



HUTCHISON CHINA MEDITECH LIMITED

Press Release

Chi-Med Initiates FRUTIGA, a Phase III Trial of Fruquintinib in Second-Line Gastric Cancer

London: Tuesday, October 31, 2017: Hutchison China MediTech Limited (“Chi-Med”) (AIM/Nasdaq: HCM) has initiated **FRUTIGA**, a pivotal Phase III clinical trial of **fruquintinib** in combination with paclitaxel (**Taxol**[®]) for the treatment in advanced **g**astric or gastroesophageal junction (“GEJ”) **a**denocarcinoma patients in China. Fruquintinib is a highly selective and potent oral inhibitor of vascular endothelial growth factor receptors (“VEGFR”) 1, 2 and 3. This randomized, double-blind, placebo-controlled, multicenter trial is being conducted in patients with advanced gastric cancer who have progressed after first-line standard chemotherapy. Advanced gastric cancer is a major medical need, particularly in Asian populations, with limited treatment options for patients who have failed first-line standard chemotherapy with 5-fluorouracil (5-FU) and platinum doublets. For gastric cancer, there are approximately 679,100 new cases and 498,000 deaths in China each year.^[1]

“Fruquintinib was designed to be a highly selective inhibitor of VEGFR 1, 2 and 3, which has shown the potential ability to combine with chemotherapy – a novel approach in the treatment of advanced gastric cancer,” said Christian Hogg, Chief Executive Officer of Chi-Med. “With fruquintinib’s New Drug Application (“NDA”) in third-line colorectal cancer (“CRC”) under review and its Phase III trial in third-line non-small cell lung cancer nearing full enrollment, we are excited to now also enter the final phase of development in second-line gastric cancer, a very large indication in which there is significant patient need for new treatment options in China.”

About FRUTIGA

Over 500 patients will be enrolled into FRUTIGA, a randomized, double-blind, Phase III trial to evaluate the efficacy and safety of fruquintinib combined with paclitaxel compared with paclitaxel monotherapy for second-line treatment of advanced gastric or GEJ adenocarcinoma. The trial will enroll patients with disease that has been confirmed through histology or cytology and who did not respond to first-line standard chemotherapy containing platinum and fluorouracil. All subjects will receive fruquintinib or placebo combined with paclitaxel. Patients will be randomized at a 1:1 ratio and stratified according to factors such as stomach vs. GEJ tumors and ECOG performance status. An Independent Data Monitoring Committee (IDMC) will be established to review safety and efficacy data.

The Primary efficacy endpoint is overall survival (“OS”). Secondary efficacy endpoints include progression-free survival (“PFS”, as defined by RECIST 1.1), objective response rate (“ORR”), disease control rate (“DCR”), duration of response, and quality-of-life score (EORTC QLQ-C30, version 3.0). Biomarkers related to the antitumor activity of fruquintinib will also be explored.

Additional details about this study can be found at clinicaltrials.gov, using identifier [NCT03223376](https://clinicaltrials.gov/ct2/show/study/NCT03223376).

FRUTIGA was initiated following the results of an open label, multi-center Phase Ib dose finding/expansion study of fruquintinib in combination with paclitaxel (Taxol[®]) in second-line patients with advanced gastric cancer (clinicaltrials.gov identifier [NCT02415023](https://clinicaltrials.gov/ct2/show/study/NCT02415023)). Results were [presented](#) at the American Society of Clinical Oncology Gastrointestinal Cancers Symposium in January 2017. A total of 32 patients were enrolled in the study and 28 of 32 patients were evaluable for efficacy, with an ORR rate of 36% and a DCR of 68%. At the fruquintinib recommended Phase II dose (“RP2D”), ≥16 week PFS rate was 50% and ≥7 month OS was 50%. Tolerability of the RP2D combination was as expected with common treatment related Grade ≥3 adverse events (AEs) being neutropenia (41%), leukopenia (28%), decreased hemoglobin (6%), and hand-foot syndrome (6%).

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. 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 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, 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.

At an advanced stage, tumors secrete large amounts of VEGF, a protein ligand, to stimulate formation of excessive vasculature (angiogenesis) around the tumor to provide greater blood flow, oxygen, and nutrients to the tumor. VEGF and VEGFR play pivotal roles in tumor-related angiogenesis, and fruquintinib inhibits the VEGF/VEGFR pathway. This represents an important therapeutic strategy in blocking the development of new blood vessels essential for tumors to grow and invade.

Fruquintinib is currently under joint development in China by Chi-Med and its partner Eli Lilly and Company.

About Fruquintinib Development in Other Cancer Types

The China Food and Drug Administration (“CFDA”) acknowledged [acceptance of the NDA](#) for fruquintinib for the treatment of patients with advanced colorectal cancer in June 2017, and was subsequently awarded priority review status in view of its significant clinical value, according to the CFDA announcement in September 2017. The NDA is supported by data from the successful FRESCO study, a Phase III pivotal registration trial of fruquintinib in 416 patients with CRC in China, which was highlighted in an [oral presentation](#) at the American Society of Clinical Oncology Annual Meeting on June 5, 2017 (clinicaltrials.gov identifier [NCT02314819](#)).

In addition to the FRUTIGA and FRESCO Phase III trials, fruquintinib is being studied in China in a Phase III pivotal trial in non-small cell lung cancer (“NSCLC”), known as FALUCA (clinicaltrials.gov identifier [NCT02691299](#)); and a Phase II study using fruquintinib combined with Iressa[®] (gefitinib) in the first-line setting for patients with advanced or metastatic NSCLC (clinicaltrials.gov identifier [NCT02976116](#)). Other studies currently being planned include new studies in the United States (clinicaltrials.gov identifier [NCT03251378](#)), and certain exploratory studies in combination with other oncology agents.

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.

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. 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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¹ CA Cancer J. Clin., 2016, 66: 115-132.