Cyclacel Pharmaceuticals, Inc. (Nasdaq: CYCC) recently announced that the company has initiated a multicentre randomised Phase II clinical trial of sapacitabine (CYC682), an orally available nucleoside analogue, in patients with advanced cutaneous T-cell lymphoma (CTCL). The study is the first of several Phase II clinical trials the company plans to begin this year to evaluate sapacitabine’s potential in haematological and solid tumours.

The primary objective of the study is to evaluate the tolerability and response rate of high-dose and low-dose regimens in patients with CTCL who have had progressive, recurrent, or persistent disease on or following two systemic therapies. The study uses a selection design with the objective of choosing an optimal dose in the event that both doses are active. Secondary objectives are to assess response duration, time to response, time to progression and relief of pruritus or itching.

Sapacitabine appears to act through a dual mechanism that is unique among nucleoside analogs. It interferes with DNA synthesis by causing single-strand DNA breaks and induces arrest of the cell division cycle at G2 phase. Both sapacitabine and its major metabolite, CNDAC, have demonstrated potent anti-tumour activity in preclinical studies. In a liver metastatic mouse model, sapacitabine was shown to be superior to gemcitabine or 5-FU, two widely used nucleoside analogs, in delaying the onset and growth of liver metastasis.

The study follows four Phase I trials in which sapacitabine has been given as a single agent to approximately 150 patients: three in patients with incurable solid tumours and one in patients with advanced leukaemias or myelodysplastic syndromes.

In addition, Cyclacel Pharmaceuticals, Inc. also announced preclinical results from a combination study of seliciclib, an orally-available cyclin dependent kinase (CDK) inhibitor, with epidermal growth factor receptor (EGFR) inhibitor erlotinib (Tarceva®). The study demonstrated that the drugs act synergistically in suppressing tumour growth in models of non-small cell lung cancer (NSCLC). Currently, seliciclib is being evaluated in a Phase II randomised double-blinded clinical trial as a single agent in NSCLC. Cyclacel Pharmaceuticals, Inc. also plan to commence in the second half of 2007 clinical development of seliciclib as a treatment for patients with nasopharyngeal cancer (NPC).

In the first quarter of 2007, Cyclacel Pharmaceuticals, Inc. raised a further $36 million through a registered direct financing. This funding will allow the company to pursue clinical trials with the three development-stage candidates, sapacitabine, seliciclib and CYC116, in multiple indications.

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Axis-Shield receives marketing clearance for assay for rheumatoid arthritis.

Axis-Shield (LSE:ASD, OSE:ASD) the international in vitro diagnostics company, recently announced that it has received US 510(k) marketing clearance from the Food and Drug Administration (FDA) for its anti-CCP assay for early detection of rheumatoid arthritis (RA).

Axis-Shield’s anti-CCP assay is regarded by many experts as the most significant recent development in the early diagnosis of RA. By enabling early detection, the assay facilitates improved management of this widespread and debilitating condition. The assay is the latest to be developed under the AxSYM xtra programme, in which Axis-Shield has contracted to produce a number of new markers for Abbott’s successful AxSYM immunoassay platform.

This proprietary test follows the recently approved Axis-Shield-labelled assay, AxSYM Active-B12, which is used for the effective determination of vitamin B12 deficiency.

In addition, Axis-Shield plc recently appointed Ronny Hermansen as Group Finance Director to replace the previous post-holder, Paul Garvey. Ronny Hermansen was previously Finance Director of Axis-Shield ASA and has extensive experience in the Norwegian pharmaceutical industry.

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Translational Medicine Research Collaboration seeks new projects

The Translational Medicine Research Collaboration (TMRC) – the multifaceted collaboration to facilitate the translation of basic scientific and clinical research into new and effective drug discoveries – has moved into its second year and has invited further research proposals from its partners.

Almost £8 million of funding was released in early 2007 to support 28 new research projects covering a wide range of therapeutic areas including cardiovascular and metabolic disease, the central nervous system, oncology, inflammation and women’s health. The collaboration comprises four of Scotland’s leading universities (Aberdeen, Dundee, Glasgow and Edinburgh), Wyeth Pharmaceutical Co., Scottish Enterprise and NHS Scotland, Grampian, Greater Glasgow, Lothian and Tayside. The main focus of the collaboration is the development of biomarkers and experimental systems to address the major challenges of innovative and safe drug discovery and development in the 21st century.

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Board Appointment at IDMoS plc

IDMoS plc (AIM: IDO) which specialises in disease detection and monitoring has recently announced the strengthening of its Board with the promotion of Dr Mikael Bronnegard MD PhD.

Dr Bronnegard joined the company in September 2006 as business development director with the initial remit to finalise the business strategy for the medical activities of the Group. He is a specialist in Pediatrics, Pediatric Endocrinology and Diabetes and has extensive experience in clinical and basic research. He also has several years of pharmaceutical industry experience and previously worked in the venture capital industry.

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BBInternational Dundee to expand

BBInternational Dundee (BBI Dundee), formerly Alchemy Laboratories, has announced plans to expand its manufacturing facilities to meet increased overseas demand, creating 27 new jobs over the next two years.

The company, which specialises in rapid diagnostic test technology including colloidal gold manufacture and custom conjugation services, became part of BBI Holdings in May 2006. The BBI group develops and manufactures rapid diagnostic tests for the point-of-care market globally and the acquisition provided BBI Dundee with capability to undergo technical manufacture and down stream processing of diagnostic tests and greater access to the US rapid diagnostic testing market. The market size for point of care tests is in the region of $2.1 billion, with BBI Dundee predicting that there is market growth potential of up to 27% over the next 5 years.

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Honours for Dundee scientists

Several University of Dundee scientists have had their works recognised with major international awards. Professor Michael Ferguson has been elected a Fellow of the Academy of Medical Sciences, the seventh member of the College of Life Sciences to receive this accolade. Professor David Lilley has been named as a recipient of one of the Royal Society of Chemistry's Interdisciplinary awards. In addition, Dr John Rouse has been awarded the 2008 Colworth Medal by the Biochemical Society.

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Dundee Cell Products

Dundee Cell Products Ltd., a Dundee based company which develops novel products and services to enhance drug and medical research, was formally launched following a six figure investment from the Discovery Investment Fund.

The company is targeting pharmaceutical life science research firms, and consists of two core operational areas: manufacturing and sales of research reagents and the provision quantitative proteomics, delivering new, innovative technology which interprets and analyses cell protein. With DCP technology it will be possible to analyse in detail the dynamics of the cellular proteins and develop interventions that will improve the performance of the cell.

The company, founded last year by internationally-renowned academics Professor Angus Lamond and Dr Paul Ajuh from Dundee University, is targeting clients in the pharmaceutical and biotechnology sector as well as academic life science research groups.

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CXR Biosciences agrees global marketing of HRN™

CXR Biosciences Ltd., Dundee, Scotland recently announced an agreement with Taconic Farms, Inc., (Hudson, New York) to provide the Hepatic Reductase Null (HRN™) mouse commercially.

CXR Biosciences’ patented HRN™ is an innovative new model that has essentially no hepatic cytochrome P450 activity, the major enzyme system involved in drug disposition. This valuable model represents a significantly improved in vivo tool for the assessment of the role of metabolism in determining the efficacy, bioavailability and toxicity of drug candidates. Use of the HRN™ model will improve the lead selection and development process significantly.

CXR Biosciences has also entered into a collaboration with Ingenuity Systems (Redwood City, CA) to help validate their new IPA-tox™ software within the Ingenuity Pathways Analysis 5.0 (IPA 5.0) package.

CXR Biosciences will advise Ingenuity about pathways associated with drug disposition and toxicity so that they can improve the IPA software that CXR currently use in investigative toxicology applications to help elucidate mechanisms of toxicity from microarray data. At CXR Biosciences overlaying results from IPA 5.0 with statistical clustering of microarray data has provided new insights into the mechanisms of toxicological responses such as oxidative stress response, interactions of drugs with individual enzymes such as P450’s, and xenobiotic metabolism. This approach is extremely useful for discovering biomarkers, determining toxicity in humans, and evaluating the utility of new toxicological models for risk assessment.

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Research Focus

Cell Cycle and Apoptosis

The correct balance between cell death and cell division must be controlled and adjusted during development, in response to injuries and when tissues are modified by exercise and nutrition. An abnormal prevalence of cell death is associated with degenerative diseases. Conversely, in cancer, cells proliferate by uncontrolled cell division but fail to undergo cell death by the process of apoptosis. This can cause resistance to cancer therapies that are aimed at the destruction of cancer cells.

Professor Paul Clarke's research team studies the molecular processes that control cell death and cell division, with particular emphasis on their roles in the development and treatment of cancer. In one area of their work, they are investigating the control of the mitochondrial or intrinsic apoptotic pathway. A critical enzyme in this pathway, a protease called caspase-9, is inhibited by modification through phosphorylation at certain amino acid residues. Phosphorylation of caspase-9 is catalysed by several protein kinases that restrain apoptosis in proliferating cells and in response to cellular stresses. During cell division, phosphorylation of caspase-9 by a cyclin-dependent protein kinase, CDK1-cyclin B1, restrains apoptosis and is critical for resistance to apoptosis in response to microtubule poisons such as paclitaxel which arrest cells during mitosis (Allan & Clarke 2007, Mol Cell 26, 301-310). The phosphorylation status of caspase-9 and its regulators can be analysed by specific antibodies, and these provide potential predictors of anti-mitotic drug sensitivity and biomarkers for tissue responses to therapeutic drugs.

In other work, the Clarke group studies the response of cells to DNA damage and has developed a number of potential biomarkers for drug toxicity and cellular responses. They also study the spatial and temporal control of cell division and the role of Ran, a GTPase of the Ras superfamily. Paul Clarke is Professor of Cancer Cell Biology and Head of Laboratory Research in the College of Medicine, Dentistry and Nursing at the University of Dundee.

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Lead compounds for the development of novel antifungals

Researchers at the University of Dundee have identified a number of compounds that inhibit family 18 chitinases and the team is currently funded with a view to produce a hit series of inhibitors against this target.

Specific potent chitinase inhibitors would be of considerable interest for the development of novel therapeutics with antifungal potential. Natural Inhibitors are already known but none are suitable as drug leads.

Previous work in Dundee has revealed compounds with drug like properties and co-crystallisation of these with the target enzyme has led to the design of novel chemical entities. Data is available to demonstrate inhibition of family 18 chitinase from Aspergillus fumigatus (chitinase B1) using a fluorogenic substrate. Inhibition of human chitotriosidase and acid mammalian chitotriosidases has also been demonstrated.

Commercial opportunity. The University is seeking potential partners in the area of anti-fungal drug development.

A patent application protecting the compounds has been filed D345

Novel non-genotoxic activators of p53

Researchers at the Universities of St Andrews and Dundee have identified a series of compounds activating the p53 tumour suppressor. Data is available showing one of these compounds preferably kills tumour cells expressing normal p53 and reduces tumour growth in a xenograft model.

The p53 tumour protein is a central mediator of cellular stress response and plays a major role in preventing tumour development. Its importance as a tumour suppressor is reflected by its high rate of mutation in human cancer; approximately 50% of adult human tumours bear inactivating mutations or deletions in the TP53 gene. Many current therapies give rise to DNA damage leading to the appearance of mutations in p53 that are associated significantly with poor outcome and drug resistance. Improving the treatment of those cancers in which p53 function is not abolished by mutation may depend on finding novel non-genotoxic activators of the p53 response.

Non-genotoxic activation of the p53 pathway may open the way to long-term cancer treatment including prophylactic treatments where toxicity and resistance are issues. Molecules which are consistent with this requirement may be useful as therapeutic agents for the management of patients with hyperproliferative conditions.

The University of Dundee is now seeking a commercial partner to further this programme.

D293
Patent pending

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