

## Chi-Med Announces the Approval of Fruquintinib Capsules for Previously Treated Colorectal Cancer in China

*– Fruquintinib capsules provide a new oral treatment option for patients with metastatic colorectal cancer and will be marketed as Elunate<sup>®</sup> –*

*– Elunate<sup>®</sup> data published in JAMA demonstrated increased overall survival versus placebo –*

*– First ever approval of an innovative medicine by Chi-Med –*

*– The first China-discovered and developed treatment for CRC approved in China –*

**London: Wednesday, September 5, 2018:** Hutchison China MediTech Limited (“Chi-Med”) (AIM/Nasdaq: HCM) today announces that fruquintinib capsules have been granted approval for drug registration by the National Medical Products Administration of China (“NMPA”, formerly the China Food and Drug Administration) for the treatment of metastatic colorectal cancer (“CRC”) patients, who have failed at least two prior systemic antineoplastic therapies including fluoropyrimidine, oxaliplatin and irinotecan, with or without prior use of anti-vascular endothelial growth factor (“VEGF”) or anti-epidermal growth factor receptor (“EGFR”) therapies. Fruquintinib is a highly selective and potent small molecule oral inhibitor of vascular endothelial growth factor receptors (“VEGFR”) 1, 2 and 3 designed to be a global best-in-class VEGFR inhibitor for many types of solid tumors. Fruquintinib capsules are to be marketed in China under the brand name Elunate<sup>®</sup>. The approval is based on results from the Phase III FRESCO trial, which were presented at the American Society of Clinical Oncology 2017 Meeting and published in the [JAMA](#) (Journal of the American Medical Association) in 2018.

“Today’s approval is a major achievement for Chi-Med,” said Simon To, Chairman of Chi-Med. “Elunate<sup>®</sup> is the first home-grown, China-discovered and developed drug we are aware of in an oncology indication to be unconditionally approved through a randomized clinical trial in China,” he added, “This is the result of over a dozen years of steadfast commitment by Chi-Med in research and development in China’s emerging biotech ecosystem.”

“We are particularly grateful to the patients, their families, investigators, nurses, caregivers and study team members who participated in the clinical development of Elunate<sup>®</sup> and now look forward to making this world-class new therapy available as quickly as possible to patients with CRC in China.”

In the FRESCO trial led by Dr. Jin Li and Dr. Shukui Qin, Elunate<sup>®</sup> was shown to provide a statistically significant and clinically meaningful improvement in overall survival (“OS”) versus placebo, with median OS of 9.3 (95% CI 8.2, 10.5) vs. 6.6 (95% CI 5.9, 8.1) months, respectively (HR=0.65, 95% CI 0.51-0.83; p<0.001), and a manageable safety profile. In addition to the significant efficacy, fruquintinib’s good kinase selectivity has been shown to limit off-target toxicity and deliver what Chi-Med assesses to be best-in-class tolerability. This allows it to be evaluated in combination with other agents such as chemotherapies, targeted therapies and immunotherapies, thereby maximizing the number of potential patients who may benefit from this novel cancer treatment.

CRC is the second most common cancer type in China,<sup>1</sup> with about 380,000 new cases per year.<sup>2</sup> There were approximately 1.5 million new CRC cases globally in 2015 which are expected to increase to approximately 1.7 million new cases per year by 2020, according to Frost & Sullivan.

The market launch of Elunate<sup>®</sup> in China will be through collaboration with our partner Eli Lilly & Company (“Lilly”). Dr. Wang Li, Senior Vice President, Head of Lilly China Drug Development & Medical Affairs Center, said, “The approval is a testament to the overall clinical profile of Elunate<sup>®</sup> and is an important step forward for our collaboration with Chi-Med.” This approval also triggers an approximately US\$13.6 million milestone payment to Chi-Med from Lilly.

## About Elunate®

Elunate® is the brand name of fruquintinib capsules. Fruquintinib (HMPL-013) is a small molecule, selective and highly potent inhibitor of VEGFR 1, 2 and 3. VEGFR inhibitors play a pivotal role in tumor-related angiogenesis, cutting off the blood supply that a tumor needs to grow rapidly. The global market for anti-angiogenesis therapies was estimated at approximately US\$18 billion in 2017, with both monoclonal antibodies and small molecules approved in around 30 tumor types. During the discovery research process, which began at Chi-Med in 2007, fruquintinib was successfully designed to be differentiated by improving kinase selectivity in comparison to other approved small molecule tyrosine kinase inhibitors (TKIs), to minimize off-target toxicities, improve tolerability and provide more consistent target coverage, resulting in better clinical efficacy. The superior tolerability, along with fruquintinib's low potential for drug-drug interaction based on preclinical assessment, suggests that it may be highly suitable for innovative combinations with other anti-cancer therapies.

In October 2013, Chi-Med entered into a licensing, co-development and commercialization agreement in China with Lilly for fruquintinib. Under the terms of the agreement, the costs of development of fruquintinib, carried out by Chi-Med, are shared; Chi-Med has received upfront payments and development and regulatory approval milestone payments; and upon commercialization in China, Chi-Med would receive royalties. Chi-Med and Lilly agreed to develop fruquintinib in three initial solid tumor indications, CRC, non-small cell lung cancer ("NSCLC") and gastric cancer.

The most common adverse reactions included hypertension, hand-foot syndrome and proteinuria. Clinically effective management of these adverse effects is feasible. For important safety information about Elunate®, please see [www.chi-med.com](http://www.chi-med.com).

## About Fruquintinib Development in CRC in China

Clinical development of fruquintinib began in 2011 with an initial Phase I trial in 40 solid tumor patients, followed by a Phase Ib study in 62 CRC patients, and a Phase II clinical trial in 71 CRC patients. Chi-Med began enrollment in December 2014 of the FRESCO study, a Phase III pivotal registration trial of fruquintinib in 416 patients in China, and subsequently reported positive top-line results in March 2017.

In October 2016, fruquintinib was the first novel drug to be granted Market Authorization Holder ("MAH") designation under the Shanghai FDA, a new system designed to improve speed and efficiency of novel drug development in China. The New Drug Application ("NDA") for fruquintinib in CRC, that was submitted in June 2017 and awarded priority review status in September 2017, was supported by data from the successful FRESCO study. FRESCO was highlighted in an [oral presentation](#) at the ASCO Annual Meeting held on June 5, 2017, and then the full results were published in the [JAMA](#) on June 26, 2018. Additional details about the FRESCO study can be found at [clinicaltrials.gov](http://clinicaltrials.gov), using identifier [NCT02314819](https://clinicaltrials.gov/ct2/show/study/NCT02314819).

Fruquintinib is only approved for use in mainland China with the approved dose in CRC being 5mg orally once per day, on a three-weeks-on / one-week-off cycle and it will be made available in the market in both 1mg and 5mg capsule packages.

## About Other Fruquintinib Development Programs

*Lung cancer in China:* FALUCA is an ongoing randomized, double-blind, placebo-controlled, multi-center, Phase III registration study of fruquintinib treating patients with advanced non-squamous NSCLC, who have progressed after two lines of systemic chemotherapy. The trial [completed enrollment](#) of 527 patients in February 2018 ([clinicaltrials.gov](http://clinicaltrials.gov) identifier [NCT02691299](https://clinicaltrials.gov/ct2/show/study/NCT02691299)) and top-line results are expected in late 2018. FALUCA was initiated following a similar Phase II clinical trial in 91 third-line NSCLC patients. Results were highlighted in an oral presentation at the 17<sup>th</sup> World Conference on Lung Cancer on December 6, 2016 ([clinicaltrials.gov](http://clinicaltrials.gov) identifier [NCT02590965](https://clinicaltrials.gov/ct2/show/study/NCT02590965)).

Along with FALUCA, fruquintinib is concurrently being studied in a Phase II study in combination with Iressa® (gefitinib) in patients with untreated advanced or metastatic NSCLC ([clinicaltrials.gov](http://clinicaltrials.gov) identifier [NCT02976116](https://clinicaltrials.gov/ct2/show/study/NCT02976116)). Preliminary results were highlighted in an [oral presentation](#) at the 18<sup>th</sup> 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, in approximately 500 patients with advanced gastric or gastroesophageal junction ("GEJ") adenocarcinoma who have progressed after first-line

standard chemotherapy (clinicaltrials.gov identifier [NCT03223376](#)). An interim analysis on FRUTIGA, to establish proof-of-concept ("POC"), is anticipated during the first half of 2019 and if successful could trigger a POC milestone from Lilly. The FRUTIGA study followed a Phase I/II clinical trial in 34 patients with gastric cancer that demonstrated that combination therapy of fruquintinib and Taxol<sup>®</sup> was generally well-tolerated with promising tumor response (clinicaltrials.gov identifier [NCT02415023](#)).

*United States:* 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](http://www.chi-med.com).

*Iressa<sup>®</sup> is a trademark of the AstraZeneca PLC group of companies. Taxol<sup>®</sup> is a trademark of The Bristol-Myers Squibb Company group of companies.*

## 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 ability of Elunate<sup>®</sup> (fruquintinib capsules) to gain commercial acceptance in China, the potential market of Elunate<sup>®</sup> for patients with metastatic CRC who have failed two prior treatments in China, the ability for Chi-Med to quickly provide Elunate<sup>®</sup> to patients by year end, and the clinical development of Elunate<sup>®</sup> in other indications. Forward-looking statements involve risks and uncertainties. Such risks and uncertainties include, among other things, assumptions regarding Chi-Med's ability to commercialize Elunate<sup>®</sup>, that the benefits obtained from Elunate<sup>®</sup> during clinical trials will be the same for all patients who are prescribed Elunate<sup>®</sup>, that no unidentified side effects will occur which could result in the NMPA pulling Elunate<sup>®</sup> from the market and the sufficiency of funding to support commercialization of Elunate<sup>®</sup> in metastatic CRC and the development of Elunate<sup>®</sup> in other indications. In addition, as certain studies rely on the use of Iressa<sup>®</sup> (gefitinib) or Taxol<sup>®</sup> (paclitaxel) as combination therapeutics with Elunate<sup>®</sup>, such risks and uncertainties include assumptions regarding the safety, efficacy, supply and continued regulatory approval of Iressa<sup>®</sup> and Taxol<sup>®</sup>. 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.*

## Inside Information

This announcement contains inside information for the purposes of Article 7 of Regulation (EU) No 596/2014.

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<sup>1</sup> R. Zheng, H. Zeng et al, Cancer Lett. 2016 Jan 1;370(1):33-8. National estimates of cancer prevalence in China, 2011. doi:[10.1016/j.canlet.2015.10.003](https://doi.org/10.1016/j.canlet.2015.10.003). Epub 2015 Oct 13.

<sup>2</sup> W. Chen, R. Zheng et al, CA Cancer J Clin. 2016 Mar-Apr;66(2):115-32. Cancer Statistics in China, 2015. doi:[10.3322/caac.21338](https://doi.org/10.3322/caac.21338). Epub 2016 Jan 25.