



HUTCHISON CHINA MEDITECH LIMITED

## Chi-Med initiates sulfatinib Phase II clinical trial in thyroid cancer

**London: Wednesday, 2 March 2016:** Hutchison China MediTech Limited (“Chi-Med”) (AIM: HCM) today announces that Hutchison MediPharma Limited (“HMP”), its drug R&D subsidiary, has initiated an open-label Phase II clinical trial to evaluate the efficacy and safety of sulfatinib (HMPL-012) in patients with locally advanced or metastatic radioactive iodine-refractory differentiated thyroid cancer (“DTC”) or medullary thyroid cancer (“MTC”) in China. The first patient was dosed on 1 March 2016.

HMP plans to enroll approximately 50 DTC and MTC patients into this study, with approximately 25 patients in each tumor type. The primary objective is to evaluate the objective response rate (“ORR”), while secondary and exploratory objectives include the evaluation of safety and tolerability, other efficacy parameters, pharmacokinetics, and tumor biomarkers. The study employs a two-stage design in which 15 subjects of each tumor type will be enrolled in the first stage. An additional 10 subjects in each tumor type will be enrolled after efficacy assessment in the second stage. Additional details about this study may be found at [clinicaltrials.gov](http://clinicaltrials.gov), using identifier [NCT02614495](https://clinicaltrials.gov/ct2/show/study/NCT02614495).

Sulfatinib is an oral drug candidate that selectively inhibits the tyrosine kinase activity associated with the vascular endothelial growth factor receptor (“VEGFR”) and fibroblast growth receptor (“FGFR”), two tyrosine kinase receptors associated with angiogenesis and tumor growth. HMP believes that sulfatinib’s VEGFR/FGFR1 inhibition profile has strong potential in second-line thyroid cancer patients, particularly in China where there are few safe and effective treatment options for this patient population.

In addition to the thyroid cancer trial, HMP is conducting or in the process of initiating four clinical trials in neuroendocrine tumors (“NETs”).

### Ends

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#### Notes to Editors

#### About thyroid cancer

Thyroid cancer is the most commonly diagnosed endocrine malignancy. Global incidence rates have increased sharply and continuously over the past few decades. According to the National Cancer Institute (“NCI”), in the U.S., incidence rates of thyroid cancer have

increased by an average of 5% each year over the last 10 years. Further, an article published in Cancer Research estimates that it could become the fourth most commonly diagnosed cancer by 2030. In China, thyroid cancer is now the fastest growing tumor type and accounted for approximately 2% of all new cancer cases reported in 2015, according to the National Central Cancer Registry of China (“NCCRC”).

This rise in incidence has been most dramatic in women. According to through the NCCRC, 67,900 new cases were reported in women compared to just 22,200 in men in China in 2015. Thyroid cancer now represents the most frequently diagnosed cancer in Chinese women under the age of 30. In the U.S., incidence rates of thyroid cancer are three-fold higher in women than in men, according to the NCI.

## **Overview of sulfatinib clinical development in NETs**

NETs arise from neuroendocrine cells and develop predominantly in the digestive or respiratory tracts but can also occur in many areas of the body. Diagnosing NETs is difficult due to the small tumor size and diverse occurrence with patients showing varied or no symptoms. As a result, it has been difficult to accurately estimate the number of NETs incidences per year. There were approximately 19,000 new cases of NETs and a cumulative prevalence of approximately 144,000 cases in the U.S. in 2015, according to Frost and Sullivan.

In 2014, HMP completed the first-in-human Phase I clinical trial of sulfatinib in China; the detailed results were presented at the American Association for Cancer Research-National Cancer Institute-European Organisation for Research and Treatment of Cancer International Conference on Molecular Targets and Cancer Therapeutics in early November 2015 ([www.chi-med.com/sulfatinib-ph1-eortc-2015/](http://www.chi-med.com/sulfatinib-ph1-eortc-2015/)). The Phase I clinical data indicates that sulfatinib has a superior ORR in NET patients. An ORR of 44% was observed for sulfatinib in 18 evaluable patients, compared to less than 10% for sunitinib and everolimus, the two approved targeted therapies for pancreatic NET patients. Additional details about this study may be found at [clinicaltrials.gov](http://clinicaltrials.gov), using identifier [NCT02133157](https://clinicaltrials.gov/ct2/show/study/NCT02133157).

In October 2014, HMP initiated a multi-center, single-arm, open-label Phase Ib/II study in broad spectrum NET patients (pancreatic, gastrointestinal, liver, lymph and lung, among others) in China to further evaluate the efficacy, safety, tolerability, and pharmacokinetic characteristics of sulfatinib. This study completed enrolment of 81 patients in December 2015. HMP expects to report top line results of this study during the course of 2016. Additional details about this study may be found using identifier [NCT02267967](https://clinicaltrials.gov/ct2/show/study/NCT02267967).

In December 2015, HMP initiated SANET-ep, a Phase III sulfatinib registration trial in China in patients with extra-pancreatic NETs (non-pancreatic). SANET-ep is a randomized, double-blind, placebo-controlled, multi-center registration study to treat pathologically low or intermediate grade NET patients whose disease has progressed, locally advanced or distant metastasized and for whom there is no effective therapy. Additional details about this study may be found using identifier [NCT02588170](https://clinicaltrials.gov/ct2/show/study/NCT02588170).

In the first quarter 2016, HMP intends to initiate a second sulfatinib Phase III registration trial, SANET-p, in pancreatic NET patients. SANET-p employs a similar treatment regimen and has primary and secondary endpoints similar to those for SANET-ep trial. HMP plans to enroll about 195 patients in SANET-p. Additional details about this study may be found using identifier [NCT02589821](https://clinicaltrials.gov/ct2/show/study/NCT02589821).

A Phase I study in Caucasian patients also began in November 2015 in the U.S. Once HMP has established the Phase II dose among Caucasian patients in this U.S. Phase I study, HMP expects to start a U.S. Phase II study in broad spectrum NET patients in the second half of 2016. Additional details about this study may be found using identifier [NCT02549937](https://clinicaltrials.gov/ct2/show/study/NCT02549937).

## **About VEGFR and FGFR in cancer**

At an advanced stage, tumors secrete large amounts of vascular endothelial growth factor ("VEGF"), a protein ligand, to stimulate formation of excessive vasculature (angiogenesis) around the tumor in order to provide greater blood flow, oxygen, and nutrients to fuel the rapid growth of the tumor. Anti-angiogenesis drugs have demonstrated benefits in a wide variety of tumor types. VEGF and other ligands can bind to VEGF receptors, which have been shown to play a role in angiogenesis. Inhibition of the VEGF/VEGFR signaling pathway can act to stop the growth of the vasculature around the tumor and thereby starve the tumor of the nutrients and oxygen it needs to grow rapidly.

Fibroblast cell growth factor ("FGF") also plays a key role in tumor angiogenesis. Aberrant activation of the FGF/FGFR signaling pathway is shown to be associated with cancer progression by promoting growth, survival, migration and invasion of the tumor. There is evidence that anti-VEGF therapy treatment could increase FGFR pathway activation, leading to drug resistance to anti-VEGF therapies. It is believed that simultaneously targeting VEGFR and FGFR could be an attractive approach to improve clinical efficacy.

## **About HMP**

HMP is a novel drug R&D company focusing on discovering, developing and commercializing innovative therapeutics in oncology and autoimmune diseases. With a team of around 290 scientists and staff, its pipeline is comprised of novel oral compounds for cancer and inflammation in development in North America, Europe, Australia and Greater China. HMP is a subsidiary of Chi-Med. For more information, please visit: [www.hmpglobal.com](http://www.hmpglobal.com).

## **About Chi-Med**

Chi-Med is a China-based, globally-focused healthcare group which researches, develops, manufactures and sells pharmaceuticals and health-related consumer products. Its Innovation Platform focuses on discovering and developing innovative therapeutics in oncology and autoimmune diseases for the global market. Its Commercial Platform manufactures, markets and distributes prescription drugs and consumer health products in China.

Chi-Med is majority owned by the multinational conglomerate CK Hutchison Holdings Limited (SEHK: 0001). For more information, please visit: [www.chi-med.com](http://www.chi-med.com).

## **Forward-Looking Statements**

*This announcement contains forward-looking statements that reflect Chi-Med's current expectations regarding future events, including its plans to initiate clinical studies for its drug candidates in the targeted indications, its expectations as to whether such studies 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 enrolment 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 a drug candidate to meet the primary or secondary endpoint of a study, the ability of a drug candidate to obtain regulatory approval in different jurisdictions, the ability of a drug candidate to gain commercial acceptance after obtaining regulatory approval and the sufficiency of funding. Existing and prospective investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. Chi-Med 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.*