (BLA) has been submitted to the FDA for the treatment of recurrent or metastatic NPC. The FDA has granted two Breakthrough Therapy designations for toripalimab in combination with chemotherapy for the first line treatment of recurrent or metastatic NPC and also for toripalimab monotherapy in second or third line treatment of recurrent or metastatic NPC. Additionally, FDA has granted Fast Track designation for toripalimab for the treatment of mucosal melanoma and orphan drug designations for NPC, mucosal melanoma and soft tissue sarcoma.

## 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 1,400 personnel has advanced eleven cancer drug candidates from in-house discovery into clinical studies around the world, with its first three oncology drugs now approved. For more information, please visit: [www.hutch-med.com](http://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 surufatinib for the treatment of patients with NEC 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 NEC 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 press release, whether as a result of new information, future events or circumstances or otherwise.*

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<sup>1</sup> Shen L, Yu X, Lu M, et al. Surufatinib in combination with toripalimab in patients with advanced neuroendocrine carcinoma: Results from a multicenter, open-label, single-arm, phase II trial. *J Clin Oncol.* 39, 2021 (suppl 15; abstr e16199). doi: [10.1200/JCO.2021.39.15\\_suppl.e16199](https://doi.org/10.1200/JCO.2021.39.15_suppl.e16199).

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- <sup>2</sup> Klöppel G. Neuroendocrine Neoplasms: Dichotomy, Origin and Classifications. *Visc Med.* 2017 ;33(5):324-330. doi:[10.1159/000481390](https://doi.org/10.1159/000481390).
- <sup>3</sup> 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. *Lancet Oncol.* 2020;21(11):1500-1512. doi: [10.1016/S1470-2045\(20\)30496-4](https://doi.org/10.1016/S1470-2045(20)30496-4).
- <sup>4</sup> 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. *Lancet Oncol.* 2020; 21(11):1489-1499. doi: [10.1016/S1470-2045\(20\)30493-9](https://doi.org/10.1016/S1470-2045(20)30493-9).