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News in Brief...

Phase 2 Trial Results

CRT licensees Biomira^[Apr06] and Antisoma^[Sept06] both report positive final phase 2 survival results in NSCLC

Temozolomide Approved in Japan

Ministry of Health, Labour and Welfare approval for patients with malignant gliomas^[Jul06]

Exclusive Rights to Increasing Research Spend

Record £257m (\$483m) funding by Cancer Research UK in 2005/2006^[Sept06]

AstraZeneca Collaboration

Characterisation of gene expression patterns in colorectal cancer^[Sept06]

B-RAF Drug Discovery

GSK, ICR and Wellcome Trust alliance builds on original programme including CRT^[Jul06]

Satraplatin Phase 3

Progression-free survival endpoint reached in pivotal prostate cancer trial^[Sept06]

Non-Invasive Therapies

New photodynamic^[Sept06] and ultrasound therapy^[Jul06] anti-cancer collaborations

Enhancing Chemotherapy with AS1404

Promising final phase 2 survival results in NSCLC patients have been released for AS1404, a small-molecule 'vascular targeting agent'^[Sept06]. Patients who received AS1404 on top of standard chemotherapy had a median survival of 14.0 months, compared with 8.8 months in patients treated with chemotherapy alone. This 5.2 month difference is one of the largest ever seen in a trial combining a novel agent with first-line chemotherapy for lung cancer. AS1404 was discovered by Professors Bruce Baguley and William Denny and their teams at the Auckland Cancer Society Research Centre. The drug was licensed to UK biotechnology company Antisoma by CRT in August 2001.

First data from the phase 2 trial of AS1404 administered in combination with docetaxel to patients with hormone-refractory prostate cancer has also recently been released^[Sept06]. These show a markedly higher rate of PSA responses among men receiving AS1404. Preliminary data show a PSA response rate of 57% in those receiving AS1404 plus docetaxel chemotherapy compared with 35% in those receiving docetaxel alone. In addition new preclinical data highlights other targeted therapies with which AS1404 can be combined to enhance treatment efficacy. These therapies include the anti-VEGF antibody Avastin[®] in colon and lung cancer^[Apr06] and anti-EGFR antibody Erbitux[®] (cetuximab) in lung cancer^[Sept06]. AS1404 is also undergoing a phase 2 trial in ovarian cancer and Antisoma are preparing for phase 3 trials of AS1404 in NSCLC.

Telomere Targeted Signalling Agents Agreement

Pharminox Limited, a UK-based biotechnology company, have signed a new agreement with CRT to secure rights to a preclinical oncology programme focused on telomere signalling targeted agents (TSTAs)^[Apr06]. The programme has come out of research by Professor Malcolm Stevens OBE, Director of the Cancer Research UK Experimental Cancer Chemotherapy group at the University of Nottingham, and Chief Scientific Officer of Pharminox. Under the terms of the agreement, CRT has granted Pharminox an exclusive 12-month option to in-license exclusive worldwide development and commercialisation rights to the programme. A lead candidate, RHPS4, has already been selected and is expected to move into formal preclinical development within the next 12 months.

The TSTA programme is Pharminox's third collaboration with CRT, building on the Phortress (phase 1) and Quinols (preclinical) programmes which are currently under development by Pharminox for treatment of solid tumours including breast and colorectal cancer and melanoma.

Molecular Insights into Bowel Cancer Treatment

CRT and the Cancer and Immunogenetics Laboratory at the Weatherall Institute of Molecular Medicine led by Sir Walter Bodmer are collaborating with AstraZeneca to characterise the expression of key genes involved in colorectal cancer.

Critical reagents and data will be provided by the Cancer and Immunogenetics Laboratory and the programme of research will be undertaken by AstraZeneca. The data generated will enhance our understanding of the link between the molecular pathology of colorectal cancers and the success of targeted treatments. In addition results will assist the identification of novel drug targets and the development of drugs that are effective against chemoresistant tumours. The findings of the collaboration will be shared by both CRT and AstraZeneca and will be used to advance AstraZeneca's anti-colorectal cancer programmes.

CRT News

Reagent Sales Forecast Exceed £1.6m

In addition to facilitating the development of anti-cancer therapeutics and diagnostics, CRT has been successfully commercialising research reagents created in academic institutes for over 20 years. Forecast revenues for the current financial year now exceed £1.6m (\$3m). Our activities ensure that new research tools are made widely available to scientists, thereby supporting biomedical research worldwide.

CRT has exclusive rights to commercialise reagents created through programmes funded by Cancer Research UK, and also markets antibodies generated by the National Institute for Biological Standards and Control and the Leukaemia Research Immunodiagnosics Unit at the University of Oxford. More recently CRT completed a further antibody commercialisation agreement with Birmingham University^[Jun06]. The new relationship expands CRT's antibody portfolio to over 450 monoclonals.

New Technology Platforms

CRT has granted Geneservice Ltd., a UK genomics products and contract research company, worldwide exclusive rights to distribute the pSUPER RNAi vector system and pRETROSUPER vector-based short hairpin RNA library^[Sept06]. Researchers at the Netherlands Cancer Institute (NKI) developed the platform technology which enables stable and prolonged inhibition of target gene expression in mammalian cells. The oncology-focused library includes approximately 8000 genes and contains a high proportion of candidate drug targets.

CRT has also begun marketing a powerful protein-genome interaction mapping technology named 'DamID'^[Aug06]. The technology was developed by scientists at the NKI and Fred Hutchinson Cancer Research Center. DamID maps protein-genome interactions by using the enzyme DNA adenine methyltransferase to create unique molecular tags which track DNA-binding sites of specific proteins. CRT are seeking a licensee to directly supply biomedical researchers and develop protein-genome interaction mapping services.

Drug Discovery Developments

Substantial progress has been made in the joint cancer drug discovery collaboration between Sareum Holdings PLC, the specialist structure-based drug discovery company, the Institute of Cancer Research (ICR), and CRT^[Aug06]. Together Sareum, the ICR and CRT have discovered novel compound series which show efficacy in cancer cell models. Several novel compound series have been identified that specifically target a key enzyme involved in resistance to chemotherapy. The team is now working to fully optimise a lead series of compounds to provide a validated candidate to take forward into clinical development. Successful development of a cancer therapeutic could allow effective treatment of tumours which do not respond to current treatments, as well as lowering the dose required of existing therapies and reducing adverse side effects.

Advancements have also been made in a B-RAF drug discovery collaboration. GlaxoSmithKline have joined a partnership involving the Wellcome Trust, Astex Therapeutics, the ICR and CRT, that aims to discover, develop and commercialise novel small molecule inhibitors of key signal transduction enzyme B-RAF for use in the treatment of cancer^[Jul06]. The new Research, Development and Collaboration Agreement grants the Wellcome Trust and the ICR a licence to three of GlaxoSmithKline's lead series of relevant compounds. Cancer Research UK continues to contribute funding to this programme, which is led by Prof. Richard Marais and Prof. Caroline Springer at the ICR.

Light and Sound to Treat Cancer

CRT has established new development programmes with leading research groups investigating two different types of non-invasive therapies, Photodynamic Therapy (PDT)^[Sept06] and High-Intensity Focused Ultrasound (HIFU)^[Jul06].

Prof. David Russell at the University of East Anglia will receive funding from Cancer Research UK and will work closely with Prof. Giulio Jori, a leading expert in PDT at the University of Padua, to perform key proof of concept studies on a novel combination of photosensitisers and gold nanoparticles. This new technology is likely to offer several advantages over existing therapies including greater efficacy, reduced side-effects of photosensitivity and improved formulation.

Prof. Jeffrey Hand and Mr Paul Abel at Hammersmith Hospital, London are leading development of 'Phased Array' HIFU for the treatment of cancer. Cancer Research UK will fund both the development of a prototype Phased Array HIFU device and proof of concept studies. HIFU therapy utilises ultrasound energy to heat and destroy tumour tissue, offering precise tumour targeting with very few side effects. Current HIFU applications are generally limited by treatment times of several hours duration, which is impractical for routine therapy. Phased Array HIFU has the potential to target larger volumes of tissue than can be currently treated with most existing HIFU technologies. This should result in dramatically reduced treatment times, making HIFU more clinically and economically viable.

Vaccine Moving Forward

Encouraging final phase 2b survival results have been released for Stimuvax[®], the MUC1 liposomal peptide vaccine under clinical development by Biomira Inc.^[May06]. Stimuvax[®] was developed under a portfolio of patents originating from the laboratory of Prof. Joyce Taylor-Papadimitriou of Guy's Hospital London and licensed by CRT. The randomised, open-label trial tested the clinical potential of Stimuvax[®] in patients with stage 3B and 4 NSCLC. The analysis confirms a median survival in stage 3B patients on vaccine being 30.6 months, while stage 3B patients on the control had a median survival of 13.3 months.

Phase 2 prostate cancer trial results of Stimuvax[®] have also been published^[Jul06]. The data showed that Stimuvax[®] could slow rising Prostate Specific Antigen (PSA) levels in some post-surgical prostate cancer patients, potentially delaying the need for initiation of androgen deprivation therapy (ADT).