

## **ASX ANNOUNCEMENT**

24 November 2009

### **Dosing in Cytopia's CYT387 clinical trial begins**

Cytopia Ltd (ASX:CYT) announced today that dosing in its Phase I/II clinical study of CYT387, a potent, orally-active JAK1/JAK2 inhibitor, has commenced at the Mayo Clinic, Rochester, Minnesota, USA. This follows favourable review of the company's submissions to the Mayo Clinic Institutional Review Board and the US Food and Drug Administration (FDA).

CYT387 potently inhibits the JAK2 enzyme, a mutated form of which has been implicated in a variety of haematological conditions known as the myeloproliferative neoplasms (MPNs) including myelofibrosis, polycythemia vera and essential thrombocythemia. CYT387 attenuates MPN symptoms in an in vivo preclinical model and disrupts JAK2 hyperactivity in cells from patients with MPNs. This data suggests that the compound may exert a profound effect on the human diseases.

The Phase I/II study will investigate the safety and tolerability of CYT387 administered as a daily oral capsule dose in patients with myelofibrosis. Myelofibrosis is a chronic, debilitating condition where the patient's bone marrow is replaced by scar tissue. This results in a compromised ability of patients to produce sufficient blood cells and a reliance on organs other than the bone marrow, including the liver and spleen, to produce cells.

Typical symptoms include an enlarged spleen, progressive anaemia and poor overall survival. The study will also allow preliminary assessment of the compound's activity in these patients including its effect on spleen size, haematological symptoms and quality-of-life as well as markers of aberrant JAK2 activity in blood.

Dr Ayalew Tefferi, Professor of Hematology at the Mayo Clinic, Rochester, will be Study Chairman for the programme, with Dr Animesh Pardanani acting as a leading investigator.

"Patient safety is very important with this class of compounds and can be reliably predicted only by testing in humans. As such, it is premature to select the best JAK2 inhibitors in clinical development as there is a need for longer follow-up data on safety and efficacy than is currently available", said Dr Tefferi.

"The commencement of our CYT387 clinical study is another significant milestone delivered by Cytopia, and we look forward to its progress under the guidance of Dr Tefferi and his colleagues", said Mr Andrew Macdonald, CEO. "Cytopia will also seek to demonstrate the activity of CYT387 in other disease indications with high unmet medical need where JAK1 and JAK2 activity is important".

Significant commercial interest in the JAK2 target is already evident with no selective JAK inhibitors having yet completed late stage clinical trials and few compounds in development with a desirable product profile. A similar clinical-stage JAK2 inhibitor was licensed by Onyx Pharmaceuticals for US\$550 million including a US\$25 million up-front payment and double-digit royalties.

Over-activity of the JAK2 enzyme has also been noted in certain cancers and in inflammatory conditions, such as rheumatoid arthritis and psoriasis. The dual JAK1/JAK2 inhibition of CYT387 is likely to increase the clinical benefit in these diseases, markedly expanding the clinical and commercial opportunities for CYT387 beyond MPNs alone.

**Enquiries:**

Mr Andrew Macdonald  
Chief Executive Officer  
T: +61 3 9926 0403

[andrew.macdonald@cytopia.com.au](mailto:andrew.macdonald@cytopia.com.au)

Dr Gregg Smith  
Director: Drug Development  
T: +61 3 9926 0406

[gregg.smith@cytopia.com.au](mailto:gregg.smith@cytopia.com.au)

**About the trial**

The following table provides a summary of the key aspects of the Phase I/II myelofibrosis study.

<b>Name of Trial</b>	A Phase I/II, Open-Label, Dose-Escalation Study Evaluating the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of Orally-Administered CYT387 in Primary Myelofibrosis or Post-Polycythemia Vera or Post-Essential Thrombocythemia Myelofibrosis (CCL09101)
<b>Primary Endpoints</b>	To assess the safety and tolerability and maximum tolerated dose of escalating doses of CYT387. To determine the pharmacokinetics of CYT387 and to obtain preliminary information on the effectiveness of the compound.
<b>Secondary Endpoints</b>	To determine the effect of CYT387 on a range of pharmacodynamic markers including cytogenetics, JAK2 mutant burden and myeloid colony formation.
<b>Blinding Status</b>	Not blinded
<b>Product Development Status</b>	Drug substance and drug product are manufactured to cGMP
<b>Treatment Method</b>	
<b>Route</b>	Oral capsule
<b>Frequency</b>	Daily
<b>Dose-levels</b>	Dose-escalation to maximum tolerated dose
<b>Number of Trial Subjects</b>	30-60 (subject to dose-escalation)
<b>Subject Selection Criteria</b>	Patients must have been diagnosed with primary myelofibrosis or post-PV or post-ET myelofibrosis. Other inclusion and exclusion criteria are detailed in the approved clinical trial protocol.
<b>Trial Location</b>	Mayo Clinic, Rochester, Minnesota, USA
<b>Expected Completion</b>	It is estimated that unaudited Phase I data will be available by mid 2010 with unaudited Phase II data available by mid 2011.
<b>Trial Standard</b>	ICH-GCP

## **About Cytopia**

Cytopia Ltd is an Australian biotechnology company focused on the discovery and development of new drugs to treat cancer and other diseases. Cytopia conducts its research and drug development through subsidiaries based in Melbourne, Australia and California, USA and specialises in developing new small molecule compounds with an improved therapeutic profile for the treatment of cancer.

The company's lead drug candidate is CYT997, a vascular disrupting agent (VDA) for the treatment of various cancers, which is currently being trialled in Phase II clinical studies. CYT387, a novel oral JAK1/JAK2 inhibitor focused on the treatment of myeloproliferative neoplasms, is also being investigated in a Phase I/II clinical study.

On 6 October 2009, Cytopia announced a proposed merger with Toronto-based YM BioSciences Inc. Details can be found at [www.cytopia.com.au](http://www.cytopia.com.au). A Scheme Booklet, further explaining the basis and details for the merger, is currently being prepared for Cytopia shareholders.