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Media Release

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CYTOPIA IN \$3.6 MILLION DRUG DISCOVERY PROJECT WITH MONASH UNIVERSITY

Cytopia is pleased to announce that it has commenced a three-year, \$3.6 million project with Monash University's Department of Biochemistry and Molecular Biology to design drugs to treat immune diseases, cancer and cardiovascular disorders. The project is being assisted by the largest ever Australian Research Council linkage grant of \$1.2 million.

Dr Kevin Healey, Managing Director and Chief Executive Officer of Cytopia, said, "The grant will allow us to accelerate the refinement of existing drug leads into candidates for preclinical testing, using rational, structure-based computer design.

"It will also broaden our range of drug discovery targets," Dr Healey said.

The targets, which include the JAK kinases, are a family of enzymes that are over-active in various diseases and Cytopia is developing drugs that can switch off these enzymes and treat the diseases.

The Monash team, led by Dr Jamie Rossjohn is determining the 3-dimensional structures of Cytopia's drug discovery targets using a technique known as X-ray crystallography.

Dr Andrew Wilks, Cytopia's Chief Scientific Officer, said that knowing the structure of a drug target is the same as knowing the detailed mechanism of a lock. "Once you know that, it becomes easier to design the most effective key. We have already applied this knowledge to the design of drug leads that are being tested in various animal models of cancer, immune diseases and cardiovascular disorders."

Dr Jamie Rossjohn said, “Monash is pleased to be working with Cytopia, which has already developed a number of exciting drug leads against the JAK kinase targets. We believe the combination of our expertise in structure determination, together with Cytopia’s skills in medicinal and computational chemistry, will create an internationally competitive drug discovery team.”

Dr Healey said that the collaboration with Monash was an excellent example of how a University research group could interact effectively with industry in a commercially focused way.

ABOUT THE DEPARTMENT OF BIOCHEMISTRY AND MOLECULAR BIOLOGY, MONASH UNIVERSITY

The Department of Biochemistry and Molecular Biology, part of the School of Biomedical Sciences, was established in 1961 and hosts more than 300 researchers. It has recognized strengths in molecular, cellular and structural biology. The Protein Crystallography Unit, led by Dr Jamie Rossjohn, was established in the School of Biomedical Sciences at the Clayton campus in January 2002.

The million-dollar unit has four laboratories - a main laboratory where proteins for study are purified, a crystallisation laboratory, an X-ray diffraction laboratory and a graphic laboratory where crystal structures are determined.

In its two-and-a-half years of operation, the unit has worked out the structures of numerous important proteins, providing unique insights into their function.

These include:

- the crystal structure of a key receptor in multiple sclerosis;
- the crystal structure of a therapeutic immunosuppressant, OKT3, in complex with a critical T cell antigen.
- discovering a group of proteins in bacteria called serpins that have exposed a new mechanism for preventing a range of human diseases;
- the crystal structure of a human T-cell receptor (receptors are a group of proteins that other proteins bind to) and the structure of this receptor in complex with a peptide from the Epstein Barr Virus. Also solved were the crystal structures of related receptors, called HLA B44, which are a significant barrier in human organ transplantation;
- finding that the protein that gives reef-building corals their blue colour could be useful as a biotechnological tool capable of highlighting structures and interactions within cells.

ABOUT CYTOPIA LIMITED

Cytopia Limited (formerly Medica Holdings) is an Australian biotechnology company focused on the discovery and development of new drugs to treat cancer, immune disorders and cardiovascular diseases.

Cytopia Limited is a registered Pooled Development Fund and conducts its research and development *via* a subsidiary company Cytopia Research Pty Ltd (formerly Cytopia Pty Ltd).

Cytopia Research Pty Ltd

Cytopia Research specialises in discovering new molecules that can inhibit enzymes known as kinases, an exciting new class of drugs.

It holds a worldwide exclusive license from the Ludwig Institute for Cancer Research to a number of these enzymes known as JAK1 and JAK2 kinases which are over-active in many inflammatory diseases and some cancers. These JAK kinases, which were discovered by Cytopia's Chief Scientific Officer Dr Andrew Wilks, are well-validated drug targets, and Cytopia has developed a number of inhibitors with therapeutic potential.

Cytopia applies structure based rational drug design techniques that can accelerate the identification of active molecules and their refinement into drug candidates.

Cancer program

Cytopia's candidate drug has shown efficacy in six *in vivo* animal models of various cancers, including prostate cancer, breast, lymphoma and leukaemia.

Cytopia's candidate has entered formal preclinical testing during which short and long term toxicity will be assessed and clinical grade material will be manufactured. We currently expect the Phase I human trial to be in early 2005 subject to approval by regulatory authorities.

Anti-Inflammatory Program

Cytopia has generated highly specific and potent inhibitors of the JAK3 kinase which is of major interest to pharma companies for the prevention of transplant rejection and treatment of several inflammatory diseases such as asthma, dermatitis, psoriasis and eczema.

A number of pharma companies are either currently evaluating Cytopia's molecules or have expressed an interest to do so.

Cardiovascular Program

Cytopia has entered into a collaborative R&D Agreement with New York-based Myomatrix to explore the use of JAK2 inhibitors to treat a number of cardiovascular problems such as heart failure and pulmonary hypertension. Myomatrix has shown that JAK 2 inhibitors are effective in an *in vivo* model of heart failure.

Cytopia and Myomatrix plan to test one or more of Cytopia's molecules in animal models of pulmonary hypertension and heart failure in calendar 2004.

Cytopia's other Assets

Xenome Limited last month gained Investigatory New Drug approval by the US Federal Drug Administration for its novel anti-pain molecule, Xen2174 and a Phase I human trial commenced in July . (Cytopia owns 22.4%of Xenome).

Alchemia Limited is ahead of schedule in its development of a generic version of synthetic heparin in partnership with Dow Chemical for manufacturing, and with American Pharmaceutical Products for marketing and regulatory matters. Alchemia has negotiated a 50:50 profit share with both companies.

In addition, Alchemia has made good progress in applying its VAST™ technology platform to the discovery of drug leads for cancer and novel antibiotics. (Cytopia owns 14.3% of Alchemia).

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