



Cytopia announces major licence and R&D collaboration

At the end of May, Cytopia announced the signing of a global licence and research and development collaboration with Novartis to develop orally active, small-molecule therapeutics targeting JAK3 kinase. The collaboration will focus on a number of therapeutic applications including the prevention of transplant rejection and the treatment of a number of autoimmune diseases such as rheumatoid arthritis.

Under the terms of the agreement, Cytopia will receive payments from Novartis of approximately A\$12.5 million over three years, including an up-front payment and research funding. Over the life of the agreement, Cytopia may become eligible to receive

development, regulatory and sales milestones which could total approximately A\$274 million if an agreed number of multiple indications are successfully commercialised. In addition, Cytopia will also receive royalties on product sales.

This is the largest deal achieved by any Australian biotech company and the first in Australia for Novartis.

Both companies will contribute expertise and intellectual property relating to JAK3 inhibitors with the ultimate aim of bringing compounds into the clinic. Novartis will assume responsibility for product development and commercialisation. Cytopia has retained co-promotion rights for Australia and New Zealand.

Transplantation and Autoimmune disease markets

The current market for drugs to prevent transplant rejection is approximately US\$3 billion and Novartis is a key player. The transplant market is set for significant growth with the number of transplants reported to grow from 440,000 to 700,000 by 2010 and more specific and potent drugs could significantly penetrate this market.

Autoimmune diseases include rheumatoid arthritis (RA), inflammatory bowel disease, psoriasis, atopic diseases and multiple sclerosis. The RA market alone is forecast to grow to US\$15 billion by 2009. Current drugs for this application either treat pain, slow disease or "mop up" immune stimulators. JAK3 inhibitors potentially offer a way to intervene more specifically and earlier in the progression of this disease.

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Cytopia has a strong structural-based design approach to the development of kinase inhibitors and has been able to achieve impressive levels of both potency and specificity for a number of targets, particularly on JAK3. Cytopia was the first to publish the crystal structure for JAK2, a related target and employs a proprietary software platform (ChemaPhore) for the in silico screening, design and refinement of drug leads.

This deal is an important recognition of Cytopia's industry-leading position in the development of kinase inhibitors, particularly for the JAK family of kinases. Novartis is a global leader in transplantation, one of the major target areas for the alliance.

About JAK3

JAK3 is a member of the janus kinase (JAK) family. JAK1 and JAK2 were discovered by Cytopia's Chief Scientific Officer, Dr Andrew Wilks, whilst at the Melbourne Branch of the Ludwig Institute for Cancer Research and Cytopia has become a world leader in the development of highly specific inhibitors for this class of enzymes.

Without JAK3, the immune system cannot perform normally and individuals missing the JAK3 gene are severely immunocompromised. Current therapies for transplant rejection and autoimmune diseases (such as rheumatoid arthritis) also act on cells other than those of the immune system and in many cases cause severe side effects. JAK3 only occurs in cells of the immune system and so there is a strong possibility that JAK3 specific drugs offer a novel approach to treating these disorders with a reduced side-effect potential.

About Novartis

Novartis, based in Basel, Switzerland, is the world's fourth largest pharmaceutical company with sales in 2005 of US\$25 billion. The Novartis Institutes for Biomedical Research (NIBR) is Novartis' global research organisation. NIBR is headquartered in Cambridge, Massachusetts, USA with research facilities across Europe, USA and Japan. NIBR currently has 42 collaborations with major biotech companies and 79 collaborations with academic centres.

In March 2004, NIBR decided to integrate some groups of diseases which share similar fundamental immunological mechanisms and created a new Autoimmunity & Transplantation Disease Area (DA), focusing mainly on transplantation, psoriasis and rheumatoid arthritis.

Message from the Executive Chairman

Dear shareholders

Cytopia's Managing Director, Dr Kevin Healey, stepped down from his executive role with the company on the 9th of June. Mr Andrew Macdonald, Cytopia's Chief Financial Officer, has been appointed Managing Director from this date.

Dr Healey was a co-founder of Cytopia (formerly Medica Holdings Limited) and has been Managing Director since August 1997. Dr Healey will remain as a non-executive director of the company and will act as a consultant to the company on corporate strategy and business development.

I would like to take this opportunity to thank Dr Healey for his contribution to the company over many years. Since founding Cytopia in 1997, Dr Healey has worked tirelessly to transform the company from its origins as a small biotechnology investment fund to one of the leading Australian drug discovery and development companies. We look forward to Dr Healey's ongoing contribution as a non-executive director.

I would like to strongly endorse the appointment of Mr Macdonald as the new Managing Director. Mr Macdonald joined Cytopia in August 2005 as CFO, following other senior executive roles for various public and private companies including Biota Holdings, Willis Ltd, and



Andrew Macdonald
Chief Executive Officer

Sharinga Networks. He has worked in both the USA and the UK and brings extensive international experience to the company. In the time he has been with the company, Mr Macdonald has demonstrated very strong leadership and commercial skills and has worked closely with Dr Healey in jointly laying the foundations for the next phase in the growth of the company.

Cytopia is at an exciting stage of development, with a major pharmaceutical deal now in place; a drug candidate in the clinic and a broad range of compounds emanating of our various kinase programs. Given our scientific assets and the highly skilled team we now have in Australia and the USA, I am confident that we will continue to generate significant value for our stakeholders.

Bob Watson
Executive Chairman



Bob Watson
Executive Chairman

Cytopia announces publication of new drug lead

Cytopia recently announced the publication of important new research in collaboration with the University of Queensland's Institute of Molecular Bioscience (IMB) which potentially opens a new approach to the treatment of chronic inflammatory diseases and cancer.

The collaborative research is important as it could lead to an additional drug candidate for Cytopia.

The research which will appear in the FASEB Journal (September 2006 issue) has shown that molecules developed by Cytopia can block the

survival and function of macrophages - cells which play a key role in the immune system. The inappropriate activity of these cells is implicated in chronic inflammatory diseases such as rheumatoid arthritis, as well as a range of other disorders including renal graft rejection, atherosclerosis and cancer.

The collaborative research is important as it could lead to an additional drug candidate for Cytopia.

Cytopia has generated a range of highly potent molecules with good drug-like properties for testing in a range of animal models including cancer, rheumatoid arthritis, renal transplant rejection, atherosclerosis and osteoporosis. It is possible that Cytopia could be in a position to select a clinical candidate in early 2007.

The molecules work by inhibiting a kinase enzyme known as c-fms which is activated during an immune response.

Alchemia investment

During recent weeks, the company sold its holding in Alchemia Ltd to a range of institutional investors for a total of \$15m.

As one of the early investors in Alchemia, Cytopia has generated a significant return on its investment cost of \$6.8m and these funds will now be used to support the clinical progress of cancer drug candidate CYT997 and the various kinase research programs including JAK2.

The company commences the new reporting period in a very healthy financial state and well positioned for further growth.



CYT997 Phase I trial well advanced

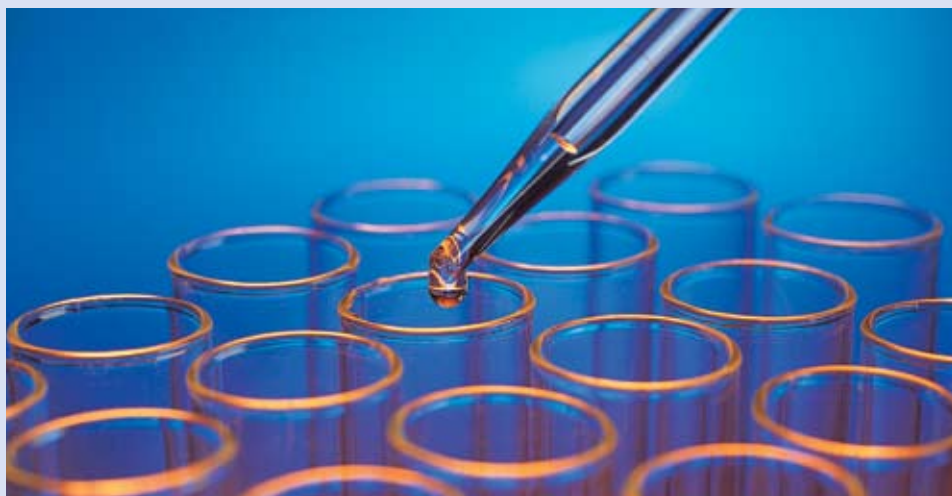
The Phase I trial of cancer drug candidate CYT997 commenced in June 2005 and is continuing to progress to expectation. CYT997 has been well tolerated to date and no dose-limiting toxicities (DLT) have yet been identified. In accordance with the clinical trial protocol, dose escalation will continue until two or more patients within a dose level exhibit a DLT.

Whilst the Company cannot be certain when DLTs will be observed, Cytopia anticipates the trial will continue through Q3 2006. The lack of toxicity increases the prospects for a good margin between efficacious and toxic doses.

MORE DETAILS ON CYT997

CYT997 is an orally available vascular targeting and cytotoxic drug candidate that has proven effective in animal models of a wide range of tumour types including breast, prostate and colon, as well as some leukemias.

In March 2005 Cytopia successfully lodged an Investigational New Drug Application for CYT997 with the Food and Drug Administration of the United States and in June 2005 commenced a Phase I dose escalation study in cancer patients at the Royal Brisbane and Women's Hospital. This study is predominantly designed to determine the safety and tolerability, the dose-limiting toxicities and maximum tolerated dose of CYT997 when given as a 24-hour intravenous infusion every three weeks to cancer patients that have failed one or more front-line therapies. Pharmacokinetic and biological activity data is also being collected.



ORAL APPLICATIONS OF CYT997

The company will apply later this year to various regulatory authorities to conduct a Phase I clinical trial with oral administration of CYT997. Subject to regulatory approval, this clinical trial will commence at a site in Australia in November 2006. This clinical trial will have similar objectives to the current intravenous trial, including the determination of safety and tolerability of CYT997 when given by mouth.

EFFICACY STUDIES

The company is currently concluding planning for future Phase II studies for CYT997, including the application of the compound in highly-vascular cancers with poor prognosis such as hepatoma. Advancement of the compound into Phase II efficacy studies is necessarily

contingent on the findings from the Phase I clinical trials programme and regulatory approval, however the company intends to commence a Phase II trial very shortly after the conclusion of each of the Phase I programmes.

COMMERCIAL READY GRANT

In December 2005 Cytopia was awarded an AusIndustry grant of \$3 million over three years to assist in the clinical development of CYT997. The grant will provide matching funds for the oral safety trial and initial efficacy studies of CYT997 as a monotherapy and potentially in combination with a front-line cytotoxic drug.



Cytopia's new website can be found at www.cytopia.com.au.

Electronic shareholder communication

Effective and efficient communication with shareholders is a very important issue for Cytopia. The best way for shareholders to achieve this is to register for electronic communications through the company's share registry, Link Market Services (formerly ASX Perpetual), and we would strongly encourage you to do so.

There are many advantages, including:

- Email alerts on all company announcements
- Notification of shareholder meetings
- Lodgement of online proxy forms

- Viewing holding details and making address changes

To register, please take a few minutes to visit the company website: www.cytopia.com.au and click on the Share Registry link under Investor Centre. All you will need to access the Link site is your name, postcode and holder identifier (HIN/SRN), which is an 11 digit number usually starting with "X", "I" or "C" and supplied at the time of acquiring your shares.

PDF Status

Cytopia Ltd is a registered Pooled Development Fund (PDF), which confers special tax concessions on both the company and its shareholders.

For most Australian taxpayers, this will mean that any gains, or losses, on disposal of shares will be exempt from capital gains tax whilst the company retains PDF status.

To remain as a PDF, the company is required to meet certain criteria. It is possible that retention of PDF status may become inconsistent with the growth strategies of the company and in late 2004, shareholders granted the Cytopia board discretion as to when it may choose to relinquish registration.

However, the PDF Board has recently extended registration through to June 2007, at the request of Cytopia, and there are no current plans to deregister.

Congratulations

Congratulations to our Non-Executive Director, Dr Geoffrey Vaughan AO, on being awarded the Officer of the Order of Australia for service to scientific research and development, particularly through contributions to the development of government policy initiatives, to the growth of innovative technology-based Australian companies, and to education as a mentor and supporter of young scientists.



Recruitment

Specific job openings will be posted on the Cytopia website from time to time. Please refer to the following link for details:

www.cytopia.com.au/careers.html

cyTopics

Further copies of *cyTopics* are available from the company website:

www.cytopia.com.au

Conference Presentations

In recent months, Cytopia has presented at a number of international conferences. In summary we have attended and presented at:

- **Biotechnology Expo**
Melbourne, Australia
– 14 June 2006
- **Drug Discovery Technology China® BioPharma Opportunities**
Shanghai, China
– 13 - 15 June 2006
- **Protein Kinase Targets – Drug Discovery and Design**
Boston, USA – 12 - 14 June 2006
- **Bio 2006**
Chicago, USA – 9 - 12 April, 2006
- **Australian-Biotechnology Expo**
New York, USA – 6 April 2006

Patent Update

The following table summarises the developments since the 2005 Annual Report was completed.

Title	Lodgement date	Number	Update
Kinase Inhibitors I	17 Feb 2004	PCT/AU03/00628	30 Nov 2005 South Africa – notice of acceptance 4/9346
Kinase Inhibitors II	23 May 2003	PCT/AU03/00629	30 Nov 2005 Grant of South African patent 2004/9341
Kinase Inhibitors III	15 Dec 2004	PCT/AU2003/01666	13 Jun 2005 Entry into National Phase EP-03767297.9, JP-2005-502389, USA-TBA
Tubulin polymerisation Inhibitor I	11 Dec 2003	PCT/AU03/001661	11 Jun 2005 Entry into National Phase CA-2508170 JP-2005-502293 IL-168833
Tubulin polymerisation Inhibitors II	3 Dec 2004	PCT/AU2004/001689	15 Jun 2005 5 Salt form provisional applications filed 2005903101(to 5)
A crystal structure and uses thereof	12 May 2005	Provisional applications AU-2005902240 US-11/248478	3 May 2006 PCT (number not available)



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