

FINSIA -Small Cap  
Series  
"The Survivors:  
strong business and  
balance sheet"

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CEO & Managing Director



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## CIRCADIAN TODAY

*A cashed up company developing novel anti-angiogenic therapeutics for cancer  
With a dominant IP platform  
And the potential for generating significant revenues in the near term.*



## Developing therapeutics for cancer

- Developing **angiogenesis-based therapies** for cancer
- World's **most comprehensive patent** estate covering key angiogenesis targets VEGF-C, VEGF-D and VEGFR3
- **Partnered programs** with leading international biotechs in their field providing existing cash flows
  - Ark Therapeutics plc (LSE:AKT) - Phase 3 clinical trial
  - ImClone Systems Inc (NSDQ:IMCL) - developing anti-cancer drug
  - Healthscope Limited (ASX:HSP) - developing cancer diagnostic test
- **Strong financial position** - \$45 million in cash & listed investments
- **Existing royalties and potential for future significant royalty income** from Ark, cancer diagnostic test and ImClone (Lilly) as well as other applications of portfolio.



# CIRCADIAN

Why have we focused on developing antibody therapies in cancer?

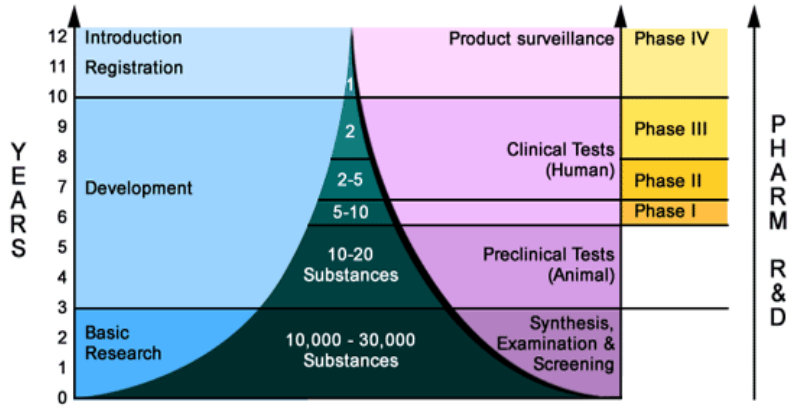


## Therapeutic Antibodies - A major development opportunity for biotech company development

- Exquisite targeting-improved probability of success
- A significant market opportunity - major focus of big pharma
- High value early stage deals and M&A opportunities
- Major successes in cancer treatment - Avastin®, Herceptin®, Erbitux®
- Significant product opportunity in angiogenesis-Avastin®
- Extremely large markets
- Unique, deep and dominant IP

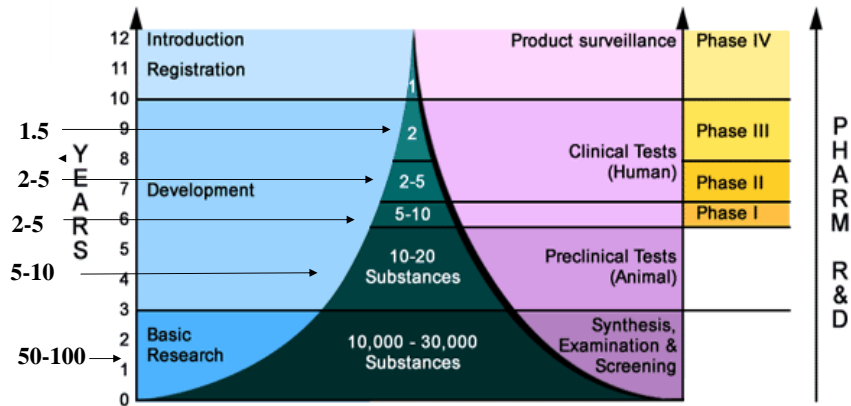


## Background - The Drug Development process Small molecules



**circadian**  
technologies limited

## The Drug Development process Therapeutic Antibodies - A higher probability of success



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## Antibodies represent significant market opportunities

21 antibody drugs on the market (mostly cancer and inflammation)

- Current sales of top ten antibodies > US\$20bn p.a;
- Total antibody sales growing by >30% annually
- greater competitive barrier to entry
- targeted profiles can provide cost v health economic advantage
- probability of success is higher



## Antibodies represent significant market opportunities (cont'd)

- Strong interest in antibodies from pharma in M&A and early stage licensing:
- M&A over last 2 years:
  - Medimmune/AstraZeneca - US\$15.5b
  - CAT/AstraZeneca - US\$1.30b
  - Domantis/GSK - US\$435m
  - Adnexus/BMS - US\$425m
  - Morphotek/Eisai - US\$325m
  - Cephalon/Arana - US\$215m



## Oncology Antibodies: Ability for large partnering deals before clinical trials commence

<i>Parties</i>	<i>Date</i>	<i>Size</i>	<i>Technology</i>
Micromet/Bayer-Schering	Jan 09	\$US396M	Option to Ab against undisclosed oncology target
Abbott/LICR	Nov 08	\$US150-200M	Exclusive licence to 2 <sup>nd</sup> generation EGFR Ab in oncology, which has completed 8 person Phase 1 study.
Bioinvent/Thrombogenics/ Roche	Jun 08	\$US800M	Exclusive licence to PIGF Abs in oncology. \$US75M upfront. \$US700M milestones. Double digit royalties
Dyax/Sanofi-Aventis	Feb 08	\$US500M	Exclusive licence to Tie-1 Ab DX-2240 and phage display in selected applications
GSK/OncoMed	Dec 07	\$US1.4B	Exclusive licence/co-development of 4 selected stem cell Abs in cancer



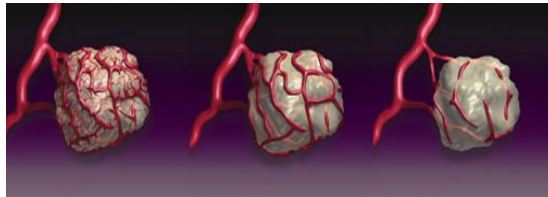
## Where does Circadian come in?

- Focused on developing better anti-angiogenesis treatments
- Anti-angiogenesis therapies have been shown to be a breakthrough concept in cancer therapy as evidenced by the drug Avastin<sup>®</sup> developed and sold by Genentech/Roche



## 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 - The first targeted anti-angiogenesis drug

- First targeted anti-angiogenesis therapy to become drug (developed & sold by Genentech Inc and Roche)
- Antibody that blocks angiogenic protein VEGF-A to starve tumours
- First approved Feb 2004
- 2007 sales: in US \$US2.3B, worldwide: \$US6B (\$10B+ 2009)
- Fastest sales growth of any drug



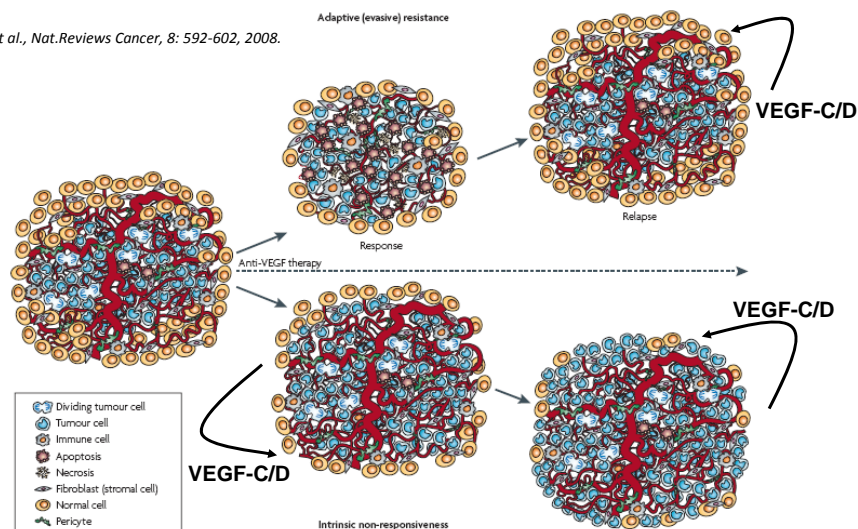
## $\alpha$ -VEGF Therapy (Avastin®): Effective but not across the board....

- Not all patients respond to therapy (30-50% response rate)
- 25-50% of responders become “resistant” within 12-18 months
- Likely reasons:
  - tumour growth due to factors other than VEGF-A; and/or
  - other angiogenic factors being turned-on when VEGF-A blocked



## $\alpha$ -VEGF Therapy (Avastin®): Effective but not across the board....

Bergers et al., *Nat.Reviews Cancer*, 8: 592-602, 2008.



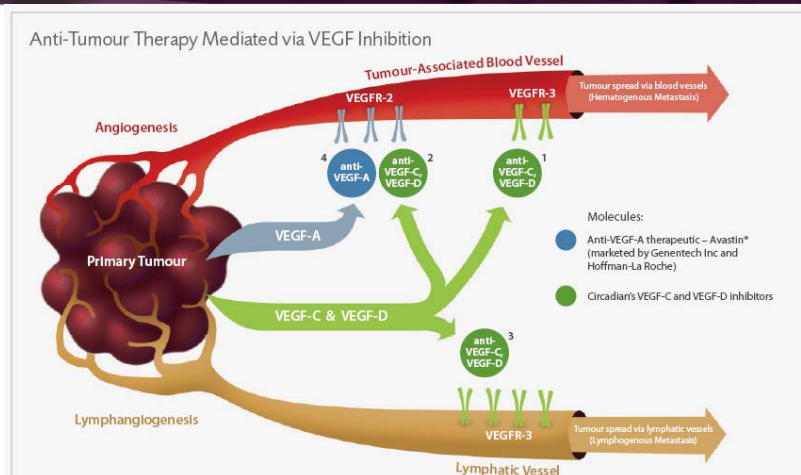


## The Product Opportunity

Opportunity to develop a new class of drugs to address resistance and/or non-responsiveness to anti-angiogenic therapies in cancer.



## Circadian's VEGF-C/D Inhibitors Blocking Tumour Growth AND Spread

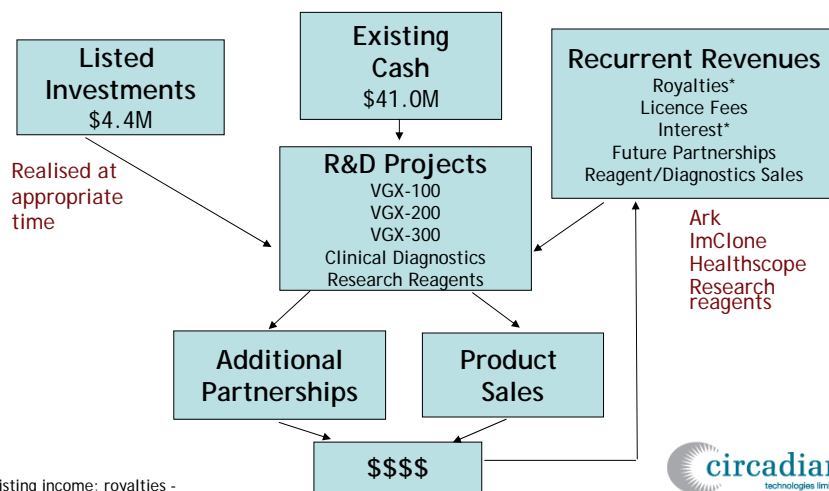


## Our strategy

- Develop 3-4 products with slightly different mechanisms of action targeting VEGF-C/D blockade
- Develop selected therapeutics to proof of efficacy in Phase II trials
- Subsequent clinical development with partners - large pharmaceutical/biotechnology companies
- Seize opportunity for earlier therapeutic partnerships if appropriate
- Selectively exploit/commercialise parts of therapeutic portfolio not in cancer area at earlier stages and exploit other applications of our portfolio such as clinical diagnostics and reagents for early revenues



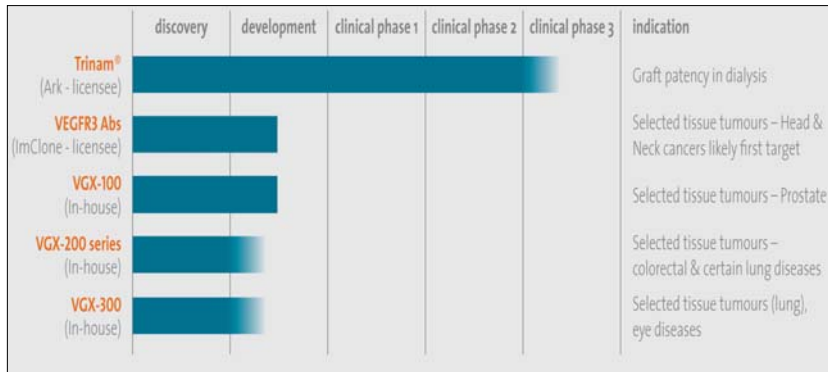
## CIRCADIAN'S BUSINESS MODEL



\* Existing income; royalties - potential for significant increase



## Deep Product Pipeline with mechanistically distinct mechanisms

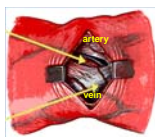


## Other Potential Revenue generating assets

- **VEGF-C, VEGF-D molecules themselves** as research tools, therapeutic development in wound healing, cardiovascular disease, lymphedema, neurodegenerative disease
- Ownership and exclusive commercialisation rights to **molecular diagnostic for Cancers of Unknown Primary (CUP)** in US, Europe, Japan; partnered with Healthscope for other territories
  - US incidence of CUP 60,000-100,000 per annum
  - Test to sell between \$500-1500 due to significant health cost savings

## Phase 3 Product Trinam® - Ark Therapeutics

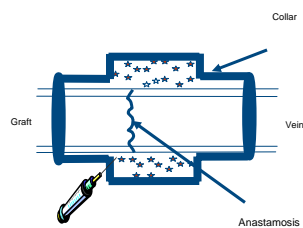
- Commenced Phase 3 trials Jan 2009 under SPA. Expected recruitment 250 patients over 18 months.
- VEGF-D gene therapy product. License under Circadian patents
- Extends lifetime of dialysis access grafts. Phase 2 clinical trials 17 months v 4.5 months.
- Major patient impact by reduced need for repeated surgery and increased survival time of patients undergoing ongoing dialysis.
- Market estimates > \$US750M+ per annum



Step 1: Surgical isolation of vein and artery



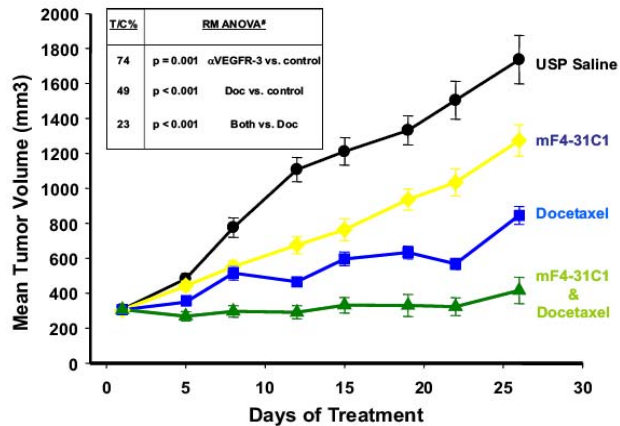
Step 2: Insert flexible plastic tube graft to provide access for dialysis



## IMC-3C5 (human anti-VEGFR-3 mAb) *ImClone/Lilly*

- Formal internal product development candidate
- Clinical trial commencement planned H1 2010
- Currently completing manufacturing development and animal safety testing
- Wide range of peer reviewed literature
- Likely first indication head & neck cancer

## VEGFR3 Ab +/- chemotherapy in Non-Small Cell Lung Cancer xenograft model (NCI-H292)



AACR 2009 Abstract #4089 O'Mahoney et al



## Circadian has dominant IP rights in respect of VEGF-C/D antagonists

- Over 500 granted and pending patents worldwide
- Granted IP rights in major territories to VEGF-C/D proteins and VEGFR-3 and blockers
- Applications in cancer and certain other diseases
- IP rights over product candidates extend beyond 2020
- Further strategic IP filings being made to extend patent life
- Freedom to operate in respect of competitors

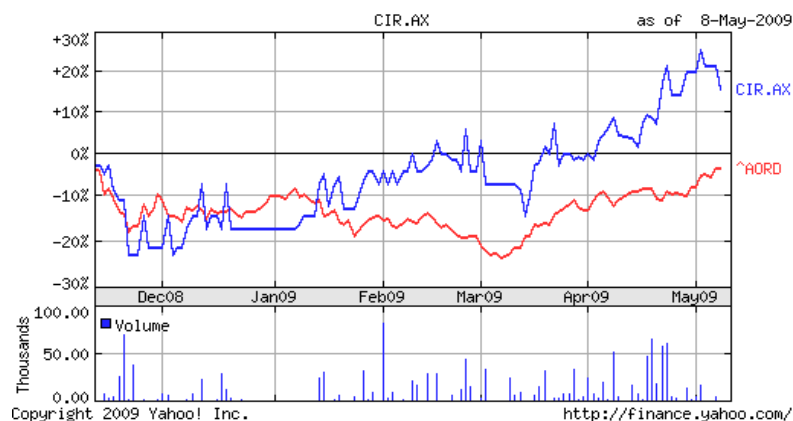


## Deal-making drug development and operational track record

- **Robert Klupacs (CEO)** Founder and former CEO, ES international and six other early stage companies. Entrepreneur and IP expert with extensive history of industry deals including Sanofi, Baxter, Aventis, Pharmacia, Novartis, Alexion, Pfizer.
- **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.
- **Product Development Advisory Committee**  
The nine members together bring vast experience in international drug development and oncology. Past roles have included positions with Amgen, GSK, Aventis, Schering, Affymax, Maxygen. Over 150 drug development experience.



## CIR v All Ords Last 6 months



## An investment with significant upside

- Dominant IP position over VEGF-C and VEGF-D key mediators of angiogenesis.
- Phase 3 product partnered and pipeline of product opportunities- potential for multi-million royalty flow within 24-36 months.
- Strong financial assets to support development/deal making
- Extremely high value space for partnerships/deals (Roche/BioInvent \$500M+)
- World class drug development expertise and management
- Share price currently trading at 15% below cash and investments with no apparent value ascribed for our IP assets or existing and future royalty flows.

