



HUTCHISON CHINA MEDITECH LIMITED

Press Release

Chi-Med Presents Further Fruquintinib FRESCO Trial Data at ASCO 2018 Annual Meeting

– Chi-Med makes additional FRESCO presentations at ASCO 2018, following oral presentation at ASCO 2017 showing that study met all endpoints with a manageable safety profile and lower off-target toxicities compared to other targeted therapies –

– Subgroup analysis showed consistent survival benefit across all key subgroups –

– Quality-adjusted survival analysis showed quality-of-life benefits –

London: Monday, June 4, 2018: Hutchison China MediTech Limited (“Chi-Med”) (AIM/Nasdaq: HCM) today announced that further data from the FRESCO Phase III study in 416 patients with locally advanced or metastatic colorectal cancer (“CRC”) were presented at the 2018 American Society of Clinical Oncology (“ASCO”) Annual Meeting, held in Chicago, Illinois from June 1 to 5, 2018.

Fruquintinib is a highly selective and potent oral inhibitor of vascular endothelial growth factor (“VEGF”) receptors 1, 2 and 3. The FRESCO dataset is a part of the New Drug Application (“NDA”) filed and accepted by the China National Drug Administration (the “CND”). Additional clinical trials are ongoing in China for lung cancer (the third-line FALUCA Phase III study and the first-line Iressa® combination Phase II study) and gastric cancer (the second-line FRUTIGA Phase III study), as well as in the United States (Phase I bridging study).

The two presentations were as follows:

Subgroup analysis by prior anti-VEGF or anti-EGFR target therapy in FRESCO, a randomized, double-blind, Phase III trial comparing fruquintinib versus placebo plus best supportive care in Chinese patients with metastatic colorectal cancer

Presenter: Ruihua Xu
Other Authors: Jin Li, Yu-Xian Bai, Yanhong Deng, Lei Yang, Haijun Zhong, Zhendong Chen, Hongming Pan, Weijian Guo, Yongqian Shu, Ying Yuan, Jianming Xu, Lin Shen, Ning Wang, Xin Wang, Haidong Chi, Jack Peng, Ye Hua, Weiguo Su, Shukui Qin
Time & Location: Sunday, June 3, 08:00 – 11:30 CDT; Hall A, Poster Board: #30
Session: Gastrointestinal (Colorectal) Cancer
Abstract No. & Link: #3537; abstracts.asco.org/214/AbstView_214_215579.html
Poster Link¹¹: [16ea1jfSDOCUUwuY6Icm22](https://www.asco.org/abstracts/2018/abstract/16ea1jfSDOCUUwuY6Icm22)

In FRESCO, fruquintinib demonstrated a statistically significant and clinically meaningful benefit in third-line metastatic CRC patients in China. This analysis explored possible effects of prior target therapy on the efficacy and safety of fruquintinib by analyzing the subgroups of patients with prior target therapy (“PTT”) and those without prior target therapy (“non-PTT”). The results of this analysis showed that fruquintinib had clinically meaningful benefits in third-line metastatic CRC patients regardless of PTT without observed accumulative toxicity.

Results previously presented at the 20th Annual Meeting of the Chinese Society of Clinical Oncology showed that the benefits of fruquintinib were generally consistent across all subgroups. Among a total of 278 fruquintinib-treated patients, 111 received PTT. In the PTT subgroup, fruquintinib significantly prolonged overall survival (“OS”) (Median OS: 7.69 months vs 5.98 months; HR = 0.63; p = 0.023) and progression-free survival (“PFS”) (Median PFS: 3.65 months vs 1.84 months; HR = 0.24; p < 0.001) compared to placebo. Patients who received prior anti-VEGF treatment (N = 84) also benefited from fruquintinib in OS (Median 7.20 months vs 5.91 months; HR = 0.68; p=0.066) and PFS (Median 3.48 months vs 1.84 months; HR = 0.24; p < 0.001). In the non-PTT subgroup, the median OS was 10.35 months for fruquintinib vs 6.93 months for placebo (HR = 0.63; p = 0.01), and the median PFS for fruquintinib was 3.81 months vs 1.84 months for placebo (HR = 0.28; p < 0.001).

Additional data presented at this year's ASCO showed that there were no observed accumulative Grade ≥ 3 treatment-emergent adverse events in the PTT subgroup. The Grade ≥ 3 treatment-emergent adverse events rates of fruquintinib were similar in PTT and non-PTT subgroup (61.3% and 61.1%). This subgroup analysis result is consistent with the previously reported FRESCO intent-to-treatment population result.

Quality-adjusted time without symptoms or toxicity (Q-TWiST) of patients with metastatic colorectal cancer treated with fruquintinib in the randomized Phase III FRESCO trial

Presenter: Yu-Xian Bai
Other Authors: Hongyan Li, Ning Wang, Xiaojun Guo, Wei Wang, Songhua Fan, Jian-Ming Xu, Lin Shen
Time & Location: Sunday, June 3, 08:00 – 11:30 CDT; Hall A, Poster Board: #37
Session: Gastrointestinal (Colorectal) Cancer
Abstract No. & Link: #3544; abstracts.asco.org/214/AbstView_214_224293.html
Poster Link^[iii]: [419OppVsv6UKE20CM4uQYy](https://www.asco.org/abstracts/2018/abstract/419OppVsv6UKE20CM4uQYy)

This ad-hoc analysis aimed to compare the quality-adjusted survival between the two arms of the FRESCO study using quality-adjusted time without symptoms or toxicity (“Q-TWiST”) methodology and to investigate the Q-TWiST benefit of fruquintinib treatment among subgroups. Q-TWiST is a tool to evaluate relative clinical benefit-risk from patient’s perspective and has been widely used in oncology treatment assessment. The survival time for each patient was divided into 3 portions: TOX (time with \geq Grade 3 toxicity before progression), TWiST (time without symptoms or \geq Grade 3 toxicity), and REL (time from progression or relapse until death or end of follow-up).

Patients treated with fruquintinib had longer Q-TWiST periods compared to patients treated with placebo. Q-TWiST benefits were observed regardless of prior lines of chemotherapy and target treatment with anti-VEGF or anti-EGFR. The relative improvement of Q-TWiST with fruquintinib represents a clinically important quality-of-life benefit for metastatic CRC patients.

Further information about the ASCO annual meeting is available at am.asco.org.

About Fruquintinib

Fruquintinib (HMPL-013) is a highly selective small molecule drug candidate that has been shown to inhibit VEGF receptors 24 hours a day via an oral dose, with lower off-target toxicities compared to other targeted therapies. Its 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. VEGF receptors 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.

About Fruquintinib in CRC in China

The CNDA, formerly the China Food and Drug Administration, acknowledged [acceptance of the NDA](#) for fruquintinib for the treatment of patients with advanced CRC in June 2017. Fruquintinib was subsequently awarded priority review status in view of its significant clinical value, according to a CNDA announcement in September 2017. The NDA is supported by data from the successful FRESCO study, which was highlighted in an [oral presentation](#) at the ASCO Annual Meeting held on June 5, 2017. Additional details about this study can be found at clinicaltrials.gov, using identifier [NCT02314819](https://clinicaltrials.gov/ct2/show/study/NCT02314819). The FRESCO study followed an initial Phase I trial in 40 solid tumor patients, a Phase Ib study in 62 CRC patients, and a Phase II clinical trial in 71 CRC patients.

Other Fruquintinib Development Programs

Lung cancer in China: Fruquintinib is being studied in China in a Phase III registration study, known as FALUCA, in non-small cell lung cancer (“NSCLC”) patients. FALUCA is a randomized, double-blind, placebo-controlled, multi-center study of fruquintinib targeted at treating patients with advanced non-squamous NSCLC who have failed two lines of systemic chemotherapy. The trial [completed enrollment](#) of 527 patients in February 2018 (clinicaltrials.gov identifier [NCT02691299](https://clinicaltrials.gov/ct2/show/study/NCT02691299)). It was initiated following a

similar Phase II clinical trial in 91 third-line NSCLC patients. Results of the Phase II study were highlighted in an oral presentation at the 17th World Conference on Lung Cancer on December 6, 2016 (clinicaltrials.gov identifier [NCT02590965](#)).

Along with FALUCA, fruquintinib is concurrently being studied in a Phase II study in combination with Iressa[®] (gefitinib) in the first-line setting for patients with advanced or metastatic NSCLC (clinicaltrials.gov identifier [NCT02976116](#)). Preliminary results were highlighted in an [oral presentation](#) at the 18th World Conference on Lung Cancer on October 16, 2017.

Gastric cancer in China: In October 2017, Chi-Med initiated a pivotal Phase III clinical trial of fruquintinib in combination with Taxol[®] (paclitaxel), known as the FRUTIGA study, for the treatment of patients with advanced gastric or gastroesophageal junction (“GEJ”) adenocarcinoma. The FRUTIGA study is a randomized, double-blind, placebo-controlled, multi-center trial expected to enroll over 500 gastric or GEJ adenocarcinoma patients who have progressed after first-line standard chemotherapy (clinicaltrials.gov identifier [NCT03223376](#)). The FRUTIGA study follows a Phase Ib/II clinical trial that demonstrated that combination therapy of fruquintinib and Taxol[®] in such patients was generally well-tolerated with promising tumor response (clinicaltrials.gov identifier [NCT02415023](#)).

In China, fruquintinib is jointly developed with Eli Lilly and Company.

United States bridging trial: In December 2017, Chi-Med initiated a multi-center, open-label, Phase I clinical study to evaluate the safety, tolerability and pharmacokinetics of fruquintinib in U.S. patients with advanced solid tumors (clinicaltrials.gov identifier [NCT03251378](#)).

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: 1). For more information, please visit: www.chi-med.com.

Iressa[®] is a trademark of the AstraZeneca PLC group of companies. Taxol[®] is a trademark of The Bristol-Myers Squibb Company group of companies.

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 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 Iressa[®] (gefitinib) or Taxol[®] (paclitaxel) as combination therapeutics with fruquintinib, such risks and uncertainties include assumptions regarding the safety, efficacy, supply and continued regulatory approval of Iressa[®] and Taxol[®]. 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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