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Chi-Med and AstraZeneca Amend Co-development Agreement to Accelerate Savolitinib Global Development Program

First global pivotal Phase III in c-Met-driven papillary renal cell carcinoma (“PRCC”) to be initiated in the near future

London: Monday, August 1, 2016: Chi-Med and AstraZeneca today announced an amendment (the “Amendment”) to the 2011 global licensing, co-development, and commercialisation agreement (the “2011 Agreement”) regarding savolitinib. Based on data from multiple Phase I/II studies, savolitinib has shown early clinical benefit as a highly selective c-Met inhibitor in a number of cancers.

As a consequence, savolitinib’s global development plan now covers multiple c-Met-driven solid tumor indications including non-small cell lung cancer (“NSCLC”), kidney, gastric and colorectal cancers. For a detailed summary of all current savolitinib clinical trials, please [click here](#).

Chi-Med and AstraZeneca have agreed to the amendment in order to accelerate savolitinib’s global development and increase Chi-Med’s participation in the programme. The Amendment provides that Chi-Med will contribute up to \$50 million, spread primarily over three years, to the joint development costs of the global pivotal Phase III study in c-Met-driven PRCC. Subject to approval in the PRCC indication, Chi-Med will receive a 5 percentage point increase in the global (excluding China) tiered royalty rate payable on savolitinib sales across all indications. All other provisions of the 2011 Agreement will remain unchanged.

Final results from savolitinib’s recently completed open-label global PRCC Phase II study (NCT02127710) will be presented at an upcoming scientific meeting. Chi-Med and AstraZeneca have now agreed to proceed to Phase III.

The global Phase III trial of savolitinib will be the first pivotal study conducted in c-Met-driven PRCC, a rare histological subtype of renal cell carcinoma (“RCC”) that is associated with alterations in the c-Met gene (e.g. mutations, amplifications, and/or chromosomal changes). Currently, available RCC therapies have demonstrated only modest benefit in PRCC and there are no therapies specifically approved for the treatment of c-Met-driven PRCC. Ongoing interactions with health authorities will determine the final design of the global pivotal Phase III trial, and its initiation will be aligned with availability of a companion diagnostic for c-Met-driven PRCC. The PRCC Phase III companion diagnostic platform will be largely similar for other indications such as NSCLC and gastric cancer.

AstraZeneca is also continuing to lead the development of savolitinib in other c-Met-driven types of cancer. Most notably, a Phase II expansion of the ongoing TATTON trial (NCT02143466) to evaluate savolitinib in epidermal growth factor receptor (“EGFR”) mutant NSCLC patients has been initiated. This trial is a single-arm global Phase II study of savolitinib in combination with *Tagrisso* (osimertinib) in advanced NSCLC patients who have developed resistance to approved EGFR tyrosine kinase inhibitors. The Phase II expansion was initiated following early data from the TATTON study.

Susan Galbraith, Senior Vice President, Head of Oncology, Innovative Medicines and Early Development, AstraZeneca, said: “The accelerated development of savolitinib in RCC and NSCLC

reflects our ongoing commitment to deliver world-class medicines to patients with limited treatment options. We are pleased to be building on our established collaboration with Chi-Med, as this reinforces our enterprise leadership approach to drug development.”

Christian Hogg, Chief Executive Officer of Chi-Med, said: “Bringing savolitinib to a global launch in multiple areas of unmet medical need is our very clear focus. We believe that savolitinib has the potential to become the first approved therapy in kidney cancer in a molecularly selected patient population, as well as in multiple c-Met-driven lung and gastrointestinal tract cancers. As we enter a period where pivotal trials in multiple indications are close at hand, we are now happy to take on a small minority of the investment in order to help accelerate development while increasing our share in the long-term economic value of savolitinib.”

NOTES TO EDITORS

About savolitinib, a uniquely selective c-Met inhibitor

Savolitinib is a potential global first-in-class inhibitor of c-Met (also known as mesenchymal epithelial transition factor) receptor tyrosine kinase, an enzyme which has been shown to function abnormally in many types of solid tumors. It was developed as a potent and highly selective oral inhibitor specifically designed to address issues observed in the clinic with first-generation c-Met inhibitors, including renal toxicity.

Market potential and unmet medical need in c-Met-driven PRCC patients

Worldwide, about 366,000 new patients are diagnosed with kidney cancer annually, and the total market for kidney cancer treatments is expected to reach \$4.5 billion in 2020, according to Frost & Sullivan. RCC accounts for approximately 80-85% of kidney cancer and has several histological sub-types with different genetic and biochemical characteristics. Among these histologic variants of RCC, clear cell RCC (“ccRCC”) is the most common, accounting for 75-80% of RCC.

PRCC is the most common of the non-clear cell renal carcinomas accounting for 10-15% of RCC. The proportion of PRCC patients whose tumors are c-Met-driven has historically been estimated at 40-70%. In the largest study to date, presented at the annual meeting of the American Association for Cancer Research 2014, analysis of 220 frozen tumor samples catalogued in the French RCC Network indicated that 55-60% of PRCC patients showed gains in Chromosome 7 (i.e. c-Met amplification).

The biology and molecular characteristics of PRCC are different from those of ccRCC. This results in significantly worse prognosis and treatment outcomes for patients with PRCC when compared to patients with ccRCC. Highlighting the unmet need is the fact that, although there are several drugs approved for use in RCC (the latest being approved in April 2016), these approvals were generally on the basis of studies conducted with a preponderance of ccRCC patients. The need for different agents and more specific data tailored to the PRCC disease setting has been identified as a critical gap in the care of these patients.

Savolitinib clinical development in PRCC

Australia Phase I Study – A Phase I dose escalation study in a range of tumor types demonstrated the clinical activity and safety profile of savolitinib 600mg once-daily, with a confirmed partial response observed at an early point in the study in a patient with c-Met-driven PRCC. In total, confirmed partial responses were observed in 3/8 (38%) PRCC patients, all of whom harbored c-Met-driven disease, and durations of response were approximately 10-37 months (ongoing). Phase I safety data (n=33) reported that the most common Grade 3 or 4 events included fatigue (9%), dysphonia (hoarseness) (6%), peripheral edema (6%) and headache (3%). Based on these Phase I

findings, which were reported at the American Society of Clinical Oncology annual meeting in 2014 ([click here](#)), AstraZeneca and Chi-Med agreed to proceed with a global Phase II study in PRCC.

Global Phase II Study – The global open-label single arm Phase II study of savolitinib in patients with locally advanced or metastatic PRCC was initiated in May 2014, reaching a total of 22 clinical centers in the U.S., Canada, UK, and Spain, and completing enrollment of 109 PRCC patients in October 2015. This Phase II study is the largest prospective clinical study ever conducted in PRCC. The primary objective of the study is to assess the anti-tumor activity of savolitinib in patients with PRCC, with secondary assessment objectives including median Progression Free Survival, duration of response, safety and tolerability, and pharmacokinetics and pharmacodynamics. Importantly, tumor samples from each patient were concurrently subjected to molecular analysis to determine c-Met status in order to better understand the relationship between c-Met aberration and clinical outcome. The results of the Phase II study will be presented at an upcoming scientific meeting.

Companion diagnostic development

The savolitinib c-Met-driven PRCC pivotal Phase III study will be the first molecularly selected trial in RCC. The molecular analysis of each patient in the PRCC Phase II study has provided an understanding of the biomarker and selection criteria needed to identify PRCC patients most likely to benefit from treatment with savolitinib. AstraZeneca and Foundation Medicine, Inc. (Nasdaq: FMI) have an agreement to develop companion diagnostic assays to facilitate personalized medicine in oncology by identifying patients most likely to benefit from novel targeted therapies, including savolitinib. The companion diagnostic assays assess multiple cancer-related genes as well as classes of genomic alterations, and are being developed in parallel with the clinical development of savolitinib as part of a coordinated regulatory strategy. The PRCC Phase III companion diagnostic platform will be largely similar for other indications such as NSCLC and gastric cancer.

Overview of AstraZeneca collaboration

Under the 2011 Agreement, we granted to AstraZeneca co-exclusive, worldwide rights to manufacture and commercialize savolitinib for all diagnostic, prophylactic and therapeutic uses. AstraZeneca paid \$20 million upon execution and agreed to pay royalties and additional amounts upon the achievement of development and sales milestones. As of June 30, 2016 we had received a further \$20 million in milestone payments. We may potentially receive future clinical development and first sales milestones of up to \$100 million for clinical development and initial sales of savolitinib, plus significant further milestone payments based on sales. AstraZeneca also reimburses us for certain development costs. Additionally, AstraZeneca is obligated to pay us a fixed royalty of 30% annually on all sales made of any product in China and tiered royalties from 9% to 13% annually on all sales made of any product outside of China. Under the Amendment, Chi-Med will contribute up to \$50 million, spread primarily over three years, to the joint development costs of the global pivotal Phase III study in c-Met-driven PRCC. Subject to approval in the PRCC indication, Chi-Med will receive a 5 percentage point increase in the global (excluding China) tiered royalty rate payable on savolitinib sales across all indications, thereby increasing the tiered royalty to 14% to 18%. After total aggregate sales of savolitinib have reached \$5 billion, the royalty will step down over a two year period, to an ongoing royalty rate of 10.5% to 14.5%. All other provisions of the 2011 Agreement will remain unchanged.

About Chi-Med

Chi-Med is an innovative biopharmaceutical company which researches, develops, manufactures and sells pharmaceuticals and healthcare-related consumer 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.

About AstraZeneca in Oncology

AstraZeneca has a deep-rooted heritage in Oncology and offers a quickly growing portfolio of new medicines that has the potential to transform patients' lives and the Company's future. With at least 6 new medicines to be launched between 2014 and 2020 and a broad pipeline of small molecules and biologics in development, we are committed to advance New Oncology as one of AstraZeneca's six Growth Platforms focused on lung, ovarian, breast and blood cancers. In addition to our core capabilities, we actively pursue innovative partnerships and investments that accelerate the delivery of our strategy, as illustrated by our investment in Acerta Pharma in haematology.

By harnessing the power of four scientific platforms – immuno-oncology, the genetic drivers of cancer and resistance, DNA damage response and antibody drug conjugates – and by championing the development of personalized combinations, AstraZeneca has the vision to redefine cancer treatment and one day eliminate cancer as a cause of death.

About AstraZeneca

AstraZeneca is a global, science-led biopharmaceutical company that focuses on the discovery, development and commercialisation of prescription medicines, primarily for the treatment of diseases in three therapy areas – Respiratory and Autoimmunity, Cardiovascular and Metabolic Diseases, and Oncology. The company is also active in inflammation, infection and neuroscience through numerous collaborations. AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide. For more information please visit: www.astrazeneca.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 can be identified by words such as “will,” “plans,” “expects,” “long-term,” “priorities,” “pipeline,” “could,” “accelerate,” “potential,” “believe,” “first-in-class,” “designed to,” “objective,” “guidance,” “pursue,” or similar terms, or by express or implied discussions regarding potential drug candidates, potential indications for drug candidates, or regarding potential future revenues from any such drug candidates; potential shareholder returns; or regarding any potential financial or other impact on Chi-Med of our acceleration of the savolitinib global development program; or regarding any potential financial or other impact on Chi-Med of the amendment to the co-development agreement with AstraZeneca; or by discussions of strategy, plans, expectations or intentions. You should not place undue reliance on these statements. Such forward-looking statements are based on the current beliefs and expectations of management regarding future events, and are subject to significant known and unknown risks and uncertainties. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those set forth in the forward-looking statements. There can be no guarantee that any of our drug candidates will be approved for sale in any market, or that any approvals which are obtained will be obtained at any particular time, or that any such drug candidates will achieve any particular revenue levels. In particular, management’s expectations could be affected by, among other things: unexpected regulatory actions or delays or government regulation generally; the uncertainties inherent in research and development, including the inability to meet our key study assumptions regarding enrollment rates, timing and availability of subjects meeting a study’s inclusion and exclusion criteria and funding requirements, changes to clinical protocols, unexpected adverse events or safety, quality or manufacturing issues; the inability of a drug candidate to meet the primary or secondary endpoint of a study; the inability of a drug candidate to obtain regulatory approval in different jurisdictions or gain commercial acceptance after obtaining regulatory approval;

global trends toward health care cost containment, including ongoing pricing pressures; uncertainties regarding actual or potential legal proceedings, including, among others, actual or potential product liability litigation, litigation and investigations regarding sales and marketing practices, intellectual property disputes, and government investigations generally; and general economic and industry conditions, including uncertainties regarding the effects of the persistently weak economic and financial environment in many countries and uncertainties regarding future global exchange rates. 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 is providing the information in this announcement as of this date and does not undertake any obligation to update any forward-looking statements as a result of new information, future events 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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