

24 October 2007

The Companies Section  
The Australian Stock Exchange Limited  
530 Collins Street  
MELBOURNE VIC 3000

*No of Pages: 24*

Dear Sir/Madam

**Annual General Meeting – 25 October 2007**  
**Managing Director's address**  
**Presentations on research projects**

Please find enclosed the following presentations to be made at tomorrow morning's annual general meeting of Circadian Technologies Limited:

- Managing Director's address by Leon Serry;
- Graeme Kaufman's presentation on two of the company's research projects; and
- Robert Klupacs' presentation on Vegenics Limited and its cancer therapeutics technology.

Yours faithfully

**Leon Serry**  
**Managing Director**

**CIRCADIAN TECHNOLOGIES LIMITED**  
**ANNUAL GENERAL MEETING**  
**THURSDAY, 25 OCTOBER 2007 AT 9.00 AM**

**MANAGING DIRECTOR'S ADDRESS TO SHAREHOLDERS**

I would also like to welcome you to the 23rd Annual General Meeting of Circadian Technologies Limited and I am pleased to provide you with a summary of some of the highlights in our financial statements during the year as well as an update on our listed holdings and projects.

As you are aware, the mineral resources boom continues to overshadow the biotechnology sector as well as some sections of the general market. However, there is still sound interest in the biotechnology sector and we look forward to 2008 as being a year in which some of Circadian's projects and those of its listed holdings experience success in their development, and that this success is reflected in the share price of the company.

Circadian would be one of the few biotech research companies in Australia with a market capitalisation of under \$500 million that has had a net profit after tax in three of the last four financial years after expensing our research & development costs and patent costs. Circadian's consolidated profit after tax for 2004 was \$5.8 million, in 2005 we had a profit of \$21.7 million, in 2006 there was a loss of \$6.5 million and this year a net profit after tax of \$6.3 million. I will elaborate further on the company's operating results in a few moments.

In July 2006, Circadian formed a collaboration (through the entity Vegenics Limited) with the Ludwig Institute for Cancer Research (Ludwig) and Licentia Limited, the commercial arm of the University of Helsinki, with Circadian having a 50% interest and control on the payment of \$4 million in subscription monies. Subsequent to the formation of Vegenics, Circadian contributed an additional \$17.5 million capital into that company. This new equity into Vegenics satisfied the requirements of the relevant Licence and Shareholders Agreements under the collaboration and gave effect to the assignment to Vegenics of Ludwig's and Licentia's patent estates in respect of molecules known as vascular endothelial growth factors (VEGF). Circadian's interest in Vegenics is currently 67%.

The various licences granted by Ludwig to its licensees including Ark Therapeutics Group plc (LSE: AKT) and Imclone Systems Inc (NASDAQ: IMCL) have now been novated to Vegenics. On 22 May 2007, Ark Therapeutics announced that it had been given clearance by the US Recombinant DNA Advisory Committee for its planned Phase 3 US clinical study of Trinam<sup>®</sup>. Trinam<sup>®</sup>, a novel gene therapy product which seeks to prevent blood vessels blocking in kidney dialysis patients, utilises technology licensed from Vegenics. Ark expects this Phase 3 trial to commence in the second half of 2007. For further information see Ark Therapeutics' website <http://www.arktherapeutics.com>.

On 22 August 2006, Vegenics announced that it had signed an agreement with CoGenesys Inc (based in Rockville, Maryland USA). The agreement provides Vegenics with further rights to intellectual property in the field of the vascular endothelial growth factor, VEGF-C. Under the agreement, Vegenics also obtained an option to develop an existing VEGF-C antibody developed by CoGenesys in collaboration with Cambridge Antibody Technologies plc. This option was exercised during the year to acquire the relevant rights.

The Vegenics project is the largest project undertaken by Circadian in its 23 year history with funding to date of \$21.5 million. We are all very excited about our involvement in this project and Robert Klupacs, Circadian's Manager, Strategic Development and Vegenics' Managing Director, will provide further information on this collaboration after Graeme Kaufman's presentation.

A detailed review of the Company's listed technology holdings is provided in the Annual Report, however I would like to provide you with an update on these holdings as well as a brief overview of the operating results for the period under review.

### **Brief Overview of Operating Results**

The consolidated profit after tax of the Company for the year was \$6.3 million compared with a loss after tax in the previous year of \$6.5 million.

The profit of \$6.3 million is after expensing the acquisition costs of the Vegenics intellectual property acquired from the Ludwig, Licentia and CoGenesys of \$7.9 million. Also an amount of \$1.8 million has been expensed in respect of patent costs incurred by Vegenics during the period under review.

The main items comprising the gains during the year were: a total gain of \$12.6 million in respect of the disposal of the company's holding in Zenyth Therapeutics Limited to CSL Limited (this includes the recoupment of impairment losses of \$5.1 million); a gain of \$8.3 million on the sale of 12 million shares in Metabolic Pharmaceuticals Limited (Circadian retains 36 million ordinary shares in Metabolic); and a gain of \$6.8 million on the disposal of 22.5 million shares in Avexa Limited (Circadian retains 13.7 million ordinary shares in Avexa as at today's date).

The net asset backing per share as at 30 June 2007 was \$1.52 (2006: \$1.41). The value of Circadian's listed holdings as at 30 June 2007 was \$19.7 million and as at Monday's close (22 October 2007) was \$19.1 million.

As in previous years, all research and development costs incurred during the year have been expensed.

The Company had cash reserves of \$30 million as at Monday 22 October 2007.

### **Holdings in listed companies**

As you are aware, Metabolic Pharmaceuticals, Optiscan Imaging and Antisense Therapeutics are companies in which Circadian has listed to the ASX after providing management, funding and other assistance prior to their listings. The investment in these three shareholdings is currently \$3.2 million whereas the total market value of these holdings as at Monday 22 October 2007 was \$9.4 million, reflecting an unrealised pre-tax gain of \$6.2 million. Also Circadian retains 13.7 million shares in Avexa Limited with a market value as at 22 October 2007 of \$9.7 million.

#### Metabolic Pharmaceuticals Limited

Circadian worked for many years on the obesity project with Monash University and in November 1998 listed Metabolic Pharmaceuticals Limited on the Australian Stock Exchange. Metabolic advised its shareholders on 21 February 2007 that the results of its phase 2b clinical trial of its obesity drug AOD9604 did not support further clinical development and that the program had been terminated. Unfortunately Metabolic also announced on 14 August 2007 that they did not intend at the present time to continue the development of their ACV1 as a compound to treat neuropathic pain.

On a positive note, Metabolic announced on 20 September 2007 that results from rodent studies showing that several peptide drugs modified by Metabolic have oral availability from 10 percent to greater than 30 percent. Next steps include testing in larger animal species, and exploring additional peptide drugs for modification.

Metabolic had cash reserves of \$20.6 million as at 30 June 2007.

Circadian is the largest shareholder of Metabolic with a 12% shareholding which had a market value at the close of trade on Monday 22 October 2007 of \$2.1 million compared with a cost of \$10,000. Since Metabolic's listing, Circadian has sold 18 million shares in Metabolic for a profit of \$14.5 million.

#### Antisense Therapeutics Limited

Circadian listed Antisense Therapeutics Limited on the Australian Stock Exchange in December 2001. Circadian has direct and indirect shareholdings totalling 23.6% of that company which had a market value of \$5.8 million as at close of trade on Monday 22 October 2007.

Antisense Therapeutics' lead project is a compound for multiple sclerosis, namely ATL1102. That company is currently conducting an 80 patient trial to assess the safety and efficacy of ATL1102 in relapsing-remitting MS patients in Poland, Czech Republic, Bulgaria, Romania, Slovak Republic and Germany. The study is a multi-centre, randomized, double-blinded, placebo-controlled clinical trial in patients with relapsing-remitting MS. Antisense Therapeutics reported on 12 September 2007 that all the patients will have been enrolled and the study completed in time for trial results to be reported in the first quarter of 2008.

#### Optiscan Imaging Limited

Optiscan Imaging Limited was Circadian's first company to be listed on the Australian Stock Exchange in 1997, with a mission to further develop a miniature microscope to be built into an endoscope, enabling immediate cellular level examination without the need for a biopsy for early cancer detection. Circadian's shareholding has been diluted over the years due to capital raisings by Optiscan and Circadian presently holds 6% of that company's issued capital.

Optiscan has advised that it had product sales revenue for the 2007 financial year of \$5.7 million which included the export to Pentax of 88 endo-microscope systems and associated miniaturised scanners.

Optiscan announced on 2 October 2007 that investigators at the Royal Women's Hospital in Melbourne have received ethics approval and commenced patient recruitment for a pilot clinical trial to study the use of Optiscan's rigid endomicroscopes in the women's health condition, endometriosis.

The present pilot study will assess the ability to predict relevant histopathology results in patients which have either known or suspected endometriosis. A total of 20 patients will be recruited for the study.

Detailed information on the activities of Metabolic Pharmaceuticals Limited, Antisense Therapeutics Limited and Optiscan Imaging Limited may be obtained from their respective websites. The website details are shown in the Circadian annual report.

### Avexa Limited

Avexa was demerged and listed by Zenyth in September 2004. At the time, Circadian was Zenyth's major shareholder.

Circadian has a 3.4% shareholding in Avexa Limited which has a cost base of \$6 million and a market value of \$9.7 million as at close of trading on Monday, 22 October 2007. Circadian sold 22.5 million shares in Avexa during the year under review for a net consideration of \$13.9 million, resulting in a net gain of \$6.8 million.

Avexa announced on 4 September 2007 positive 24 week data from the phase 2b clinical trial of ATC (apricitabine). The data demonstrate that, in over 80% of patients treated with ATC, the level of HIV in the blood was reduced to below detectable levels after 24 weeks.

### **Summary and Closure**

In summary, Circadian has invested \$21.5 million in Vegenix, demonstrating our confidence in Vegenix' technology and the potential of its license agreements. This is substantially more than Circadian has funded for other individual projects in the past, however we feel that this asset has the potential to create further value for our shareholders. We have an exciting pipeline of projects being developed and Vegenix is a licensor to Ark Therapeutics in respect of Trinam<sup>®</sup>, which if successfully developed, may provide significant royalty income in the future for Vegenix.

Circadian's listed holdings have seen some of their low points during the year with regard to their market values, however the market value of these holdings is still considerably in excess of Circadian's investment in these companies, and we look forward to better results from these entities during the forthcoming year.

On completion of my presentation, Graeme Kaufman, Executive Director of Circadian, will provide you with a summary of two of Circadian's main R&D projects, namely the Dicarba Analogues Project and the Cancer Vaccine Project, both with Monash University.

Also on completion of Graeme's short presentation, Mr Robert Klupacs, who is Circadian's Manager, Strategic Development and Managing Director of Vegenix, will provide a brief presentation on Vegenix.

We have a management team and board who are passionate and motivated to progress Circadian's intellectual property portfolio. Your company is in a strong financial position with \$30 million in cash reserves, Vegenix with a further \$15.6 million in cash reserves, a share portfolio with a market value of \$19.1 million and in addition to our research portfolio, we have a very exciting IP portfolio in Vegenix which we intend to actively develop further.

On behalf of the Board and Circadian's management, I would like to thank you our shareholders for your continued support. Many of you have been with us for 23 years and we look forward to sharing with you future successes for Circadian.

## About Circadian Technologies Limited

Circadian Technologies Limited (ASX: CIR) was listed on the Australian Stock Exchange in 1985 and provides management and funding for the development and commercialisation of Australian biomedical research.

It aims to identify high potential scientific research projects from within Australian universities and research institutes, focussing on opportunities that have the potential to address large markets or significant unmet medical needs. Circadian is able to provide funds for further project development, in addition to providing the management expertise that is essential if the project is to meet its goal of commercialisation.

Circadian has shareholdings in Optiscan Imaging Limited, Metabolic Pharmaceuticals Limited and Antisense Therapeutics Limited, companies in which Circadian has provided management, funding and assistance in their listing. Circadian also has a shareholding in Avexa Limited, an Australian pharmaceutical research company which was demerged from Zenyth Therapeutics Limited.

In addition to retaining shareholdings in these companies, Circadian maintains an active research and development program. Circadian is the founder and a major shareholder (67%) of Vegenic Limited, which has a collaboration with the Ludwig Institute for Cancer Research and Licentia Ltd to develop antagonists of VEGF-C and/or VEGF-D as therapeutic agents, initially as anti-tumour agents. Other current research projects include a cancer vaccine project aimed at developing novel immunising agents with potential application in the development of vaccines against cancer, and a dicarba analogues project which is based on novel technology for the development of stable peptides, with potential application across a broad range of therapeutic agents.

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## INHERENT RISKS OF INVESTMENT IN BIOTECHNOLOGY COMPANIES

Shareholders should be aware of the risks involved in drug discovery and development. Some of the risks inherent in the development of a product to a marketable stage include the uncertainty of patent protection and proprietary rights, whether patent applications and issued patents will offer adequate protection to enable product development, the obtaining of the necessary drug regulatory authority approvals and difficulties caused by the rapid advancements in technology. Also a particular compound may fail the clinical development process through lack of efficacy or safety. Companies such as Circadian are dependent on the success of their research projects and technology investments. Investment in research projects and technology-related companies cannot be assessed on the same fundamentals as trading and manufacturing enterprises. Thus investment in these areas must be regarded as speculative taking into account these considerations.

This announcement may contain forward-looking statements regarding the potential of the company's projects and interests and the development and therapeutic potential of the company's research and development. Any statement describing a goal, expectation, intention or belief of the company is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to certain risks and uncertainties, particularly those inherent in the process of

discovering, developing and commercialising drugs that are safe and effective for use as human therapeutics and the financing of such activities. There is no guarantee that the company's research and development projects and interests (where applicable) will receive regulatory approvals or prove to be commercially successful in the future. Actual results of further research could differ from those projected or detailed in this report. As a result, you are cautioned not to rely on forward-looking statements. Consideration should be given to these and other risks concerning research and development programs referred to in this announcement.

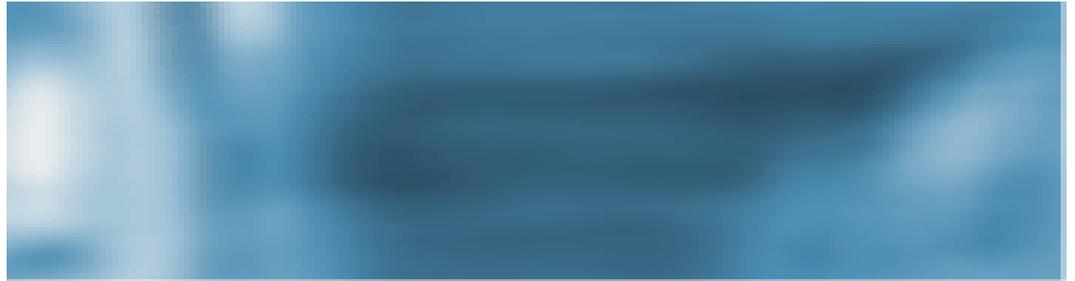


# **Circadian Technologies Limited**

**2007**

**Annual General Meeting**





# Corporate overview

**Presentation to Annual General Meeting  
October 2007**

**Presenter: Leon Serry, Managing Director**



## **DISCLAIMER**

**Investment in Circadian Technologies Limited ('Circadian') is subject to investment risk, including possible loss of income and capital invested. Neither Circadian nor any other member company of the Circadian Group guarantees any particular rate of return or performance, nor do they guarantee the repayment of capital.**

**This presentation is not an offer or invitation for subscription or purchase of or a recommendation of securities. It does not take into account the investment objectives, financial situation and particular needs of the investor. Before making any investment in Circadian, the investor or prospective investor should consider whether such an investment is appropriate to their particular investment needs, objectives and financial circumstances and consult an investment advisor if necessary.**

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## □ **Vegenics progress**

- **assignment of patent estate and novation of agreements**
- **acquisition of CoGenesys rights**
- **licensee Ark Therapeutics prepares for Phase 3 trial**

# Financial year highlights

<b>Profit after tax*</b>	<b>\$6.3m</b>
<b>Market value of listed holdings before tax</b>	<b>\$19.7m</b>
<b>Net asset backing</b>	<b>\$1.52 per share</b>
<b>* after expensing all R&amp;D, plus \$9.7m acquisition costs of Vegenics IP and patent costs</b>	

- sale of Zenyth to CSL – total gain of \$12.6m
- sale of shares in Metabolic – gain of \$8.3m
- sale of shares in Avexa – gain of \$6.8m

## Strong financial position

**As at 22 October 2007:**

- ☐ cash of \$30m**
- ☐ Vegenics cash of \$15.6m**
- ☐ share portfolio market value \$19.1m**

# Research projects

(Cancer vaccine and Dicarba analogues)

**Presentation to Annual General Meeting**  
**October 2007**

**Presenter: Graeme Kaufman, Executive Director**

# Cancer vaccine

- ❑ **Increasing global interest in development of vaccines to treat cancer**
  
- ❑ **Circadian research project to improve stability and efficacy of peptide-based cancer vaccines**
  - makes peptides more resistant to breakdown in the body – more stable
  - potential to also improve recognition by the body's immune system – better efficacy
  - partners Monash and Melbourne universities
  
- ❑ **Early promising results in models of anti-tumour immunity**
  - effective immune response
  - program to develop vaccine against multiple targets
  
- ❑ **\$671,000 ARC Linkage grant**

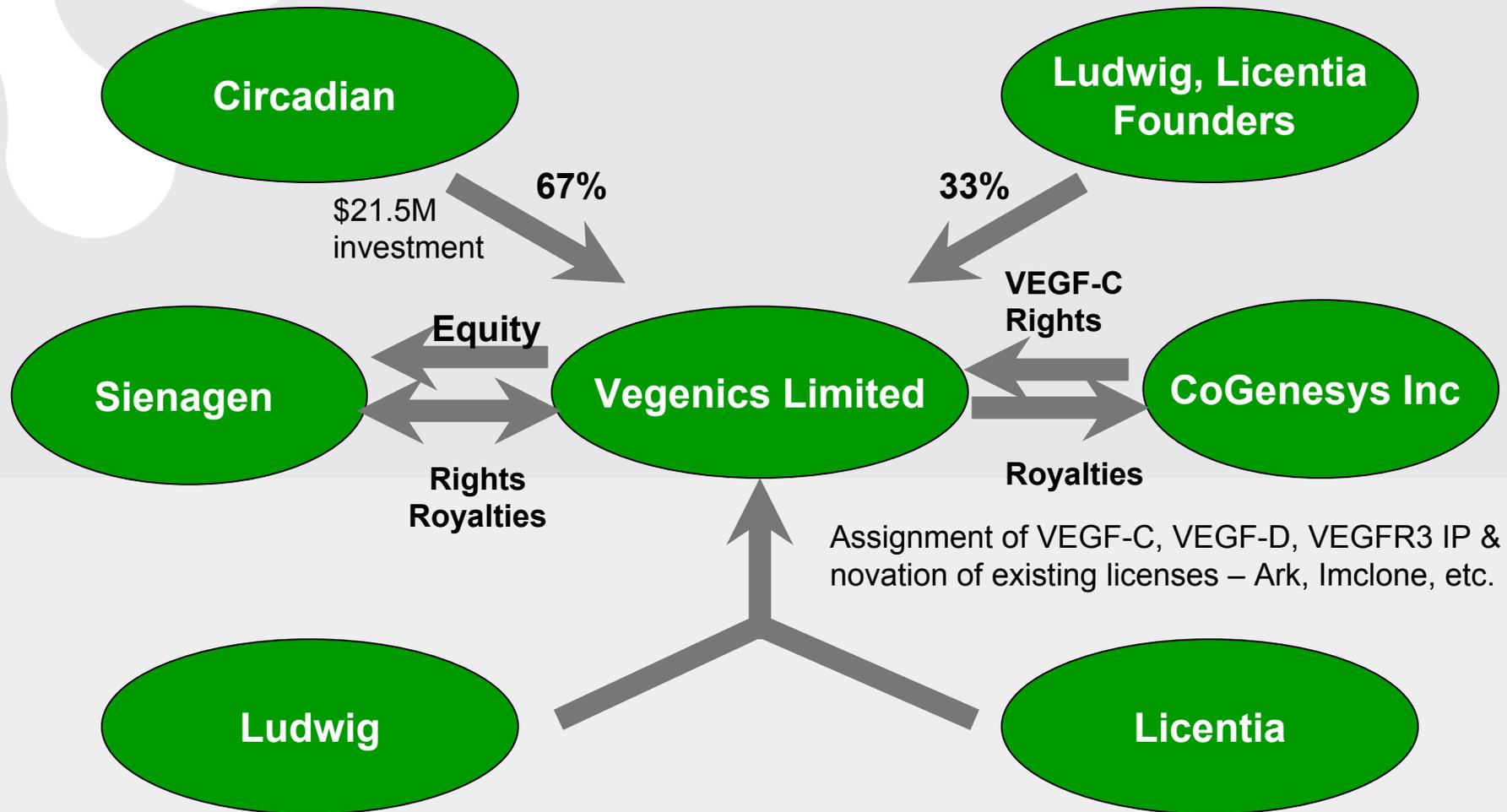
# Dicarba analogues

- Method for replacing weak internal links in peptide molecules with strong carbon bonds**
- Potential to produce more stable peptide drugs – resistant to breakdown in the body**
- Development program centred on insulin**
- Has potential for out-licensing on a compound by compound basis**
- Partner Monash University**
- \$280,000 ARC Linkage grant**

**Presentation to Circadian AGM  
by Robert Klupacs**

**Managing Director  
Vegenics Limited**

**Oct 25 2007**



## Background

### Targeted VEGF Inhibitors-A Hot Space

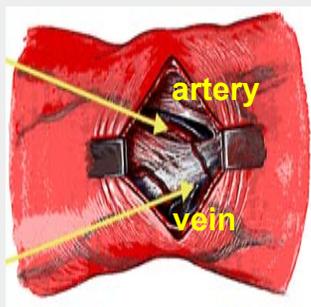
- **Avastin® (Roche/Genentech) a VEGF-A Ab for cancers projected 2007 sales of \$US3B+**
- **Lucentis® (Novartis/Genentech) a VEGF-A antibody fragment for AMD projected 2007 sales of \$US1B+**
- **Regeneron –VEGF Trap (soluble VEGF Receptor) deals with Aventis and Bayer 2004/2005 \$200M up front for pre-clinical compounds**

## Key Assets

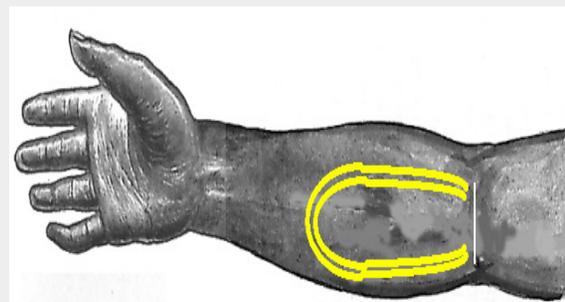
- \$15M cash at bank
- Circadian 67% ownership
- Broad and deep IP portfolio
- Existing Major Licence Partners-Ark (AKT:LSE), Imclone (IMCL:NSDQ)
- Close relationships with major researchers –LICR, Helsinki
- World class advisors and management

## Trinam<sup>®</sup> - Being Developed by Ark Therapeutics

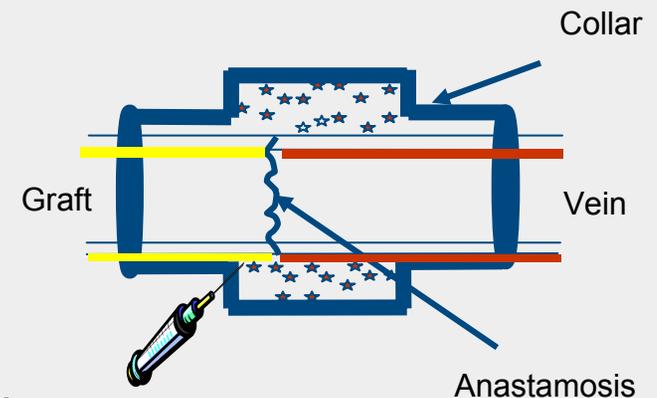
- Prevention of blockage of haemodialysis access grafts
- Combination of adenoviral VEGF gene and proprietary bio-degradable local drug delivery device
  - “Collar” fitted around vein/graft junction during normal surgical procedure
  - “Drug” injected into cavity between “collar” and blood vessel
- Market opportunity - 150,000 suitable cases per year (US and Europe)
- Potential \$US500m per annum peak sales product
- Positive Phase 2. Commence Phase 3 Q1 2008
- Approval end 2010?



**Step 1: Surgical isolation of vein and artery**



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



Source:  
Ark web-  
site

## Achievements First 12 months

- CoGenesys IP Licence and access to lead product candidate (VEGF-C Ab)
- Evogenix collaboration-VEGF-D antibodies
- Siena VEGF-D IP Licensing
- Collaboration with global pharma co - eye disease
- Product Development Advisory Group formed
- Manufacturing relationships-Abs, peptides

## Achievements First 12 months

- Research contracts with Uni Helsinki, LICR, others including CSIRO
- Progressed VEGF-D Ab and VEGFR3 to near product candidate status
- Identified potential opportunities for non-core licensing
- Built relationships with Stanford and Harvard Key Opinion Leaders in areas of lymphedema and cornea inflammation

## Key Targets next 12 months

- Further IP consolidation
- Confirm Product Candidate Development Status for VEGF-D Ab, VEGFR3, proteins
- Partnering deals in eye disease, gene therapy, cancer vaccine space
- Partner aspects of oncology portfolio