MD on FY13 Results & Outlook

Open Briefing interview with MD & CEO Robert Klupacs

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Circadian Technologies Limited (ASX:CIR, OTCQX:CKDXY) is an Australian biotechnology company developing biologics-based therapies for the treatment of cancer and eye diseases. Circadian owns a portfolio of products and intellectual property related to Vascular Endothelial Growth Factors (VEGFs), a class of proteins that play a critical role in regulating blood supply in tumours and other diseases.

In this Open Briefing®, MD & CEO Robert Klupacs discusses:

- FY2013 result and forecast FY2014 expenditure
- Ceres progress in VGX-100 Phase I update
- Opthea planned IND filing for VGX-300
- FY2014 royalty and license fees

Record of interview:

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Circadian Technologies Limited (ASX:CIR, OTCQX:CKDXY) booked net cash outflow of $5.38 million in FY2013 versus $5.74 million FY2012, partly reflecting the receipt of a $1.32 million R&D tax refund (FY2012 $0.62 million). Cash stood at $11.00 million as at 30 June 2013, down from $16.44 million a year earlier. What is your expected cash burn in FY2014 and do you have adequate cash to fund your planned activities over the next 12 to 18 months?

MD & CEO Robert Klupacs
We're targeting a cash burn of between $5 million to $8 million over the next 12 months, so we have at least 12- months of required capital in hand. Our actual annual spend will be influenced by the timing and size of our R&D tax refund from the Australian government and the progress and management of our two key drug development projects, as well as how quickly royalties and sales in our diagnostics and reagents business progress.

Also, as we noted in our FY2013 annual report, in addition to strong expense management, we will be seeking to augment our cash reserves in FY2014 by one of, or a combination of, IP licensing, sales of all or part of our investments in ASX listed companies and/or sale of equity in the parent company or subsidiaries.

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Total R&D expenditure, including personnel costs and other R&D support costs, was $5.20 million for the year (FY2012: $5.13 million). How was this spending divided across your three key areas of oncology, eye disease and clinical diagnostics and what will be the focus of your R&D spending in the current year?

MD & CEO Robert Klupacs
The spend ratio was approximately 45 percent for oncology, 45 percent for eye disease and 10 percent for clinical diagnostics. In the next 12 months we expect a higher proportion to be spent on the ophthalmology business given that we will be manufacturing and starting our

IND-enabling studies in the ophthalmology program.

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Ceres Oncology, your wholly owned subsidiary focused on developing VGX-100 in oncology applications, presented the progress of its ongoing Phase I trial of VGX-100 in patients with advanced or metastatic solid tumours at the June 2013 annual meeting of the American Society of Clinical Oncology (ASCO). Can you provide an update on the trial and expected completion date?

MD & CEO Robert Klupacs
We've progressed the Phase 1 trial since the ASCO update and we expect the last patient cohorts, both in the single agent VGX-100 arm of the trial and the combination VGX-100 plus Avastin® arm to complete enrolment in October. We have enrolled over 35 patients to date who have received VGX-100 at doses ranging from 1 to 30 mg/kg given weekly. So far VGX-100 appears to be well tolerated when used as a monotherapy and in combination with Avastin®, which is a key outcome for us to move into later stage clinical development. We also believe we've identified a dose of VGX-100 which provides biological coverage of the VEGF-C target, to take into our planned Phase II studies in breast cancer related lymphoedema and solid tumour indications.

In the ongoing Phase 1 clinical study, preliminary data from the first 25 patients indicates about a third of the patients have had a best tumour response of stable disease, with some showing durable responses of their disease not progressing for ≥ 15 weeks whilst on therapy. This is encouraging data given that these patients have advanced cancer that is refractory to standard treatments. Further detailed evaluation of VGX-100 alone or in combination with Avastin® in the later patient cohorts is ongoing and we plan to present the trial data at a major international oncology conference in the coming year.

We're excited about reaching the major clinical milestone of completing all Phase 1 patient enrolment in October, and that VGX-100 appears to be well tolerated without showing overlapping toxicities when combined with Avastin®. This milestone will allow us to quickly move into planned Phase 2 proof-of-concept clinical studies in patient populations with major unmet medical needs and in which VEGF-C is known to be an important mediator of the pathophysiology of the disease.

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What is the likely schedule for development of VGX-100 in other oncology applications, such as breast-cancer related lymphedema, and which applications look most promising in terms of potential partnering interest?

MD & CEO Robert Klupacs
Our current plan is to move into the lymphoedema setting first. As we've flagged previously, we're expecting to start those studies in the United States around January/February 2014 in order to get interim data about mid 2014. We'd like to get that data before we expand our Phase 2 studies into solid tumour indications. Assuming that time line, we'd expect to initiate a small Phase 2 study probably in Australia, of VGX-100 in combination with the FDA approved drug Avastin® in patients with recurrent glioblastoma multiforme around mid 2014.

We're also exploring the possibility of doing a Phase Ib/II study in patients with recurrent ovarian cancer using VGX-100 in combination with Taxol® chemotherapy, which could start around late 2014.

In terms of potential partnering interest, there are a group of companies very interested in the use of VGX-100 in the lymphedema indication, given their existing commercial strength in oncology supportive care. There are also several companies we have an ongoing dialogue with that are very interested in our approach of targeting VEGF-C with VGX-100 in solid tumour indications. They like the combination approach we're developing, particularly now that we've shown tolerability of VGX-100 with Avastin® which generates sales in excess

of US$6 Billion a year in oncology but is limited by tumour escape and relapse due to up-regulation of pro-angiogenic factors including VEGF-C.

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Opthea, your wholly owned subsidiary focused on developing VGX-300 in eye disease such as age-related macular degeneration (AMD), plans to submit an IND application for VGX-300 in AMD in late 2014. What further work is required before Opthea can submit the application and is the process on track to meet the planned time line?

MD & CEO Robert Klupacs
We're happy to say we remain on track to meet that time line. We're focused on preparing for the IND filing, including the manufacture of the drug to clinical grade quality and quantity. We need that material to undertake toxicology studies to comply with US Food and Drug Administration (FDA) guidelines for the safety testing of new biological agents. We also need to develop unique assays for both quality control drug release and for monitoring the effectiveness of our drug and how it's distributed in the human body. All of those activities are ongoing.

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US ophthalmology focused company Ophthotech Corporation recently filed an IPO application with the US SEC and its core product Fovista®, which is an anti-platelet-derived growth factor (anti-PDGF) agent for the treatment of wet AMD (in combination with Lucentis®, Eylea® or Avastin®), is due to start Phase III clinical trials later this year. Can you comment on VGX-300's competitive positioning versus Fovista®?

MD & CEO Robert Klupacs
Fovista® targets one part of the disease pathway involved in AMD and we're targeting a different pathway so we are not directly competing with Fovista®. The great thing for us about Fovista®'s development is that four to five years ago the concept of developing combination therapy for AMD was not being considered. The great results Ophthotech have achieved in its Phase II studies combining two agents in a safe way suggests that our concept of combining our drug with the existing agents is also valid.

Some of the data that's been generated with Fovista® is very exciting but we still think there's a very significant opportunity for better drug combinations for the 60 percent of patients with AMD who have been treated with existing agents or with existing agents and Fovista® but don't seem to experience sustained vision gain. Notwithstanding the benefits Fovista® has as a combination therapy, we believe very strongly that our combination can still have a major impact in improving vision in people with AMD.

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Your wholly owned diagnostics subsidiary Precision Diagnostics saw its revenue increase in FY2013, with group royalty and licence fee income totalling $622,701, up from $510,270. With your CUPGUIDE® cancer of unknown primaries (CUP) diagnostic test now released in Australia by marketing partner Healthscope, what is the outlook for royalty and licence income in FY2014?

MD & CEO Robert Klupacs
Our royalties have been hit over the last few years by the very strong Australian dollar, so the recent depreciation of the Australian dollar will have a positive impact on the size of royalties we receive. Also, we believe royalties will now start to flow from CUPGUIDE® over the next 12 months and that there will be continuing growth. At the same time, we now see our recently launched research reagents business getting some traction, with ordering interest increasing significantly now the northern hemisphere scientific community is returning from summer holidays.

This year we think it's also likely we'll form partnerships for CUPGUIDE® outside Australia, in Europe and the US, and we'd expect to be getting licence fees as well as royalties from

the test.

And finally, we expect the VEGF-D kit we recently announced had been granted humanitarian use device (HUD) status, will be approved by the FDA early in 2014, enabling us to expand sales of the kit and its uses. That product should also have a positive impact on our royalty revenue. We're optimistic that our royalty and licence income can reach seven figures in FY2014, with continued growth thereafter.

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Can you comment on how the restructure of the company into three focused business streams is impacting the progress of your key programs and their potential opportunities?

MD & CEO Robert Klupacs
The restructure has been good from a couple of perspectives. It's enabled our people to focus on their particular business segments and given them profit and loss accountability for their part of the business rather than having more blurred responsibilities across the whole spectrum. It's also helped our marketability in terms of specific business development activities and investor relations activities. We can now talk about one project at a time on a company by company basis and that's been very effective. Importantly, it's also allowed us to open up the dialogue for potential equity investment.

Investors have traditionally viewed Circadian as an incubator, and haven't attributed the full value of our technology to the public vehicle. But we think that's changing. The restructure has enhanced our ability to talk about potential partnering or investment into specific programs or businesses such as Opthea, Precision Diagnostics or Ceres Oncology and allows us to have different valuation discussions. It also allows us to have very specific dialogues with investors who want to focus on particular specialisations within Circadian rather than having their interest diluted across a larger combined Circadian conglomerate.

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Thank you Robert.

For more information about Circadian Technologies, visit www.circadian.com or call Robert Klupacs on (+61 3) 9826 0399

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