

Developing biological therapeutics for cancer
Managing Director's Presentation
AGM 14 November 2008



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Presentation Outline

- **2007/08 – Year in Review: Key Events**
- **Circadian Today**
- **Ongoing Strategic Directions**
- **Circadian – The Investment Opportunity**

2007/08 Review: A year of major change

- Retirement of Leon Serry after 24 Years



2007/08 Review: A year of major change

- Transformation of the business model from “biotechnology investor and incubator of early stage technologies” to **focused drug development company in cancer**
- New leadership, Robert Klupacs MD, expanded management team, expert advisors
- Retirement of long serving directors: John Stocker and James MacKenzie
- Appointments of new directors:
Tina McMeckan (commercialisation of science, corporate fund raising)
Carlo Montagner (experience in heading oncology therapeutic businesses)
Jonathan Skipper (Ludwig IP executive)
- Acquisition of 100% of Vegemics (Ludwig and Licentia’s minority interest holdings)
- Licentia and Ludwig Institute becoming significant shareholders
- Divestment of remaining MBP holding

Key Events

ImClone (NASDAQ: IMCL) announces IMC-3C5 is product development candidate (licensed VEGFR-3 antibody technology for this product from Vegenics)	October 2008
Arana completes humanisation of Vegenics' VGX-200 series drug candidates	October 2008
Circadian completes 100% acquisition of Vegenics	August 2008
Vegenics granted key strategic patent in US covering angiogenesis inhibitors	August 2008
"Nature" publication reporting major role of VEGFR-3 in angiogenesis – confirming role of target in cancer therapy	July 2008
Circadian establishes a world class team to develop cancer drugs using its VEGF technology	June 2008
Robert Klupacs appointed Managing Director	March 2008

Key financials – 30 June 2008 (consolidated)

	30 June 2008	13 Nov 2008 (unaudited)
	\$000	\$000
Cash	46,217	42,900
Listed investments (market value)	12,754	6,800
Net assets	51,407	
Revenue	8,148	
Operating costs (incl R&D)	(9,264)	
Loss before tax	(1,117)	
Loss after tax	(2,286)	
NTA per share	\$1.28	
Cash & listed assets per share	\$1.46	\$1.10
Share price	\$0.88	\$0.665



CIRCADIAN TODAY

Developing therapeutics for cancer and other serious diseases

- Developing **angiogenesis-based** therapies for cancer and other serious diseases
- World's **most comprehensive** patent estate covering key angiogenesis targets VEGF-C, VEGF-D and VEGFR-3
- **Partnered programs with leading international biotechs**
Ark Therapeutics plc (LSE:AKT) – Phase 3 clinical trial
ImClone Systems Inc (NSDQ:IMCL) – developing anti-cancer drug
- **Strong financial position - \$50 million** in cash & listed investments
- **ASX:CIR**

What is angiogenesis?

- Angiogenesis is the growth of new blood vessels
- Tumour growth is caused by stimulation of new blood vessel growth by proteins (e.g. proteins VEGF-A, C, D)
- Blocking these proteins blocks blood vessel growth, leading to tumour starvation



Avastin® Story

- First targeted anti-angiogenesis therapy to become drug (developed & sold by Genentech Inc)
- Antibody that blocks angiogenic protein VEGF-A
- First approved Feb 2004
- 2007 sales: in US \$US2.3B, worldwide: \$US6B
- Fastest sales growth of any drug



Circadian's approach and technology

Developing four drug programs targeting different mediators of the process of angiogenesis to treat cancer

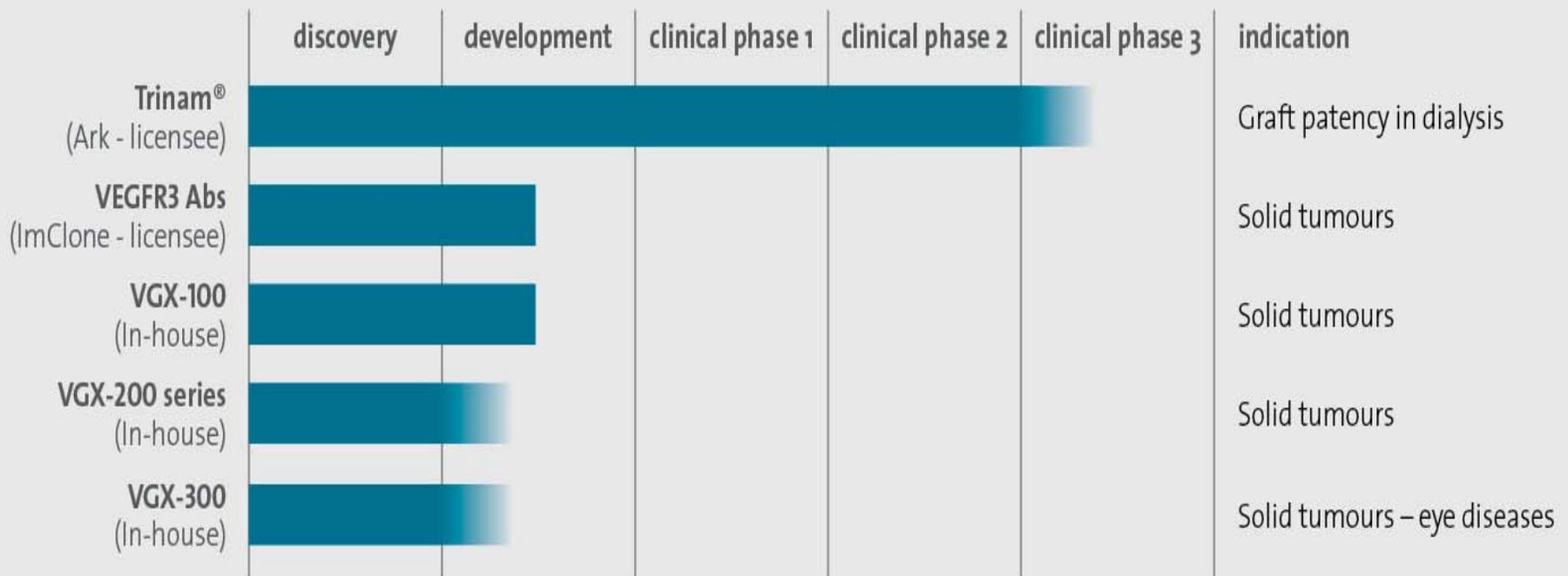
- We are focused on the two other angiogenic VEGF proteins (VEGF-C & D) which are involved in tumour growth **as well** as in tumour spread (metastasis).
- By blocking VEGF-C/D - not only **starves** tumours but has additional major therapeutic potential for **inhibiting tumour spread**.
- Angiogenesis and metastasis blockade are a major area of oncology drug development internationally.
- Drugs complementary to, or improved on Avastin®, are recognised as important areas in drug development.
- Our products target **multiple indications** – cancer first target.

Antibodies represent significant market opportunities

- Strong interest in antibodies from pharma in new product opportunities. Recent partnerships/M&A over last 2 years:
 - Medimmune/AstraZeneca – US\$15.5b
 - CAT/AstraZeneca – US\$1.30b
 - Bioinvent/Tx/Roche – US\$800m
 - Domantis/GSK – US\$435m
 - Adnexus/BMS – US\$425m
 - Morphotek/Eisai – US\$325m
- 19 antibody drugs on the market
 - Current sales of top ten antibodies > US\$20bn p.a;
 - Total antibody sales growing by >30% annually

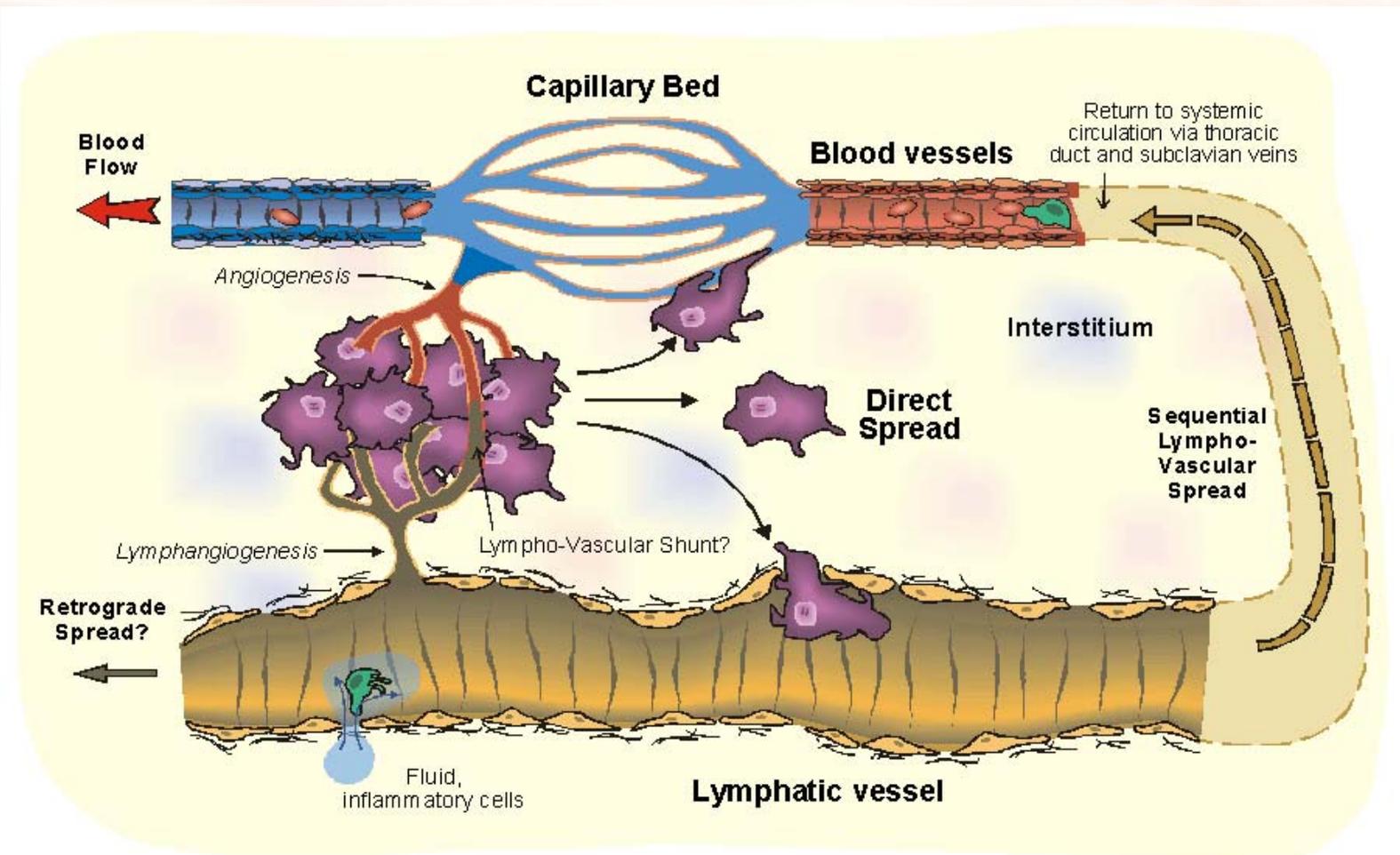
Circadian's products

Product Pipeline



VEGF-C / D Blockade: Inhibiting Angiogenesis AND metastasis

VEGF-C/D blockers can block tumour spread through lymph system

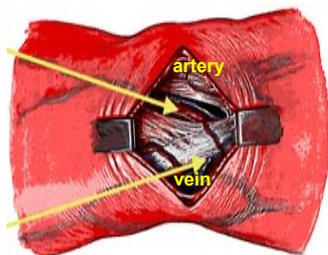


Creating value for shareholders

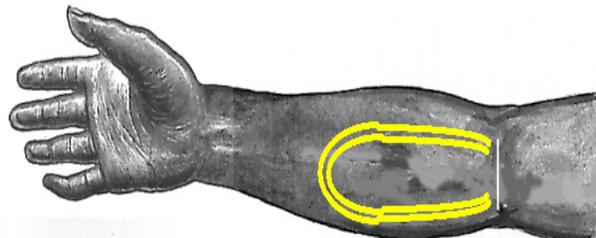
- **Dominant IP position** over key mediators of angiogenesis and tumour spread with control over major IP portfolio
- **Phase 3 product** partnered and **pipeline of product opportunities** in development
- **Significant cash reserves** and other financial assets to undertake ongoing development and strength in negotiating future licensing/partnering deals
- **High value space for partnerships** – Recent early stage deals (e.g. Roche/Bioinvent) in angiogenic antibody space of US\$500M +
- **Deal making and drug development expertise** to achieve partnering

Phase 3 Product Trinam®

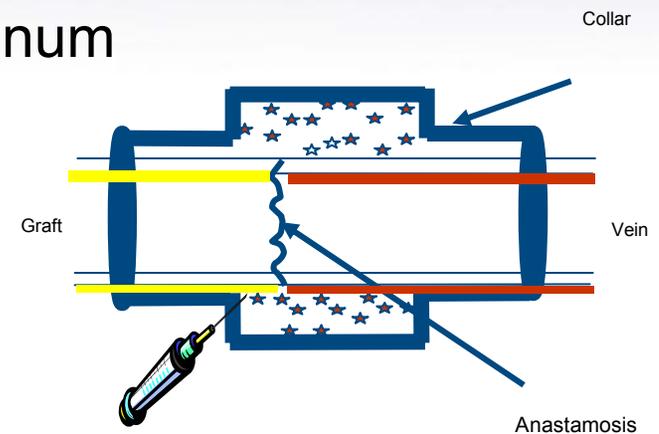
- Commencing Phase 3 second half 2008
- VEGF-D gene therapy product
- Extends lifetime of dialysis access grafts by keeping veins open for longer. Phase 2 clinical trials: 17 months v 4.5 months.
- Major patient impact by reduced need for repeated surgery and increased survival time of patients undergoing ongoing dialysis.
- Market estimates > \$US500M+ per annum



Step 1: Surgical isolation of vein and artery



Step 2: Insert flexible plastic tube graft to provide access for dialysis



Deal-making, drug development and operational track record

Management

- **Robert Klupacs (CEO)** - Over 3 years in executive position with Circadian. Founder and former CEO, ES international and six other early stage companies. Entrepreneur and IP expert with extensive history of industry deals.
- **Dr Alex Szabo (Head, Business Development)** - Formerly Bionomics, Beckman-Coulter, Affymetrix, Pharmacia. Recent deals include Aventis, Eisai, Genmab, LabCorp, Merck-Serono
- **Natalie Korchev (CFO & Head of Operations)** ACA - Formerly Ernst & Young, global finance, risk management experience. Over 10 years experience in biotech industry – over 8 years with Circadian.
- **Dr Megan Baldwin (Scientific Affairs)** – PhD in angiogenesis with over 10 years experience in the field; ex Genentech R&D
- **Ms Sue Foran (Product Development Manager)** – Over 15 years experience in drug development. Ex GlaxoSmithKline and Kandle
- **Dr Mike Gerometta (CMC and Manufacturing Manager)** – Over 18 years experience in diagnostic and antibody therapeutic development. Ex Agenix
- **Dr Richard Chadwick (IP Counsel)** - European and Australian patent attorney. Over 15 years experience in patent management with multi-nationals and biotechs. Ex FB Rice & Co

Deal-making drug development and operational track record

Product Development Advisory Committee

- **Dr Errol Malta** - ex Amgen Team leader for cancer drug Neulasta and other projects.
- **Dr George Morstyn** - Formerly CMO and Head of Development Amgen
- **Mr Ralph Smalling** – Formerly Head of Amgen Regulatory Affairs
- **Dr Russell Howard** – ex Head R&D Affymax, currently CEO Nasdaq listed Maxygen Inc
- **Dr Richard Morgan** – Formerly Head of Toxicology Glaxo Wellcome (now GlaxoSmithKline)
- **Mr Carlo Montagner** – Circadian Director. Formerly Head of Oncology Franchises at Aventis, Schering AG and Abraxis.

Over 150 drug development projects collective experience of above members of the Committee.

Deal-making drug development and operational track record

Board of Directors

- **Ms Dominique Fisher** – Entrepreneur, professional director - Pacific Brands, ex AIG, various private cos
- **Mr Don Clarke** – Partner Minter Ellison. Professional director - Metabolic, Webjet, various private companies
- **Ms Tina McMeckan** – Strategist, corporate fund-raising specialist. Professional director – Vision CRC, Melbourne Zoo, ex Alinta, various other companies
- **Dr Jonathan Skipper** – Executive Director IP & Licensing Ludwig Institute for Cancer Research
- **Mr Carlo Montagner** (see previous slide)
- **Mr Robert Klupacs** (see management slide)



Ongoing Strategic Directions

Our strategy

- Develop at least one therapeutic to proof of efficacy in Phase II trials
- Subsequent clinical development with partners – large pharmaceutical/biotechnology companies
- However seize opportunity for earlier partnerships if and when appropriate
- Selectively exploit/commercialise parts of portfolio not in angiogenesis area at earlier stages (e.g. similar to the Ark Therapeutics partnership)
- Prudently manage our cash. Our objective is net cash outflows of \$10-12M p.a. with increases in activities subject to increased revenue/ other cash inflows

Our Strategy Addresses Financial Market Challenges

- Market conditions are likely to adversely effect capital raisings for biotechs over the short to medium term.
- We are addressing this through prudent cash management and pursuing earlier partnerships where appropriate as stated in the previous slide.
- This, however, needs to be balanced against astute value adding investments.
- Although healthcare industry deal making still seems relatively stable, our plans consider the possibility of slow-down or reduction in industry deal value metrics.

Expected Milestones (next 6 to 18 months)

- Commencement of Phase 3 studies with licensee's product Trinam®
- Imclone/Eli Lilly commence clinical studies with IMC-3C5
- Successful divestment of listed investments
- VGX-100 completes pre-clinical developments
- VGX-200 series lead designated product development candidate
- VGX-300 designated product development candidate
- At least one strategic partnership in place
- Scientific presentations at leading international conferences on successful animal trials with VGX candidates

Why Circadian is a major investment opportunity

- ✓ **Competitive IP** - Dominant IP position over key mediators of angiogenesis and tumour spread
- ✓ **People** – Track record of deal making & drug development success
- ✓ **Cash** – \$50m cash/listed investments. Among a handful of biotechs in strong financial position
- ✓ **Product Advantages** – Compelling advantages over existing treatments
 - Trinam® – 4-fold increase in kidney dialysis graft lifetime
 - VGX-Compounds – Potential to inhibit *both* tumour growth *and* metastasis

Why Circadian is a major investment opportunity (cont)

- ✓ **Pipeline** - Four drug development programs targeting different mediators of cancer
- ✓ **Partnership opportunities**
 - 2 existing deals
 - High value for early deals in angiogenesis space: e.g. Roche/Bioinvent antibody US\$500M (Phase 1) – see separate slide for other deals in the sector
- ✓ **Revenue stream** – existing *and increasing* royalty flow
- ✓ **News flow** – Potential for many upcoming product development/scientific/partnership milestones
- ✓ **Value**
“Exceptional Cash Resources” and a “stand out offering” (*Bioshares*, 10 Oct, 2008)

Questions