ASX and Media release

3 December 2014

Circadian Announces Formation of Clinical Advisory Board

- **Formation of initial Clinical Advisory Board comprising internationally recognised and experienced key opinion leaders from Australia and US**
- **Advisors bring breadth of experience in drug development of emerging and FDA approved ophthalmic therapeutics for wet AMD, including Macugen®, Fovista®, Eylea® and Lucentis®**
- **Provides key scientific, clinical and regulatory strategic guidance for the OPT-302 ophthalmic development program which is on-track to initiate a Phase 1 clinical trial in 2Q 2015**

MELBOURNE, Australia – 3 December 2014: Australian biologics drug developer, Circadian Technologies Limited (ASX:CIR, OTCQX:CKDXY) today announced the formation of a Clinical Advisory Board (CAB) focused on the development of its VEGF-C/-D 'trap', OPT-302, for the treatment of ophthalmic diseases including wet age-related macular degeneration (wet AMD).

The CAB will provide insight into the regulatory and clinical development strategy for OPT-302. Dr Megan Baldwin, CEO and Managing Director of Circadian Technologies stated, "We have assembled an impressive group of internationally recognised key opinion leaders who will be instrumental in assisting us move this important clinical program forward. The quality of the members of the CAB is testimony to the potential of OPT-302 to address the unmet medical need for patients with wet AMD."

The CAB will initially be comprised of four members, including:

Pravin Dugel, MD – Managing Partner of Retinal Consultants of Arizona, founding member of the Spectra Eye Institute and Clinical Professor, Department of Ophthalmology, Keck School of Medicine, University of Southern California

Mark Gillies, MBBS, PhD - Professor of Retinal Therapeutics, Save Sight Institute, University of Sydney/Professor of Clinical Ophthalmology

Peter Campochiaro, MD - Professor of Ophthalmology and Neuroscience, Johns Hopkins Wilmer Eye Institute

Kameran Lashkari, MD – Associate Professor, Schepens Eye Research Institute at Harvard Medical School/Massachusetts Eye and Ear

The CAB will work closely with Circadian's management team as the company prepares to initiate a Phase 1 clinical study at US sites under an IND in 2Q 2015. The CAB will provide scientific, clinical and regulatory advice for the OPT-302 program as well as invaluable perspectives on ophthalmic drug development and commercialisation strategies.

"The combined experience of the advisory group in the development of novel and commercially approved therapeutics, including Macugen®, Fovista®, Eylea® and Lucentis®, will provide tremendous guidance to the OPT-302 clinical development program. We look forward to welcoming additional members to the CAB following selection of sites and investigators for the Phase 1 clinical trial. This process is actively underway with invaluable input from existing advisors" said Dr Ian Leitch, Director of Clinical Research, Circadian.

Circadian's key advisors in ophthalmology also include Dr Emmett Cunningham (Chairman of the Ophthalmology Innovation Summit, San Francisco), Dr Denis O'Shaughnessy (formerly Senior Vice President of Clinical Affairs at Oraya Therapeutics, clinical consultant to Xcovery Vision and founding member of Eyetech Pharmaceuticals), Dr David Worsley (retinal ophthalmologist, Hamilton Eye Clinic, New Zealand) and Dr Robert Finger (retinal ophthalmologist, Royal Victorian Eye and Ear Hospital and Centre for Eye Research Australia).

Circadian is developing OPT-302 for the treatment of wet AMD, the leading cause of blindness in the Western world with significant unmet medical need and large market opportunity. OPT-302 is a soluble receptor that 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.

Detailed biographies of each CAB member:

Pravin Dugel, MD
Dr Dugel serves as Managing Partner of Retinal Consultants of Arizona and Founding Member of the Spectra Eye Institute. He is also Clinical Professor, Department of Ophthalmology, Keck School of Medicine, University of Southern California (USC). Dr Dugel is internationally recognised as a major clinical researcher having served as Principal Investigator for over 50 multicenter clinical trials for emerging and subsequently FDA approved therapies for wet AMD, including Fovista®, Lucentis® and Eylea® and was recently named "one of the best 35 ophthalmologists in the USA" by the Becker Institute.

Dr Dugel graduated Summa Cum Laude from Columbia University and attended UCLA School of Medicine. He then completed his residency in ophthalmology at the Doheny Eye Institute, USC School of Medicine. Thereafter, he completed his medical retina fellowship at the Bascom Palmer Eye Institute and his surgical retina fellowship at the Doheny Eye Institute, where he was elected to serve on the faculty as the Resident Director.

Dr Dugel has authored more than 200 papers, 35 book chapters and has been invited to lecture at prestigious meetings, visiting professorships and universities worldwide. He is on the Editorial Board of several major journals. His research and educational contributions earned him the prestigious Senior Honor Award from the American Academy of Ophthalmology (AAO).

Dr Dugel is on the Board of Directors of the American Society of Retina Specialists (ASRS), Chairman of the ASRS Research and Therapeutics Committee and Chairman of the AAO Media Relations Committee. Internationally, he is on the Board of Directors of the Asia Pacific Vitreoretinal Society. Dr Dugel has received numerous awards including amongst others, the Heed Foundation Fellowship Award, The Ronald G. Michels Surgical Fellowship Award, AAO Senior Honor Award, ASRS Honor Award and the AAO Secretariat Award.

Prof Mark Gillies, M.B.B.S, PhD., F.R.A.N.Z.C.O.
Professor Mark Gillies is a retinal clinician with a 25 year history of laboratory and clinical research in retinal disease. He was the first Australian ophthalmologist to be awarded a PhD, which he received for his work on diabetic retinopathy at the Walter and Eliza Hall Institute. Having trained in ophthalmology at Prince of Wales Hospital he moved to the University of Sydney's Save Sight Institute, after a period of sabbatical study in Boston and London, where he is currently a Sydney Medical School Foundation Fellow.

Directing the Macular Research Group at the University of Sydney, Mark Gillies is a clinician-scientist with an interest in developing improved treatments for macular disease, particularly macular oedema, and degenerative macular conditions. Professor Gillies is the Scientific Manager of the MacTel Project, an international project to identify a cure for Macular Telangiectasia Type 2. He has been a scientific advisor to the Macular Photocoagulation Study group, the world's leading investigator initiated study group for retinal diseases, and the United States' National Eye Institute-funded Diabetic Retinopathy Collaborative Research Network. Dr Gillies serves as the Vice Chairman of the Board of the Ophthalmic Research Institute of Australia and has also served on the Board of the Fred Hollows Foundation since its inception in 1992. In addition, he is on advisory boards and has received research support from Bayer, Novartis and Allergan. He has more than 140 publications, mostly concerned with the treatment of macular diseases and retinal cell biology.

Peter Campochiaro, MD
Dr Campochiaro is the George S. and Dolores Dor Eccles Professor of Ophthalmology and Neuroscience at the John Hopkins Wilmer Eye Institute. He was trained at the University of Notre Dame, Johns Hopkins School of Medicine, the University of Virginia, and Wilmer, joining the Wilmer Faculty in 1991.

Dr Campochiaro is a clinician-scientist with an interest in understanding the molecular pathophysiology of ocular neovascularization and vascular leakage with the goal of developing new treatments for retinal diseases. His laboratory research group helped to demonstrate the importance of the vascular endothelial growth factor (VEGF) pathway in retinal and choroidal vascular diseases and as a clinician he has had significant experience in many of the clinical studies evaluating anti-VEGF-A therapies such as Lucentis® (Genentech/Roche) and Eylea® (Regeneron/Bayer). As a respected and prominent clinical researcher, Dr Campochiaro serves as a member of the Scientific Advisory Boards of Asclepix Therapeutics, CoMentis, Inc., Eyegate Pharmaceuticals, Inc, Potentia Pharmaceuticals and RXi Parmaceuticals. Dr Campochiaro has more than 300 articles published in peer-reviewed medical journals.

Kameran Lashkari, MD
Dr. Lashkari currently holds several academic positions including Clinical Assistant Scientist, Schepens Eye Research Institute and Clinical Instructor of Ophthalmology at Harvard Medical School. He is Assistant in Ophthalmology at the Massachusetts Eye and Ear Infirmary.

Dr Lashkari received his medical degree from New York Medical College and is board certified in the fields of ophthalmology and internal medicine. He completed his Internal Medicine residency at St. Vincent's Hospital and Medical Center in New York City, and his Ophthalmology residency at the University of Missouri Eye Foundation of Kansas City. Dr Lashkari completed medical and surgical fellowships in vitreoretinal disease at Massachusetts Eye and Ear Infirmary, Harvard Medical School, and Schepens Retina Associates. In addition, he has completed a research fellowship at Schepens Eye Research Institute.

Company and media enquiries

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About Circadian Technologies Limited
Circadian (ASX:CIR; OTCQX:CKDXY) and its 100% owned subsidiary Opthea Pty Ltd 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.