



HUTCHISON CHINA MEDITECH LIMITED

## Press Release

### Chi-Med Presents Phase I Clinical Data for Selective Syk Inhibitor HMPL-523 at the 2016 ACR/ARHP Annual Meeting

**London: Monday, November 14, 2016:** Hutchison China MediTech Limited (“Chi-Med”) (AIM/Nasdaq: HCM) today announces that data from a recent Phase I, first-in-human, dose escalating study of the safety, tolerability and pharmacokinetics (“PK”) and pharmacodynamics (“PD”) of single and multiple doses of HMPL-523, will be presented at the Annual Meeting of the American College of Rheumatology/Association of Rheumatology Health Professionals (the “ACR/ARHP Annual Meeting”), being held in Washington DC, USA from November 11 to November 16, 2016. The presentation will include additional data on HMPL-523, a highly selective, potent and orally available inhibitor of Spleen Tyrosine Kinase (“Syk”).

Syk plays a pivotal role in the regulation of downstream signaling in immune receptors, including B cell receptors (“BCRs”), which play a key role in autoimmune diseases such as rheumatoid arthritis (“RA”). A Phase I dose-escalating study to assess safety, tolerability and PK of HMPL-523 was completed in healthy volunteers in Australia in late 2015. HMPL-523 was administered at up to 800mg as a single dose and up to 400mg in multiple doses in 14 cohorts. The treatment was generally well tolerated without material off-target toxicities, including lower rates of diarrhea and hypertension compared to what had been observed in first-generation Syk inhibitors. Furthermore, HMPL-523 demonstrated a dose-dependent suppression of B-cell activation. The Company plans to initiate a Phase II study in the U.S. in 2017.

HMPL-523 is also being studied in oncology indications. A Phase I dose escalation study was initiated in Australia in January 2016 and is expected to complete in the first half of 2017. This study is in patients with relapsed and/or refractory B-cell non-Hodgkin’s lymphoma or chronic lymphocytic leukemia for whom there is no standard therapy.

The ACR/ARHP Annual Meeting brings together more than 16,000 physicians, health professionals and industry partners from over 100 countries for six days of networking and educational events covering the latest cutting-edge research on clinical and basic science of rheumatologic care, as well as prevention, diagnosis, and treatment of rheumatic diseases.

#### **ACR/ARHP 2016 Poster Presentation**

**Title:** A Phase I, Randomized, Double Blind, Placebo-Controlled, Dose Escalating Study of the Safety, Tolerability and Pharmacokinetics and Pharmacodynamics of Single and Multiple Doses of HMPL-523 in Australian Male Healthy Subjects

**Abstract number:** 1621

**Track:** Rheumatology

**Date & Time:** Monday, November 14, 2016, 9:00AM – 11:00AM EST

The presentation will be made available at <http://chi-med.com/news/>. Further information about the 2016 ACR/ARHP Annual Meeting and the abstracts are available at <http://acrannualmeeting.org/>.

#### **ACR/ARHP 2016 Presentation Abstract**

**A Phase I, Randomized, Double Blind, Placebo-Controlled, Dose Escalating Study of the Safety, Tolerability and Pharmacokinetics and Pharmacodynamics of Single and Multiple Doses of HMPL-523 in Australian Male Healthy Subjects**

**Background:** Syk plays a pivotal role in the regulation of downstream signals in immune receptors, including BCRs, which play a key role in autoimmune diseases such as RA. This abstract reports the

results of the first-in-human study of HMPL-523, a highly selective, potent, and orally available inhibitor of Syk.

**Methods:** We conducted a 3-part study to investigate the safety, tolerability, and PK of HMPL-523 as well as its PD measured by CD63+ as the biomarker, and the effect of food on PK in healthy adult male subjects. The study design is summarized in the table below.

#### Study Design

Endpoints	Part A (Single Ascending Dose) PK												Part B (Multiple Ascending Dose)PK/PD				Part C Effect of Food on PK	
General design	A randomized, double- blind, placebo-controlled design																Cross over	
Dose	Single dose												Once daily for 14 days				Once on Day 1 and Day 8, respectively	
Meal condition	Fasted						Fed						Fed				Fasted on Day 1; wash-out for 7 days; after the consumption of a high-calorie meal on Day 8	
Dosage (mg, N)	5, N=6	20, N=6	50, N=6	100, N=6	200, N=6	300, N=6	Pbo, N=12	300, N=6	400, N=6	600, N=6	800, N=6	Pbo, N=8	200, N=12	300, N=6	400, N=6	Pbo, N=8	100, N=6	

Pbo = Placebo

**Results:** A total of 118 adult male healthy subjects were enrolled at baseline. 114 (96.6%) subjects completed the study. A total of 83 treatment emergent adverse events (“TEAEs”) were reported as the following: 38.9% in the HMPL-523 groups, and 32.1% in the placebo groups, respectively. The majority of TEAEs were mild (63/83 or 75.9%) with 18/83 (21.7%) moderate events. Two serious adverse events (SAEs) were reported due to elevated lipase (HMPL-523 200mg) and febrile illness (HMPL-523 400mg) in Part B (multiple ascending doses [“MAD”]). As a result, HMPL-523 was discontinued in the two subjects. All of the TEAEs and SAEs were resolved.

Part A (single ascending dose [SAD]) PK results revealed that HMPL-523 was rapidly absorbed with median time to maximum plasma concentration ( $T_{max}$ ) between 3 and 6 hours under both fasted and fed conditions. The maximum plasma concentration ( $C_{max}$ ) and area under the plasma concentration-time curve (AUC) of HMPL-523 increased proportionally with dose increased up to 800mg. The terminal half-life ( $t_{1/2}$ ) ranged between 9.808 hours and 13.488 hours across HMPL-523 doses of 100 to 800mg. Part B (MAD) PK results showed that steady state was achieved within 48 hours of daily administration and accumulation of 1.3 to 1.5 folds was observed over 14 days of dosing. In an *ex vivo* human whole blood PD assay, HMPL-523 inhibited anti-IgE-induced basophil activation (CD63<sup>+</sup>) in a concentration-dependent manner with an estimated half maximal effective concentration ( $EC_{50}$ ) of 47.70ng/mL. The human PK exposures at 200mg once daily and above can be expected to provide the target coverage required for clinical efficacy based on the preclinical PK/PD analysis.

In Part C, systemic exposure of HMPL-523 was increased up to 1.5 folds when administered in the fed condition compared to the fasted condition, indicating that food consumption increases the relative bioavailability of HMPL-523.

**Conclusions:** Overall, the safety and laboratory data suggests that the single and multiple doses of HPML-523 were generally well tolerated. A multiple-dose regimen of 300mg or less of HMPL-523, administered once daily, is recommended for future Phase II clinical trials for autoimmune diseases.

#### About B-cell signaling

As one of the major cellular components of the immune system, B-cells play pivotal roles in several immune system related diseases, such as autoimmune diseases including rheumatoid arthritis, systemic lupus erythematosus and allergy, as well as hematological cancers (i.e. B-cell malignancies) including lymphoma and leukemia. Targeted B-cell receptor signaling therapies, including monoclonal antibodies and small molecules, have been proven to be clinically effective for the treatment of rheumatoid arthritis as well as B-cell malignancies, leading to scientific and commercial success.

Syk is a key protein involved in the B-cell signaling pathway.

## About Chi-Med

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

## Forward-Looking Statements

*This press release 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 reflect Chi-Med's current expectations regarding future events, including its expectations for the clinical development of HMPL-523, plans to initiate clinical studies for HMPL-523, 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 HMPL-523 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 HMPL-523 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 U.S. 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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