

## ASX / Media Release

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### **CIRCADIAN PARTNERS WITH CINCINNATI CHILDREN'S HOSPITAL IN U.S. TO DEVELOP BLOOD TEST DIAGNOSTIC FOR POTENTIALLY FATAL LUNG DISEASE**

- First non-invasive diagnostic to test for LAM – a serious lung disease that often goes undiagnosed
- Data published in CHEST shows VEGF-D levels key to successfully diagnose the lung disease lymphangioleiomyomatosis (LAM).
- Testing to become available in the U.S. from early 2011, through CCHMC
- Circadian retains rights to rest of world

Circadian Technologies (ASX.CIR) has announced today that it has partnered with Cincinnati Children's Hospital Medical Centre (CCHMC) to develop and market a blood test to diagnose LAM, a serious lung disease that strikes women, usually in their child bearing years.

The diagnostic is being developed following the discovery that high levels of vascular endothelial growth factor-D, or VEGF-D – to which Circadian owns intellectual property rights – holds the key to detecting the disease.

The test is expected to be available in the U.S. from early 2011, and Circadian will work with CCHMC and other groups throughout the world to make the test available in other global markets.

LAM, which is short for lymphangioleiomyomatosis, is a serious lung disease that affects women, causing shortness of breath and lung collapse. The disease occurs when an unusual type of cell invades the lungs and causes tissue destruction by creating holes or cysts in the lung. It can be fatal and the only known treatment is a lung transplant.

To date, LAM has been difficult and expensive to diagnose, usually requiring a biopsy or high resolution CT scan. Due to low awareness of LAM, the early symptoms are often mistaken for other respiratory conditions such as asthma, bronchitis or emphysema.

Although only a small number of patients have been diagnosed with LAM to date the recent discovery of a link between LAM and the genetic abnormality, *Tuberous Sclerosis Complex (TSC)*, has led scientists to estimate that more than 250,000 women worldwide are unaware they have LAM.

The availability of this non-invasive diagnostic test may eliminate the need for a surgical lung biopsy to diagnose LAM, significantly improving the quality of life in women who may be suspected LAM sufferers. It will also be helpful in screening for LAM in women with TSC, a genetic disorder that causes tumours to form in many different organs. TSC is a risk factor for the development of LAM.

Robert Klupacs, CEO of Circadian Technologies said he is very proud to be working with the team from CCHMC to make a test available that offers straightforward and accurate identification of LAM.

“This test will be able to reduce, and hopefully, remove the need for surgical intervention for accurate diagnosis of LAM which we believe will have a huge impact on the quality of life for women who may have this terrible disease. Being able to provide an early indication of LAM, particularly in those who have the genetic disorder, TSC, should greatly assist in helping these patients to manage their condition.”

“The development of this test adds to the portfolio of diagnostics in development by Circadian and our partners. Diagnostics is an important part of Circadian’s business that is progressing in parallel to our drug development activity, as a source of early potential revenue and to complement our product portfolio.”

The findings of the diagnostic link between LAM and VEGF-D were made by a team of scientists at the University of Cincinnati (UC) and CCHMC led by Dr Lisa Young and Dr Frank McCormack, Director of Pulmonary, Critical Care and Sleep Medicine at UC and were published in the August 2010 edition of CHEST<sup>1</sup>.

Dr Frank McCormack stated that “These findings are the result of a team effort by clinicians around the world to collect blood samples and clinical data from patients with very rare lung diseases.

“Through their efforts and the generosity of patients who participated, we are optimistic that this new diagnostic, serum VEGF-D, will join the ranks of diagnostic tests for lung disease, reduce the need for surgical lung biopsy and allow for intervention and trial recruitment earlier in the disease course.”

Circadian controls exclusive worldwide rights to an extensive intellectual property portfolio enabling it to develop diagnostic tests to detect VEGF-D.

“We look forward to working with the Cincinnati team and other groups to make this test also available outside the United States in the near future,” concluded Mr Klupacs.

*Company Enquiries:*

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

*Media Enquiries – Australia:*

Kyahn Williamson  
Buchan Consulting  
Tel: +61 (0) 3 9866 4722  
[kwilliamson@bcg.com.au](mailto:kwilliamson@bcg.com.au)

*Media Enquiries – International:*

Lauren Glaser  
The Trout Group LLC  
251 Post Street, Suite 412  
San Francisco, CA 94108  
Tel +1 215 740 8468  
[lglaser@troutgroup.com](mailto:lglaser@troutgroup.com)

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<sup>1</sup> Chest (2010) Sep; 138(3) pp674-81

## **About Circadian Technologies Limited**

Circadian (ASX:CIR) is a biologics drug developer focusing on cancer therapies. It controls exclusive worldwide rights to a significant intellectual property portfolio around Vascular Endothelial Growth Factor (VEGF) C and D. The applications for the VEGF technology, which functions in regulating blood and lymphatic vessel growth, 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.

## **About Circadian's pipeline of treatments for 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, had U.S. sales in 2009 of US\$5.7 billion and worldwide sales in excess of US\$8.6 billion. Avastin is approved by the US FDA in the following indications: metastatic colorectal cancer, non-squamous-cell lung cancer, metastatic breast cancer, glioblastoma, metastatic renal cell carcinoma.

The VEGF-C inhibitor, VGX-100, a key therapeutic in Circadian's portfolio, block this alternative stimulator for VEGFR-2. As such, it has 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 along with the molecule VEGF-D. are also the only known proteins to bind and activate VEGFR-3 which drives lymphatic vessel and tumour-associated blood vessel growth. Inhibitors of VEGF-C 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.

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### **Inherent risks of Investment in Biotechnology Companies**

There are a number of inherent risks associated with the development of pharmaceutical products to a marketable stage. The lengthy clinical trial process is designed to assess the safety and efficacy of a drug prior to commercialisation and a significant proportion of drugs fail one or both of these criteria. Other risks include uncertainty of patent protection and proprietary rights, whether patent applications and issued patents will offer adequate protection to enable product development, the obtaining of necessary drug regulatory authority approvals and difficulties caused by the rapid advancements in technology. Companies such as Circadian are dependent on the success of their research and development projects and on the ability to attract funding to support these activities. Investment in research and development projects cannot be assessed on the same fundamentals as trading and manufacturing enterprises. Thus investment in companies specialising in drug development must be regarded as highly speculative. Circadian strongly recommends that professional investment advice be sought prior to such investments.

### **Forward-looking statement**

Certain statements in this ASX announcement may contain forward-looking statements regarding Company business and the therapeutic and commercial potential of its technologies and products in development. Any statement describing Company goals, expectations, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to certain risks and uncertainties, particularly those risks or uncertainties inherent in the process of developing technology and in the process of discovering, developing and commercialising drugs that can be proven to be safe and effective for use as human therapeutics, and in the endeavor of building a business around such products and services. Circadian undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events, or otherwise. Actual results could differ materially from those discussed in this ASX announcement.