

ASX and Media release

30 January 2012

VGX-100 identified as potential new therapy for improving corneal graft survival

- Data published in the scientific journal *Investigative Ophthalmology & Visual Science* generated by investigators at The Schepens Eye Research Institute led by Harvard University Professor Reza Dana.
- VEGF-C markedly up-regulated in corneal graft rejection.
- VGX-100 significantly improved corneal graft survival in a mouse corneal graft model.
- Data indicates potential opportunity for VGX-100 as a therapeutic for major unmet clinical need of improving corneal graft survival.

Melbourne, Australia January 30, 2011– Circadian Technologies Limited (ASX: CIR, OTCQX:CKDXY) announced today the publication of data in the scientific journal, *Investigative Ophthalmology & Visual Science (IOVS)*, showing that VEGF-C expression is markedly up-regulated in corneal graft rejection. Importantly the data also showed that VEGF-C blockade, through administration of Circadian’s lead development candidate VGX-100, a human antibody against VEGF-C, significantly improved corneal graft survival in an animal model. The data indicates a major new therapeutic opportunity for VGX-100 to improve corneal graft survival.

The manuscript entitled “Vascular Endothelial Growth Factor-C Promotes Alloimmunity by Amplifying Antigen Presenting Cell Maturation and Lymphangiogenesis” *IOVS Papers in Press*, published as manuscript iovs.11-8668 is accessible via the *Investigative Ophthalmology and Visual Science* website (www.iovs.org)

The Eye Bank Association of America reports that more than 40,000 corneal transplants are performed annually in the United States (Statistical Report on Eye Banking activity for 2008. *Eye bank Association of America; 1-25, 2009*). While most grafts take very well it is estimated that between 10 and 30% of grafts will be rejected within 6-12 months, particularly in “at-risk” patients who have a highly vascularized eye bed or in whom a graft has previously failed. Improving graft survival in these “at-risk” patients is a major unmet clinical need.

The study, which was led by Professor Reza Dana and Dr Amir R. Hajrasouliha, of the Schepens Eye Research Institute, Harvard Medical School Department of Ophthalmology, showed that VEGF-C was markedly upregulated in rejected corneas and that administration of VGX-100 was able to significantly improve corneal graft survival.



Prof Reza Dana, MD MSc MPH Claes Dohlman Chair in Ophthalmology, Professor of Ophthalmology, Harvard Medical School, Co-Director of Research at Schepens Eye Research Institute and senior author of the study said "Corneal grafting can have enormously positive results for patients who may otherwise become blind. While grafting success has improved significantly over the past 20 years there are still a large number of grafts which continue to fail. Our findings demonstrating that VEGF-C is up-regulated in graft failure and that blockade of VEGF-C could significantly improve graft survival identify VEGF-C blockade as an exciting new therapeutic possibility for improving corneal graft survival."

Mr. Robert Klupacs, CEO of Circadian Technologies, said: "This very exciting data generated by our collaborators at Schepens provides a significant new therapeutic development opportunity for our VGX-100 program in addition to our ongoing clinical oncology programs. We are currently undertaking additional preclinical studies with VGX-100 in the corneal grafting setting with the aim to commence clinical trials in H1 2013."

Circadian's wholly owned subsidiary, Vegemics Pty Ltd, owns worldwide rights to an extensive intellectual property portfolio covering the angiogenesis and lymphangiogenesis targets VEGF-C, VEGF-D and the receptor protein VEGFR-3. Vegemics has also been granted exclusive worldwide rights to intellectual property filed by Schepens Eye Research Institute covering the use of anti-lymphangiogenic molecules for the treatment of Dry Eye Disease.

Company and media enquiries

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



About Circadian Technologies Limited

Circadian (ASX:CIR; OTCQX:CKDXY) is a biologics drug developer focusing on cancer and 'front of the eye' 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 focussed 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 for 'front of the eye' disease such as corneal neovascularisation and/or dry eye disease applications. 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 antibody-based drug IMC-3C5 targeting VEGFR-3.

About Schepens Eye Research Institute

Schepens is a subsidiary of the Foundation of the Massachusetts Eye and Ear Infirmary,

Founded in 1950 by famed retinal surgeon Charles L. Schepens, M.D., Schepens Eye Research Institute, Massachusetts Eye and Ear is one of the largest eye research institutes in the United States and an affiliate of Harvard Medical School. Since its inception, it has trained more than 600 postdoctoral fellows in various disciplines of eye research; trained more than 500 eye surgeons who now practice around the world; and published more than 4,600 scientific papers and books about health and eye disease.

Schepens Eye Research Institute, Massachusetts Eye and Ear fights blindness by developing new technologies, therapies and knowledge to retain and restore vision. Through a continuum of discovery, the Institute works toward a future in which blindness is prevented, alleviated, and, ultimately, cured.

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. 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 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.

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

Level 1 10 Wallace Avenue Toorak Victoria 3142 Australia

T +61 (3) 9826 0399 F +61 (3) 9824 0083 www.circadian.com.au

ABN 32 006 340 567



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 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.