Circadian’s partner Eli Lilly presents Phase 1 oncology clinical trial of VEGFR-3 antibody IMC-3C5 (LY3022856) at ASCO

Melbourne, Australia – Circadian Technologies Limited (ASX:CIR, OTCQX:CKDXY) is pleased to announce that its partner Eli Lilly has presented clinical data from the Phase 1 oncology clinical trial of the VEGFR-3 antibody IMC-3C5 (LY3022856) at the 2015 Annual Meeting of the American Society of Clinical Oncology (ASCO) in Philadelphia (USA).

IMC-3C5 (LY3022856) is a fully-human IgG1 monoclonal antibody being developed by Eli Lilly as a treatment for cancer. Eli Lilly has an exclusive license to Circadian intellectual property to develop the VEGFR-3 antibody. Eli Lilly pays Circadian an annual license fee and potential royalties on future product sales.

The First-in-Human oncology trial, run under an Investigational New Drug (IND) program with the Food and Drug Administration (FDA), completed enrolment with a total of 44 patients refractory to standard therapy in two parts: Part A dose escalation (dose levels 5, 10, 20 and 30 mg/kg) enrolled 23 patients with advanced solid tumors; Part B was an expansion cohort to evaluate IMC-3C5 (LY3022856) monotherapy at 30 mg/kg in 21 patients with colorectal cancer (CRC).

Weekly intravenous administration of IMC-3C5 (LY3022856) was shown to be well tolerated up to the highest planned dose of 30 mg/kg and a maximum tolerated dose (MTD) was not reached in the study. The pharmacokinetic profile of IMC-3C5 (LY3022856) was favourable with dose-related increases in exposure observed following weekly infusions. Overall, the most common treatment emergent side effects observed were nausea, fatigue, vomiting and anorexia.

In Part A, 4/8 patients with CRC refractory to standard therapy treated at 30 mg/kg had prolonged progression free survival (PFS) (10-39 weeks) while in Part B the median PFS was 6.3 weeks. Interestingly, biomarker analysis revealed an increase in soluble VEGFR-3 levels in patient plasma samples following IMC-3C5 (LY3022856) administration suggesting engagement with the VEGFR-3 target. Plasma VEGF-C and VEGF-D levels were not significantly changed following dosing.

IMC-3C5 (LY3022856) blocks VEGF-C/D activation of VEGFR-3, which inhibits blood and lymphatic vessel growth. IMC-3C5 (LY3022856) does not block VEGFR-2 which VEGF-C and VEGF-D also activate. Eli Lilly will consider future development of IMC-3C5 (LY3022856) in indications in which lymphatic vessel growth plays a prominent role.

A copy of the ASCO poster presentation is attached in the Appendix. In addition, the IMC-3C5 Phase 1 abstract can be found on the ASCO 2015 Annual Meeting website at: http://abstracts.asco.org/156/AbstView_156_143954.html. More information on the IMC-3C5 clinical trial (Study ID: NCT01288989) is available at www.clinicaltrials.gov.
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.

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.
Phase 1 Study of Anti-VEGF Receptor-3 (VEGFR-3) Monoclonal Antibody (mab) LY022856/IMC-3C5

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BACKGROUND

VEGF-A and VEGF-C, secreted by tumor lymphangiogenic activity in breast cancer treatment, is hypothesized to attract lymphangiogenesis. The results of VEGF-A or VEGF-C expression is higher in the majority of tumor blood vessels and cancer cells and is dependent, not dose dependent, of VEGF receptor (Part A and B) or co-receptor (Part A). 

METHODS

Tufts University School of Medicine, Tufts Cancer Center - Medical Center, Boston, MA; Illinois Cancer Care, Peoria, IL; University of Washington, Seattle, WA; Eli Lilly and Company, Bridgewater, NJ; Eli Lilly and Company, Indianapolis, IN; Eli Lilly and Company, New York, NY; Indiana University, Indianapolis, IN

PART A: Dose escalation (n = 23)

Tufts Cancer Center - Med Center, Boston, MA; Illinois Cancer Care, Peoria, IL; University of Washington, Seattle, WA; Eli Lilly and Company, Bridgewater, NJ; Eli Lilly and Company, Indianapolis, IN; Eli Lilly and Company, New York, NY; Indiana University, Indianapolis, IN

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Dose escalation (n = 23) study at the recommended phase II dose (RP2D)

• Advanced solid tumors without systemic therapy or for which no standard therapy is available (Part A).

• Measurable Part A and B or non-measurable (Part A) disease according to RECIST version 1.1 and/or biopsy confirmed (Part B) lymphatic oncology pathology.

• Tumor was evaluable (Part A) or treatable with investigational agent within 30 days prior to enrollment.

• Adequate hematological and visceral function (ECOG PS 0-2).

• Eastern Cooperative Oncology Group performance status (ECOG PS) score 0, 1, or 2.

• 18 years of age or older and the expiration within 3 months.

• Uncontrolled hyperthyroidism (TSH > 50 mIU/L).

• Adequate renal function (creatinine clearance > 50 mL/min).

Part IA/B: VEGFR3 (LY022856/IMC-3C5) was administered as a single IV bolus injection on a 28-day schedule on days 1 of cycles 1, 2, 3, and 4 of each 28-day cycle. The recommended phase II dose (RP2D) was determined based on the following criteria: dose-limiting toxicity (DLT) was defined as any toxicities of grade 3 or 4 (common terminology criteria for adverse events [CTCAE] v4.0) and occurred within the first 30 days after treatment. Maximum tolerated dose (MTD) was the dose at which either one or more dose-limiting toxicities occurred.

Other toxicities (e.g., non-dose-limiting toxicities [DLTs], dose modifications, dose interruptions [DI], and dose delays [DD]) were analyzed descriptively. Study completion was based on the last evaluable date at any time point after the last dose of study treatment. All data were analyzed descriptively using descriptive statistics at the 21-day or 28-day post-dose.