

## **Circadian subsidiary terminates licence to Ark Therapeutics**

### **- To also initiate arbitration against Ark's subsidiary Lymphatix Oy -**

- Ark licence terminated for non-payment of licence fees
- Ark claims license to use Vegenics' IP in Trinam™ through subsidiary Lymphatix. Strongly disputed by Circadian
- Circadian action instigated now to ensure clarity of rights prior to Ark's sales of Trinam™

Circadian Technologies Limited (ASX:CIR), a developer of novel, biologics-based treatments for cancer, announced today that its subsidiary Vegenics Limited has terminated the licence previously granted to Ark Therapeutics Limited, under its VEGF-D gene therapy intellectual property (IP) to exploit Ark's product Trinam™. The licence was terminated for non-payment of fees.

Trinam™, which is currently undergoing Phase 3 clinical trials, is a treatment being developed by Ark to extend the functioning of intravenous access grafts used by kidney dialysis patients.

Circadian, through Vegenics, will also commence arbitration proceedings against Ark's Finnish subsidiary, Lymphatix Oy, to rule out Ark's claim that it retains a license covering the use of Vegenics' IP in Trinam™ through Lymphatix (Lymphatix has a license from Vegenics for certain VEGF-C and VEGF-D gene therapy rights). Circadian is strongly of the view that Lymphatix, and therefore its parent Ark, have no rights to use Vegenics' IP to sell Trinam™ under the Lymphatix license.

Circadian has initiated these actions to ensure that these matters can be resolved and clarified before Trinam™ comes to the market in the next 2 to 3 years, assuming ongoing Phase 3 trials are successful.

Circadian expects that arbitration may take between 6 and 12 months and the associated time and costs are not expected to have a significant effect on management resources or on the overall operating expenditures of the company, respectively. Updates on the timetable will be provided as the process continues.

Robert Klupacs, CEO of Circadian said: "It is disappointing that it has been necessary to take this action to enforce our rights, despite our attempts to rectify the disputes with Ark and Lymphatix. We are confident in our position that neither Ark nor Lymphatix have rights to market

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Trinam™ using our VEGF-D technology through the Lymphatix license which we expect to resolve through the arbitration process.”

“Addressing this issue now, before Trinam™ completes Phase 3 studies and/or obtains marketing approval, will enable all parties to get clarity for their shareholders in respect of any future revenues that may arise from this product.”

“We take the enforcement of our intellectual property rights very seriously, however this dispute is unrelated to the company’s major assets which are our three novel anti-cancer therapies in development: VGX-100, VGX-200 and VGX-300 as well as our partnered programs with ImClone Systems Inc and Healthscope Limited. These will remain the business focus for our management team.”

### **Background relating to the License Agreements**

In 2001 the Ludwig Institute for Cancer Research (“LICR”) and Licentia Ltd granted Ark Therapeutics Limited a non-exclusive licence under its VEGF-D intellectual property to exploit the VEGF-D gene therapy combination product, now branded as Trinam™ by Ark, in return for an upfront fee, minimum annual royalties, product development milestone payments and royalties on sales (“the Ark License”). Ark Therapeutics Limited, a wholly owned subsidiary of Ark Therapeutics Group plc (LSE:LKT; market capitalisation of £94 million), is developing Trinam™ to inhibit the closure of vascular grafts in renal dialysis patients.

In 2004 LICR and Licentia (the commercial arm of the University of Helsinki) together with founding scientists formed the Finnish company Lymphatix Oy. LICR and Licentia granted that company an exclusive licence under its VEGF-C and VEGF-D intellectual property to develop VEGF-C and VEGF-D gene therapy products (“the Lymphatix License”). It is Circadian’s position that the Lymphatix License expressly excludes rights previously granted to a third party.

In 2007 LICR and Licentia assigned all of their interest in VEGF-C and VEGF-D intellectual property to Vegenics Limited. The Ark License and the Lymphatix License were also novated to Vegenics with Vegenics taking over all rights and responsibilities as licensor.

In 2008 Lymphatix Oy was acquired by Ark Therapeutics Limited and is now a 100% owned Finnish based subsidiary of Ark.

In 2009 Vegenics issued Ark with its annual invoice for payment of the minimum royalty in accordance with the Ark License. Ark, which had paid all previous years’ fees, refused to pay the 2009 fee. Ark considers that it does not require the Ark License as it owns Lymphatix, which it considers has the rights to market Trinam™ using Vegenics’ VEGF-D intellectual property.

In October 2009 due to:

- Ark failing to remedy its breach of the Ark License for non-payment; and
- Vegenics being unable to resolve the dispute over the scope of rights granted to Lymphatix under the Lymphatix License,

Vegenics terminated the Ark License. Vegenics is now in the process of initiating arbitration under the dispute resolution provisions of the Lymphatix License to resolve the dispute on contract interpretation.

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## **About Circadian Technologies Limited**

Circadian (ASX:CIR) is a biologics drug developer utilising the significant intellectual property portfolio around Vascular Endothelial Growth Factor (VEGF) C and D that it has accumulated in its unlisted wholly owned subsidiary Vegedics. The applications for the VEGF technology, which functions in regulating blood supply, are substantial and broad. Circadian's internal product development programs are focussed 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 to ImClone Systems (a wholly owned subsidiary of Eli Lilly & Company - NYSE: LLY). ImClone Systems is currently developing an antibody-based drug targeting VEGFR-3 for the treatment of solid tumours.

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

## **About VEGF Technology and angiogenesis**

### **In Cancer**

The clinical and outstanding commercial success of Avastin®, an antibody that blocks the activity of VEGF-A, clinically validated anti-angiogenic drugs as an effective means of inhibiting solid tumour growth. By blocking the interaction of VEGF-A with its receptors, primarily VEGFR-2, the multi-billion dollar cancer therapeutic slows tumour growth by inhibiting blood vessel recruitment into the tumour, effectively starving tumours of essential nutrients and oxygen required for growth. Avastin®, which is sold by Genentech, now part of Roche, and Hoffman-La Roche, had U.S. sales in 2008 of US\$2.7 billion and worldwide sales in excess of US\$7.5 billion.

VEGF-C and VEGF-D inhibitors, key therapeutics in the portfolio of Circadian's unlisted subsidiary Vegedics, blocks the alternative ligands for VEGFR-2. As such, they have the potential to block blood vessel growth in tumours resistant to anti-VEGF-A therapy and, when used in combination with drugs like Avastin, may completely shut down angiogenesis (the growth of blood vessels) mediated by VEGFR-2, resulting in greater clinical efficacy.

VEGF-C and VEGF-D also bind and activate VEGFR-3 which drives lymphatic vessel and tumour-associated blood vessel growth. Inhibitors of VEGF-C, VEGF-D and VEGFR-3 thus have therapeutic potential to inhibit not only primary tumour growth through their anti-angiogenic activities, but to also inhibit tumour spread or metastasis via the lymphatic vessels - a mechanism of tumour dissemination that is often the deadliest aspect of many tumour types and a mechanism that is not effectively blocked by anti-VEGF-A or anti-VEGFR-2 therapeutics.

### **Other Disease Applications**

VEGF Technology also has applications in other diseases, where shutting down angiogenesis and/or lymphatic vessel growth is important, such as eye diseases including age related macular degeneration and diabetic retinopathy.