

ASX and Media release

28 January 2015

US Patent Granted for Soluble VEGFR-3 Traps

- **1980 days of patent term adjustment (PTA) awarded extending patent expiry to 22 June 2026**
- **Patent coverage for soluble VEGFR-3 fusion proteins, such as OPT-302**
- **Equivalent patents granted in Europe, Japan, Canada and Australia**

MELBOURNE, Australia – Wednesday, 28 January 2015: Circadian Technologies Limited, through its wholly-owned subsidiary Vegenics Pty Ltd, is pleased to announce the grant of US Patent Number 8,940,695 on 27 January 2015. This US patent protects compositions containing soluble VEGFR-3 fusion proteins, such as OPT-302. Circadian is developing OPT-302 for the treatment of wet AMD (age-related macular degeneration) through its wholly-owned subsidiary Opthea Pty Ltd.

In our Media Release of 23 September 2014, we advised of the expected award of substantial patent term adjustment (PTA) on this patent. We are pleased to confirm that the US Patent Office has awarded 1980 days PTA, which extends the patent expiry date for US 8,940,695 to 22 June 2026.

The equivalent patent case has already been granted in Europe, Japan, Canada and Australia.

Circadian has a further patent family directed to the OPT-302 molecule which has the potential to extend the patent protection for this molecule out to 2034.

OPT-302 blocks VEGF-C and VEGF-D and inhibits the hallmarks of wet AMD in preclinical models, including blood vessel growth and vessel leakage. Wet AMD is the leading cause of blindness for people over the age of 50 in the US and Europe and is estimated to affect over 1.5 million people worldwide, with an estimated market of \$5BN in the US alone.

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About Circadian Technologies Limited

Circadian (ASX:CIR; OTCQX:CKDXY) is a biologics drug developer focusing on 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 OPT-302 (formerly VGX-300, soluble VEGFR-3) for 'back of the eye' disease such as wet age-related macular degeneration (wet AMD). 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 Wet AMD

Wet (neovascular) age-related macular degeneration, or wet AMD, is a disease characterised by the loss of vision in the middle of the visual field caused by degeneration of the central portion of the retina (the macula). Abnormal growth of blood vessels below the retina, and the leakage of fluid and protein from the vessels, causes retinal degeneration and leads to severe and rapid loss of vision.

Wet AMD typically affects individuals aged 50 years or older, and is the leading cause of blindness in the developed world. The prevalence of AMD is increasing annually as the population ages. Sales of the drug Lucentis® (Roche/Novartis), which targets VEGF-A but not VEGF-C, were over \$US3BN in 2012. Sales of EYLEA™ (Regeneron/Bayer), which also targets VEGF-A but not VEGF-C first marketed in November 2011 for the treatment of wet AMD, were \$US1.4BN in 2013 and are forecast to reach \$US1.7BN in 2014. Approximately half of the people receiving Lucentis®/Eylea® are classified as non-responders or 'poor' responders and experience no significant gain in vision and/or have persistent retinal vascular leakage. There is great opportunity to improve patient responses by targeting more than one factor involved in disease progression. Existing therapies, such as Lucentis®/Eylea®, target VEGF-A that promotes blood vessel growth and leakage through its receptor VEGFR-2. VEGF-C can also induce angiogenesis and vessel leakage through the same receptor. Combined inhibition of VEGF-A and VEGF-C, has the potential to improve patient response by more effective inhibition of the pathways involved in disease progression.

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.