

## **MEDIA RELEASE**

13 November 2007

### **Cytopia reports final data from Phase I cancer trial**

***Trial also shows stabilisation of cancers after conventional drugs did not succeed and preliminary evidence of vascular-targeting activity***

Cytopia Limited (ASX: CYT) announced today that its anti-cancer drug CYT997 not only achieved its Phase I primary safety and tolerability objectives but final data also reveals preliminary evidence of vascular-targeting activity.

Seven of the trial's 31 patients completed six cycles of therapy, suggesting stabilisation of their cancers for approximately 4 months. These findings are promising given that most of the study patients had failed therapy with approved anticancer agents and that CYT997 was given as a single agent in these chemo-resistant subjects. Two patients continued to receive the drug following the trial under the Commonwealth Government's compassionate use scheme.

"Stabilisation of disease in patients who have failed standard anticancer treatments is an encouraging finding, particularly as CYT997 was given alone," said Dr Jason Lickliter, Principal Investigator for the study. "The data obtained in this study indicate that further investigation of CYT997 is warranted in a range of clinical settings."

Secondary objectives included a preliminary investigation of the anti-tumour properties of the compound, determination of a recommended dose for Phase II studies and pharmacokinetic assessment.

Data collected during the study suggests that CYT997 may be disrupting the tumour blood vessels in some patients, leading to changes in tumour blood flow and signs of blood vessel damage.

"Although the anti-tumour activity of CYT997 administered as a single agent was a secondary objective for this study, the company is encouraged by the findings of these initial assessments," said Mr Andrew Macdonald, CEO of Cytopia. "These early data auger well for the compound including CYT997's utility in combination with other anticancer agents. In addition CYT997 is readily administered, with predictable pharmacokinetics and concentrations in plasma well in excess of those thought necessary for activity."

The GCP-compliant clinical study report is currently being prepared for submission to regulatory agencies.

Given the favourable findings of the Phase I study, the company is well advanced in planning for its multi-trial Phase II programme, including single-arm and randomised studies in a range of tumour indications.

Subject to regulatory approval, the company also intends to commence dosing in its single-arm Phase II study in relapsed or refractory multiple myeloma patients in December 2007. This study will be conducted in Melbourne.

The company is also undertaking a second Phase I dose-escalation study of CYT997 as an oral capsule dose.

## **ABOUT THE PHASE I INTRAVENOUS CLINICAL TRIAL**

### **Patient demographics and diagnoses**

Patients enrolled in the study had advanced cancer which had failed to respond to other therapies. Each patient was eligible to receive a maximum of six cycles of CYT997 therapy, subject to ongoing clinical stabilisation. In total, 31 patients (16 female) with a diverse range of solid tumours were enrolled into the study in twelve dosing cohorts over the dose range of 7 to 358 mg/m<sup>2</sup> (approximately 0.2 to 9.7 mg/kg). The median age of the patients at first dose was 59 years (range 21 to 75 years).

Patients with a diverse range of diagnoses were included in the trial, with the most common tumour types being metastatic melanoma and mesothelioma (5 patients each).

In total, 98 doses of CYT997 were administered during the Phase I study. The median number of doses per patient was 2 (range 1 to 6).

### **Tumour response**

Seven of the 31 patients treated on study completed the planned six cycles and two additional patients completed five cycles of CYT997 therapy, indicating cancer disease stabilisation for a period in excess of three months. Significantly, two patients with symptomatic progressive disease prior to study entry experienced stabilisation of their tumours that persisted beyond 6 cycles of CYT997. These patients continued to receive CYT997 under the Commonwealth Government's Special Access Scheme, which is designed to facilitate the administration of experimental agents to terminally-ill patients where potential therapeutic benefit may be observed.

Of the 22 patients evaluable for tumour response measurements, 17 achieved a best response of stable disease. The remaining five patients experienced progressive disease as their best response.

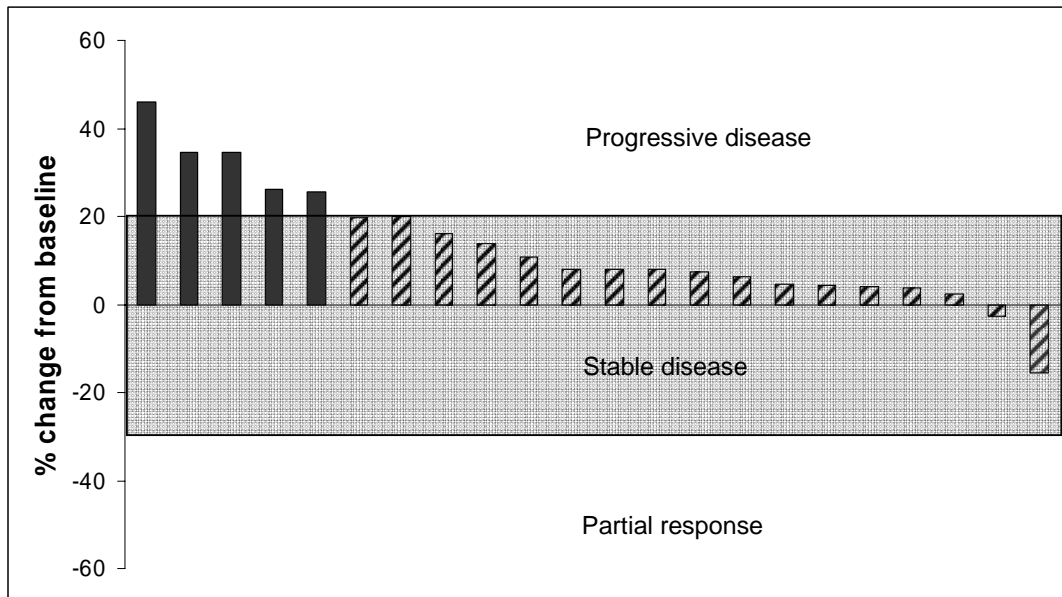


Figure 1: Waterfall plot of best response (by RECIST tumour measurement) of 22 evaluable patients.

*[In accordance with standard criteria, greater than a 20% increase in the sum of the longest tumour axes is progressive disease (PD; solid bars); a reduction of greater than 30% in summed tumour axes is a partial response and a change within those parameters is stable disease (SD; shaded area)].*

### Pharmacodynamic data

Cytopia collected a range of pharmacodynamic data during the Phase I study, including serial DCE-MRI (dynamic contrast-enhanced magnetic resonance imaging) images to gauge the antivascular effect of CYT997 and measurement of plasma von Willebrand factor (vWf), a biomarker for tumour blood vessel damage by CYT997.

Significant aberrations of median tumour blood flow parameters were observed in seven of the 17 patients evaluable for DCE-MRI, indicating that CYT997 may be targeting tumour blood vessels.

In addition, a dose-dependent increase in circulating vWf was observed in patients with normal baseline vWf levels at CYT997 doses above 152 mg/m<sup>2</sup>, again suggesting damage to blood-vessel endothelial cells.

Together these promising preliminary data sets suggest that CYT997 may be ablating tumour blood vessels leading to alterations in tumour blood perfusion. This data therefore lays the foundation for future clinical studies and will assist in the design of dosing regimes.

DCE-MRI and biomarker analysis designed to further elucidate the activity of CYT997 is ongoing.

## Adverse events

CYT997 was comparatively well tolerated in this study, with the maximum tolerated dose (358mg/m<sup>2</sup>) and plasma concentration of CYT997 exceeding those shown tolerable in preclinical species. As previously reported, the dose-limiting toxicities in this study were grade 3 QTc interval prolongation (in two patients) and grade 4 dyspnoea (in one patient). Other toxicities associated with CYT997 administration included a case of acute visual disturbance, IV site reaction, elevated serum creatinine, acute neutropaenia and grade 1-2 QTc interval prolongation. Nausea, vomiting and diarrhoea were also observed.

The range and severity of the adverse events observed in this study were typical of those seen with other vascular-disrupting and cytotoxic agents.

The following table provides a summary of key aspects of the trial:

Name of trial	A Phase I dose-escalation study of CYT997 given as a 24-hour intravenous infusion every three weeks in patients with solid tumours (QP04C07)
Primary endpoints	Determination of the dose-limiting toxicities and maximum tolerated dose of CYT997 given as a 24-hour intravenous infusion
Secondary endpoints	Pharmacokinetics; definition of recommended dose for Phase II studies; preliminary evaluation of vascular-targeting activity
Blinding status	Not blinded
Product development status	Drug substance and drug product are manufactured to GMP standards
Treatment method	
Route	Intravenous infusion
Frequency	Three weekly cycle
Dose-levels	Dose-escalation study over 12 dose-levels (7 to 358 mg/m <sup>2</sup> )
Number of trial subjects	31
Subject selection criteria	Eligible patients must have a solid tumour that is metastatic or unresectable for which standard therapies do not exist or are no longer effective
Trial location	Brisbane, Australia
Trial standard	ICH-GCP

## About Cytopia

Cytopia Ltd is an Australian biotechnology company focused on the discovery and development of new drugs to treat cancer. Cytopia conducts its research and development via subsidiaries based in Melbourne and New York and specialises in discovering new molecules that can inhibit enzymes known as kinases, an exciting new class of drugs.

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