



HUTCHISON CHINA MEDITECH LIMITED

## Press Release

### Chi-Med Highlights Oral Presentations at CSCO Annual Meeting

– Three oral presentations given at CSCO for fruquintinib, savolitinib and theliatinib –

– Plenary keynote presentation for FRESKO Phase III trial details analysis showing consistent survival benefit in all key subgroups –

**London: Friday, September 29, 2017:** Hutchison China MediTech Limited (“Chi-Med”) (AIM/Nasdaq: HCM) announced that new clinical data on three of its novel tyrosine kinase inhibitors, fruquintinib, savolitinib and theliatinib, were presented at the 20<sup>th</sup> Annual Meeting of the Chinese Society of Clinical Oncology (“CSCO”), held in Xiamen, China, from September 26 to 30, 2017.

The three oral presentations were as follows:

#### **Fruquintinib: Further in-depth results from FRESKO**

Session: Plenary Keynote Presentation  
Presenter: Shukui Qin  
Date: Wednesday, September 27  
Presentation Slides: [www.chi-med.com/cSCO-2017-fresco/](http://www.chi-med.com/cSCO-2017-fresco/)

FRESKO is the Phase III trial assessing fruquintinib in patients with colorectal cancer (“CRC”) in China. Overall results presented earlier at the American Society of Clinical Oncology annual meeting in June 2017 showed that the trial met all primary and secondary efficacy endpoints. Fruquintinib is a novel vascular endothelial growth factor (“VEGF”) receptor kinase inhibitor.

Dr. Qin, Director of the PLA Cancer Center and Deputy Director of the 81<sup>st</sup> Hospital in Nanjing, presented data from prespecified subgroup analyses of overall survival (“OS”) and progression-free survival (“PFS”), which showed that the benefits of fruquintinib were generally consistent amongst all subgroups including, but not limited to, the following important subgroups:

1. Significant improvements in OS and PFS were demonstrated irrespective of whether patients had received prior anti-VEGF therapy or anti-epidermal growth factor receptor (“EGFR”) therapy. Median OS for those who had not received such prior therapies (250 of 416 patients enrolled, i.e. 60%) was 10.4 months for the fruquintinib group, versus 6.9 months for the placebo group, with a hazard ratio of 0.63 (95% CI 0.46–0.86;  $p = 0.010$ ). Median PFS for this group was 3.8 months for the fruquintinib group versus 1.8 months for the placebo group, with a hazard ratio of 0.28 (95% CI 0.21–0.37;  $p < 0.001$ ).
2. Significant OS and PFS improvements were demonstrated particularly amongst *K-RAS* wild-type patients (i.e. without mutation of the *K-RAS* gene). Median OS for patients that were *K-RAS* wild-type (231 of 416 patients enrolled, i.e. 56%) was nearly five months longer in the fruquintinib group at 10.7 months, versus 6.1 months for the placebo group, with a hazard ratio of 0.56 (95% CI 0.40–0.78;  $p < 0.001$ ). *K-RAS* mutant patients (44%) also demonstrated OS and PFS improvements, with median OS of 8.2 months in the fruquintinib group and 7.0 months in the placebo group, with a hazard ratio of 0.75 (95% CI 0.53–1.07;  $p = 0.114$ ).

The FRESKO plenary presentation received the “2017 First Prize, CSCO Outstanding Research Paper Award” by the Academic Committee of CSCO based on votes by the committee members.

### **Savolitinib: Results from a Phase Ib trial in advanced aberrant c-MET gastric cancer**

Session: Precision Therapy for Late-Stage Gastric Cancer  
Presenter: Jifeng Feng  
Date: Thursday, September 28  
Presentation Slides: [www.chi-med.com/csco-2017-savolitinib-ph1b-gastric/](http://www.chi-med.com/csco-2017-savolitinib-ph1b-gastric/)

Dr. Feng, Chief Physician of the Jiangsu Cancer Hospital, presented results from the Phase Ib clinical trial of the safety and anti-tumor activity of savolitinib in aberrant c-MET advanced gastric cancer patients. Savolitinib is a highly selective c-MET kinase inhibitor.

The study cohort included 31 locally advanced or metastatic gastric cancer patients who had failed at least two lines of therapy. C-MET status was determined using fluorescent in situ hybridization (FISH) and immunohistochemistry (IHC). The primary endpoint was to evaluate the safety and tolerability of savolitinib, with secondary endpoints including objective response rate ("ORR"), disease control rate ("DCR"), PFS and determining the pharmacokinetic profile.

As of June 15, 2017, of the 441 patients screened, 58 patients (13.2%) were determined to have aberrant c-MET, of which 22 (5.0%) were *MET* gene amplified. 31 patients were enrolled. Amongst the efficacy evaluable *MET* gene amplified patients, ORR was 42.9% (3/7) and DCR was 85.7% (6/7), with ORR of 13.6% (3/22) and DCR of 40.9% (9/22) amongst the overall efficacy evaluable aberrant c-MET set. As of the database cut-off, the longest PFS was in excess of two years.

Savolitinib monotherapy was determined as safe and well tolerated in patients with advanced gastric cancer. Grade 3 or above adverse events occurring in at least two patients included abnormal hepatic function in 12.9% (4/31), each of gastrointestinal bleeding or decreased appetite in 9.7% (3/31 each), and each of diarrhea or gastrointestinal perforation in 6.4% (2/31 each).

The study concluded that savolitinib monotherapy demonstrated promising anti-tumor efficacy in gastric cancer patients with *MET* gene amplification, and the potential benefit to patients with *MET* gene amplification warrants further exploration.

### **Theliatinib: Preliminary results from a Phase I trial in solid tumors, focusing on esophageal cancer**

Session: Esophageal Cancer  
Presenter: Jifang Gong  
Date: Thursday, September 28  
Presentation Slides: [www.chi-med.com/csco-2017-theliatinib-ph1/](http://www.chi-med.com/csco-2017-theliatinib-ph1/)

Dr. Gong of the Beijing Cancer Hospital presented results from the Phase I trial of the safety and anti-tumor activity of theliatinib. Theliatinib is a novel EGFR inhibitor designed with strong affinity to the wild-type EGFR kinase, and has been shown to be five to ten times more potent than erlotinib, which holds importance because tumors with wild-type EGFR activation have been found to be less sensitive to current EGFR inhibitors. This is notable in certain cancer types such as esophageal cancer, where 8-30% have EGFR gene amplification and 30-90% have EGFR over-expression.

Up to 500mg QD was determined to be safe and well-tolerated, with no dose-limiting toxicities (DLT) and no clear maximum tolerated dose (MTD). Pharmacokinetic exposure increased with dose, with a 300mg QD or more considered to be sufficient to inhibit EGFR phosphorylation. Amongst the 21 patients that received 120mg to 500mg QD, there were only four adverse events of grade 3 or above: gastrointestinal bleeding, decreased white blood cell count, anemia or decreased platelet count (1/21 = 4.8% each). There were no incidences of grade 3 or above rash or diarrhea. Amongst seven esophageal cancer patients, five had measurable lesions and could be evaluated for response. All five had stable disease. Of the efficacy evaluable patients in the 120mg to 500mg cohorts, 44.4% (8/18) had stable disease after 12 weeks.

The study concluded that further study of theliatinib at 400mg QD amongst esophageal cancer patients with EGFR activation was warranted.

In addition to the oral presentation, Yongxin Ren et al published preclinical study data regarding EGFR as a target for advanced esophageal cancer treatment using theliatinib. The summary abstract is available at [www.chi-med.com/csco-2017-theliatinib-preclinical/](http://www.chi-med.com/csco-2017-theliatinib-preclinical/).

## **About Fruquintinib**

Fruquintinib (HMPL-013) is a highly selective small molecule drug candidate that has been shown to inhibit VEGFR receptor (“VEGFR”) 24 hours a day via an oral dose, with lower off-target toxicities compared to other targeted therapies. VEGFR is known to play a pivotal role in tumor-related angiogenesis, and inhibition of VEGFR represents an important therapeutic strategy in blocking the development of new blood vessels essential for tumors to grow and invade. Fruquintinib’s tolerability, along with its clean drug-drug interaction profile demonstrated to date, may enable rational combination with other cancer therapies such as in our ongoing clinical trials of fruquintinib in combination with chemotherapy and targeted therapy.

Fruquintinib is currently under joint development in China by Chi-Med and its partner Eli Lilly and Company. The New Drug Application (NDA) for fruquintinib in CRC was accepted by the China Food and Drug Administration (CFDA) in June 2017. In addition, fruquintinib is being studied in China in a Phase III pivotal trial in non-small cell lung cancer (NSCLC), known as FALUCA; and a Phase II study using fruquintinib combined with Iressa® (gefitinib) in the first-line setting for patients with advanced or metastatic NSCLC. Other studies currently being planned, and soon to be initiated, include a Phase III study in gastric cancer in combination with paclitaxel in China, new studies in the United States, and certain exploratory studies in combination with other oncology agents.

## **About Savolitinib**

Savolitinib (AZD6094/HMPL-504) is a potential first-in-class selective 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 other selective c-MET inhibitors, such as renal toxicity.

Savolitinib was discovered by Chi-Med and is being developed in collaboration with AstraZeneca PLC. Savolitinib is currently being studied in Phase Ib/II and III studies in multiple tumor types worldwide including kidney, lung and gastric cancers, both as a monotherapy or in combination with other targeted and immunotherapy agents. A global Phase III registration study in papillary renal cell carcinoma (PRCC) was initiated in June 2017. Later in 2017, Phase II data is expected to be presented at a major scientific conference on savolitinib in combination with Tagrisso® and Iressa®, in both second- and third-line NSCLC.

## **About Theliatinib**

Theliatinib (HMPL-309) is a novel molecule EGFR inhibitor under investigation for the treatment of solid tumors. Tumors with wild-type EGFR activation, for instance, through gene amplification or protein over-expression, have been found to be less sensitive to currently marketed EGFR inhibitors. Theliatinib has been designed with strong binding affinity to the wild-type EGFR kinase and has been shown to be five to ten times more potent than erlotinib. Theliatinib may benefit patients with esophageal and head and neck cancers, tumor-types with a high incidence of wild-type EGFR activation.

## **About Chi-Med**

Chi-Med is an innovative biopharmaceutical company which researches, develops, manufactures and sells pharmaceuticals and healthcare products. Its Innovation Platform, Hutchison MediPharma Limited, 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).

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## **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 Chi-*

*Med's current expectations regarding future events, including its expectations for the clinical development of fruquintinib, savolitinib and theliatinib; plans to initiate clinical studies for fruquintinib, savolitinib and theliatinib; 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 drug candidates fruquintinib, savolitinib and theliatinib to meet the primary or secondary endpoint of a study, to obtain regulatory approval in different jurisdictions, to gain commercial acceptance after obtaining regulatory approval, the potential markets of fruquintinib, savolitinib and theliatinib for targeted indications 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 press release, whether as a result of new information, future events or circumstances or otherwise.*

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