



HUTCHISON CHINA MEDITECH LTD

**Hutchison China Mediatech Limited ("Chi-Med")  
(AIM: HCM)**

**Initiation of AZD6094 (HMPL-504/volitinib) Global Phase II Study in Papillary Renal Cell Carcinoma**

**London: Friday, 23 May 2014:** Chi-Med today announces that Hutchison MediPharma Limited ("HMP"), Chi-Med's majority owned R&D company, and AstraZeneca AB (publ) ("AstraZeneca") have initiated a global Phase II study to evaluate the efficacy and safety of AZD6094 (HMPL-504/volitinib) ("AZD6094"), HMP's potent and highly selective c-Met inhibitor, in patients with papillary renal cell carcinoma ("PRCC"). Under the terms of the global licence granted to AstraZeneca by HMP in 2011, AstraZeneca will now make a milestone payment to HMP, and will lead and fund this development outside of China.

PRCC represents about 10 to 15% of all new cases of kidney cancer and advanced disease has no approved therapy today. Molecular alterations leading to aberrant activation of the c-Met signalling pathway have been well documented in PRCC and effective inhibition of c-Met has been considered a potential treatment pathway for PRCC.

AZD6094 has been demonstrated to inhibit the growth of tumours in a series of preclinical disease models, selectively for those tumours with aberrant c-Met signalling. Phase I dose escalation studies were initiated in Australia and China in 2012 and 2013 respectively. AZD6094 has demonstrated good safety and tolerability and favourable pharmacokinetic properties in late stage cancer patients, and has shown encouraging anti-tumour activity in several tumour-types, in particular for metastatic PRCC. The results from the Phase I studies are planned to be released at the 50th annual meeting of the American Society of Clinical Oncology which will be held from 30 May to 3 June 2014 in Chicago, Illinois, USA.

This trial is an open-label, single-arm, multicentre, Phase II, study designed to evaluate the efficacy and safety of AZD6094 in patients with locally advanced or metastatic PRCC. Approximately 20 centres in the United States, Canada, and Europe will participate in the study. The primary objective of this study is to assess the anti-tumour activity of AZD6094 in patients with PRCC as measured by overall response rate according to Response Evaluation Criteria in Solid Tumours ("RECIST") (version 1.1). The secondary objectives for this study are to: assess the progression free survival and duration of response in patients with PRCC according to RECIST (version 1.1); assess the safety and tolerability of AZD6094 in the treatment of patients with PRCC; characterise the pharmacokinetics and pharmacodynamics of AZD6094 and metabolites following administration to steady state after multiple dosing when given orally; and obtain a preliminary assessment of AZD6094 activity in blood and tumour by evaluation of biomarker changes which may include, but not limited to, phosphorylated c-Met. Exploratory objectives include an investigation of predictive markers and acquired resistance to AZD6094 that may be observed in blood and tumour from patients treated with AZD6094.

"It is pretty exciting to see trials being developed in this rare histology. PRCC is an unmet medical need in the field of kidney cancer and targeting MET is a very reasonable strategy," said Toni Choueiri, MD, of the Dana-Farber Cancer Institute and Head of the Steering Committee of the Phase II trial.

Christian Hogg, Chief Executive Officer of Chi-Med said, "We are delighted to see the initiation of this Phase II trial for AZD6094 in PRCC as this represents a major milestone for both the compound and for HMP. The data which has driven this decision to invest in a PRCC study is compelling and shows the quality of both the compound itself and the joint development team which has been built between HMP and AstraZeneca. There are enormous opportunities for AZD6094 in other cancer types and we are particularly excited by the potential to combine with other compounds."

“Through this great collaboration we are able to increase our understanding of the genetic changes which drive different cancers to grow and to develop medicines designed to address and overcome those genetic drivers. This is a core part of our oncology strategy to deliver personalised healthcare to patients,” said Susan Galbraith, Vice President, Head of Oncology Innovative Medicines, AstraZeneca.

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### Notes to Editors

#### About renal cell carcinoma (kidney cancer)

Renal cell carcinoma (“RCC”) accounts for approximately 3% of all adult malignancies. In the United States, there are more than 65,000 new cases of RCC diagnosed each year and 13,500 RCC deaths annually. Worldwide, 270,000 new patients are diagnosed each year and up to 116,000 deaths occur due to RCC. RCC is more common in men than in women and it usually occurs between 50-70 years of age.

RCC is a heterogeneous disease made up of several histological subtypes with different genetic and biochemical characteristics. Among the histologic variants of RCC, clear cell RCC is the most common, accounting for 75-90% of all renal malignancies. Papillary RCC is the most common of the non-clear cell renal carcinomas (10-15%).

#### About the c-Met signal pathway

The c-Met (also known as HGFR) signalling pathway has specific roles particularly in normal mammalian growth and development. However, this key pathway has been shown to function abnormally in a range of different cancers. Aberrant pathway activation can lead to uncontrolled tumour cell growth, invasion and survival. There are four different mechanisms of c-Met pathway activation: c-Met gene amplification, HGF/c-Met over-expression, mutation, and cross talk with other receptors.

c-Met gene amplification is more prevalent in stomach, head & neck and colon cancers; whereas c-Met over-expression is found in many solid tumours, including lung, stomach, head & neck, colon, and oesophageal cancers. Moreover, many of these tumours are of relevance to the Asian population, such as lung, stomach, and oesophageal cancers (with EGFR mutations). Mutations in the tyrosine kinase domain of c-Met have been positively identified in patients with a hereditary form of PRCC, directly implicating c-MET in human tumourigenesis.

#### About AZD6094 (HMPL-504/volitinib)

AZD6094 is a potent and highly selective small molecule inhibitor of the c-Met receptor with opportunities in lung, gastric, renal and other cancers. It has been demonstrated to inhibit the growth of tumours in a series of

preclinical disease models, especially for those tumours with aberrant c-Met signalling such as gene amplification or c-Met over-expression. In addition, these biomarkers provide the potential to explore patient selection strategies in later stage clinical trials. In December 2011, HMP signed a global licensing deal with AstraZeneca on AZD6094 and then followed up with the start of Phase I study in Australia in February 2012. In June 2013 HMP initiated a Phase I study in Asian patients in China.

### **About HMP**

HMP is a novel drug R&D company focusing on discovering, developing and commercialising innovative therapeutics in oncology and autoimmune diseases. With a team of around 200 scientists and staff, its pipeline is comprised of novel oral compounds for cancer and inflammation in development in North America, Europe, Australia and Greater China.

HMP is majority owned by Chi-Med. For more information, please visit: [www.hmpglobal.com](http://www.hmpglobal.com).

### **About Chi-Med**

Chi-Med is a China-based healthcare group focused on researching, developing, manufacturing and selling pharmaceuticals and health-related consumer products. Its China Healthcare Division manufactures, markets and distributes prescription and over-the-counter pharmaceuticals in China. Its Drug R&D Division focuses on discovering and developing innovative therapeutics in oncology and autoimmune diseases. Its emerging Consumer Products Division focuses on organic and natural consumer products in Asia.

Chi-Med (LSE:HCM) is majority owned by the multinational conglomerate Hutchison Whampoa Limited (SEHK:13). For more information, please visit: [www.chi-med.com](http://www.chi-med.com).