ASX and Media release

13 September 2011

VGX-100 identified as potential new therapy for Dry Eye Disease

- Data published in the scientific journal Archives of Ophthalmology generated by investigators at The Schepens Eye Research Institute led by Harvard University Professor Reza Dana.
- VGX-100 significantly reduced inflammation and corneal epitheliopathy in a mouse model of Dry Eye Disease.
- Data indicates major potential opportunity for VGX-100 as a therapeutic for Dry Eye Disease.

Melbourne, Australia September 13, 2011– Circadian Technologies Limited (ASX: CIR, OTCQX:CKDXY) announced today the publication of data in the scientific journal Archives of Ophthalmology showing that its lead development molecule VGX-100, a human antibody against the angiogenic and lymphangiogenic molecule VEGF-C, can significantly reduce inflammation and corneal tissue damage associated with Dry Eye Disease (DED). The data indicates a major new therapeutic opportunity for VGX-100 in the DED setting.

The manuscript entitled “Blockade of Prolymphangiogenic Vascular Endothelial Growth Factor C in Dry Eye Disease” Arch Opthamol. Dol:10.1001/archopthamol.2011.266 is accessible via the Archives of Ophthalmology website (http://archopht.ama-assn.org)

DED is a complex, immune-mediated disorder of the ocular surface that has multiple causes and affects about 5 million Americans above the age of 50 years. It is estimated that 10% of Australians will suffer from the condition at some point in their lives. DED severely impacts the vision-related quality of life and the symptoms, including persistent dryness, burning, light sensitivity, pain and blurred vision, can be both psychologically and physically debilitating. The current therapeutic options for DED are limited and mostly palliative. Currently, topical cyclosporine-A is the only approved treatment for DED.

The study, which was led by Professor Reza Dana and Dr. Sunali Goyal of the Schepens Eye Research Institute, Harvard Medical School Department of Ophthalmology, showed that administration of VGX-100 was able to significantly reduce inflammation, lymphangiogenesis and corneal damage in a mouse model of DED.

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 "Dry Eye Disease is suffered by millions of people in the U.S but current treatments have significant limitations, and effective treatments are not available for many patients. This current study builds on our previous findings demonstrating

that VEGF-C, VEGF-D and VEGFR-3 are upregulated in DED corneas, and demonstrates for the first time that an anti-lymphatic effect, caused by the blockade of VEGF-C, has significant beneficial effects in treating the condition. We strongly believe that blocking lymphangiogenic molecules could become a major new paradigm for the treatment of DED".

Mr. Robert Klupacs, CEO of Circadian Technologies, said: "We have always believed that blockade of VEGF-C will have clinical utility in a variety of conditions, in addition to treating solid tumours. This very exciting data generated by our collaborators at Schepens offers significant opportunities for us to leverage our investment in the VGX-100 oncology program and undertake additional preclinical and clinical development activities for VGX-100 in DED, a disease which still remains extremely difficult to treat".

Circadian's wholly owned subsidiary, Vegenics 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. Vegenics has also been granted exclusive worldwide rights to intellectual property filed by Schepens Eye Research Institute covering the use of anti-lymphangiogenc molecules for the treatment of DED.

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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 Dry Eye Disease

Dry Eye Disease (DED) is a complex, multifactorial, immune-mediated disorder of the ocular surface affecting about 5 million Americans above the age of 50 years [1, 2]. Millions more suffer from manifestations which are precipitated under adverse environmental conditions such as low humidity. DED severely impacts the vision-related quality of life and the symptoms can be both psychologically and physically debilitating [1]. The current therapeutic options for DED are limited, mostly palliative and costly [3]. Currently, topical cyclosporine-A is the only approved treatment for this disease [1].

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.

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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 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.

1. *Research in dry eye: report of the Research Subcommittee of the International Dry Eye WorkShop.* Ocular Surface, 2007. **5**(2): p. 179-193.
2. Schaumberg, D.A., et al., *Prevalence of dry eye syndrome among US women.* Am J Ophthalmol, 2003. **136**(2): p. 318-26.
3. Reddy, P., O. Grad, and K. Rajagopalan, *The economic burden of dry eye: a conceptual framework and preliminary assessment.* Cornea, 2004. **23**(8): p. 751-61.

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