2 December 2015, Melbourne, Australia: Opthea Limited (ASX:OPT) has featured in the Eureka Report in an interview with Alan Kohler.

Eureka Report provides astute investors with strategies and advice to grow their wealth. Founded by Alan Kohler in 2005, Eureka Report is Australia's #1 online investment report and the partner of choice for hands-on investors.

A transcript of the interview is provided in the following pages.

To view the interview, please click on the link:
http://bcove.me/j3if0h8g

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About Opthea Limited

Opthea (ASX:OPT; 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. Opthea'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).

TRANSCRIPT

Eureka Report: DEC 2 2015
Opthea Limited, Megan Baldwin (MB) CEO & Managing Director
Alan Kohler (AK)

AK: G'day, Megan.

MB: Hi, Alan.

AK: Thanks for coming in.

MB: Thank you.

AK: Now, soon to be renamed Opthea.

MB: That's correct. Yes, we're going to rename Circadian Technologies, Opthea Limited. We had that resolution passed at our AGM this week.

AK: And the reason for that of course is that Opthea is the main subsidiary which does the macular degeneration work.

MB: Yes.

AK: So let's just go in to the background of that. You ran that subsidiary of Circadian up until you were appointed CEO 18 months ago, right?

MB: Yes. That's right. That's correct.

AK: And how long did you run that for?

MB: We created Opthea as a private subsidiary in Circadian in September 2012 and that was created to house the eye disease asset as a separate programme to what we had within Circadian. So Circadian at that time also had some diagnostics programmes and a cancer programme and so Opthea was created to really separate it out and give that programme its chance to be pitched to investors and analysts as a separate programme itself.

AK: And where did that programme come from?

MB: Well, our technology actually came out of the Ludwig Institute for Cancer Research here in Melbourne. There was intellectual property that came out of that group, which is where I did my PhD and have a background on this particular molecule, and we also got some intellectual property out of the University of Helsinki where there was a leading investigator there studying the role of VEGF-C (Vascular Endothelial Growth Factor C) and he created the first form of the drug that we're now developing and we've optimised that and we're moving it forward in to clinical trials and commercialisation.

AK: And in fact that drug has become the main thing in the company, right.

MB: That's right.

AK: Which is why the name is changing to Opthea.

MB: Exactly. So we've parked the oncology programme.

AK: Is that because those things failed?

MB: No, it's not that it failed. We got to a natural point in the oncology programme where we are now in a position to explore partnership opportunities for cancer development. But really what we saw emerge out of the eye disease programme was very interesting preclinical data showing that when we have our OPT-302 molecule and we test it in a mouse model of the wet AMD (Age-related Macular Degeneration) disease that it was very active in preventing the lesions growing in the mouse eye and was also able to block vessels leaking very, very effectively. And so what we found was a lot of investor interest and a lot of pharmaceutical company interest in the molecule and its activity, so we've restructured the company around developing that molecule and we're now a focussed company on this therapy for eye diseases, not just wet AMD but there's a potential across other eye diseases as well.

AK: So I'll get you to explain all the technology in detail in a moment.

MB: Sure.

AK: The other thing to talk about is the board renewal that's just taken place.

MB: Yes, yes.

AK: You've in fact got a whole new board.

MB: We have got a whole new board. We went to our AGM and at that time it coincided with a resolution for our Chairman to be re-elected. She decided not to go up for re-election at that meeting and we've had a significant number of board changes just this week. We've welcomed two new individuals to the board to join me. We now have three people on the board. The first one is Geoffrey Kempler. He's a very experienced biotechnology executive. He currently is CEO and Executive Chairman of Prana Biotechnology, but has a very deep bio… a business development expertise and very good US investor contacts around the world and he is also… he has a lot of experience on chairing a biotechnology company, so I'm very confident in his approach to the board and his role. We've also welcomed Michael Sistenich who has a very deep background in investment management and investment banking. He has run funds and also was involved in our fundraising which we completed in November 2014. A lot of investor contacts, again, a lot of capital market experience and he's a real asset to the company, just given that he knows our story and with his investment background. That is really a skill set that he is bringing to the board and that's really going to help facilitate us moving the programme forward in the most effective way.

AK: Right. So but you've lost three and gained two, is that it?

MB: We have at the moment, so we're currently a three person board, but we will be looking at expanding that in the near term and we're currently looking at a number of candidates that will bring complementary skill sets to this new board structure that we have at Circadian.

AK: Yeah. I'm sure it will be quite efficient for a while at three people.

MB: It is actually very efficient, but it's also exciting to know that we're building on our biotechnology relevant experience for the board and I think strategically that's going to be a real asset for the company.

AK: So tell us about the technology. You did your PhD on VEGF-D (Vascular Endothelial Growth Factor D) which is one of the causes of age-related macular degeneration, is that correct?

MB: Well, it's involved in making vessels grow, as is vascular endothelial growth factor C (VEGF-C). So our drug hits VEGF-C and VEGF-D and these are signals that tell blood vessels to grow and they tell vessels to leak. So what our drug does, when you inject it – and it's a drug that injected directly in to the eye at the site of the disease, it binds to both VEGF-C and VEGF-D and so in binding, it blocks the ability for those signals to tell vessels to grow. So the effect of that is that it can stop vessels from growing abnormally and stop those vessels from leaking. And in the disease process of wet age-related

macular degeneration or wet AMD these are the two key hallmarks of that disease. Patients that have wet AMD experience abnormal growth of vessels at the back of the eye and those vessels grow and they leak and that disrupts the tissue at the back of the eye and so when light hits that tissue, the signals to the brain cannot be effectively transmitted. There's a lot of cell death and inflammation that can also occur and that results in a chronic and very rapid loss of vision. It's largely a vision loss in the centre of the visual field, so patients lose their ability to read, drive a car, see their family members because that's the region of the eye required for sharp, detailed focussed vision. So we hope that by patients receiving this drug, either as a single agent where it's injected on its own or when it's injected with the existing therapies that are on the market currently, that we can improve upon the vision in those patients.

AK: So these other therapies that are on the market at the moment are Lucentis and Eylea?

MB: That's correct, yes.

AK: Now, there's a lot of money going in to those already, isn't there?

MB: Yes. They're huge blockbuster, successful drugs. Together they generated over $7 billion revenue last year. And the interesting thing about those two drugs is that they're the only two targeted therapies that are currently approved for the treatment of wet age-related macular degeneration (wet AMD), but they both target exactly the same molecule or signal and that molecule is VEGF-A (Vascular Endothelial Growth Factor A). What we offer with our drug is the ability to block different family members of the same pathway, so we're effectively shutting down the other half of the pathway that's not blocked by those existing therapies.

AK: So Lucentis and Eylea just do half the job, is that correct?

MB: Effectively they do only do half the job. They hit only one molecule or one signal that's involved. Patients that receive those drugs, many of them do well, but there's still room for improvement in vision.

AK: That exactly describes my mum.

MB: Right. It's a very common disease.

AK: Who has wet AMD and she's getting… I don't know which one of those things she's getting, but she's getting injections in her eye and sort of is improving a bit, but not entirely.

MB: That's exactly right. So what you see in many of these patients is that there's persistent leakage or fluid that can occur at the back of the eye because hitting only one signal that's involved in a very complex disease process is frequently not enough and more completely shutting down those processes may be indeed the answer to having a much more effective therapy. We are positioning our drug as adding on to what's already out there which means that entire market potentially is open to us. So patients will come to their clinic. They receive the existing therapy. Thirty minutes later, they receive a second injection with our drug and in doing that, we hope to much more completely block the signals that are involved in making the vessels grow and making the vessels leak and by doing that, we hope that their vision improves over time.

AK: So here's another question for you. My daughter has diabetic problems with her eyes.

MB: Right.

AK: Which is the blood vessels leaking blood in to the eye because of the diabetes, right.

MB: Right.

AK: Does your drug deal with that?

MB: We haven't got a programme in diabetic eye disease at this time.

AK: Or could it?

MB: Potentially it could. I think that's a really interesting development opportunity actually. Diabetic macular oedema (DME) is one disease which affects…

AK: That's what she's got.

MB: DME. So that's often called DME or diabetic macular oedema. And being an oedema disease – exactly what you said – it is characterised by a diabetes involvement that causes oedema or leakage. One of the key things about our drug is that it blocks signals that cause vessels to leak. So the existing therapies that are on the market have seen that they've got approval for wet AMD, but that's also translated in to efficacy in other diseases as well, including DME. So we're hopeful our drug will also have the potential to be used across those other diabetic eye diseases as well.

AK: So where are you at in the trials? I mean how far off being on the market are you?

MB: Our current clinical trial is a Phase 1/2a clinical study. There are clinical trials. As you know, they're run in essentially Phase 1, Phase 2, Phase 3. So we're in the earliest phases of clinical trials right now, but the clinical trial that we have going on is a very robust, good sized Phase 1/2a clinical study. By that I mean we are looking at the safety parameters around injecting the drug, but we've incorporated a lot of measures of activity of the drug as well. So we'll dose patients once a month for three months and that's a good number of months to dose these patients in the early trials in order to start, we hope, seeing evidence that our drug is actually having a benefit to patients.

AK: Where are you running it?

MB: We're running it completely in the United States at this point at trial centres that have access to a large geographical area servicing wet AMD patients. We're working with the leading clinical investigators from the US. Ophthalmology is a relatively small field of retinal specialists and it's important that we work with really the leading names and principal investigators who have experience in doing trials for the commercially successful drugs. That way we can most effectively and efficiently get our trials completed. So that's where we're doing our clinical trials. It's all being done under the US regulatory system which means that we've done all of our preclinical and manufacturing work to the highest regulatory standards, which is also important.

AK: Right. But so what's the sort of timeline that we are looking at?

MB: We expect the first clinical results from that study to be released late in the first quarter of 2016, so by April next year we'll put out some data around the first Phase 1 component of the study and then towards the end of next year we have a larger group of patients that will be dosed at the highest dose level and that's an additional 30 patients.

AK: Is that still Phase 1?

MB: That's called the 2a component, so it's a Phase 1/2a study, so we roll directly from the Phase 1 directly in to the Phase 2a component through the same clinical trial protocol. And that data is expected, as I said, at the end of next year. So near term clinical milestones are Phase 1, late March and then the larger, extra 30 patients by the end of the year. We're pretty excited given the trial is already up and running and recruiting patients with wet AMD and we're hopeful given the way we've designed the trial that we'll get very meaningful measures of whether or not we can improve vision or help to resolve fluid at the back of the eye in these patients as well, which are two very important parameters.

AK: Well, my mum is 84.

MB: Yes

AK: You're not going to get in to her eyes until she's 90.

MB: I'm not going to get in to her eyes?

AK: Yeah, her eyes. You know, fix her eyes up until she's 90, are you?

MB: So this is a disease of the ageing process, so it's typically said that it affects people over the age of 50 or 55. A lot of the people that have the more severe forms of wet AMD are over the age of 70, so…

AK: No, I'm just looking at the time it's going to take for you to…

MB: Oh, I see what you're saying, in terms of our development span.

AK: Yeah, to be on the market and injected in my mum's eye for five years or six years.

MB: The development process for therapies is indeed… it's usually a couple of years for Phase 2 and then two years to three years in this particular disease space for Phase 3, but as a company, we may consider exits or partnering licensing agreements or relationships to be entered in to prior to embarking on Phase 3. I take your point for getting to the market, but as a company in terms of potential licensing milestone agreements that we could potentially enter in to, it's a much shorter timeframe than that, so…

AK: Oh, so you could monetise it earlier.

MB: Earlier than getting to market.

AK: So you reckon you might be able to monetise it I assume – I'm inferring here – after the Phase 1/2a trial?

MB: Well, really I think the sweet spot for a company, pharmaceutical company partnership or joint venture or licensing agreement is often the end of a Phase 2b clinical study which is a larger randomised, controlled study which we also have funding to complete from our fundraising at the end of last year. But like you said, we will look at the results that we get from the earlier trial, the one that we've got currently going on, we'll look at those results, we'll assess it and we are currently also constantly updating potential partners, so that they're aware of our programme and if the conversations go well and our trial shows certain parameters that they're interested in, there's a potential for an earlier discussion, but we're going to play that by ear as we move on.

AK: So Sasha says… Let's go to the audience now. Sasha says, in the meantime how much cash are you burning? And what's the ideal path to cash flow positive?

MB: We're currently burning between $6 million and $7 million a year, but we get a good proportion of that back in an R and D tax rebate.

AK: Which you just got this very day.

MB: This very day we've just announced we got $3 million back from our R and D activities last year, so you can see from that the R and D tax credit rebate is around 43.5 per cent on all R and D activities, both conducted in Australia and internationally. So you can see that our development activities cost us last year around about the sort of $6 million to $7 million mark. So that's our cash burn. When are we cash positive? Well, drug development, as I said, is really focussed on exits at certain pivotal points in your clinical development programme. As a small company, we'd likely be looking to partner prior to getting in to Phase 3 because Phase 3 is such a, you know, a significant commitment to conduct those sort of sized trials.

AK: So who are the potential partners? Are we talking about the people who do Lucentis and the other drug, Eylea? Who are they? They're Eyetech Pharmaceuticals?

MB: Well, Eyetech is no longer around.

AK: Oh, right.

MB: They did the original Macugen molecule, so they were actually… they sold that asset off and they no longer exist. But the big potential partnerships, so yes, the marketers of the existing therapies, so we're looking at Genentech, Roche and Novartis for Lucentis, for Eylea it's Regeneron, Bayer and there are a number of other ophthalmology companies or companies that are looking to really build a pipeline in ophthalmology, so you're looking at, you know, large pharmaceutical companies like Allergan, Alcon, even Ophthotech who started as a private company very successfully, NASDAQ listed, has an interesting asset in development in Phase 3 and now has a valuation in excess of $1.8 billion, for example. You can see the potential uplift and those sorts of companies are also looking to build their pipelines as well. And we have a very interesting molecule in that we have the potential to be combined with not only a Lucentis or an Eylea to make their drugs work better, but other drugs that are coming through as well .

AK: Is there any guidance as to what these sorts of molecules produce in terms of corporate value in the US?

MB: So I think a great model is that… You know, it's often said that wet AMD is about a $10 billion worldwide market opportunity. That's just for wet AMD. And I think you can see that the real potential of that is supported by the current sales of Lucentis and Eylea which together they sold in excess of $7 billion last year. And it's a growing market opportunity as the population gets older. In addition, with this sort of family or class of drugs working well in wet AMD and the potential across those other diabetic eye diseases where there are also additional market opportunities, you can see in terms of the potential revenue streams, it's multibillion dollar potential there. It really will obviously depend on how amenable you are to combinations. And even a small piece of that pie which we anticipate we'll be able to potentially have the whole market open to us, but very large market opportunity by any way that you sort of cut and dice where the molecule may be used and how it may be used and in what proportion of patients. There's really a large opportunity.

AK: Yeah. Ben says, when you do make it to market, what is the strategy to break through when there are other drugs already being used?

MB: Yeah. I think this question of where does our drug fit in the landscape is best answered really relatively to what's out there now. We offer something that is very novel that we don't know of anyone else that has intellectual property. We have a very good controlling intellectual property position on these targets and we're not sure of anyone else who's working on a drug to block the same targets as us, so we have a differentiated mechanism. And the fact that we hit the other half of the pathway which is currently being addressed means that the clinical ophthalmologists and patients are familiar with the processes that these drugs target. So we think that that positions us very well for clinical use. And frankly there are a lot of other drugs being developed in this space that aren't competitive with us, but what they do or may offer down the track are alternative ways of delivering the existing therapies that are on the market. So we're not competing with that.

AK: So has anyone else got a molecule like OPT-302?

MB: Not that targets VEGF-C and VEGF-D. We really have the controlling IP position and therefore we are also the company that's the most advanced in terms of targeting those two signals. So it is differentiated, it is novel, but yet it hits a pathway that we know is involved in the disease process.

AK: And you've got just the right PhD.

MB: Well, my PhD was actually done on the function of VEGF-D, so I did a lot of the early characterisation work around what VEGF-D did and how it works to make vessels grow and how it works to be involved in tumour growth and eye disease. I then backed that I guess scientific background up by moving to San Francisco in 2002 and I undertook further postdoctoral studies working with the founder of VEGF-A and that was the company, Genentech, that also discovered and commercialised Lucentis as well as Avastin and these are really blockbuster drugs that work via a similar mechanism.

AK: So you were involved in the development of those drugs?

MB: I was involved in a lot of the basic research around our target as well as some of the development around Lucentis and Avastin, yes, and then I moved in to the commercial division, again, working on a similar pathway. So I have a research and commercial background on factors that target this pathway, yes.

AK: Serge wants to know, how important is it for those on your board and for you to have a scientific background in a company like yours?

MB: Yeah look, I think what you need on the board as well as in your management team and executives is a balance of backgrounds. I certainly joined the company as someone who had the commercial and research background on this particular pathway, but I'm complemented now with a board that has investment banking experience and business development experience. I've certainly done a lot of those activities over a number of years now, both at Genentech and at Circadian Opthea, but it is great to have that supported with people that bring new skills to the board. And, as I said, Geoffrey Kempler has also got a very deep background and US investor network. So I think it is important to have relevant biotechnology expertise, but not just spanning the science but spanning the timelines and the strategies around drug development as well. So I think it is a very selective, specific thing being on a biotechnology company's board, but you want a diversity of skills.

AK: Someone else wants to know, you've slated primary data analysis for the OPT-302 programme to be completed by second half 2016. What are the next steps in getting the products generated? Well, I think we've been through that kind of, haven't we?

MB: Yes.

AK: The next step will be…

MB: A larger Phase 2 clinical study.

AK: 2b?

MB: It's a 2b study and it's a randomised, controlled study, yes.

AK: Yeah. And then Phase 2?

MB: So that would be a Phase 2, so Phase 2b because it's a bigger Phase 2 study than what 2a is and along that whole path of development we keep the dialogue with potential partners or acquirers of the technology updated on our progress and they're certainly watching to see what results we'll be getting out of the clinical trial as well.

AK: And what's happened to the other things that Circadian was doing, the oncology things? Are they just sitting there or what?

MB: When we restructured the company, we took a very deep dive in to the commercial prospects and really the business model potential of all of those other assets. Certainly as a small company, you can't do everything and we didn't want to be spreading our cash and resources too thinly across too many things. I think it becomes important in a company's evolution to start to focus on really the lead

asset, so that you can then focus your attention and your cash on getting to meaningful clinical milestones with that asset. So what have we done with the oncology trial? That was an ongoing study where we conducted a Phase 1a, 1b clinical study in cancer patients. It's a different drug. It's an antibody drug only to VEGF-C, but that drug still sits within Circadian. It's a partnership opportunity and it's something that we can reinitiate partnership discussions. We've been focussed over the last 12 months really on advancing the eye disease asset, but it is still sitting within Circadian and in the IP and drug is a potential opportunity there. The diagnostics programmes, we had CUP and LAM programmes. They're essentially smaller opportunities, but they're being run and managed by our partners. So in the case of the LAM kit, it's the University of Cincinnati who can advance that.

AK: LAM?

MB: It's lymphangioleiomyomatosis diagnostic kit, doesn't matter.

AK: Well said.

MB: It's basically for the diagnosis of a rare lung condition. It's not a large market opportunity and that's why we've allowed the University of Cincinnati to manage that and then we don't lose our focus. And the CUP test is with Peter MacCallum [Cancer Institute] and Healthscope [Pathology] and so that also doesn't take our time nor our resources to move forward. And we're focussing on what we think is the real lead asset that has the best chance to return value for shareholders. As a small company, [it's] important for us to focus and that's what we've achieved recently.

AK: I suppose Geoffrey Kempler coming on the board as Chairman is a bit of an endorsement of what you're doing, more than a bit of one.

MB: Yeah, Geoffrey has a very strong background in biotechnology and he's looked very deeply in to our programme, as have a lot of our new investors that came on to our register with our capital raising at the end of last year. There's been a lot of due diligence by a lot of people on our programme and the potential of where this molecule sits in terms of other competitors and the market opportunity as well. Itt's really comforting to know that a lot of people have looked at it and dived in very, very deeply. Like you said, Geoffrey's background in this space is also I think a good endorsement of the potential of the technology as well.

AK: I had an idea that Prana also did something to do with the eyes, but it's not; it's entirely Alzheimer's, is it?

MB: I think at one point they may have been interested in that and I'm not sure of the status of their focus on that at this point in time.

AK: There's no talk about combining Opthea and Prana in some way?

MB: No. They're very separate. The role of Geoffrey as Chairman of Circadian is very separate to his role on Prana and he's really coming to Circadian because he has a lot to offer in terms of his strategic input to the company.

AK: Right. Well, if you're all done, I'm all done.

MB: Thank you.

AK: It's been great talking to you, Megan. Thanks very much for coming in.

MB: Thank you. Thank you.

AK: I've been talking to Megan Baldwin who's the Managing Director of Circadian Technologies, soon to become Opthea.