

Press Release

Chi-Med and BeiGene Enter into Clinical Collaboration to Evaluate Combinations of Surufatinib and Fruquintinib with Tislelizumab

– Collaboration to explore multiple solid tumor cancer indications –

– Initial development focused on multi-cohort trials in the U.S., Europe, China and Australia –

LONDON, UK; CAMBRIDGE, Mass. and BEIJING, China: May 26, 2020: Hutchison China MediTech Limited (“Chi-Med”) (Nasdaq/AIM: HCM) and BeiGene, Ltd. (“BeiGene”) (Nasdaq: BGNE; HKEX: 06160) today announced that they have entered into a clinical collaboration agreement to evaluate the safety, tolerability and efficacy of combining two of Chi-Med’s drug candidates, surufatinib and fruquintinib, with BeiGene’s anti-PD-1 antibody tislelizumab, for the treatment of various solid tumor cancers, in the U.S., Europe, China and Australia.

Under the terms of the agreement, Chi-Med and BeiGene each plan to explore development of the combination of surufatinib with tislelizumab or fruquintinib with tislelizumab in different indications and regions. The companies have agreed to provide mutual drug supply and other support.

“We are very pleased to enter into this clinical collaboration with BeiGene, a company with which we share a vision to discover, develop and commercialize innovative targeted therapies and immunotherapies worldwide,” said Dr. Marek Kania, Senior Vice President and Chief Medical Officer, Hutchison MediPharma International.¹

“By working together with a partner like Chi-Med, we hope to understand and develop innovative combination therapies that may bring meaningful treatments to cancer patients around the world. Through this collaboration we plan to further evaluate tislelizumab in combination with oral VEGFR inhibitors to target a variety of solid tumor cancers,” said Lai Wang, Ph.D., Senior Vice President, Head of Global Research, Clinical Operations & Biometrics and APAC Clinical Development, at BeiGene.

Each of these three compounds are currently in late-stage global clinical development across many countries outside of China. Tislelizumab is a humanized IgG4 anti-programmed death-1 (“PD-1”) monoclonal antibody specifically designed to minimize binding to Fc receptor gamma (“FcγR”), which is believed to play an essential role in activating phagocytosis in macrophages, to minimize its negative impact on T effector cells. Fruquintinib is designed to improve kinase selectivity against vascular endothelial growth factor receptors (“VEGFR”) in order to minimize off-target toxicities, and thereby provide consistent coverage and better tolerability, which is very important in combinations. Surufatinib, a VEGFR inhibitor, inhibits colony stimulating factor-1 receptor (“CSF-1R”) additionally, thereby blocking the accumulation of tumor associated macrophages and promoting infiltration of T effector cells into tumors, leading to possible synergistic anti-tumor activity with PD-1 inhibitors.

Tislelizumab and fruquintinib have both been approved by the China National Medical Products Administration (“NMPA”), which is also currently reviewing the New Drug Application (“NDA”) for surufatinib that was submitted late last year.

About Tislelizumab

Tislelizumab (BGB-A317) is a humanized IgG4 anti-PD-1 monoclonal antibody specifically designed to minimize binding to FcγR on macrophages. In pre-clinical studies, binding to FcγR on macrophages has been shown to compromise the anti-tumor activity of PD-1 antibodies through activation of antibody-dependent macrophage-mediated killing of T effector cells. Tislelizumab is the first drug from BeiGene’s immuno-oncology biologics program and is being developed internationally as a monotherapy and in combination with other therapies for the treatment of a broad array of both solid tumor and hematologic cancers.

Tislelizumab is approved by the China NMPA as a treatment for patients with classical Hodgkin’s lymphoma (“cHL”) who received at least two prior therapies and for patients with locally advanced or metastatic urothelial carcinoma (UC) with PD-L1 high expression whose disease progressed during or following platinum-containing

¹ Hutchison MediPharma International – the international arm of Chi-Med’s innovative drug R&D operations.



chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.

Currently, 15 potentially registration-enabling clinical trials are being conducted in China and globally, including 11 Phase 3 trials and four pivotal Phase 2 trials.

Tislelizumab is not approved for use outside of China.

About Fruquintinib

Fruquintinib is a highly selective and potent oral inhibitor of VEGFR 1/2/3. VEGFR inhibitors play a pivotal role in blocking tumor angiogenesis. Fruquintinib was designed to improve kinase selectivity to minimize off-target toxicities, improve tolerability and provide more consistent target coverage. The generally good tolerability in patients to date, along with fruquintinib's low potential for drug-drug interaction based on preclinical assessment, suggests that it may be highly suitable for combinations with other anti-cancer therapies.

Fruquintinib was approved for marketing in China by the NMPA in September 2018 and commercially launched by Eli Lilly and Company ("Lilly") in late November 2018 under the brand name Elunate®. Elunate® is for the treatment of patients with metastatic colorectal cancer that have been previously treated with fluoropyrimidine, oxaliplatin and irinotecan, including those who have previously received anti-VEGF therapy and/or anti-EGFR therapy (RAS wild type). Results of the FRESCO study, a Phase III pivotal registration trial of fruquintinib in 416 patients with colorectal cancer ("CRC") in China, were [published](#) in The Journal of the American Medical Association, JAMA, in June 2018 (clinicaltrials.gov identifier: [NCT02314819](#)).

Chi-Med retains all rights to fruquintinib outside of China and is partnered with Lilly in China.

Global development of fruquintinib in CRC: We intend to initiate a Phase III registration study, known as the FRESCO-2 study, in the U.S., Europe and Japan in CRC. FRESCO-2 is expected to start enrolling patients in mid-2020. Based on our agreement with the U.S. Food and Drug Administration (FDA), the FRESCO and FRESCO-2 studies, if positive, could support our NDA application.

Gastric Cancer in China: In October 2017, we initiated the FRUTIGA study, a randomized, double-blind, Phase III study in China to evaluate the efficacy and safety of **fru**quintinib combined with paclitaxel (**T**axol®) compared with paclitaxel monotherapy in the treatment of patients with advanced **g**astric **a**denocarcinoma or gastroesophageal junction (GEJ) adenocarcinoma who have progressed after first-line standard chemotherapy (clinicaltrials.gov identifier: [NCT03223376](#)). Over 540 patients are expected to be enrolled into the FRUTIGA study at a 1:1 ratio with the primary endpoint of this study being overall survival (OS). In April 2019, we conducted the first interim analysis of the FRUTIGA study for futility. Following the analysis of safety and efficacy of the first 100 patients, the Independent Data Monitoring Committee ("IDMC") recommended to continue the study without changes. We expect to conduct a second interim analysis in mid-2020 and complete enrollment of the study in 2020.

Immunotherapy combinations: In November 2018, we entered into two [collaboration agreements](#) to evaluate the safety, tolerability and efficacy of fruquintinib in combination with PD-1 monoclonal antibodies, including with Tyvyt® (sintilimab) and geptanolimab (GB226, genolimzumab).

Fruquintinib is not approved for use outside of China.

About Surufatinib

Surufatinib is a novel, oral angio-immuno kinase inhibitor that selectively inhibits the tyrosine kinase activity associated with VEGFR and fibroblast growth factor receptor (FGFR), which both inhibit angiogenesis, and CSF-1R, which regulates tumor-associated macrophages, promoting the body's immune response against tumor cells. Its unique dual mechanism of action may be very suitable for possible combinations with other immunotherapies, where there may be synergistic anti-tumor effects.

Chi-Med currently retains all rights to surufatinib worldwide.

Neuroendocrine tumors ("NET") in the U.S., Europe and Japan: We are preparing for regulatory interactions in the U.S., Europe and Japan to confirm clinical development and path to registration, based on the robust data from the two positive Phase III studies of surufatinib in NET in China, and the ongoing multi-cohort Phase Ib study in the U.S. (clinicaltrials.gov identifier: [NCT02549937](#)). In the U.S., surufatinib was granted [Fast Track](#)



[Designations](#) for development in pancreatic and non-pancreatic (extra-pancreatic) NET in April 2020, and [Orphan Drug Designation](#) for pancreatic NET in November 2019.

Non-pancreatic neuroendocrine tumors in China: In November 2019, a New Drug Application (“NDA”) for surufatinib for the treatment of patients with advanced non-pancreatic NET was [accepted for review](#) by the China NMPA and [granted Priority Review](#) status in December 2019. The NDA is supported by data from the successful SANET-ep study, a Phase III study of surufatinib in advanced neuroendocrine tumors – extra-pancreatic patients in China for whom there is no effective therapy. A 198-patient interim analysis was conducted in June 2019, leading the IDMC to determine that the study met the pre-defined primary endpoint of progression-free survival (“PFS”) and should be stopped early. The [positive results](#) of this trial were highlighted in an oral presentation at the 2019 European Society for Medical Oncology Congress (clinicaltrials.gov identifier: [NCT02588170](#)).

Pancreatic neuroendocrine tumors in China: In 2016, we initiated the SANET-p study, which is a pivotal Phase III study in patients with low- or intermediate-grade, advanced pancreatic NET in China. A second NDA for surufatinib for the treatment of patients with advanced pancreatic NET is being prepared for submission, following an interim analysis review conducted in January 2020 by the IDMC that recommended the registrational study be terminated early as the pre-defined primary endpoint of [PFS had already been met](#) (clinicaltrials.gov identifier: [NCT02589821](#)). Study results will be submitted for presentation at an upcoming scientific conference.

Biliary tract cancer in China: In March 2019, we initiated a Phase IIb/III study comparing surufatinib with capecitabine in patients with advanced biliary tract cancer whose disease progressed on first-line chemotherapy. The primary endpoint is overall survival (“OS”) (clinicaltrials.gov identifier [NCT03873532](#)).

Immunotherapy combinations: In November 2018 and September 2019, we entered into [collaboration agreements](#) to evaluate the safety, tolerability and efficacy of surufatinib in combination with anti-PD-1 monoclonal antibodies, including with Tuoyi® (toripalimab) and Tyvyt®, which are approved in China.

About Chi-Med

Chi-Med (Nasdaq/AIM: HCM) is an innovative biopharmaceutical company committed, over the past twenty years, to the discovery and global development of targeted therapies and immunotherapies for the treatment of cancer and immunological diseases. It has a portfolio of eight cancer drug candidates currently in clinical studies around the world and extensive commercial infrastructure in its home market of China. For more information, please visit: www.chi-med.com.

About BeiGene

BeiGene is a global, commercial-stage biotechnology company focused on discovering, developing, manufacturing, and commercializing innovative medicines to improve treatment outcomes and access for patients worldwide. Our 3,800+ employees in China, the United States, Australia, and Europe are committed to expediting the development of a diverse pipeline of novel therapeutics for cancer. We currently market two internally-discovered oncology products: BTK inhibitor BRUKINSA™ (zanubrutinib) in the United States, and anti-PD-1 antibody tislelizumab in China. We also market or plan to market in China additional oncology products licensed from Amgen Inc., Celgene Logistics Sàrl, a Bristol Myers Squibb (BMS) company, and EUSA Pharma. To learn more about BeiGene, please visit www.beigene.com and follow us on Twitter at @BeiGeneUSA.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the U.S. Private Securities Litigation Reform Act of 1995 and other federal securities laws, including statements regarding the clinical development of surufatinib and fruquintinib in combination with tislelizumab, Chi-Med’s and BeiGene’s roles and responsibilities in the collaboration, the opportunity and potential benefits of their product candidates both as monotherapies and in combination, and other information that is not historical information. Actual results may differ materially from those indicated in the forward-looking statements as a result of various important factors, including the ability of Chi-Med and BeiGene to develop and receive regulatory approvals for the combination therapies in the collaboration; the risk that the potential benefits of the collaboration do not materialize or do not outweigh the costs; the ability of Chi-Med and BeiGene to demonstrate the efficacy and safety of their respective drug candidates as monotherapies or in combination; the clinical results for such drug



candidates, which may not support further development or marketing approval; actions of regulatory agencies, which may affect the initiation, timing and progress of clinical trials and marketing approval; Chi-Med's and BeiGene's ability to achieve commercial success for their marketed products and drug candidates, if approved; Chi-Med's and BeiGene's ability to obtain and maintain protection of intellectual property for their respective technology and drugs; BeiGene's and Chi-Med's reliance on third parties to conduct drug development, manufacturing and other services; BeiGene's limited operating history and BeiGene's and Chi-Med's ability to obtain additional funding for operations and to complete the development and commercialization of their drug candidates; and the impact of the COVID-19 pandemic on BeiGene's and Chi-Med's clinical development, commercial and other operations. 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 or BeiGene's filings with the U.S. Securities and Exchange Commission and, in the case of Chi-Med, on AIM. All information in this press release is as of the date of this press release, and neither Chi-Med nor BeiGene undertakes a duty to update such information unless required by law.

Chi-Med Contacts

Investor Enquiries

Mark Lee, Senior Vice President	+852 2121 8200
Annie Cheng, Vice President	+1 (973) 567 3786

Media Enquiries

Americas – Brad Miles, Solebury Trout	+1 (917) 570 7340 (Mobile) bmiles@troutgroup.com
Europe – Ben Atwell / Alex Shaw, FTI Consulting	+44 20 3727 1030 / +44 7771 913 902 (Mobile) / +44 7779 545 055 (Mobile) Chi-Med@fticonsulting.com
Asia – Joseph Chi Lo / Zhou Yi, Brunswick	+852 9850 5033 (Mobile), jlo@brunswickgroup.com / +852 9783 6894 (Mobile), yzhou@brunswickgroup.com

Nominated Advisor

Freddy Crossley / Atholl Tweedie, Panmure Gordon (UK) Limited	+44 (20) 7886 2500
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BeiGene Investor Contact

Craig West
+1 857-302-5189
ir@beigene.com

BeiGene Media Contact

Liza Heapes
+1 857-302-5663
media@beigene.com