ASX and Media Release
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Circadian receives IND approval from FDA to initiate clinical trial of OPT-302 for wet AMD patients

Melbourne, Australia – Circadian Technologies Limited (ASX:CIR, OTCQX:CKDXY) through its wholly owned subsidiary Opthea Pty Ltd is pleased to announce that the US Food and Drug Administration (FDA) has approved its Investigational New Drug (IND) application to initiate its Phase 1 clinical trial of OPT-302 in patients with wet age-related macular degeneration (wet AMD).

Circadian's CEO and Managing Director Dr Megan Baldwin said "The FDA's acceptance of our IND for the Phase 1 clinical trial of OPT-302 is a major milestone for the Company. It is the result of a detailed review by the FDA of our non-clinical data package including preclinical safety/toxicology, efficacy testing and manufacturing processes for OPT-302, as well our Phase 1 study design. We look forward to bringing this important novel therapy to wet AMD patients for whom there remains a significant unmet medical need."

Opthea's first-in-human multi-centre clinical trial is a sequential dose escalation study of OPT-302 administered to patients with wet AMD on a monthly basis for three months by ocular injection either alone or in combination with ranibizumab (Lucentis®). The primary endpoint of the study will be an assessment of the safety and tolerability of OPT-302. Secondary endpoints include the pharmacokinetic profile of OPT-302 as well as preliminary measures of clinical efficacy as measured by visual acuity (eye charts) and sophisticated imaging techniques to determine retinal thickness and wet AMD lesion area using optical coherence tomography (OCT) and fluorescein angiography.

David Boyer MD, a Senior Partner at Retina-Vitreous Associates Medical Group and Clinical Professor of Ophthalmology at the University of Southern California Keck School of Medicine, and one of the clinical trial investigators, commented "We are excited to be participating in this Phase 1 clinical study of OPT-302 as it is a promising novel therapy with potential to improve outcomes for wet AMD patients."

OPT-302 is a soluble receptor or 'Trap' molecule that blocks the activity of two proteins (VEGF-C and VEGF-D) that cause blood vessels to grow and leak. In preclinical models of wet AMD, OPT-302 demonstrates significant activity as a monotherapy and additive activity when used in combination with existing agents that block VEGF-A.

Dr Baldwin commented "We are aggressively pursuing the development of this molecule following the compelling preclinical activity we have observed. Importantly, OPT-302 shuts down two proteins that are implicated in resistance to existing therapies. Our hope is that we can improve vision in patients with wet AMD when it is administered alone, and/or improve outcomes for patients when it is used in combination with existing therapies."

Wet AMD is the leading cause of blindness in the elderly in the Western world and is caused by excessive growth and leakage of blood vessels at the back of the eye that leads to a chronic and often rapid loss of vision. Existing therapies for the disease are limited and target VEGF-A but not VEGF-C or VEGF-D, and approximately half of those patients experience sub-optimal improvement in their vision following treatment.

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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, VEGF-D and VEGFR-3. 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 IMC-3C5, a monoclonal antibody targeting VEGFR-3.

About Wet AMD

Wet (neovascular) age-related macular degeneration, or wet AMD, is a disease characterised by the loss of vision of 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 $US4BN in 2014. 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 over $US1.8BN 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 as well as through an independent pathway. 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.