ASX and Media release

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VGX-100 Phase 1 Clinical Trial Program Update in Oncology presented at the 15th International Symposium on Anti-Angiogenic Therapy

Circadian Technologies Limited (ASX:CIR, OTCQX:CKDXY) announces that Dr Lee Rosen, MD, Health Sciences Clinical Professor of Medicine, UCLA Santa Monica Hematology / Oncology, who is a principal investigator on the VGX-100 (human anti-VEGF-C antibody) Phase 1 clinical trial in oncology, presented a trial update over the weekend at the 15th International Symposium on Anti-Angiogenic Therapy: Recent Advances and Future Directions in Basic and Clinical Cancer Research held in San Diego, California.

This annual symposium run by the University of Texas MD Anderson Cancer Center, is designed to continue interactions between research and clinical investigators by reviewing the current scientific understanding of vascular biology and angiogenesis. In addition, this international symposium provides a forum for presenting the most current preclinical and clinical updates on emerging anti-angiogenic agents and regimens.

In the oral presentation entitled "Phase I trial of VGX-100, an anti-VEGF-C monoclonal antibody, with or without Bevacizumab" Dr Rosen, discussed the scientific rationale for VGX-100 in oncology, reviewed the Phase 1 trial design and provided an interim clinical update. To date more than 30 patients have received weekly VGX-100 at doses ranging from 1 to 20 mg/kg. A copy of the presentation is attached.

The Phase 1 clinical trial is being conducted under an Investigational New Drug (IND) application at 2 sites in the USA in patients with advanced or metastatic solid tumours and is a dose escalation study of VGX-100 +/- bevacizumab (Avastin®). The primary objective of the clinical study is to establish the safety profile of VGX-100 while secondary objectives include determination of anti-tumour activity, biomarker levels and pharmacokinetics of VGX-100.

Circadian previously reported the commencement of the Phase 1 clinical study of VGX-100 with the first patient enrolled in January, 2012. Completion of the remaining patient enrolment for the clinical trial is expected in Q1, 2013. Phase 2 studies with VGX-100 are expected to commence in Q4 2013.

Circadian controls exclusive worldwide rights to an extensive intellectual property portfolio enabling it to commercially develop antibodies targeting VEGF-C. In addition, Circadian recently created a 100% owned subsidiary company, Ceres Oncology Pty Ltd, to specifically focus on the development of VGX-100 as a cancer therapy.

VGX-100 was recently rated by the leading pharmaceutical market research group, Windhover Conferences, a division of Elsevier Business Intelligence, as one of the Top 10 Oncology Projects to Watch in 2013.

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About Circadian Technologies Limited

Circadian (ASX:CIR; OTCQX:CKDXY)) is a biologics drug developer focusing on cancer, cancer related and ophthalmic disease 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 primarily focused on developing VGX-100 (a human antibody against VEGF-C) as a treatment for solid tumours, in particular glioblastoma and colorectal cancer, as well as developing VGX-300 (soluble VEGFR-3) for 'back of the eye' disease such as wet Age Related Macular Degeneration. 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 and Company, including the anti-lymphatic antibody-based drug IMC-3C5 targeting VEGFR-3.

About Circadian's pipeline of treatments for cancer

The clinical and 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. However after a short period of time tumors can begin to grow again in the presence of Avastin®. Avastin® is approved by the US FDA in the following indications: metastatic colorectal cancer, non-squamous-cell lung cancer, metastatic breast cancer, glioblastoma, and metastatic renal cell carcinoma.

The angiogenic receptor VEGFR-2 can also be stimulated by VEGF-C and hence an inhibitor such as VGX-100, a key therapeutic in Circadian's portfolio, can produce greater blockade of this receptor pathway. As such, VGX-100 has the potential to block blood vessel growth in tumours which grow in the presence of Avastin® therapy and hence may completely shut down angiogenesis (the growth of blood vessels) mediated by VEGFR-2.

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.

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 statements

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 endeavour 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.