



HUTCHISON CHINA MEDITECH

## **Chi-Med Announces Amendment to the 2013 License & Collaboration Agreement on Fruquintinib with Eli Lilly and Company**

- *Chi-Med acquires right to determine & conduct all future life cycle indication development of fruquintinib monotherapy as well as innovative combinations in China –*
- *Chi-Med to assume all development costs of life cycle indications in China in return for an increase in both milestone and royalty payments from Lilly –*
- *Chi-Med acquires potential future co-promotion rights for fruquintinib in China –*

**London: Thursday, December 20, 2018:** Hutchison China MediTech Limited (“Chi-Med”) (AIM/Nasdaq: HCM) today announces certain amendments (“2018 Amendment”) to the 2013 License and Collaboration Agreement (“2013 Agreement”) on fruquintinib with Lilly Shanghai an affiliate of Eli Lilly and Company (“Lilly”). The 2018 Amendment covers adjustments in the respective roles and responsibilities of Chi-Med and Lilly, in China, for the development and commercialization of fruquintinib in the areas of future life cycle planning and development, collaborations for co-development of fruquintinib with other third-party anti-cancer agents as well as promotion and distribution rights of fruquintinib.

“Through this amendment, Chi-Med is stepping forward to take on greater responsibility in return for a broader role and a larger share of the future economic interest on fruquintinib,” commented Simon To, Chairman of Chi-Med. “Lilly has been and will continue to be a most important partner for Chi-Med in bringing fruquintinib to as broad a patient population as possible and we share a common goal to maximize the commercial success of fruquintinib in China.” He added, “The recent approval and launch of fruquintinib for colorectal cancer in China is an important first step on this journey.”

### **Fruquintinib Life Cycle Indications (“LCI”):**

Under the terms of the 2013 Agreement, decision making on LCI development beyond the initial indications of third-line colorectal cancer (“CRC”), third-line non-small cell lung cancer (“NSCLC”) and second-line gastric cancer was controlled by Lilly. The majority of development costs for LCIs were to be paid by Lilly, with the minority by Chi-Med.

The 2018 Amendment now gives Chi-Med all planning, execution and decision making responsibilities for LCI development on fruquintinib in China. Chi-Med will pay all of the costs associated with fruquintinib LCI development in China. In return for this investment of capital and resources, Lilly will pay Chi-Med a \$20 million milestone upon approval of each fruquintinib LCI in China, for up to three LCIs, totaling up to \$60 million in LCI approval milestone payments. Furthermore, upon the launch of the first LCI, the tiered royalty structure, payable by Lilly to Chi-Med on total molecule sales in China, has been raised from the range of 15-20% in the 2013 Agreement to a new level of 15-29% under the 2018 Amendment.

### **China commercial - Co-Promotion rights:**

Under the terms of the 2013 Agreement, Lilly held full commercialization rights to fruquintinib in China.

The 2018 Amendment provides Chi-Med the right to promote fruquintinib in provinces that represent 30% of the sales of fruquintinib in China (“Chi-Med Territory”) upon the occurrence of certain commercial milestones. The Chi-Med Territory will expand to provinces that represent 40% of the sales of fruquintinib in China subject to additional criteria being met. Lilly will pay Chi-Med a fee for service to conduct all promotional activities in the Chi-Med Territory.

### **Immunotherapy collaborations:**

Lilly has provided consent, and freedom to operate, for Chi-Med to enter into joint development collaborations with certain third-party pharmaceutical companies to explore combination treatments of fruquintinib and various immunotherapy agents. The first such collaborations with Innovent Biologics (Suzhou) Co. Ltd. (“Innovent”) and Genor Biopharma Co. Ltd. (“Genor”) will explore the combination of fruquintinib and their respective programmed cell death protein-1 (“PD-1”) antibodies, sintilimab (IBI308) and genolimzumab (GB226), in several solid tumor settings.

## FINANCIAL GUIDANCE:

Our updated guidance for 2018, compared to the most recent guidance in our 2018 Interim Results announcement for the period ended June 30, 2018 dated July 27, 2018, includes a \$12 million increase in expected full year Innovation Platform R&D expense to \$142-152 million. This increase reflects the 2018 Amendment of the fruquintinib collaboration with Lilly; our recent co-development collaborations with multiple partners to explore immunotherapy (PD-1) combinations with our vascular endothelial growth factor receptor (VEGFR) inhibitors; as well as a general rise in clinical trial spending on our eight clinical drug candidates and discovery programs including a one-time non-cash adjustment relating to one of our joint ventures. Further, while progress has been made towards realizing the one-time property compensation gain under the Commercial Platform, it is not expected to occur in 2018. We make no other changes to the full year 2018 financial guidance as detailed below:

	2018 Previous Guidance	2018 Current Guidance	Adjustment
<b>Group Level:</b>			
• Consolidated revenue	\$155-175m	\$155-175m	None
• Admin., interest & tax	\$(16)-(18)m	\$(16)-(18)m	None
• Net loss <sup>[1]</sup>	\$(39)-(72)m	\$(71)-(84)m	\$(12)-(32)m increase
<b>Innovation Platform:</b>			
• Consolidated revenue	\$40-50m	\$40-50m	None
• Adjusted (non-GAAP) R&D expenses	\$(130)-(140)m	\$(142)-(152)m	\$(12)m increase
• Net loss <sup>[1]</sup>	\$(80)-(100)m	\$(92)-(112)m	\$(12)m increase
<b>Commercial Platform:</b>			
• Sales (consolidated)	\$115-125m	\$115-125m	None
• Sales of non-consolidated JVs <sup>[2]</sup>	\$460-480m	\$460-480m	None
• Net income on an adjusted (non-GAAP) basis excl. one-time gains <sup>[1]</sup>	\$41-43m	\$41-43m	None
• One-time gains <sup>[1]</sup>	\$0-20m <sup>[3]</sup>	\$0m	\$0-(20)m decrease
• Net income <sup>[1]</sup>	\$41-63m	\$41-43m	\$0-(20)m decrease

Notes: [1] Attributable to Chi-Med; [2] Joint ventures; [3] One-time property compensation, timing of which is dependent on Guangzhou government policy.

All dollars are expressed in US dollar currency unless otherwise stated.

## About Fruquintinib

Fruquintinib (brand name: Elunate<sup>®</sup>) 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 over \$18 billion in 2017, including both monoclonal antibodies and small molecules approved in around 30 tumor settings. 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. 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 fruquintinib, please see [www.chi-med.com](http://www.chi-med.com).

## About Other Fruquintinib Development Programs

### Global Development

*Phase I monotherapy in the U.S.:* 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](#)). This study is almost complete, and proof-of-concept (“POC”) studies are expected to begin in 2019.

*PD-1 checkpoint inhibitor combination:* It is an important part of Chi-Med’s strategy to explore the potential synergies of its drug candidates in combination with other anti-cancer treatments in several solid tumor settings. In November 2018, Chi-Med entered into a global collaboration agreement to evaluate the safety, tolerability and efficacy of fruquintinib in combination with sintilimab (IBI308), a PD-1 inhibitor being developed by Innovent.

### China Development

*CRC in China:* The National Medical Products Administration (NMPA) [approved the first New Drug Application \(“NDA”\)](#) for fruquintinib for the treatment of patients with advanced CRC in September 2018. 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 held on June 5, 2017 and was published in The Journal of the American Medical Association, [JAMA](#), in June 2018 (clinicaltrials.gov identifier [NCT02314819](#)).

*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 POC, is anticipated during the first half of 2019 and if successful could trigger a POC milestone payment 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® was generally well-tolerated with promising tumor response (clinicaltrials.gov identifier [NCT02415023](#)).

*Lung cancer in China:* 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. 527 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. On November 16, 2018, Chi-Med announced that FALUCA did not meet the primary endpoint to demonstrate a statistically significant increase in overall survival (OS) compared to placebo, however the data did show statistically significant improvement in all secondary endpoints including progression free survival (PFS), objective response rate (ORR), disease control rate (DCR) and duration of response (DoR) as compared to the placebo. The safety profile of the trial was in line with that observed in prior clinical studies. Full detailed results are expected to be disclosed at an upcoming scientific meeting. Additional details about this study can be found at clinicaltrials.gov, using identifier [NCT02691299](#).

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 identifier [NCT02976116](#)). Preliminary results were highlighted in an oral presentation at the 18<sup>th</sup> World Conference on Lung Cancer on October 16, 2017.

*PD-1 checkpoint inhibitor combination:* In October 2018, Chi-Med entered into a further collaboration in China to evaluate the combination of fruquintinib with genolimzumab (GB226), a PD-1 inhibitor being developed by Genor.

## About Chi-Med

Chi-Med (AIM/Nasdaq: HCM) is an innovative biopharmaceutical company which researches, develops, manufactures and markets pharmaceutical products. Its Innovation Platform, Hutchison MediPharma, has about 400 scientists and staff focusing on discovering, developing and commercializing targeted therapeutics in oncology and autoimmune diseases. It has a portfolio of eight cancer drug candidates currently in clinical studies around the world. Chi-Med’s Commercial Platform manufactures, markets, and distributes prescription drugs and consumer health products, covering an extensive network of hospitals across China.

Dual-listed on the AIM market of the London Stock Exchange and the Nasdaq Global Select Market, Chi-Med is headquartered in Hong Kong and 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).

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

## USE OF NON-GAAP FINANCIAL MEASURES

In addition to financial information prepared in accordance with U.S. GAAP, this announcement also contains certain non-GAAP financial measures.

*Adjusted R&D expenses:* We exclude the expected impact of the revenue received from external customers of our Innovation Platform, which is reinvested into our clinical trials, to derive our adjusted R&D expense. Revenue received from external customers of our Innovation Platform consists of milestone and other payments from our collaboration partners. The variability of such payments makes the identification of trends in our ongoing R&D activities more difficult. We believe the presentation of adjusted R&D expenses guidance provides useful and meaningful information about our ongoing R&D activities by enhancing investors’ understanding of the scope of our normal, recurring operating R&D expenses.

*Adjusted consolidated net income attributable to Chi-Med from our Commercial Platform:* We exclude the impact of one-time gains which could be triggered by the payment of land compensation from the Guangzhou government to a non-consolidated JV, dependent on Guangzhou government policy.

Management uses such measures internally for planning and forecasting purposes and to measure the Chi-Med Group’s overall performance. We believe these adjusted financial measures provide useful and meaningful information to us and investors because they enhance investors’ understanding of the continuing operating performance of our business and facilitate the comparison of performance between past and future periods. These adjusted financial measures are non-GAAP measures and should be considered in addition to, but not as a substitute for, the information prepared in accordance with U.S. GAAP. Other companies may define these measures in different ways.

<b>Reconciliation of GAAP to adjusted R&amp;D expenses</b>	<b>2018 Previous Guidance</b>	<b>2018 Current Guidance</b>
Segment operating loss — Innovation Platform	\$(80)-(100)m	\$(92)-(112)m
Less: Segment revenue from external customers — Innovation Platform	\$(40)-(50)m	\$(40)-(50)m
Adjusted R&D expenses	\$(130)-(140)m	\$(142)-(152)m

<b>Reconciliation of GAAP to adjusted consolidated net income attributable to Chi-Med from our Commercial Platform</b>	<b>2018 Previous Guidance</b>	<b>2018 Current Guidance</b>
Consolidated net income attributable to Chi-Med — Commercial Platform	\$41-63m	\$41-43m
Less: One-time gains from land compensation	\$0-(20)m	\$0m
Adjusted consolidated net income attributable to Chi-Med — Commercial Platform	\$41-43m	\$41-43m

## Inside Information

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

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