

ASX and Media release

14 Jan 2014

Opthea Signs Cell Line Commercial License Agreement with Selexis

Circadian Technologies (ASX:CIR; OTCQX:CKDXY), through its 100% owned subsidiary Opthea Pty Ltd (Melbourne, Australia), today announced that it has signed a commercial license agreement with Selexis SA (Geneva, Switzerland) covering the use of the CHO-M Cell Line and related technologies for the production of Opthea's lead molecule OPT-302 (formerly VGX-300).

OPT-302 is a soluble form of human VEGFR-3 in development for the treatment of "wet" (neovascular) age-related macular degeneration (wet AMD) and on-track to initiate a Phase I clinical trial by early 2015.

A copy of the joint Opthea/Selexis press release is attached.

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About Circadian Technologies Limited

Circadian (ASX:CIR; OTCQX:CKDXY) is a biologics drug developer focusing on cancer, cancer related and ophthalmic disease therapies. It controls exclusive worldwide rights to a significant intellectual property portfolio around Vascular Endothelial Growth Factor (VEGF)-C and -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 VGX-100 (a human antibody against VEGF-C) as a treatment for lymphedema resulting from breast cancer treatment and solid tumours, in particular glioblastoma and colorectal cancer, as well as developing OPT-302 (soluble VEGFR-3) for 'back of the eye' disease such as "wet" Age Related Macular Degeneration through its subsidiary Opthea. 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.

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About Opthea Pty Ltd

Opthea Pty Ltd is a private, 100% owned subsidiary of Circadian Technologies Limited based in Melbourne, Australia. Opthea is developing novel biologic inhibitors of VEGF-C driven angiogenesis (blood vessel growth), lymphangiogenesis (lymphatic vessel growth) and vascular leakage for the treatment of ophthalmic diseases.

Opthea's compounds have broad utility in a range of eye diseases characterised by aberrant blood and/or lymphatic vessel growth, vascular leakage or edema, and inflammation, including wet AMD, diabetic macula edema, corneal neovascularisation and transplantation, and dry eye disease.

Opthea's lead compound, OPT-302, is a soluble receptor that specifically and potently blocks the activity of two members of the vascular endothelial growth factor family, namely VEGF-C and VEGF-D that are involved in the progression of both retinal and corneal diseases. Opthea's lead program is the development of OPT-302 for the treatment of "wet" (neovascular) age-related macular degeneration (wet AMD).

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. Sales of the drug Lucentis® (Roche), which targets VEGF-A but not VEGF-C, were over \$US3B 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 \$US838M in 2012 and are forecast to reach \$1.3BN in 2013. Approximately half of the people receiving Lucentis®/Eylea® are classified as non-responders or 'poor' responders and experience no 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.

A preclinical model of "wet" AMD has demonstrated that VEGF-C blockade can significantly inhibit disease progression and that low levels of VEGF-C during development affects formation of the retinal vessels. Like VEGF-A, VEGF-C can also induce vessel permeability that leads to vascular fluid and protein leakage. Inflammatory cytokines associated with wet AMD upregulate VEGF-C levels, and increased levels of the receptors for VEGF-C are detected in AMD tissue. VEGF-C is strongly implicated in the progression of wet AMD.

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.



ASX and Media Release
January 14, 2014

Opthea Signs Cell Line Development Commercial License Agreement with Selexis SA for Wet AMD Product

Geneva, Switzerland and Melbourne, Australia January 14, 2014 – Selexis SA, a serial innovation company focused on drug discovery for lead identification and cell line development for scale-up and manufacturing of therapeutic protein drugs announced today that Opthea Pty Ltd has entered into a commercial license agreement with Selexis covering the use of the CHO-M Cell Line and related technologies for the production of OPT-302 (formerly VGX-300), an Fc fusion protein for the treatment of wet Age-Related Macular Degeneration (wet AMD).

OPT-302 is a soluble form of human VEGFR-3 that blocks the activity of both VEGF-C and VEGF-D, which promote blood and lymphatic vessel formation and are implicated in the progression of eye disease. OPT-302 is anticipated to enter Phase I clinical studies in early 2015 and is being developed by Opthea, a private, 100% owned subsidiary of Circadian Technologies (ASX:CIR; OTCQX:CKDXY) of Melbourne, Australia.

“Wet” (neovascular) AMD, is a disease characterized 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, cause retinal degeneration and leads to severe and rapid loss of vision.

“Selexis is excited about the collaboration with Opthea and looks forward to seeing OPT-302 progress to clinical studies in wet AMD patients,” said Dr. Igor Fisch, CEO, Selexis SA. “The OPT-302 cell line demonstrates the power of our new technologies for the rapid generation of CHO cell lines expressing high yields of Fc fusion recombinant proteins. We look forward to continuing to work with Opthea.”

“The productivity and speed of stable cell line generation with the SUREtechnology Platform™ is playing a key role in quickly progressing our candidate into clinical development,” said Dr. Megan Baldwin, CEO of Opthea. “By leveraging the SUREtechnology Platform™, we were able to improve our titers by several fold.”

About Opthea Pty. Ltd.

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Opthea's compounds have broad utility in a range of eye diseases characterised by aberrant blood and/or lymphatic vessel growth, vascular leakage or edema, and inflammation, including wet AMD, diabetic macula edema, corneal neovascularisation and transplantation, and dry eye disease.

Opthea's lead compound, OPT-302, is a soluble receptor that specifically and potently blocks the activity of two members of the vascular endothelial growth factor family, namely VEGF-C and VEGF-D that are involved in the progression of both retinal and corneal diseases. Opthea's lead program is the development of OPT-302 for the treatment of "wet" (neovascular) age-related macular degeneration (wet AMD).

For more information:

Please visit Opthea's website at www.opthea.com

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About Selexis SA

Headquartered in Geneva, Switzerland, Selexis SA is a global life science company with innovative technologies and world-class expert services for drug discovery, cell line development and scale-up to manufacturing of therapeutic proteins. The Company's SUREtechnology Platform™ is based on Selexis Genetic Elements™ — novel DNA-based elements that control the dynamic organization of chromatin within all mammalian cells and allow for higher and more stable expression of recombinant proteins. Selexis has generated cell lines being used in a variety of programs from drug discovery to late-stage clinical trials.

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