



HUTCHISON CHINA MEDITECH LIMITED

## Press Release

### Chi-Med and AstraZeneca Present Savolitinib Papillary Renal Cell Carcinoma Phase II Results at 2017 Genitourinary Cancers Symposium

**London: Tuesday, February 14, 2017:** Hutchison China MediTech Limited (“Chi-Med”) (AIM/Nasdaq: HCM) and AstraZeneca PLC (“AstraZeneca”) will present data from the ongoing Phase II clinical trial of savolitinib in patients with papillary renal cell carcinoma (“PRCC”) at the 2017 Genitourinary Cancers Symposium sponsored by the American Society of Clinical Oncology (“ASCO-GU”), to be held in Orlando, Florida from February 16 to 18, 2017. Savolitinib, a highly selective inhibitor of c-Met receptor tyrosine kinase, has shown early clinical benefit in multiple Phase I and II studies in a number of cancers. 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.

PRCC, the second most common histologic subtype of renal cell carcinoma (“RCC”), is associated with alterations in the c-Met gene (e.g. mutations, amplifications, and/or chromosomal changes). Therapies that are currently available for RCC patients have demonstrated only modest benefit in PRCC and there are no therapies specifically approved for the treatment of c-Met-driven PRCC. National Comprehensive Cancer Network guidelines recommend enrolling patients in clinical trials for first-line systemic therapy.

“There is a clear unmet medical need in PRCC,” said Toni Choueiri, Director of the Lank Center for Genitourinary Oncology, Dana-Farber Cancer Institute. “The dataset from this Phase II study is compelling, with a very clear efficacy signal in MET-driven patients and an encouraging long duration of response, while remaining very well tolerated.” He added, “These results support the initiation of the pivotal Phase III trial in a selected population of MET-driven PRCC. This innovative patient selection approach would be the first ever molecularly selected trial in renal cell carcinoma.”

“We are delighted to report this highly encouraging progression-free survival data in Met-driven papillary renal cell carcinoma, a disease with no approved treatment options,” said Christian Hogg, Chief Executive Officer of Chi-Med. “With development of the companion diagnostic assay to screen Met-driven disease now also complete we are preparing for the initiation of our global Phase III study, the first global registration trial for savolitinib.”

The current Phase II trial is the largest prospective clinical study ever conducted in PRCC patients. It is a global single arm study of savolitinib in 109 patients with locally advanced or metastatic PRCC and was initiated in May 2014. It is being conducted in 22 clinical centers in the US, Canada, UK, and Spain, and completed enrollment in October 2015. Additional details about this study may be found at [clinicaltrials.gov](http://clinicaltrials.gov), using identifier [NCT02127710](https://clinicaltrials.gov/ct2/show/study/NCT02127710). The most recent results of the study will be presented in detail as follows:

**Presentation Title:** A Single-Arm Biomarker-Based Phase II Trial of Savolitinib in Patients with Advanced Papillary Renal Cell Cancer

**Authors:** Toni K. Choueiri, Elizabeth Plimack, Hendrik-Tobias Arkenau, Eric Jonasch, Daniel Y. C. Heng, Thomas Powles, Melanie M. Frigault, Edwin Clark, Amir Handzel, Humphrey Gardner, Shethah Morgan, Laurence Albiges, Sumanta Kumar Pal

**Abstract No:** 436

**Session:** Session C: Penile, Urethral, and Testicular Cancers; Renal Cell Cancer

**Date & Time:** Saturday, February 18, 2017, 7:00 AM-7:55 AM and 11:30 AM-1:00 PM (EST)

Once presented, the presentation will be available at [www.chi-med.com/news](http://www.chi-med.com/news). Further information about ASCO-GU is available at [gucasym.org](http://gucasym.org).

Chi-Med and AstraZeneca are currently initiating a global pivotal Phase III trial, the first pivotal study ever conducted in c-Met-driven PRCC and the first molecularly selected trial in RCC.

Over the course of 2017, Chi-Med and AstraZeneca are also conducting a comprehensive molecular epidemiology study of approximately 300 PRCC patient samples to further understand the correlations between c-Met alterations and patient outcomes, including any predictive biomarkers.

## ABSTRACT

### ***A single-arm biomarker-based phase II trial of savolitinib in patients with advanced papillary renal cell cancer (PRCC)***

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**Background:** Savolitinib (HMPL-504/Volitinib, AZD6094) is a potent, selective mesenchymal epithelial transition (“MET”) inhibitor (IC<sub>50</sub> of 4 nM). MET and its ligand, hepatocyte growth factor (“HGF”), are known to play an important role in the molecular events underlying oncogenesis in PRCC, a disease without a clear standard of care and marked by alterations of chromosome 7 (containing both MET and HGF genes) in a majority of patients as well as gene amplification or MET kinase domain mutations (Albiges et al 2014, Linehan et al, 2015).

**Methods:** This study evaluates savolitinib in PRCC patients dosed at 600 mg daily until disease progression. Objective Response Rate (“ORR”) is the primary endpoint. Progression-Free Survival (“PFS”) & Duration of Response are secondary endpoints. Patient Reported Outcome (“PRO”) and Health-Related Quality of Life (“HRQoL”) questionnaires are exploratory endpoints. Eligibility includes naïve and previously treated metastatic PRCC, ECOG PS 0 or 1. Archival tumor was used to centrally confirm PRCC pathology post hoc and to determine MET status using Next Generation Sequencing (Foundation Medicine Inc, US).

**Results:** As of 27 June 2016, 109 patients were dosed. Best response was PR n=8, SD n=43, PD n=48 & 10 patients were not evaluable for response. 44 patients are MET-driven (MET/HGF gene copy number gain or kinase domain mutations), 46 patients were MET-negative, 19 patients are status unknown. MET-driven pts included Papillary Type I & II histologies. All 8 responders were in the MET-driven group, 18% ORR in this subset. Median PFS in the MET-driven group was 6.2 months (95% CI: 4.1–7.0) vs. 1.4 months (95% CI: 1.4–2.7) in the MET-negative group (p=0.002). Overall 10/109 patients had adverse events (“AEs”) leading to discontinuation. 23/109 patients had ≥ Grade 3 toxicity related to savolitinib. The most common AEs (all grades) includes: nausea (39%), fatigue (27%), edema (18%) and abnormal liver function tests (LFTs) (17%). One death from hepatic encephalopathy was considered related to savolitinib. PRO & HRQoL data was not statistically analyzed, descriptive data support main efficacy findings.

**Conclusions:** In the largest biomarker-profiled trial dedicated to PRCC, savolitinib was generally well tolerated with anti-tumor activity in MET-driven patients. These findings warrant further clinical investigation of savolitinib in MET-driven PRCC.

## **About the 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 US\$4.5 billion in 2020, according to Frost & Sullivan. RCC accounts for approximately 80-85% of kidney cancer and has several histological subtypes 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.

### **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](http://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 six 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 hematology.

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 commercialization of prescription medicines, primarily for the treatment of diseases in three main therapy areas – Oncology, Cardiovascular & Metabolic Diseases and Respiratory. The Company also is selectively active in the areas of autoimmunity, neuroscience and infection. 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](http://www.astrazeneca.com) and follow us on Twitter @AstraZeneca.

### **Forward-Looking Statements**

*This press release contains forward-looking statements within the meaning of the "safe harbor" provisions of the US 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 savolitinib, plans to initiate clinical studies for savolitinib in PRCC, 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 savolitinib 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 savolitinib 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 US 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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