



HUTCHISON CHINA MEDITECH LIMITED

## Press Release

### Chi-Med Presents Phase I/II Clinical Data for Selective VEGFR Inhibitor Fruquintinib at the 2017 Gastrointestinal Cancers Symposium

**London: Monday, January 16, 2017:** Hutchison China MediTech Limited (“Chi-Med”) (AIM/Nasdaq: HCM) today announces that data from the ongoing Phase I/II clinical trial of fruquintinib in combination with paclitaxel (Taxol<sup>®</sup>) in second-line patients with advanced gastric cancer will be presented at the 2017 Gastrointestinal Cancers Symposium sponsored by the American Society of Clinical Oncology (“ASCO-GI”), being held in San Francisco, California from January 19 to 21, 2017. Fruquintinib is a highly selective and potent oral inhibitor of vascular endothelial growth factor receptors (“VEGFR”).

Chi-Med completed a Phase Ib dose finding study of fruquintinib in combination with paclitaxel, which established a combination regimen that was well tolerated, and continued to enroll patients in this trial to expand the data-set. Additional details about this study may be found at [clinicaltrials.gov](http://clinicaltrials.gov), using identifier [NCT02415023](https://clinicaltrials.gov/ct2/show/study/NCT02415023).

The most recent results of the study will be presented in detail as follows:

**Presentation Title:** A Phase I/II trial of Fruquintinib in Combination with Paclitaxel for Second-line Treatment in Patients with Advanced Gastric Cancer

**Authors:** Ruihua Xu, Dongsheng Zhang, Lin Shen, Jin Li, Jing Huang, Yang Zhang, Jifang Gong, Weijian Guo, Songhua Fan, Ke Li, Ye Hua and Weiguo Su

**Abstract No:** 128

**Session:** Poster Session A: Cancers of the Esophagus and Stomach

**Date & Time:** Thursday, January 19, 2017, 12:30 PM-6:30 PM (PST)

Once presented, the presentation will be available at [www.chi-med.com/news](http://www.chi-med.com/news). Further information about ASCO-GI is available at [gicasymp.org](http://gicasymp.org).

#### ABSTRACT

##### **A Phase I/II Trial of Fruquintinib in Combination with Paclitaxel for Second-line Treatment in Patients with Advanced Gastric Cancer**

Ruihua Xu, Dongsheng Zhang, Lin Shen, Jin Li, Jing Huang, Yang Zhang, Jifang Gong, Weijian Guo, Songhua Fan, Ke Li, Ye Hua and Weiguo Su

#### Background

Advanced gastric cancer is a major public health problem, particularly in Asian countries. The treatment options are limited in patients who failed standard first-line chemotherapy. This Phase I/II study is aimed to evaluate the tolerability, pharmacokinetics (“PK”) and preliminary efficacy of fruquintinib, a selective oral VEGFR inhibitor, combined with paclitaxel as second-line therapy in Chinese patients with advanced gastric cancer.

#### Patients and methods

This open arm Phase I/II trial ([NCT02415023](https://clinicaltrials.gov/ct2/show/study/NCT02415023)) consisted of dose finding and dose expansion stages. In the dose finding stage, three dose levels of fruquintinib (2, 3, 4mg once daily; three-weeks-on and one-week-off) were evaluated in combination with standard 80mg/m<sup>2</sup> paclitaxel (once weekly on day 1, 8 and 15) in a 28-day cycle until the maximum tolerated dose (“MTD”) or recommended phase II dose (“RP2D”) was reached. Additional patients were enrolled at dose expansion phase with fruquintinib RP2D regimen to assess further the efficacy, safety and PK profile.

## Results

As of September 10, 2016, a total of 32 patients were enrolled and dosed with fruquintinib in combination with weekly paclitaxel. The RP2D of fruquintinib was determined to be 4 mg daily.

Two patients at 4 mg experienced dose-limiting toxicity, both with febrile neutropenia. Grade 3 or 4 treatment emergent adverse events ("TEAE") were neutropenia (40.6%), leukopenia (28.1%), decreased hemoglobin (6.25%), hand-foot skin reaction (6.25%), neurophlegmon (6.25%), and hypertension (6.25%), with higher frequencies in the 4mg cohort as compared with lower doses.

At steady state, fruquintinib drug exposure, i.e. the area under the curve ( $AUC_{ss}$ ), increased dose-proportionally and was within the same range as given as a single agent. Paclitaxel exposure at fruquintinib RP2D (4mg) however, increased by approximately 30% as compared to that of single agent.

28 of 32 patients were evaluable for tumor response, and of these, 10 patients achieved confirmed partial response (objective response rate, ("ORR") = 35.7%), 9 patients experienced stable disease for at least 8 weeks (disease control rate, ("DCR") = 67.9%). At fruquintinib RP2D,  $\geq 16w$  progression free survival ("PFS") = 50% and  $\geq 7m$  overall survival ("OS") = 50%.

## Conclusion

Combination therapy of fruquintinib and paclitaxel appeared to be generally well-tolerated with promising tumor response in the second-line setting in advanced gastric cancer. Further evaluation of fruquintinib in a randomized control trial is warranted.

## About Gastric Cancer

Every year, it is estimated that approximately one million new patients around the world are diagnosed with gastric cancer, according to Frost & Sullivan, and in 2015 China represented approximately 44% of all newly diagnosed gastric cancer cases worldwide. The very high prevalence of gastric cancer in China as compared to the rest of the world is thought to be linked in part to food preparation habits, such as the use of certain preservatives. In 2015 there were an estimated 679,100 incidence gastric cancer cases and 498,000 mortality cases in China, according to the National Central Cancer Registry of China.

Gastric cancer is the third of most lethal cancer worldwide. As it is often diagnosed at an advanced stage, prognosis is poor with a median OS of less than 12 months. Although targeted therapy is under development in China, chemotherapy remains the mainstay of treatment for gastric cancer patients and confers only a moderate survival advantage. Accordingly, we see a high medical need for new targeted treatment options.

## About Fruquintinib

Fruquintinib (HMPL-013) is a highly selective small molecule drug candidate that has been shown to inhibit VEGFR 24 hours a day via an oral dose, without known off-target toxicities. It is currently under the joint development in China by Chi-Med and its partner Eli Lilly and Company. Two late-stage, pivotal Phase III registration studies are ongoing in colorectal cancer (FRESCO) and lung cancer (FALUCA) along with the currently reported gastric cancer trial.

**Colorectal:** The FRESCO trial is a randomized, double-blind, placebo-controlled, multicenter, Phase III pivotal trial in patients with locally advanced or metastatic colorectal cancer who have failed at least two prior systemic antineoplastic therapies, including fluoropyrimidine, oxaliplatin and irinotecan. Enrollment was completed in May 2016. 416 patients were randomized at a 2:1 ratio to receive either: 5mg of fruquintinib orally once per day, on a three-weeks-on / one-week-off cycle, plus best supportive care ("BSC"); or placebo plus BSC. The primary endpoint is OS, with secondary endpoints including PFS, ORR, DCR and duration of response. Additional details of the FRESCO study may be found at [clinicaltrials.gov](http://clinicaltrials.gov), using identifier [NCT02314819](https://clinicaltrials.gov/ct2/show/study/NCT02314819).

**Lung:** The FALUCA trial is a randomized, double-blind, placebo-controlled, multi-center, Phase III registration study targeted at treating patients with advanced non-squamous NSCLC, who have failed two lines of systemic chemotherapy. Enrollment began in December 2015. Patients are randomized at a 2:1 ratio to receive either: 5mg of fruquintinib orally once per day, on a three-weeks-on / one-week-off cycle, plus BSC; or placebo plus BSC. The primary endpoint is OS, with secondary endpoints including PFS, ORR, DCR and duration of response. Chi-Med plans to enroll approximately 520 patients in about 45 centers across China. Additional details about this study may be found at [clinicaltrials.gov](http://clinicaltrials.gov), using identifier [NCT02691299](https://clinicaltrials.gov/ct2/show/study/NCT02691299).

## 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).

## 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, plans to initiate clinical studies for fruquintinib, 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 candidate fruquintinib 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 market of fruquintinib for a targeted indication and the sufficiency of funding. In addition, as certain studies rely on the use of paclitaxel as a combination therapeutic with fruquintinib, such risks and uncertainties include assumptions regarding the safety, efficacy, supply and continued regulatory approval of paclitaxel. 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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