HUTCHISON CHINA MEDITECH LTD

Hutchison China MediTech Limited ("Chi-Med")

(AIM: HCM)

Phase I clinical data for selective VEGFR, c-Met and VEGFR/FGFR inhibitors to be presented at the 2014 ASCO Annual Meeting

London: Thursday, 22 May 2014: Chi-Med today announces that data from recent Phase I and Phase Ib clinical studies by Hutchison MediPharma Limited ("HMP"), its majority owned R&D company, will be presented at the 50th Annual Meeting of the American Society of Clinical Oncology ("ASCO") to be held in Chicago, Illinois, USA from 30 May to 3 June 2014. These presentations will include additional data on fruquintinib (HMPL-013), AZD6094 (HMPL-504/volitinib) and sulfatinib (HMPL-012), three novel and highly selective small molecule drugs discovered by HMP. Presentations on AZD6094 were prepared jointly with HMP's collaboration partner AstraZeneca AB (publ) ("AstraZeneca").

ASCO is a non-profit organisation founded in 1964 with the goals of improving cancer care and prevention. Nearly 30,000 oncology practitioners belong to ASCO, representing all oncology disciplines and subspecialties. Members include physicians and health-care professionals in all levels of the practice of oncology. The ASCO Annual Meeting brings these people together to find cutting-edge scientific presentations and comprehensive educational content.

HMP will have one presentation on each of the three novel kinase inhibitors, as follows:

Title:	A Phase Ib study of VEGFR inhibitor **fruquintinib** in patients with pre-treated advanced colorectal cancer
Abstract:	#3548
Track:	Gastrointestinal (Colorectal) Cancer
Date & Time:	Saturday, 31 May 2014, 8:00 AM

Title:	First-in-human Phase I study of a selective c-Met inhibitor **AZD6094 (HMPL-504/volitinib)** in patients with advanced solid tumours
Abstract:	#11111
Track:	Tumour Biology
Date & Time:	Saturday, 31 May 2014, 1:15 PM

Title:	First-in-human (FIH) Phase I study of a selective VEGFR/FGFR dual inhibitor **sulfatinib** with milled formulation in patients with advanced solid tumours
Abstract:	#2615
Track:	Developmental Therapeutics
Date & Time:	Sunday, 1 June 2014, 8:00 AM

Presentations will be made available at http://chi-med.com/eng/irinfo/presentations.htm. Further information about the 2014 ASCO Annual Meeting and the abstracts are available in Notes to Editors and at am.asco.org.

Ends

Enquiries

Chi-Med	Telephone:	+852 2121 8200
Christian Hogg, CEO		
Panmure Gordon (UK) Limited	Telephone:	+44 20 7886 2500
Richard Gray		
Andrew Potts		
Citigate Dewe Rogerson	Telephone:	+44 20 7638 9571
Anthony Carlisle	Mobile:	+44 7973 611 888
David Dible	Mobile:	+44 7967 566 919

Notes to Editors

ASCO 2014 Presentation Abstracts

A Phase Ib study of VEGFR inhibitor fruquintinib in patients with pre-treated advanced colorectal cancer

Background: Fruquintinib is a novel oral small molecule compound that selectively inhibits vascular endothelial growth factor receptors (VEGFR) 1, 2, and 3 with potent inhibitory effects on multiple human tumour xenografts. In the first-in-human Phase I study, fruquintinib demonstrated good tolerability and impressive anti-tumour activity (ORR=38.2% and DCR=82.4%) in patients (pts) with various heavily pre-treated solid tumours including colorectal cancer (CRC) (ASCO 2012 Abs#3038).

Methods: This Phase Ib study was designed to evaluate the safety, pharmacokinetics, and efficacy of two fruquintinib regimens: 4mg once daily continuously (QD) or 5mg once daily for three weeks followed with one week break (3/1 wk), as treatment for pts with advanced CRC who had failed at least two prior systemic therapies. The study consists of two stages: a two-arm 1:1 randomisation stage including both QD and 3/1 wk regimens, and an expansion stage with the selected regimen. Tumour response was assessed per RECIST1.1.

Results: Forty pts were enrolled in the randomisation phase, with 20 pts in each QD or 3/1 wk group. Patient characteristics at baseline were similar between the two groups. The median treatment duration was 90 (7-280) days for QD regimen and 119 (14-364) days for 3/1 wk regimen. The most common treatment-related toxicities were hand-foot syndrome (HFS), hoarseness, proteinuria, hypertension and fatigue. The 3/1 wk group had less Grade 3/4 AEs than the QD group, particularly HFS (5% vs. 30%). Thirty-five pts were evaluable for response, 17 in QD and 18 in 3/1 wk. In QD group: DCR=76.2% (2 partial responses or PRs and 2 minor responses or MRs who achieved a 20-30% tumour reduction), 16-wk progression free survival (PFS)=40.0%, and 9-month survival=41.2%. In 3/1 wk group: DCR=83.3% (1 PR and 3 MRs), 16-wk PFS=65.0%, and 9-month survival=53.8%. 5mg 3/1 wk regimen was selected as the recommended regimen and additional 22 CRC pts were enrolled in the expansion stage.

Conclusions: Fruquintinib administered at 5mg once daily in cycles of three weeks on and one week off was well tolerated and demonstrated encouraging preliminary clinical efficacy in pts with advanced CRC. Further clinical studies are warranted.

First-in-human Phase I study of a selective c-Met inhibitor AZD6094 (HMPL-504/volitinib) in patients with advanced solid tumours

Background: AZD6094 is a selective oral small molecule inhibitor of c-Met kinase with potent in vivo inhibitory effects on a variety of human tumour xenografts.

Methods: This Phase I, first-in-human dose-escalation study was conducted to determine the maximum tolerated dose (MTD), dose-limiting toxicities (DLTs), pharmacokinetics (PK) profile, and preliminary anti-tumour activity of AZD6094.

Results: By Dec 31, 2013, 32 patients (pts) had been enrolled and treated with AZD6094 at doses of 100-1000mg QD or 300-400mg BID. Pts had a median age of 61 (27-78) yrs, 66% were male. The most common tumour types were papillary renal cell carcinoma (PRCC, 6) and CRC (5). The most common adverse events

were constipation, diarrhoea, fatigue, nausea, vomiting, dizziness and peripheral edema, mostly grade (G) 1/2. Four pts reported 5 DLTs: 1 G3 elevated ALT (600mg QD), 1 G3 fatigue (800mg QD), and 2 G3 fatigues and 1 G3 headache (1000mg QD). 800mg was identified as MTD of the QD regimen. Dose-escalation in the BID cohort is currently ongoing at 400mg BID. PK analysis showed AZD6094 was rapidly absorbed with T_{max} around 2 hours and half-life around 5 hours. Both C_{max} and AUC displayed dose-proportional increase and no obvious accumulation occurred. Two PRCC pts in the 600mg QD cohort (one with ongoing treatment at 1 year) and 1 PRCC pt in the 300mg BID cohort achieved partial response. A CRC pt in the 600mg QD cohort achieved 29% tumour reduction. A PRCC pt in the 1000mg QD cohort achieved 27% tumour reduction and remains on study. Analysis of pre-treatment tumour sample showed that the responders had either gene copy number increase (Chromosome7 gains or MET gene amplification) or high MET protein expression.

Conclusions: AZD6094 was well tolerated at doses up to 800 mg QD and demonstrated promising anti-tumour activity in pts with evidence of dysregulated MET signalling. It demonstrated linear PK without marked drug accumulation. Further clinical studies are warranted.

First-in-human (FIH) Phase I study of a selective VEGFR/FGFR dual inhibitor sulfatinib with milled formulation in patients with advanced solid tumours

Background: Sulfatinib is a highly selective oral small molecule tyrosine dual inhibitor of vascular endothelial growth factor receptors (VEGFR) and fibroblast growth factor receptors (FGFR). The data of patients (pts) treated with the original formulation dosing from 50 to 300mg once or twice daily has been reported in ASCO 2013. A milled formulation was developed to reduce the PK variability and optimise absorption recently.

Methods: This Phase I dose-escalation study were to determine the maximum tolerated dose (MTD), dose-limiting toxicities (DLTs), pharmacokinetic (PK) profiles, and preliminary anti-tumour activity of sulfatinib when given orally in continuous cycles of 28 days, until disease progression or unacceptable toxicity.

Results: Total 60 pts have been enrolled (43 were treated with the original formulation and 17 with milled formulation). For the 17 pts treated with milled sulfatinib at doses of 200mg, 300mg and 350mg once daily, the median age was 57 (23-69) yrs, with 82% male. Common adverse events included hypertension, nausea, diarrhoea and elevated AST/ALT, mostly grade1/2. No DLT was observed. MTD has not been reached. Tumour response has been observed in 4 pts including 1 HCC in 200mg QD cohort, 1 liver neuroendocrine tumour (NET) and 1 NET with unknown primary site in 300mg cohort, and 1 lymph node NET in 350mg cohort. ORR is 30% among the 13 evaluable pts. 7 (54%) pts had stable disease (SD). PK analyses showed the inter- and intra-individual variability was optimised and the exposures in terms of C_{max} and AUC were increased compared with the original formulation, indicating optimised oral absorption. A reasonable 2-fold accumulation was observed at steady-state with $t_{1/2}$ of 20.2±4.75 h and 15.4±3.66 h at 200 and 300 mg, respectively.

Conclusions: Milled sulfatinib was well tolerated at doses up to 350 mg per day and demonstrated encouraging preliminary anti-tumour activity. PK data suggests that milled formulation reduced individual variability and increase oral absorption compared to the original formulation. Milled formulation warrants further clinical development.

About vascular endothelial growth factor ("VEGF") and colorectal cancer in China

At an advanced stage, tumours secrete large amounts of VEGF, a protein ligand, to stimulate formation of excessive vasculature (angiogenesis) around the tumour in order to provide greater blood flow, oxygen, and nutrients to the tumour. VEGF and VEGF receptors ("VEGFRs") play a pivotal role in tumour-related angiogenesis, and inhibition of the VEGF/VEGFR pathway therefore represents an exciting therapeutic strategy in blocking the development of new blood vessels essential for tumour to grow and invade.

Colorectal cancer is the third most commonly diagnosed cancer in China, with 10.2% incidence in 2012. An estimated 390,000 cases of colorectal cancer were diagnosed in China. It is the fifth most common cause of cancer death after lung, liver, stomach and oesophagus cancer.

To date, several anti-VEGF/VEGFR agents have shown clinical efficacy against a number of tumour types. Given the scale and growth in the China oncology market, the market for VEGF/VEGFR inhibitors in China is expected to develop quickly in the next few years.

About fruquintinib

Fruquintinib is designed to selectively inhibit VEGF receptors, including VEGFR1, 2, and 3. In the first-in-human Phase I clinical trial, 40 late-stage cancer patients were treated with fruquintinib. Detailed results of the Phase I clinical trial were presented at the annual meeting of the American Association for Cancer Research in April 2013, and can also be found at http://chi-med.com/eng/irinfo/presentations.htm. Based on the Phase I data, the first proof-of-concept Phase II study was initiated on 2 April 2014, which was a randomised, double-blind, placebo-controlled, multi-centre Phase II clinical trial targeted at patients with metastatic colorectal cancer.

In October 2013, HMP entered into a licensing, co-development and commercialisation agreement in China with Eli Lilly and Company for fruquintinib.

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 sulfatinib (HMPL-012)

Sulfatinib is a novel small molecule that selectively inhibits the tyrosine kinase activity associated with VEGFR and fibroblast growth factor receptor ("FGFR"). Pre-clinical data shows that sulfatinib has demonstrated a narrow kinase inhibition profile affecting mainly VEGFR and FGFR and consequently has an attractive anti-tumour profile, and is a potent suppressor of angiogenesis, an established approach in anti-cancer treatment. It targets major

cancer types such as hepatocellular carcinoma (liver cancer), neuroendocrine tumours, colorectal cancer and breast cancer. The first-in-human Phase I clinical trial was started in China. To date, sulfatinib has demonstrated good safety and tolerability, favourable pharmacokinetic properties, and encouraging preliminary anti-tumour activity in multiple tumour types, including liver cancer.

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.hmplglobal.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.