



HUTCHISON CHINA MEDITECH LIMITED

## Savolitinib Global Phase II Trial Initiated in EGFR Mutant Non-Small Cell Lung Cancer

*Initiation of expanded Phase II trials in NSCLC triggers US\$10 million milestone from AstraZeneca to Chi-Med*

*New study builds on encouraging data from initial small Phase II studies of savolitinib in combination with Tagrisso or Iressa in c-Met-amplified NSCLC*

**London: Monday, June 20, 2016:** Hutchison China MediTech Limited (“Chi-Med”) (AIM/Nasdaq: HCM) today announces the initiation of a Phase II expansion of the ongoing TATTON trial (NCT02143466) to evaluate the selective c-Met inhibitor savolitinib (AZD6094) in epidermal growth factor receptor (“EGFR”) mutant non-small cell lung cancer (“NSCLC”) patients. Savolitinib has the potential to address major unmet medical needs in c-Met-driven subsets of NSCLC, a disease that is estimated to afflict approximately 1.7 million new patients annually worldwide.

The trial is a single-arm global Phase II study of savolitinib in combination with *Tagrisso* (osimertinib/AZD9291) in advanced NSCLC patients who have developed resistance to approved EGFR tyrosine kinase inhibitors (“TKIs”). This expansion was initiated following encouraging early data from a number of patients enrolled in the TATTON study who received savolitinib in combination with *Tagrisso*.

The initiation of the expanded Phase II study has triggered a US\$10 million milestone payment to Hutchison MediPharma Limited (“HMP”) (a 99.8% held subsidiary of Chi-Med) under the terms of the agreement with AstraZeneca PLC (“AstraZeneca”) signed in December 2011. HMP and AstraZeneca are conducting Phase II studies in NSCLC with savolitinib in monotherapy, as well as in combination with either *Tagrisso* or *Iressa* (gefitinib). AstraZeneca continues to lead and invest in the global NSCLC development program for savolitinib.

Susan Galbraith, Senior Vice President, Head of Oncology Innovative Medicines, AstraZeneca, said: “Savolitinib is a highly selective c-Met inhibitor that is being investigated in a number of cancers including in patients with lung cancer whose disease is driven by aberrant c-Met / HGF signaling. We are extremely excited by the data we have seen for savolitinib when used in combination with our EGFR tyrosine kinase inhibitors. We are committed to advancing research to develop a broad range of potential treatment options for patients with lung cancer.”

Christian Hogg, Chief Executive Officer of Chi-Med, said: “We estimate that the annual incidence of patients with MET-driven NSCLC in the U.S., European Union and Japan totals about 40,000-50,000 in all treatment settings. This is an important unmet medical need and one that we believe savolitinib is well suited to address because of its very high selectivity. This allows for effective target coverage of c-Met, as well as safe and tolerable combinations with other oncology agents. We believe that savolitinib either as a monotherapy in first-line NSCLC, or in proprietary combinations with AstraZeneca’s *Iressa* and *Tagrisso* in second- and third-line NSCLC, will address the key genetic drivers of cancer cell proliferation in these very difficult-to-treat NSCLC patients. We are hopeful about proceeding into Phase III in 2017 based on future data from this study.”

## NSCLC DEVELOPMENT PROGRAM HIGHLIGHTS

Savolitinib continues to be explored in a range of MET-driven NSCLC settings including:

- Savolitinib in combination with *Tagrisso* or *Iressa* in Phase II expansions of ongoing studies in advanced EGFR mutant NSCLC
- Savolitinib + *Tagrisso* combination Phase II study in third-line NSCLC (for patients progressing on T790M-directed therapies)
- Savolitinib monotherapy Phase II study in NSCLC

Savolitinib is in clinical development in multiple MET-driven solid tumor indications including NSCLC, kidney, gastric and colorectal cancer. For a detailed summary of all current savolitinib clinical trials covering multiple patient populations, please [click here](#).

## NOTES TO EDITORS

### About NSCLC and TKIs to address MET-driven and EGFR-driven NSCLC

Every year, it is estimated that approximately 1.7 million new patients around the world are diagnosed with NSCLC, according to Frost & Sullivan. Lung cancer is the leading cause of cancer death among both men and women, accounting for about one-third of all cancer deaths, and more than breast, prostate and colorectal cancers combined. TKIs are used in many cancer therapies and act by blocking the cell signaling pathways that drive the growth of tumor cells.

Around 4-5% of first-line NSCLC patients have MET-driven NSCLC, including approximately 3-4% with MET Exon-14 mutations and approximately 1-2% with c-Met gene amplification, and are generally sensitive to treatment with selective c-Met inhibitors such as savolitinib. Currently there are no approved selective c-Met TKIs for these NSCLC patients.

Separately, patients who have the EGFR mutation form of NSCLC, which occurs in an estimated 10-15% of NSCLC patients in Europe and 30-40% of NSCLC patients in Asia, are particularly sensitive to treatment with currently available EGFR-TKIs. However, tumors almost always develop resistance to treatment leading to disease progression, with median progression-free periods of approximately nine months. Among NSCLC patients treated with the approved EGFR-TKIs *Iressa*, *Tarceva* (erlotinib) or *Gilotrif* (afatinib), who build resistance to EGFR-TKIs and thus become second-line patients, approximately half of this resistance is driven by T790M, and approximately one-fifth is driven by c-Met gene amplification.

In third-line NSCLC patients treated with EGFR T790M mutation-positive TKIs, resistance pathways are only beginning to emerge as more patients are being treated with TKIs in clinical trials and *Tagrisso* was approved in the U.S., European Union, Japan and South Korea. Data is limited, but as patients become resistant to *Tagrisso* (median progression-free survival of nine months), c-Met gene amplification is emerging as a resistance pathway of significant interest.

### About savolitinib, a uniquely selective c-Met inhibitor

Savolitinib is a potential global first-in-class inhibitor of c-Met (also known as mesenchymal epithelial transition factor) receptor tyrosine kinase, an enzyme which has been shown to function abnormally in many types of solid tumors. It was developed as a potent and highly selective oral inhibitor specifically designed to address issues observed in the clinic with first-generation c-Met inhibitors, including renal toxicity.

### **About *Tagrisso*, a selective inhibitor against EGFR and T790M mutations**

*Tagrisso* (osimertinib) 80mg once-daily tablet, developed by AstraZeneca, is the first medicine indicated for the treatment of adult patients with locally advanced or metastatic EGFR T790M mutation-positive NSCLC. Non-clinical *in vitro* studies have demonstrated that osimertinib has high potency and inhibitory activity against mutant EGFR phosphorylation across the range of clinically relevant EGFRm and T790M mutant NSCLC cell lines, with significantly less activity against EGFR in wild-type cell lines.

*Tagrisso* is being compared with platinum-based doublet chemotherapy in the confirmatory AURA3 Phase III study in patients with EGFR T790M-positive, locally advanced or metastatic NSCLC who have progressed after EGFR-TKI therapy. It is also being investigated in the adjuvant and metastatic first-line settings, including in patients with and without brain metastases, in leptomeningeal disease, and in combination treatment.

### **About *Iressa*, an EGFR mutation inhibitor**

*Iressa* (gefitinib) is a targeted monotherapy developed by AstraZeneca for the treatment of patients with advanced or metastatic EGFR mutation-positive NSCLC. *Iressa* acts by inhibiting the tyrosine kinase enzyme in the EGFR, thus blocking the transmission of signals involved in the growth and spread of tumors. EGFR mutations occur in approximately 10-15% of NSCLC Caucasian patients and 30-40% of NSCLC patients in Asia. *Iressa* is approved in 91 countries worldwide.

### **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, Hutchison MediPharma Limited, is focused on discovering, developing and commercializing innovative therapeutics in oncology and autoimmune diseases. Its pipeline of eight novel oral compounds for cancer and inflammation is in development in North America, Europe, Australia and Greater China.

Chi-Med's 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).

### **About AstraZeneca in Oncology**

AstraZeneca has a deep-rooted heritage in Oncology and offers a quickly growing portfolio of new medicines that has the potential to transform patients' lives and the Company's future. With at least six new medicines to be launched between 2014 and 2020 and a broad pipeline of small molecules and biologics in development, we are committed to advance New Oncology as one of AstraZeneca's six Growth Platforms focused on lung, ovarian, breast and blood cancers. In addition to our core capabilities, we actively pursue innovative partnerships and investments that accelerate the delivery of our strategy, as illustrated by our investment in Acerta Pharma in hematology.

By harnessing the power of four scientific platforms – immuno-oncology, the genetic drivers of cancer and resistance, DNA damage response and antibody drug conjugates – and by championing the development of personalized combinations, AstraZeneca has the vision to redefine cancer treatment and one day eliminate cancer as a cause of death.

## About AstraZeneca

AstraZeneca is a global, innovation-driven biopharmaceutical business that focuses on the discovery, development and commercialization of prescription medicines, primarily for the treatment of diseases in three main therapy areas – respiratory, inflammation, autoimmune disease (RIA), cardiovascular and metabolic disease (CVMD) and oncology – as well as in infection and neuroscience. AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide. For more information please visit: [www.astrazeneca.com](http://www.astrazeneca.com).

## 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 Chi-Med's current expectations regarding future events, including its expectations for the clinical development of savolitinib, plans to initiate clinical studies for savolitinib in solid tumor 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 enrollment 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, the potential market of a drug candidate for a targeted indication 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. For further discussion of these and other risks, see Chi-Med's filings with the U.S. Securities and Exchange Commission and on AIM. 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.*

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