ASX / Media Release

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FDA GRANTS HUMANITARIAN USE DEVICE DESIGNATION TO VEGF-D KIT

- **Proprietary VEGF-D kit designated for HUD status in LAM**
- **Fast-tracks FDA approval**
- **FDA registration dossier to be lodged before year end.**

Circadian Technologies (ASX.CIR; OTCQx:CKDXY) announces that the US FDA has designated its VEGF-D assay kit as a humanitarian use device (HUD), for "the detection of circulating VEGF-D intended to monitor patients who have been diagnosed with lymphangioleiomyomatosis (LAM) for disease progression and response to therapeutic intervention."

LAM is a debilitating lung disease which affects young women world-wide, with estimates at between 1,000-3,000 women in the United States and 100-300 in Australia. VEGF-D circulating in the blood has been shown to be a unique biomarker of this disease.[1,2]

Similar in concept to the FDA's designation of orphan drug status to therapeutic drugs, an HUD is defined by the FDA as a medical device intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in fewer than 4,000 individuals in the United States per year. HUD designation enables formal approval of a HUD using a regulatory approval process known as a Humanitarian Device Exemption (HDE).

The HDE process greatly accelerates marketing approval in the United States compared to conventional routes (PMA and 510(k)) as formal clinical studies to show effectiveness in the approved indication are not required to be submitted. Circadian is currently completing the development of kits to be manufactured under current Good Manufacturing Practice (cGMP) and plans to submit its HDE application before year end.

The VEGF-D diagnostic is being developed as an enzyme-linked immunosorbent assay (ELISA), which is ideally suited to laboratory testing and could be used at pathology or hospital laboratories world-wide. The ELISA kit quantitates circulating levels of VEGF-D, which have been shown to be significantly elevated in patients afflicted with LAM. Recently, rapamycin has been shown to be an

[1] Young LR, Lee H-S, et al., Performance of serum VEGF-D as a biomarker of Lymphangioleiomyomatosis severity and treatment response: A prospective analysis from the MILES Trial. Lancet Respir. Med. 2013; doi:10.1016/S0140-6736(08)61345-8

[2] Young LR, VanDyke R, et al. Serum Vascular Endothelial Growth Factor-D Prospectively Distinguishes Lymphangioleiomyomatosis from Other Diseases. Chest. 2010; 138(3): 674-681.

effective treatment for LAM and monitoring the condition of these patients using VEGF-D as a biomarker provides physicians with a valuable tool to assist in their treatment strategy.

Robert Klupacs, CEO of Circadian said "We are delighted to have received HUD designation for our VEGF-D kit. It fast-tracks our FDA approval process while minimising development costs and provides the opportunity to conduct clinical studies while the kit is on market generating revenue. In addition, a similar registration dossier can be submitted for CE Mark, providing access for sales in the European Union. We expect to complete our regulatory submissions before the end of 2013."

He added, "LAM is an incredibly debilitating condition with limited treatment options. Recent studies have shown that VEGF-D is a useful biomarker for LAM disease. We are proud that we have been able to develop the VEGF-D kit, which offers the opportunity for improving the quality of life for LAM patients."

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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.

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.