

AUSBIOTECH INVESTMENT SHOWCASE

MELBOURNE NOVEMBER 2 2012

**CIRCADIAN TECHNOLOGIES
LIMITED**

ASX:CIR, OTCQX:CKDXY

Robert Klupacs, CEO & Managing Director



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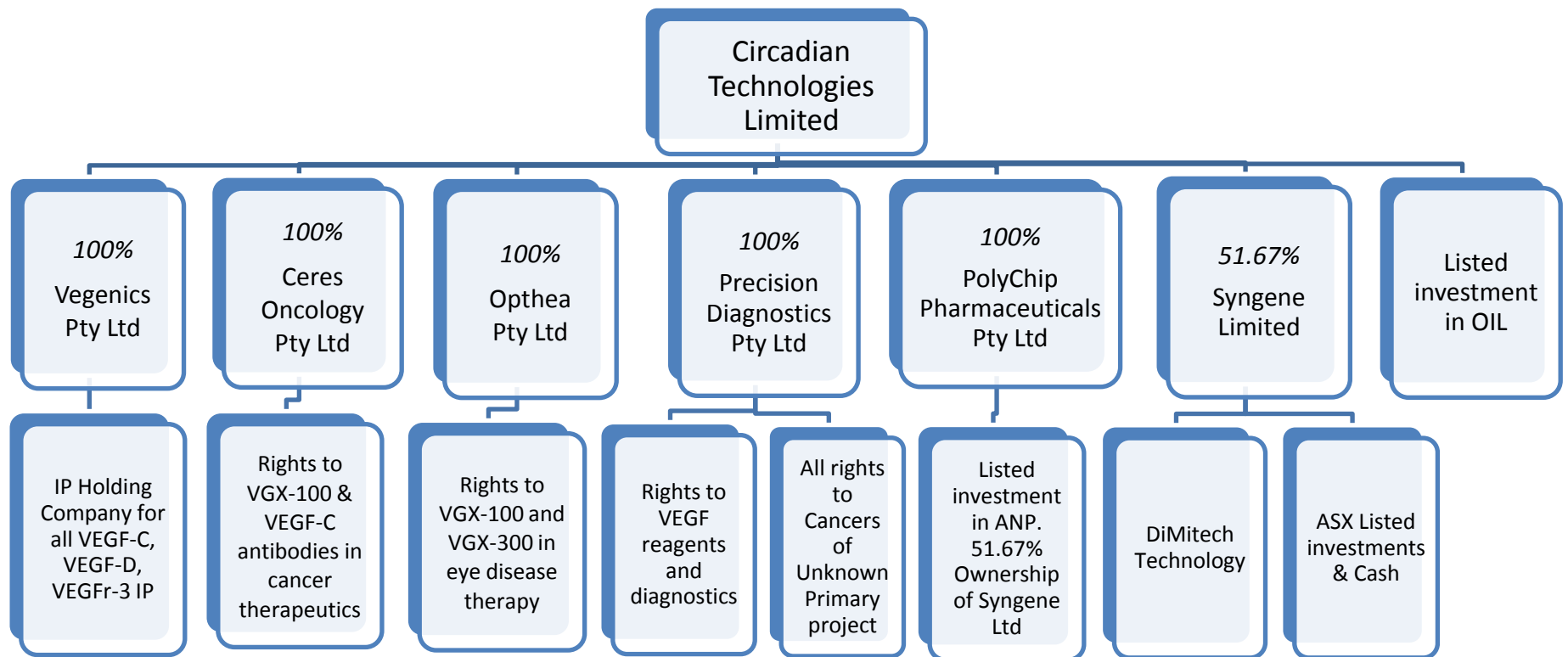
WHO WE ARE

An Australian based emerging clinical stage company developing human therapeutic and diagnostic products from our extensive and worldwide dominant intellectual property platform in respect of VEGF-C, VEGF-D and VEGFR-3 and key relationships with leading cancer and eye research organisations.

OUR PRODUCTS

- **Developing antibody therapies to treat cancer and eye disease**
 - » Based on unique ability to starve blood vessel and lymphatic vessel growth
 - » Targeting significant unmet clinical needs in oncology & ophthalmology
 - » Multi-billion dollar market opportunity
 - » Shown in range of tumour models to significantly improve chemotherapy responses
- **2 molecules currently in USA Phase 1 in cancer patients**
 - » VGX-100: Phase 2 to commence H1 2013 in brain cancer patients
 - » IMC-3C5: Being developed by Eli Lilly under licence
- **Clinical Trials in Eye diseases expected to commence H2 13**
 - » VGX-100 or VGX-300 in combination with Lucentis/Eylea for wet AMD
 - » Topical VGX-100 or VGX-300 in Dry Eye Disease
- **New generation cancer diagnostic – CUPGUIDE -developed in collaboration with Healthscope**
 - » Launched Q3 2012

OUR CORPORATE STRUCTURE



**OUR PRODUCTS ARE DESIGNED TO IMPROVE ON
EXISTING ANTI-ANGIOGENIC THERAPIES WHICH
TARGET VEGF-A**

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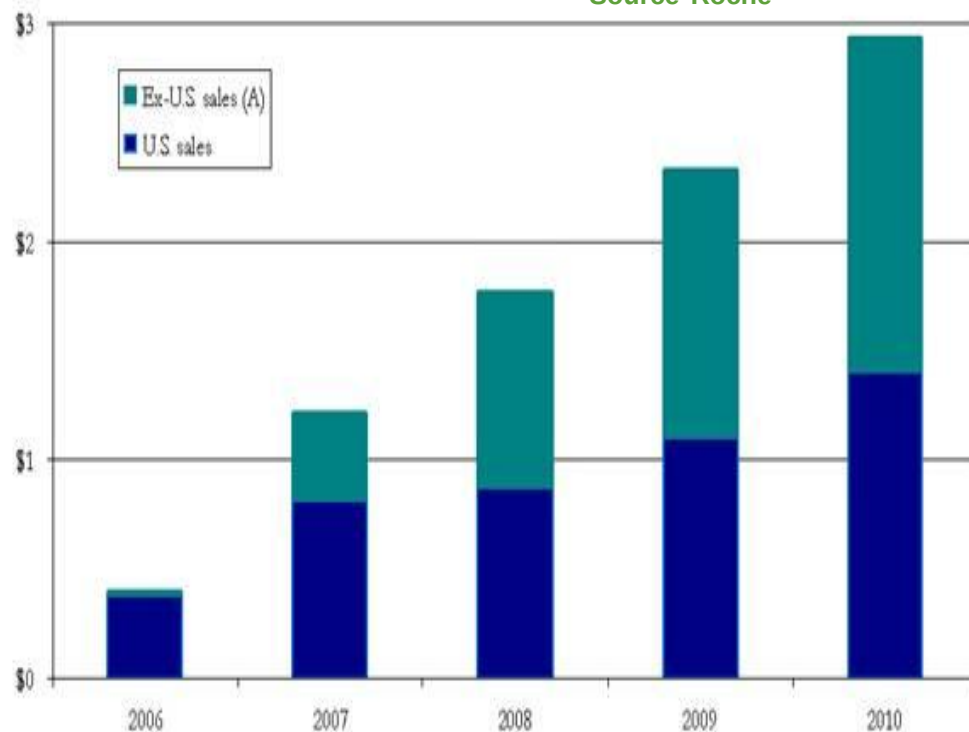


Avastin 2011 sales \$US5.8B (cancer)

Source Roche

Lucentis 2011 sales \$US2.9B (wet AMD)

Source Roche



OUR APPROACH

Combine a VEGF-C inhibitor (VGX-100/VGX-300) **with a VEGF-A inhibitor** (Avastin, Lucentis or Eylea) (or small molecule drugs which also target VEGF-A) to **improve and maintain inhibition** of new blood and/or lymphatic vessel growth to **treat cancers and various eye diseases.**

IMPROVING ANTI-ANGIOGENESIS

A MAJOR COMMERCIAL OPPORTUNITY

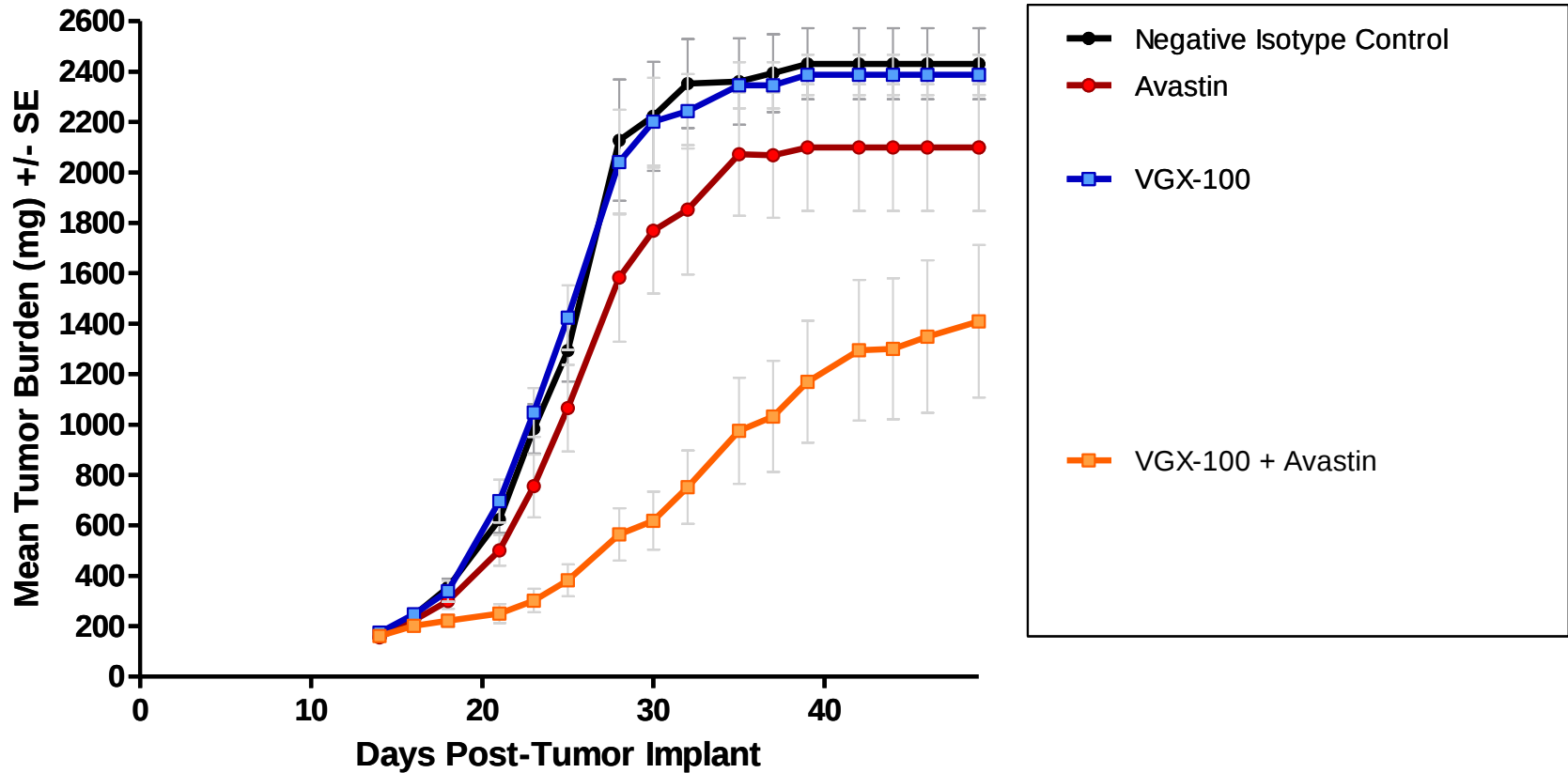
- Avastin[®] (a humanised VEGF-A Antibody):
- Effective but not in all patients
 - Not all patients respond to therapy (30-50% response rate)
 - 25-50% of responders become “resistant” within 12 to 18 months
 - Potential reasons:
 - Tumour growth due to factors other than VEGF-A; and/or
 - Other angiogenic factors being turned on when VEGF-A blocked
(i.e. VEGF-C, VEGF-D)
 - Acts only to “starve” tumours but does not target metastatic spread

IMPROVING ANTI-ANGIOGENESIS

A MAJOR COMMERCIAL OPPORTUNITY

- Lucentis® (a humanised VEGF-A Antibody):
- Approved for use in “wet” AMD (new blood vessel growth in retina causing leakage)
- Huge and Growing market due to aging
- Effective but not in all patients
 - Not all patients respond to therapy (50-70% response rate)
 - Potential reasons:
 - Blood vessel growth due to factors other than VEGF-A; and/or
 - Other angiogenic factors being turned on when VEGF-A blocked
(i.e. VEGF-C, VEGF-D)
 - Possible role of lymphatics

U87MG GLIOBLASTOMA TUMOR XENOGRAFTS: VGX-100 EFFECTIVE IN COMBINATION WITH AVASTIN



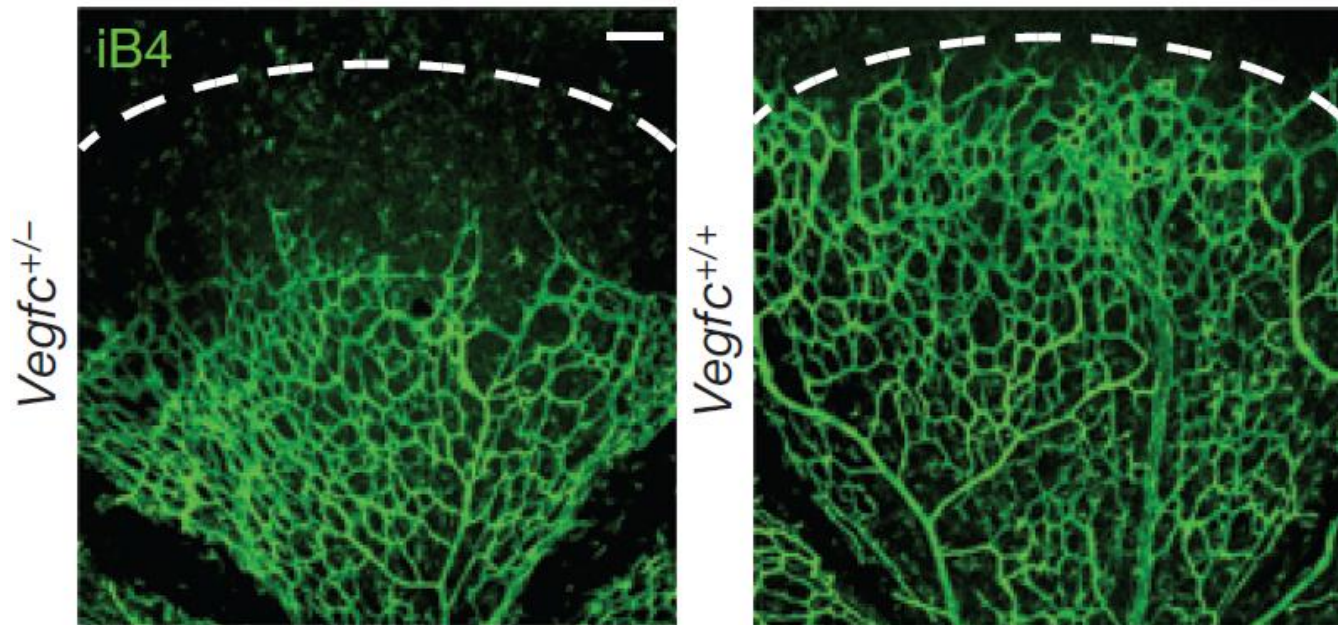
At Day 49, VGX-100 + Avastin reduces tumor burden by:

- 42% compared to control IgG
- 33% compared to single-agent Avastin.

EYE DISEASE

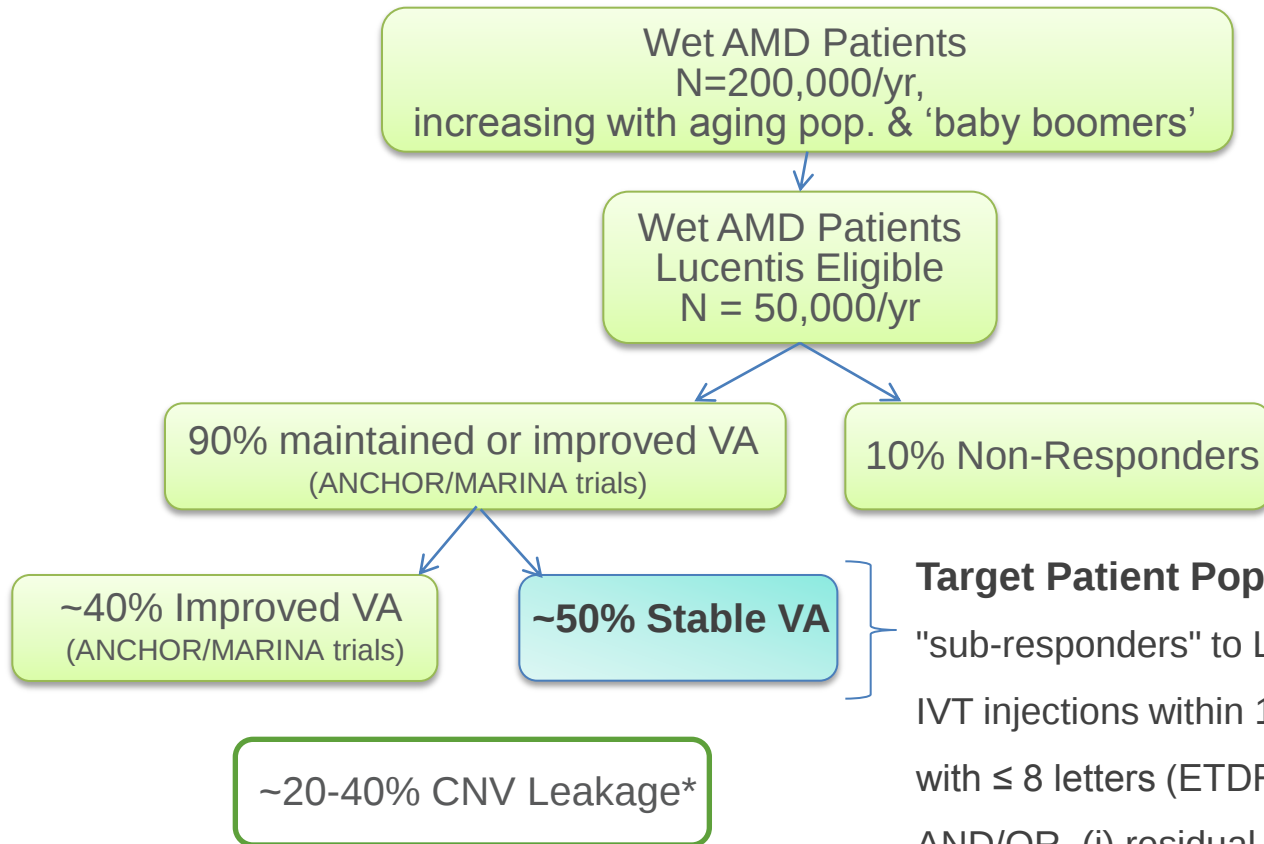
- **Age related macular degeneration (AMD) – a major unmet clinical need with significant commercial potential**
- Currently in the USA 1.75 million individuals are affected
- 200,000 new cases are diagnosed each year.
- Lucentis \$3B sales in 2011
- Our market estimates based on “niche” non-responder market of 30-50% of all patients

VEGF-C IS REQUIRED FOR RETINAL VASCULAR DEVELOPMENT



Retinas from P5 VEGF-C^{+/-} mice have reduced vascularity.

TARGET PATIENT POPULATION



Target Patient Population: Subjects who qualify as "sub-responders" to Lucentis (previously had 4-6 monthly IVT injections within 18 wks: with ≤ 8 letters (ETDRS chart) gain under treatment) AND/OR (i) residual subretinal or intra retinal fluid observed on OCT, (ii) leakage on FA and (iii) av central retinal thickness $\geq 250 \mu\text{M}$)

CANCERS OF UNKNOWN PRIMARY DIAGNOSTICS – A SOURCE OF NEAR TERM REVENUE

- Development partnered with Healthscope
- CUP 7th largest cancer fatalities
- Healthscope (Aus,NZ, Singapore & Malaysia) Circadian retains ROW rights
- Product launched in Healthscope territories July 2012
- Market size in Healthscope territories up to 10,000 tests p.a
- Pricing at \$>1000 Potential Royalty \$>1M p.a from 4 countries
- Partnership discussions in US/Europe ongoing
- Market in USA/Europe/Japan estimated to be 150,000 tests p.a

FINANCIALS – CASH FLOWS

- Current Cash - \$14.0m (Unaudited)
- Value of Listed Holdings - \$2.5M (Unaudited)
- Conservative Cash Burn 2012/13 and 2013/14 - \$8-10M p.a
- Well positioned to achieve key value adding milestones
- Does not take into consideration:
 - Increased R&D Tax Credit
 - Royalties on Sales of Diagnostics
 - Potential non-dilutive grant income (applications under review)
 - Further partnership income
 - Income from divestment of investments

KEY DEVELOPMENT MILESTONES

Activity	Timeline
Proof of concept in “back of eye” disease	Q4 2012
Expansion of Diagnostics portfolio	H1 2013
VGX-100 Phase 1b oncology studies completed	Q1 2013
IMC-3C5 Phase 1 trials reported	H1 2013
VGX-100 Phase 1 oncology studies reported	H1 2013
Phase II studies in cancer patients start (Multiple Indications)	H2 2013
Phase I Trials in Eye disease commence	H2 2013
Clinical proof-of-concept in first cancer indication	2H 2014
Clinical proof-of-concept in first eye disease indication	2H 2014
Partnering	H1 2013

AN INVESTMENT WITH SIGNIFICANT UPSIDE

Research Report from Edison Research March 14 2012

“....On a DCF basis to March 2012, Edison estimates a revised indicative value of A\$100m (A\$2.16 per share).

We expect value to develop strongly as the pipeline develops and as new VGX-100 indications become clearer...”

CIR current share price at October 31 is 36c

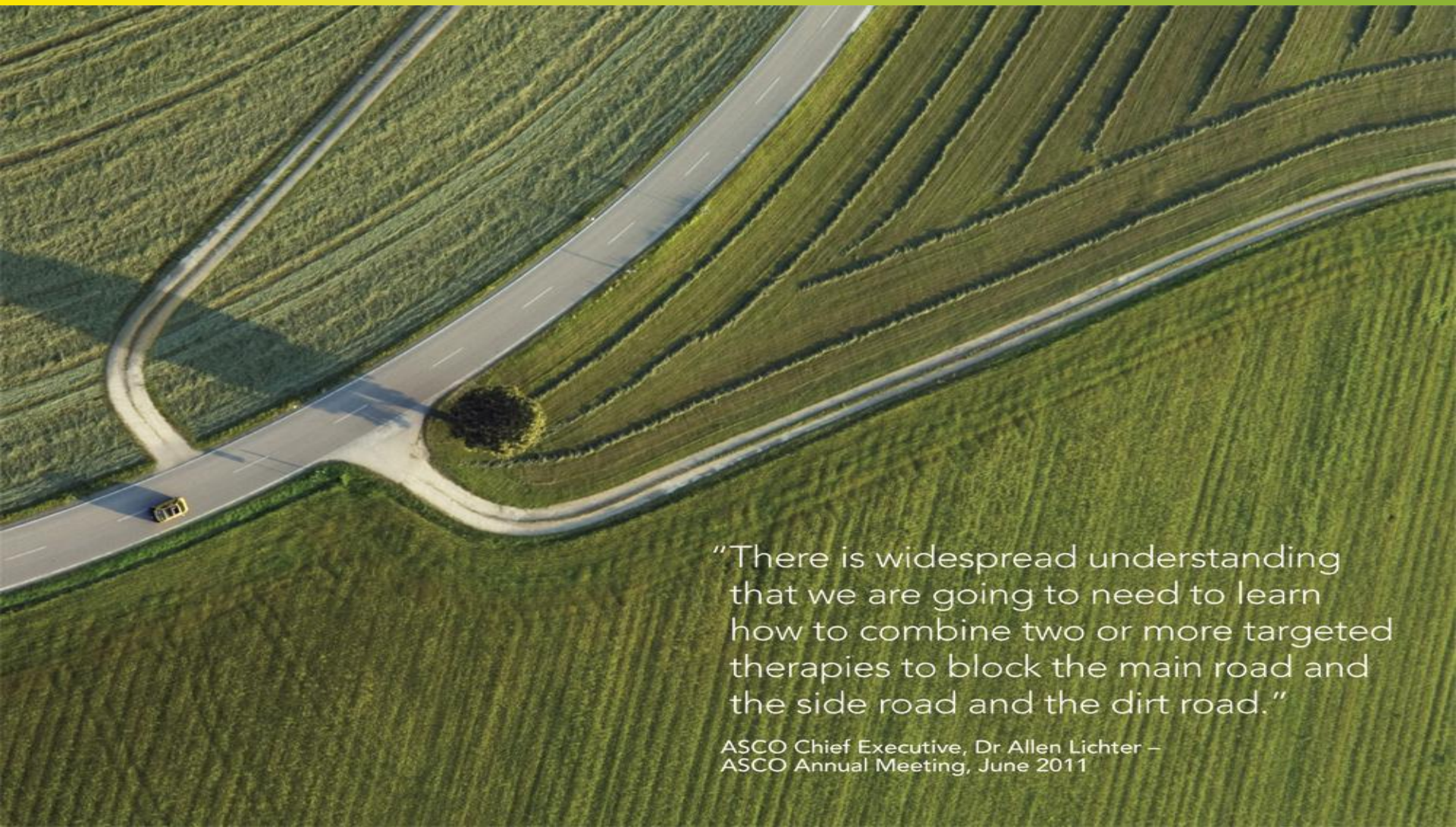
REASONS TO INVEST

- Clinical Stage Assets
- Increasing Reagents & Diagnostics Portfolio generating revenues
- A platform with major deal/partnering potential across a range of products over next 3-18 months
- Investments coming up to major re-rating events
- Capability to get to key value adding events
- Experienced and talented management & advisors

THANK YOU!

www.circadian.com.au

COMBINATION THERAPY OF TARGETED AGENTS IS BECOMING THE NEW PARADIGM IN CANCER THERAPY



"There is widespread understanding that we are going to need to learn how to combine two or more targeted therapies to block the main road and the side road and the dirt road."

ASCO Chief Executive, Dr Allen Lichter –
ASCO Annual Meeting, June 2011

ONCOLOGY

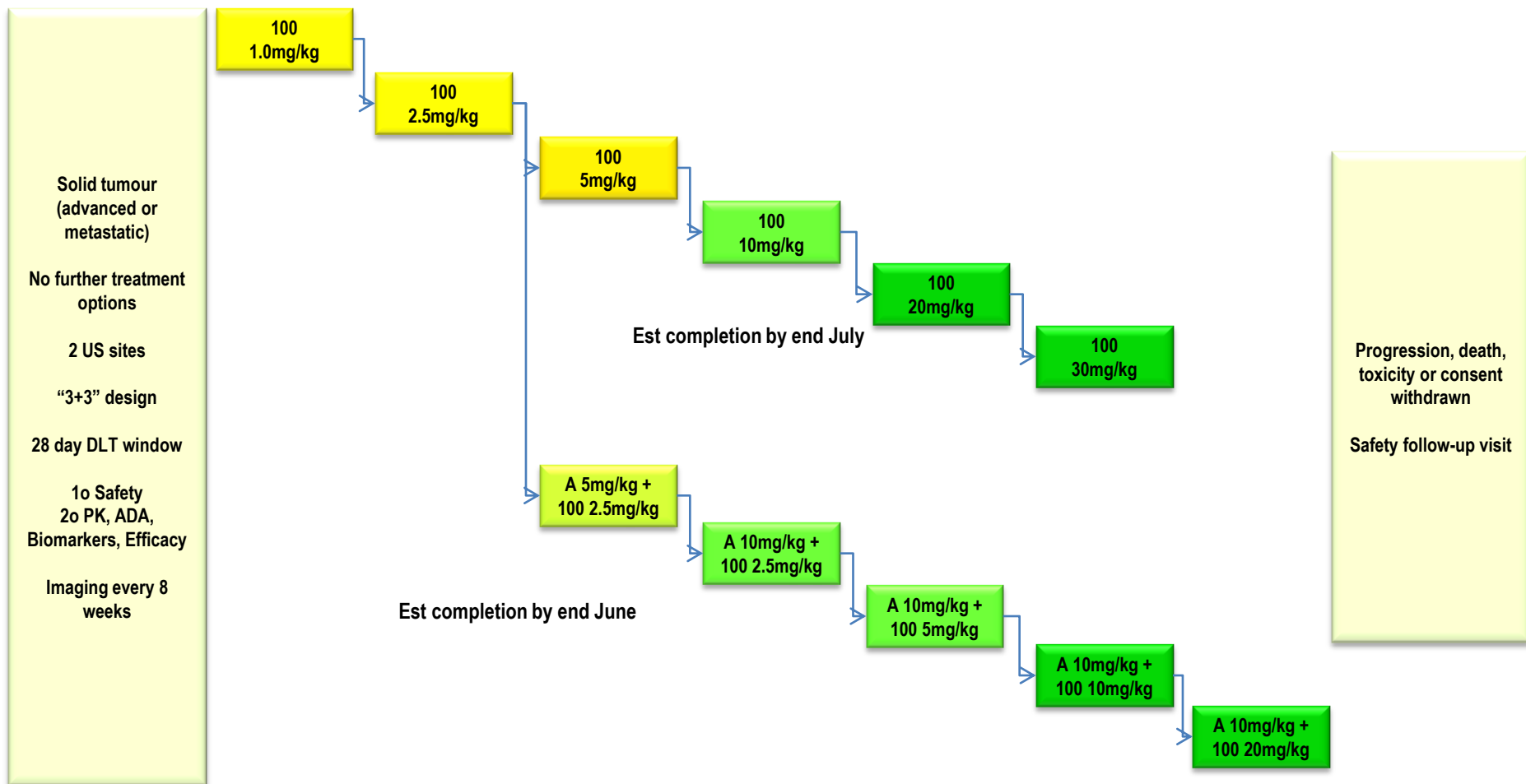
- **Phase 1 studies ongoing in USA under IND to complete Q4 12**
- **Initially targeting “niche” tumours then expanding into larger tumour types / markets after securing clinical proof.**
 - Glioblastoma (“Brain cancer”) – First Indication
 - Ovarian cancers
 - Pancreatic cancers
 - Gastric cancers
 - Colorectal cancers (“Bowel”)

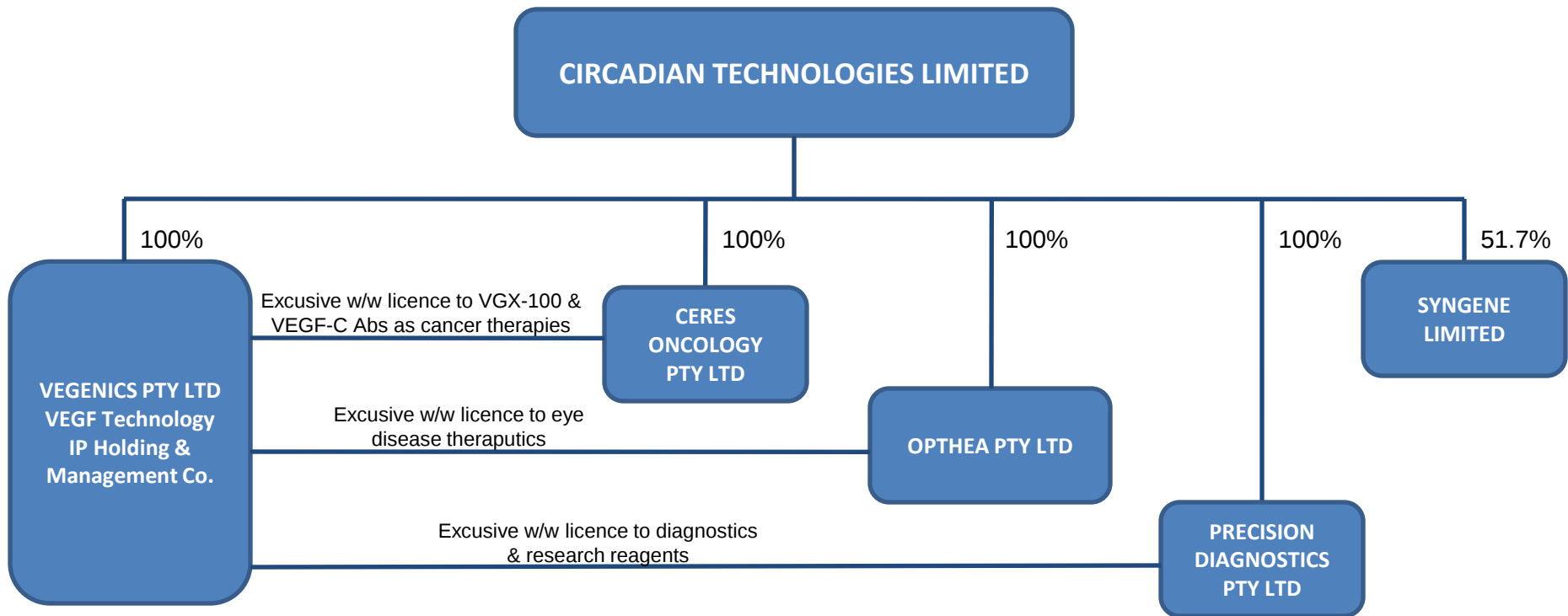
DRY EYE DISEASE

- Multifactorial, immune-mediated disorder of the ocular surface affecting vision.
- Affects ~5M people aged >50yrs in USA.
- Adverse environmental conditions significant cause of DED.
- Limited therapeutic options. Usually artificial tears.
- Now known to be lymphatic mediated. Lucentis/Avastin ineffective.
- Currently, the only approved treatment is “Restasis” – 2011 sales >\$1B
- VGX-100 very effective in mouse model

VGX-100-1001

PHASE I FIRST-IN-HUMAN STUDY





GLIOBLASTOMA - A MAJOR UNMET CLINICAL NEED

- In the US in 2010¹
 - Estimated diagnosed: 22,020
 - Estimated fatalities: 13,140
- The most aggressive malignant primary brain tumor in adults
- Nearly always fatal
- Possibility for fast track registration based on Phase 2b study.
- Phase 2a study aim to complete H2 '14.
- Fast track approval possible by H1 '17.
- Very strong interest from Key Opinion leaders worldwide
- Market estimate >\$300M p.a in USA

¹ Howlader N, Noone AM, Krapcho M, et al. *SEER Cancer Statistics Review, 1975-2008*, National Cancer Institute. seer.cancer.gov/csr/1975_2008/ based on November 2010 SEER data submission, posted to the SEER web site, 2011.