

## **MEDIA RELEASE**

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### **Cytopia concludes Phase I oral trial for vascular-disrupting agent, CYT997**

Cytopia Limited (ASX: CYT) has successfully concluded dose-escalation in its oral Phase I study for CYT997, the company's anticancer vascular-disrupting agent (VDA).

The primary objectives of this safety and tolerability study have been achieved. These were to determine the maximum tolerated dose (MTD) and the dose-limiting toxicities (DLTs) for the agent when administered orally in capsule form every two weeks to patients with a diverse range of solid tumours. Safety and tolerability data from this study augments data obtained in the company's first Phase I study where CYT997 was administered intravenously. Together, these studies suggest that the CYT997 is a potent and selective VDA which is well tolerated at biologically efficacious doses and is worthy of further investigation as a novel anticancer agent.

"Cytopia has now demonstrated the broad clinical potential of CYT997 in both intravenous and oral forms", said Mr Andrew Macdonald, CEO. "The oral activity of CYT997 is a key advantage over most other vascular disrupting agents which are administered intravenously. The oral activity of the agent should markedly improve its clinical and commercial value."

The company has already commenced Phase II studies for the intravenous form of CYT997 and intends to undertake similar efficacy studies for the oral presentation. Investigating the safety and efficacy of metronomic dosing, frequent oral administration at a comparatively low, but biologically effective dose, is of particular interest.

This oral trial was partly funded under the company's \$3 million Commercial Ready grant.

#### **Preliminary trial data**

CYT997 was generally well tolerated in this study with a maximum tolerated dose in cancer patients of *ca* 165 mg/m<sup>2</sup>. This dose resulted in maximal plasma concentrations some two-fold higher than those observed in the Phase I intravenous infusion study at a comparable dose, indicating favourable oral absorption.

Three dose-limiting toxicities were observed, namely two cases of significant drug-induced fatigue and one case of hypoxia. Importantly, no significant prolongation of the corrected QT interval (a measure of cardiac conduction) was observed.

Patients entering the trial had advanced cancer that had failed to respond to other therapies or for which no other therapy exists. Each was eligible to receive a maximum of six cycles of CYT997 therapy, subject to clinical status. One patient continued to receive the drug beyond their initial six cycles due to prolonged disease stabilisation. No patients currently remain on study.

Secondary objectives of this Phase I study included the determination of a recommended dose for Phase II studies and pharmacokinetic assessment and a preliminary investigation of the anti-tumour properties of CYT997. Analysis of biological and clinical data from the study is currently ongoing and the company expects to present a finalised trial report, including a complete list of adverse events and the recommended dose for Phase II studies, within three months.

The following table provides a summary of the key aspects of this trial.

Name of Trial	An accelerated dose-escalation study of CYT997 given as an oral capsule every two weeks in patients with advanced solid tumours (CCL06001).
Primary Endpoints	Determination of the dose-limiting toxicities and maximum tolerated dose of CYT997 given as an oral capsule dose.
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	Oral
Frequency	Two weekly cycle
Dose-levels	Dose-escalation study over 8 dose-levels (15 to 164 mg/m <sup>2</sup> )
Number of Trial Subjects	21
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 Locations	Adelaide, Brisbane, and Townsville, Australia.
Trial Standard	ICH-GCP

### About Cytopia

Cytopia Ltd is an Australian biotechnology company discovering and developing new drugs to treat cancer and other diseases. Cytopia conducts its research and drug development through subsidiaries based in Melbourne, Australia and San Francisco, 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. It is currently being trialled in Phase II clinical studies. Cytopia is continuing to build on its range of JAK inhibitors and kinase expertise. CYT387, a novel, orally administered JAK2 inhibitor focused on the treatment of myeloproliferative disorders is expected to enter Phase I clinical studies in 2009.

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