

## **Circadian Technologies announces that Ark Therapeutics receives clearance to commence Phase 3 trial of Trinam®**

Circadian Technologies Limited (ASX: CIR) announced today that Ark Therapeutics Limited, licensee of Circadian's wholly owned subsidiary Vegenics, has been notified by the US Food and Drug Administration to commence patient recruitment into its Phase 3 human trials of Trinam®, a novel treatment to improve quality of care and quality of life for kidney dialysis patients.

Trinam® is a gene-based medicine to prevent blood vessels from blocking in kidney dialysis patients who have undergone vascular access graft surgery. The product is an adenovirus-mediated VEGF-D gene delivered with a novel biodegradable local delivery device.

In March 2007, Ark reported that in a Phase 2 clinical trial the access grafts of patients given Trinam® remained functional for dialysis, on average, up to three times longer than in untreated controls.

Rights to employ the VEGF-D gene in Trinam®, are licensed from Vegenics to Ark. Under the terms of the Vegenics/Ark license agreement, Vegenics is entitled to receive milestone payments on clinical development achievements and royalties on product sales.

Circadian, through Vegenics, owns extensive intellectual property rights for the use of VEGF-D and other VEGF family members for diverse therapeutic applications. Circadian's internal product programs are focused on the development of novel therapeutics for cancer.

Robert Klupacs, CEO of Circadian commented, "This is a significant milestone for Trinam® in the path towards commercialization, and we congratulate Ark on their pioneering role in advancing this important and novel technology. We are hopeful that Trinam® will, in the future, bring considerable benefit to patients undergoing kidney dialysis. We believe that progression of this application is a reflection of the significant commercial value of our VEGF intellectual property."

Additional information is provided in the announcement below submitted by Ark Therapeutics Limited to the London Stock Exchange. Additional information on Ark Therapeutics may be found on its web-site [www.arktherapeutics.com](http://www.arktherapeutics.com)

### **For more information**

#### *Company enquiries*

Robert Klupacs  
Managing Director - Circadian  
Tel: +61 (0) 3 9826 0399 or  
[robert.klupacs@circadian.com.au](mailto:robert.klupacs@circadian.com.au)

#### *Media enquiries*

Rebecca Wilson  
Principal - Buchan  
Tel: +61 (0) 417 382 391

## **About Circadian Technologies Limited**

Circadian (ASX: CIR) is a drug developer focused on its extensive intellectual property portfolio around Vascular Endothelial Growth Factor (VEGF) C and D owned by its unlisted subsidiary Vegenics. The applications for the VEGF technology, which functions in regulating blood supply, are substantial and broad. Circadian's internal product development programs are focused on novel anti-cancer therapeutics for large unmet needs. Circadian, has also licensed rights to some parts of its intellectual property portfolio for the development of other products. UK company Ark Therapeutics Group plc (LSE: AKT) is developing Trinam®, a treatment for vascular grafts associated with renal dialysis based upon Circadian intellectual property which has commenced Phase 3 trials. Another Circadian licensee, ImClone Systems Inc (NASDAQ:IMCL), is developing an antibody-based drug to VEGFR-3 for the treatment of solid tumours.

The VEGF patent portfolio developed by LICR and Licentia has been assigned to Circadian's subsidiary Vegenics. Vegenics also has rights to CoGenesys Inc/Human Genome Sciences Inc's VEGF-C intellectual property.

RNS Number : 3035L  
Ark Therapeutics Group PLC  
08 January 2009

### **Ark completes potency test qualification enabling Trinam® Phase III trial to commence**

**8 January 2009** - Ark Therapeutics Group plc ("Ark" or the "Company") today announces that it has successfully completed the work requested by the US Food and Drug Administration (FDA) to qualify a potency test for Trinam®. As a result, the Company has now been notified by the FDA that it can commence patient recruitment into its Trinam® Phase III trial. In June 2008, Ark reported that its application for Special Protocol Assessment (SPA) for Trinam® had been successful and that, in parallel, the updated Investigational New Drug (IND) application for the trial had also been reviewed and approved by the FDA. The IND was subject to a requirement for Ark to qualify a product release test relating to potency prior to treating patients. That condition has now been met.

Trinam® is Ark's novel gene-based medicine to prevent blood vessels blocking in kidney dialysis patients who have undergone vascular access graft surgery. The product is an adenovirus-mediated VEGF D gene delivered with a novel biodegradable local delivery device (EG001). Trinam® has already been granted Orphan Drug Status in the USA and Europe and Ark now also intends to apply to the FDA for Fast Track Designation and to submit a rolling Biologic Licence Application (BLA) for sale and marketing approval in the US in due course. US regulatory review for the product comes under the responsibility of the Centre for Biologics Evaluation and Research (CBER), the specialist biologics division of the FDA.

The Phase III study is a US multi-centre, randomised, controlled trial, in which the efficacy and safety of Trinam® will be investigated in patients with end-stage renal disease (ESRD) requiring vascular access for haemodialysis. Patients with ESRD will be randomised to receive either Trinam® in addition to standard care or standard care alone at the time of surgical placement of a synthetic PTFE graft for vascular access. Primary Unassisted Patency (time to any first intervention) will be the primary regulatory end point and overall patency and a number of other important pre-defined clinical endpoints will also be measured. Safety will be assessed by an independent Data and Safety Monitoring Board (DSMB) against a pre-specified set of stopping rules defined during the SPA. The DSMB will also undertake a 'sample sizing' analysis after 150 patients have been recruited to determine the final trial size. This type of adaptive design assists groundbreaking drugs to ensure robust efficacy data are available to satisfy regulatory requirements as approval standards evolve.

Results from a Phase II open-label, non randomised, standard-care controlled trial of Trinam®, reported in March 2007, indicated that the access grafts of patients given Trinam® remained functional for dialysis, on average, up to three times longer than in untreated controls. Trinam® was well tolerated with no quantifiable systemic distribution of the product found and no serious side effects were exhibited other than those consistent with the nature of the operation and underlying condition.

Dr David Eckland, R & D Director of Ark, commented: *"Qualifying and validating batch release assays in advanced biologicals is pioneering work and is part of the evolving process of developing and improving the quality controls for these breakthrough drugs as they move nearer to market. The work requires considerable scientific capabilities and again our Finnish unit has demonstrated its capabilities in developing this potency assay."*

Nigel Parker, CEO of Ark, added: *"Following finalisation of the test work and acceptance of the assay by the FDA, we are delighted now to be commencing patient recruitment in the Phase III trial for Trinam®. Maintenance of graft access for kidney dialysis patients is vital for their survival, making this an area of high clinical need for which we are hopeful that this pioneering gene-based medicine can provide a solution. With our other lead product, Cerepro®, now filed for regulatory approval in Europe, Ark's portfolio continues to make strong progress towards the market."*

## ***Enquiries***

### **Ark Therapeutics Group plc**

Dr Nigel Parker, Chief Executive Officer  
Martyn Williams, Chief Financial Officer

Tel: +44 (0)20 7388 7722

### **Financial Dynamics**

David Yates / Sue Quigley

Tel: +44 (0)20 7831 3113

## ***Notes to Editors***

### **Trinam®**

Trinam® is a combination of a vascular endothelial growth factor gene in an adenoviral vector (Ad-VEGF-D) and Ark's biodegradable local delivery collagen collar device (EG001). At the end of the access graft surgery procedure, the collar is fitted around the outside of the vein/graft join. The Ad-VEGF-D solution, which reduces the likelihood of blood clots and intimal hyperplasia, is then injected into the space between the wall of the collar and the blood vessel. This unique method of administration of the gene localises its delivery to the target tissue site, maximising efficacy, avoiding systemic distribution and thus minimising the potential for side effects.

### **Ark Therapeutics Group plc**

Ark Therapeutics Group plc is a specialist healthcare group (the "Group") addressing high value areas of unmet medical need within vascular disease, wound care and cancer. These are large and growing markets, where opportunities exist for effective new products to generate significant revenues. With four marketed devices, Kerraboot®, Kerraped®, Flaminal® and Neuropad®, and three further lead pharmaceutical products in late stage clinical development: Cerepro®, Vitor™, and Trinam®, the Group is transitioning from an R&D company to a commercial, revenue generating business.

Ark's own products are sourced from related but largely non-dependent technologies within the Group and have been selected to enable them to be taken through development within the Group's own means and to benefit from Orphan Drug Status and/or Fast Track Designation, as appropriate. This strategy has allowed the Group to retain greater value and greater control of clinical development timelines, and to mitigate the risks of dependency on any one particular programme or development partner. Ark has secured patents or has patent applications pending for all its lead products in principal pharmaceutical markets.

Ark has its origins in businesses established in the mid-1990s by Professor John Martin and Mr Stephen Barker of University College London and Professor Seppo Yla-Herttuala of the AI Virtanen Institute at the University of Kuopio, Finland, all of whom play leading roles in the Company's research and development programmes.

Ark's shares were first listed on the London Stock Exchange in March 2004 (AKT.L).

*This announcement includes "forward-looking statements" which include all statements other than statements of historical facts, including, without limitation, those regarding the Group's financial position, business strategy, plans and objectives of management for future operations (including development plans and objectives relating to the Group's products and services), and any statements preceded by, followed by or that include forward-looking terminology such as the words "targets", "believes", "estimates", "expects", "aims", "intends", "will", "can", "may", "anticipates", "would", "should", "could" or similar expressions or the negative thereof. Such forward-looking statements involve known and unknown risks, uncertainties and other important factors beyond the Group's control that could cause the actual results, performance or achievements of the Group to be materially different from future results, performance or achievements expressed or implied by such forward-looking statements. Such forward-looking statements are based on numerous assumptions regarding the Group's present and future business strategies and the environment in which the Group will operate in the future. Among the important factors that could cause the Group's actual results, performance or achievements to differ materially from those in forward-looking statements include those relating to Ark's funding requirements, regulatory approvals, clinical trials, reliance on third parties, intellectual property, key personnel and other factors. These forward-looking statements speak only as at the date of this announcement. The Group expressly disclaims any obligation or undertaking to disseminate any updates or revisions to any forward-looking statements contained in this announcement to reflect any change in the Group's expectations with regard thereto or any change in events, conditions or circumstances on which any such statements are based. As a result of these factors, readers are cautioned not to rely on any forward-looking statement.*

This information is provided by RNS  
The company news service from the London Stock Exchange

END