# ANNUAL GENERAL MEETING 24 NOVEMBER 2011

Robert Klupacs, CEO & Managing Director

Circadian Technologies (ASX.CIR)

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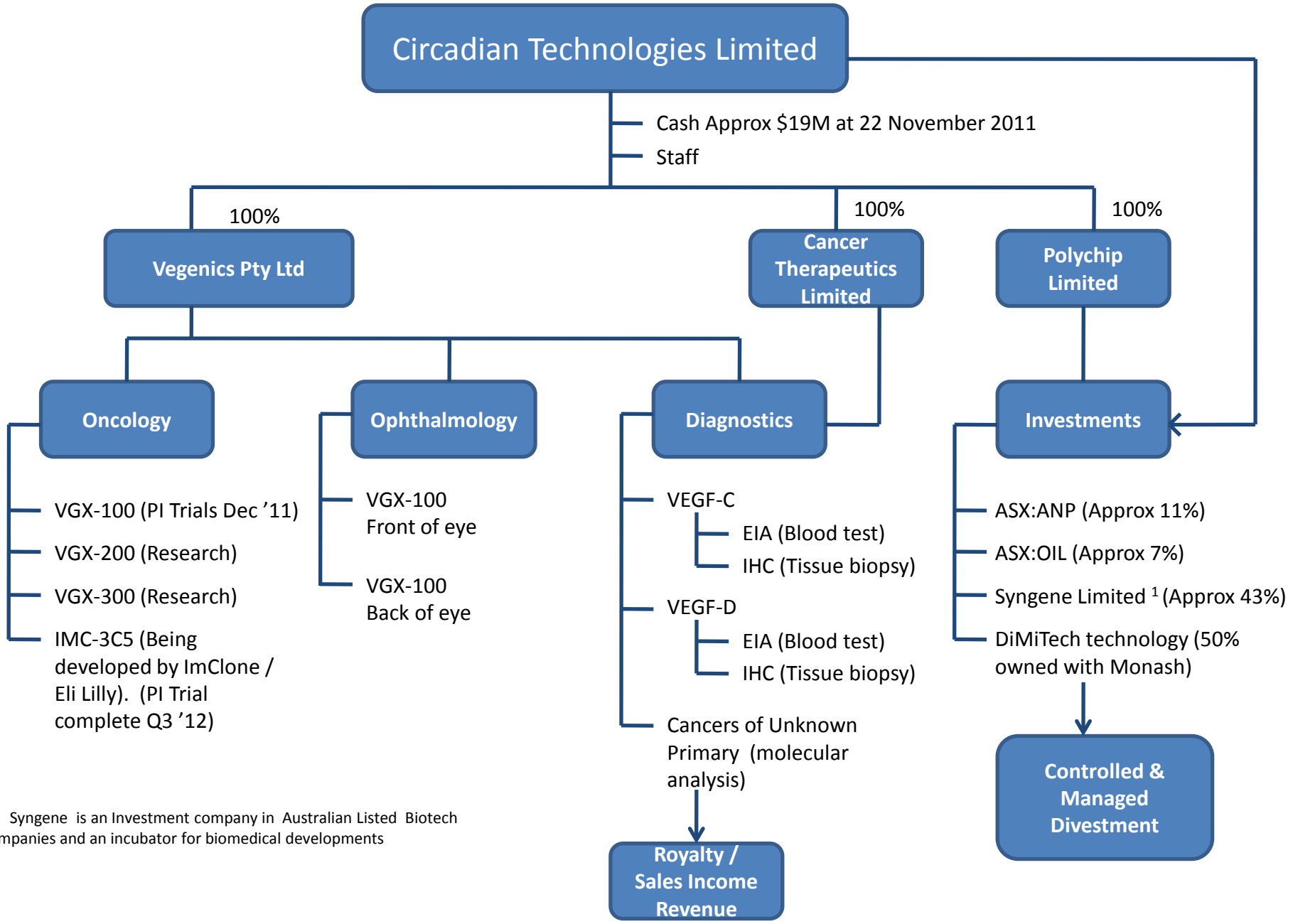
# CIRCADIAN TECHNOLOGIES LIMITED- 2011 AGM PRESENTATION OUTLINE

- **Corporate Snapshot & Structure**
- **Review of achievements since June 2010**
- **Therapeutic Development**
  - **Oncology**
  - **Ophthamology**
- **Diagnostics Development**
- **Expected milestones/value adding events next 6-18 months**
- **Circadian – the investment opportunity**

# CORPORATE SNAPSHOT

*Developing human therapeutic and diagnostic products from our extensive intellectual property assets in respect of VEGF-C, VEGF-D and VEGFR-3 and key relationships with leading cancer and ocular research organisations.*




1./ Syngene is an Investment company in Australian Listed Biotech Companies and an incubator for biomedical developments

# REVIEW OF ACHIEVEMENTS SINCE JUNE 2010

# OBJECTIVES WE SET FOR 2010/2011

- Advance drug development pipeline toward human clinical trials
- Develop partnerships for the commercialisation of our intellectual property
- Further strengthen and add skill-sets to our management team

# PROGRESS ACHIEVED IN EXECUTING BUSINESS STRATEGY

## Advancing our product pipeline

VGX-100: (human anti-VEGF-C antibody):

- Completed IND enabling studies

- IND Filed and cleared by FDA for studies in cancer patients

- Phase 1 trials to commence in USA December

- MD Anderson collaboration identified key role of VEGF-C in Avastin resistance

- Designated a product development candidate for “front-of-eye” disease

- Publication of data showing significant effects in ameliorating dry eye disease in animal models

# PROGRESS ACHIEVED IN EXECUTING BUSINESS STRATEGY

## Advancing our product pipeline

IMC-035: (VEGFR-3 Antibody being developed by Eli Lilly):

- Phase 1 Clinical Trials commenced. Results expected Q3’12

VGX-300: (recombinant VEGFR-3)

- CSIRO alliance has generated second generation molecules with significantly improved characteristics.

- Further confirmatory pre-clinical studies being undertaken as prelude to designation as product development candidate H1 2012.

# PROGRESS ACHIEVED IN EXECUTING BUSINESS STRATEGY

## Partnerships

- Healthscope-CUP Test:  Good progress. On track for launch in Q1 2012
- Cincinnati Childrens Hospital Medical Centre – VEGF-D Diagnostic for women with respiratory disease: Product launched
- Eli Lilly-IMC-3C5: Phase 1 trials commenced
- Ark Therapeutics: Arbitration settled. Phase 1 studies with VEGF-D gene therapy well underway

## Building the management and advisory team

- Establishment of International Clinical Advisory Group in ocular disease
- Appointment of Director, Clinical Trials – Dr Ian Leitch

# FINANCIAL POSITION & SHAREHOLDER BASE

## Top 10 shareholders: 52.8%

| Investor | % of issued shares |
|---|---|
| HSBC Custody Nominees (Australia) Limited | 18.88 |
| Licentia Ltd | 6.79 |
| Ludwig Institute for Cancer Research | 6.73 |
| HSBC Custody Nominees (Australia) Limited GSCO ECA | 4.57 |
| Cogent Nominees Pty Limited | 3.84 |
| Capital Macquarie Pty Limited | 2.97 |
| Citicorp Nominees Pty Limited | 2.61 |
| Chemical Trustee Limited | 2.50 |
| National Nominees Limited | 2.38 |
| JFF Steven Pty Ltd | 1.54 |
| **Total 10 shareholders own** | **52.8%** |
| **Total 20 shareholders own** | **60.1%** |

## Financial Summary @ 22 November 2011 (unaudited)

| | |
|---|---|
| **Stock code:** | **CIR** |
| Share price: | **50.0c** (AUD) |
| Shares issued: | 46,396,928 |
| Market cap: | ~ A$**23.2** mill |
| Cash holdings:<br>Listed investments:<br>(ASX: ANP, OIL) | ~ A$**19.1** mill<br>A$**3.5**mill |

**Institutions/Funds: ~ 32%**

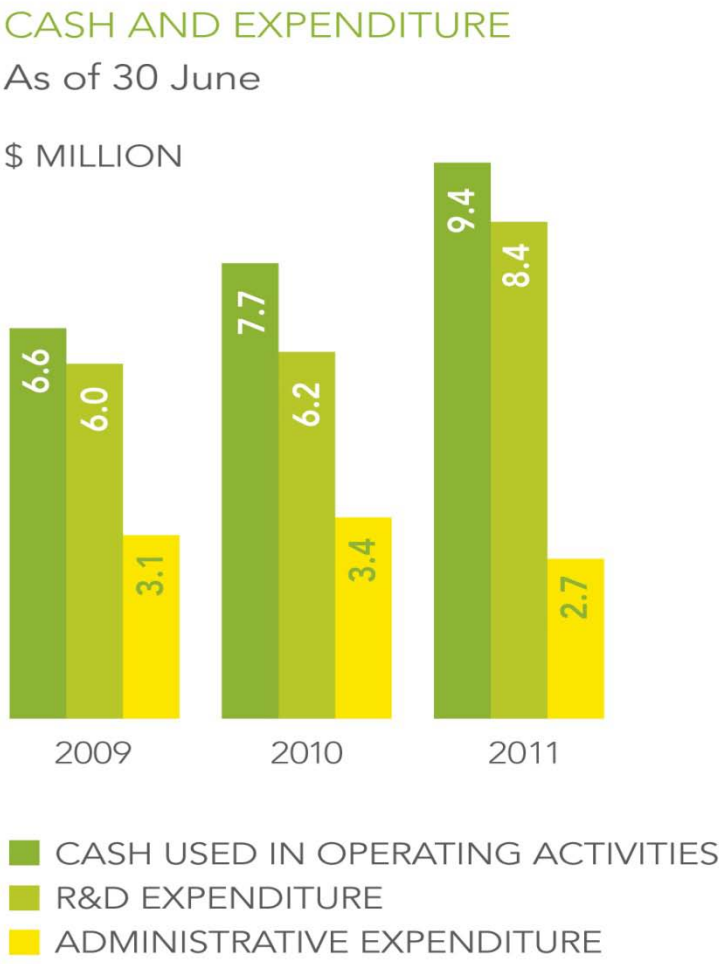
**Retail investors: ~ 40%**

**Professional investors: ~ 28%**

# KEY FINANCIALS (CONSOLIDATED)

| | 30 June 11<br><br>$000 | 22 Nov 2011 (unaudited)<br>$000 |
|---|---|---|
| Cash | 22,104 | **19,100** |
| Listed investments (market value) | 1,432 | **3,548** |
| Net assets | 21,824 | |
| Revenue | 1,850 | |
| Operating expenses (incl. R&D, investment related exp's) | (12,893) | |
| Loss before tax | (11,043) | |
| Net cash outflows | (9,477) | |
| **NTA per share** | **$0.47** | |
| **Cash & listed assets per share** | **$0.48** | **$0.49** |
| **Share price** | **$0.53** | **$0.50** |

# FINANCIALS




**A focus on funds going to R&D value generating activity and continued streamlining of business activities to reduce Administrative expenses**

# FINANCIALS

## TOTAL OPERATING COSTS

| | |
|---|---|
| RESEARCH & DEVELOPMENT | 68% |
| PATENTS | 5% |
| ADMINISTRATIVE | 22% |
| OTHER | 5% |

**Our goal is to have a ratio of R&D/IP Expense to Administrative/Other better than 80/20 on an annual basis**

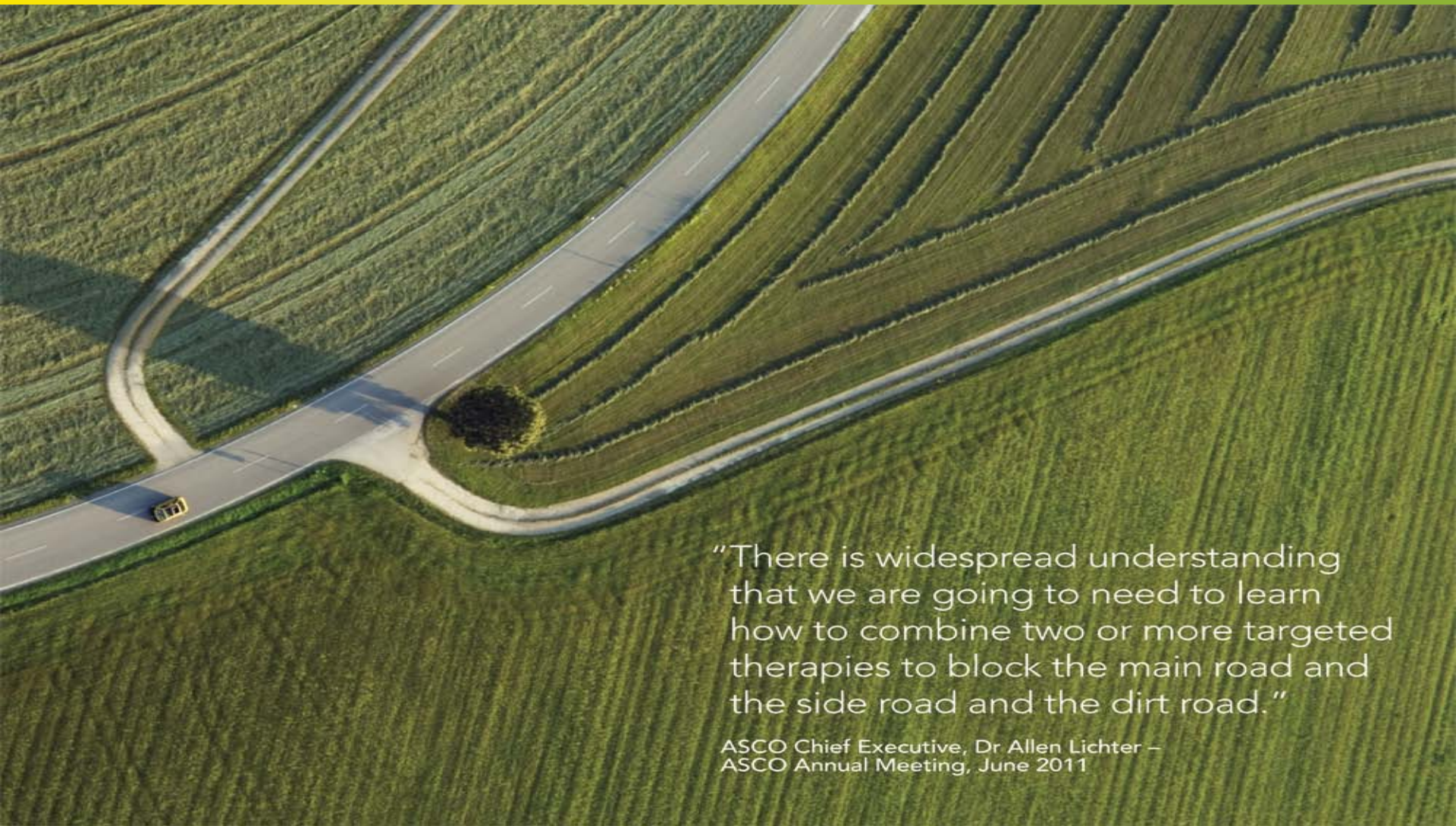
# FINANCIALS – CASH FLOWS

- Current Cash - $19.1m (Unaudited)
- Value of Listed Holdings - $3.5M (Unaudited)
- Conservative Cash Burn 2011/12 and 2012/13 - $9.0M 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

THERAPEUTIC DEVELOPMENT

# Oncology & Eye Disease

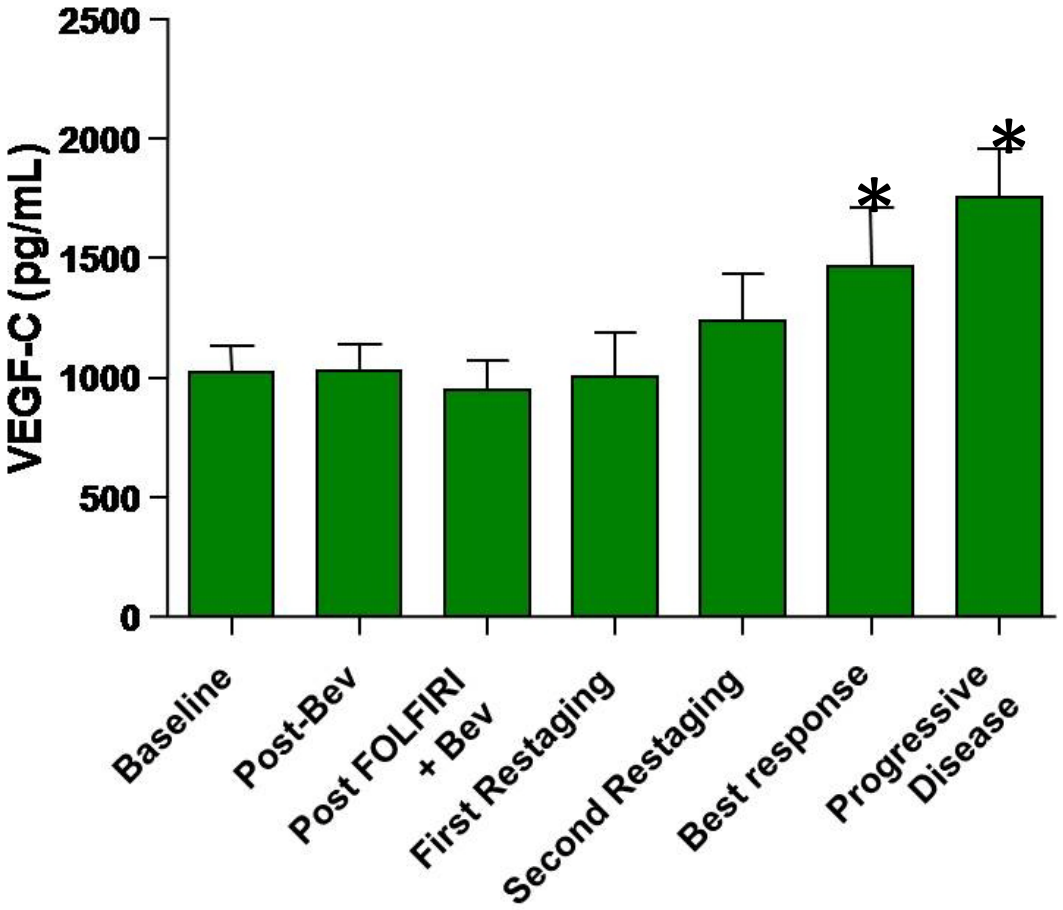
# COMBINATION THERAPY OF TARGETED AGENTS IS BECOMING THE NEW PARADIGM IN CANCER THERAPY



# IMPROVING ANTI-ANGIOGENESIS A MAJOR COMMERCIAL OPPORTUNITY

- Avastin®:  2010 Sales $US7.2B
- 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)

# HAVE NOW SHOWN THAT VEGF-C MAY BE A PREDICTIVE BIOMARKER FOR AVASTIN RESISTANCE




**VEGF-C levels begin to rise Significantly BEFORE tumours Stop responding to Avastin.**

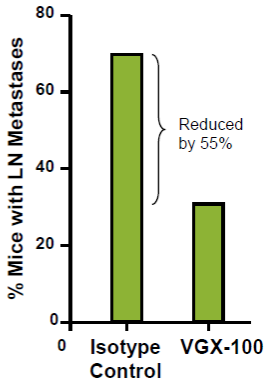
**Highlights major potential for improving therapy by combining VEGF-A and VEGF-C blockade**

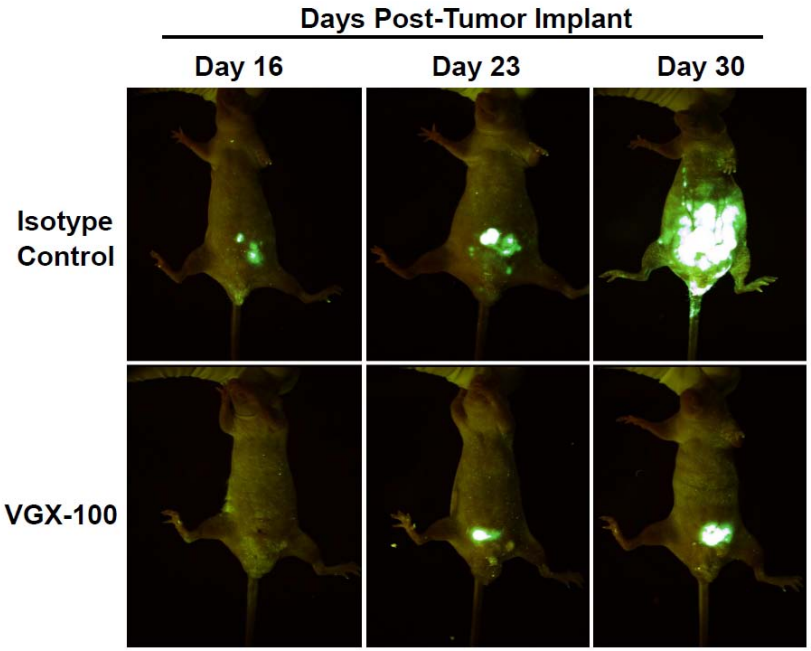
C.Lieu et al., *"The Association of Alternate VEGF Ligands with Resistance to Anti-VEGF Therapy in Metastatic Colorectal Cancer (mCRC)"*, J.Clin.Oncol. 29:2011 (suppl; Abstract #3533).

# VGX-100 REDUCES METASTASIS IN AN ORTHOTOPIC PROSTATE CANCER MODEL

| Group | # Mice | # Mice with LN Mets | % Mice with LN Mets | p value* |
|---|---|---|---|---|
| Isotype Antibody Control | 17 | 12 | 71% | - |
| VGX-100 | 19 | 6 | 32% | 0.019 |

** p value by Fisher exact test.*



# VGX-100 ONCOLOGY CLINICAL DEVELOPMENT

# VGX-100 TARGET PRODUCT PROFILE IN ONCOLOGY

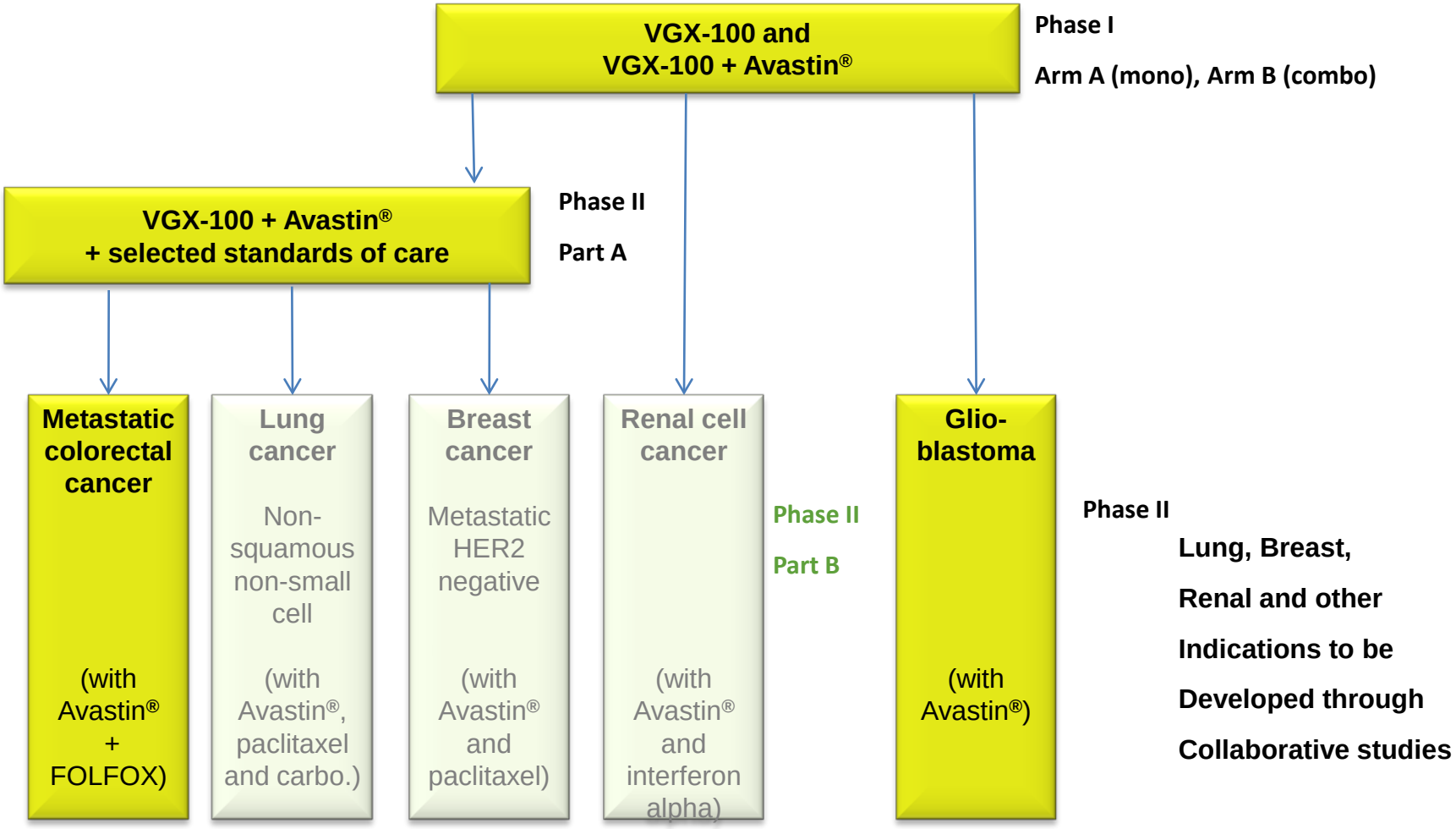
- **Indication:**
  - Co-administered with anti-angiogenic agent eg (Sutent®, Nexavar®, Avastin® ) and standard of care
  - Targeting glioblastoma and colorectal cancer as first indications
  - To develop through collaborations at least one of breast, lung, renal and/or potentially ovarian cancer in combination with anti-angiogenic agents most likely to be Avastin®

# GLIOBLASTOMA - A MAJOR UNMET CLINICAL NEED

- In the US in 2010[1]
  - 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 2b study aim to complete HI ’15.
- Fast track approval possible by H2 ’15.
- Very strong interest from Key Opinion leaders worldwide

[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.

# PHASE I AND II CLINICAL PROGRAM



# VGX-100 OCULAR DEVELOPMENT OPPORTUNITY

# LEVERAGING VGX-100 ONCOLOGY DEVELOPMENT

# DEVELOPMENT OPPORTUNITY

- Significant development opportunity for VGX-100 as a treatment for ‘front of the eye’ disease.

- Initial indications:

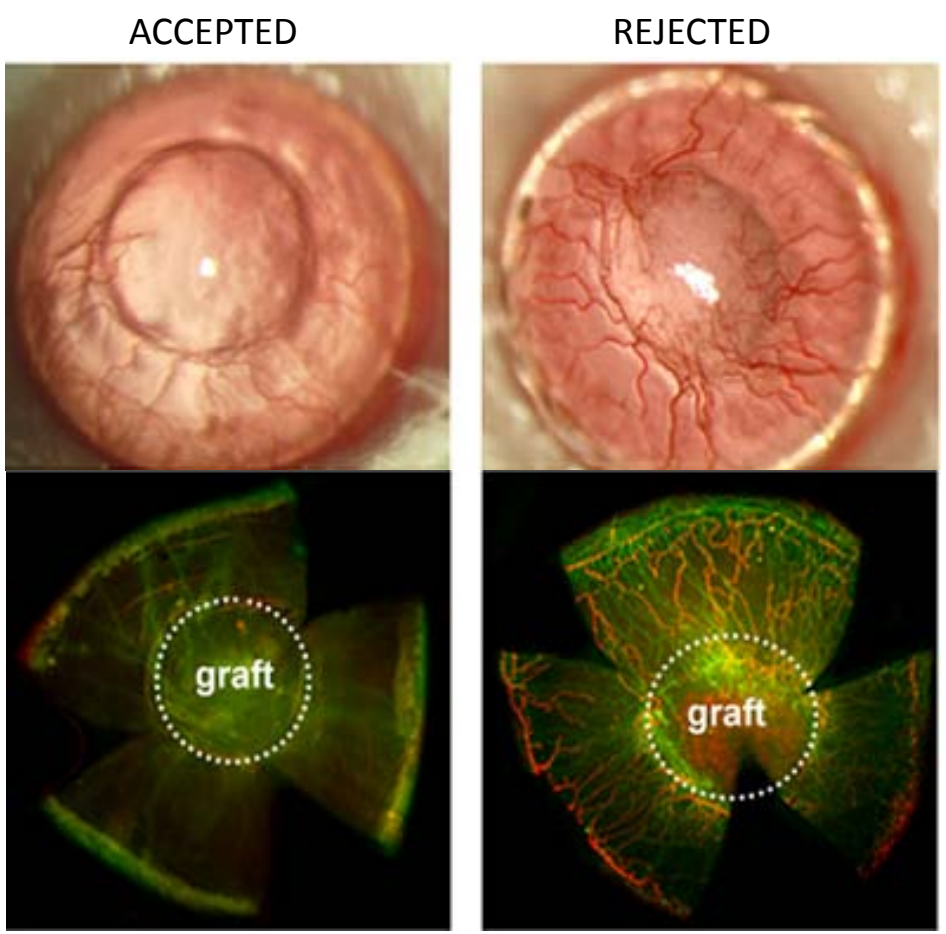
  - **Corneal Neovascularisation (CNV)**
    - Estimated that up to 4-5% of patients at eye clinics have CNV
    - Potential market >$1B p.a
    - Very limited competition

  - **High-Risk Corneal Allograft Rejection**
    - >10000 grafts/yr in USA
    - Potential market >$300M p.a
    - Major unmet clinical need
    - Existing anti-rejection drugs limited effects
    - Very high likelihood of accelerated approval

- Local ocular administration via subconjunctival injection as a single-agent.

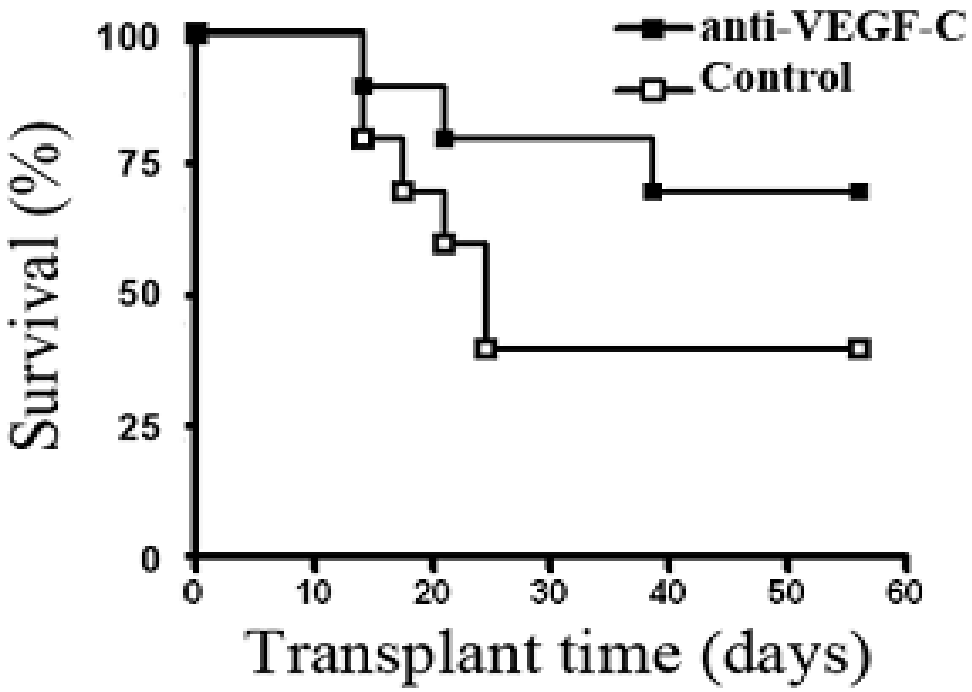
# REJECTED CORNEAS ARE INFILTRATED BY BLOOD AND LYMPHATIC VESSELS AND OVER-EXPRESS VEGF-C and VEGFR-3

Transplanted Corneas: 3 wks Post-Transplant




VEGF-C expression increased 2-fold in rejected vs accepted allografts, and 4.8 fold over non-transplanted corneas.

# VGX-100 PROMOTES CORNEAL TRANSPLANT SURVIVAL




***Our Goal is to commence clinical studies by Q1 '13 with fast track approval application lodged by H2'15***

ARVO Annual Meeting 2010. Program#/Poster#1554/D995

# OUR DIAGNOSTICS PORTFOLIO

# DIAGNOSTICS – A SOURCE OF NEAR TERM REVENUE

- **VEGF-D Diagnostics**
- **VEGF-C Diagnostics**
- **Cancers of Unknown Primaries**

# DIAGNOSTICS – A SOURCE OF NEAR TERM REVENUE

## VEGF-D Diagnostics

- Marketed as biomarker test for LAM (degenerative lung disease in women) in USA by Cincinatti Children's
- Market expected to expand to 25-50,000 tests p.a within 2-3 years
- $10-20M market (with 20-25% royalty)
- Sales significantly increasing over past 2 months following KOL marketing.

- Expansion into drug monitoring cancer sector ongoing-CLIA waiver launch around end 2012 with PMA lodged Q1 2013
- Based on results of MILES Sirolimus LAM Trial a significant opportunity for VEGF-D to be used a biomarker to monitor mTOR therapy
- Lead drug in class,  Affinitor estimated to have sales >$3B in next 2-3 years

# DIAGNOSTICS – A SOURCE OF NEAR TERM REVENUE

## VEGF-C Diagnostics

- Development accelerated
- Based on MD Anderson study appears to be a major biomarker to monitor anti-angiogenic therapy “resistance”
- Key product requirement for US re-imbursement agencies
- Possible market 250,000 tests worldwide at $200-300/test
- Generating further clinical data in larger cohorts
- Targeting CLIA waiver launch Q4 2012
- PMA with FDA by H1 2014.

# DIAGNOSTICS – A SOURCE OF NEAR TERM REVENUE

## Cancers of Unknown Primary Origin

- Market launch in Aust, NZ, Malaysia, Singapore expected Q1 2012
- Market size 10,000 tests p.a
- Pricing at $1000-1500/test (Royalty > 15%)
- Circadian retains rights to test to ROW
- Partnership discussions ongoing
- Existing Competitive Test selling for $3000/test
- Market in USA/Europe/Japan estimated to be 150,000 tests p.a

# EXPECTED NEAR TERM MILESTONES

# NEAR TERM MILESTONES

H1
2012

- **VGX-100 Phase 1 trials commenced**
- **CUP molecular diagnostic market launch**
- **VGX-100 monotherapy safety demonstrated**

# NEAR TERM MILESTONES

## H2 2012

- **VGX-100 & Avastin combination safety and acceptable toxicity demonstrated**
- **VGX-100 Phase 1 studies complete**
- **IMC-3C5 Phase 1 studies complete**
- **VEGF-C CLIA waivered diagnostic available**
- **VGX-100 corneal allograft IND lodged**

# NEAR TERM MILESTONES

H1

2013

- **VGX-100 Phase 2 oncology studies commence**
- **VGX-100 Phase ½ corneal allograft studies commenced**
- **CUP Test ROW partnership in place**

# AN INVESTMENT WITH SIGNIFICANT UPSIDE

Research Report from van Leeuwenhoeck Research 7 October 20100

"...*Based on sum-of-the-parts valuation, we believe Circadian is gravely undervalued at the current share price of AUD 0.47.*

*Using our valuation model, the Company's total value is AUD 91 million, or AUD 1.97 per share. This represents more than 300% upside from the current share price…"*

# THANK YOU!

# Q&A