

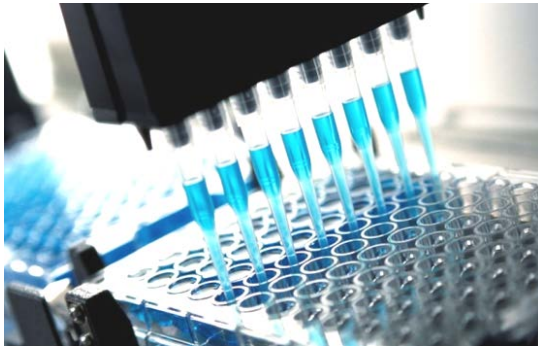


# Eco Quest's Investment in Cynata

A next generation stem cell company

Dr Ross Macdonald, CEO, Eco Quest

September 2013



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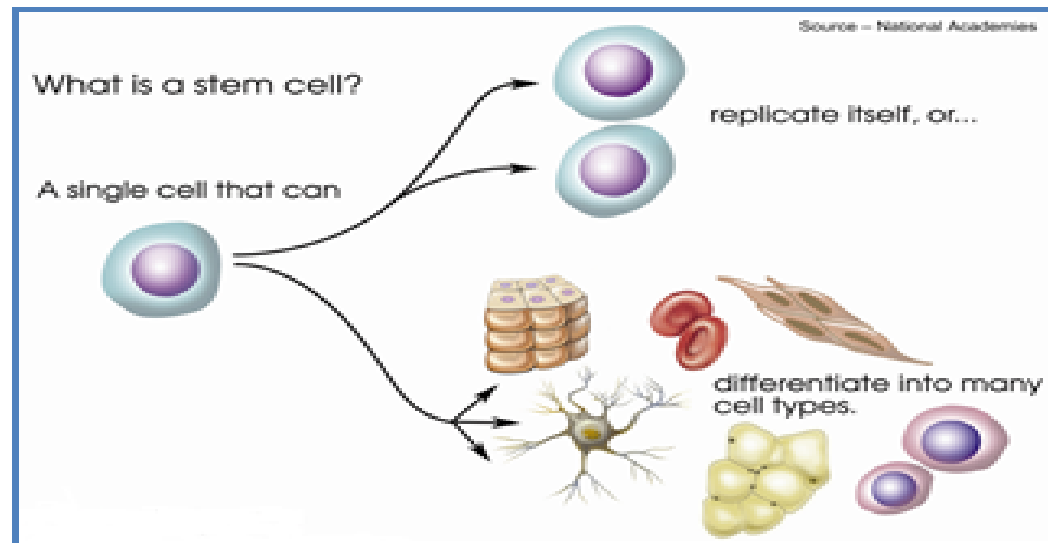
# Overview

- Cynata Inc is a California registered company with rights to certain novel stem cell technology licensed from Wisconsin University Alumni Research Foundation (WARF)
- Cynata is 33% owned by ECQ through investment of \$1m in the company to date
- ECQ has an option to acquire all remaining shares in Cynata:
  - Conditional upon ECQ shareholder approval + compliance with laws/ASX + recompliance with Chapters 1 & 2
  - Consideration: 200m ECQ shares (currently 636m out)
  - 11 shareholders will hold 23.9% of ECQ (largest with 5.7%)
- Upon completion of the potential acquisition, ECQ will be re-purposed as a biotechnology company with Cynata's technology as its chief asset



# What is a Stem Cell?

- Stem cells are unspecialised (undifferentiated) cells in the body that give rise to all functional cell types: blood, nerves, bone, muscle.....



- Stem cells may also assist in the body's own ability to repair or replace tissue that is damaged or destroyed by injury or disease:
  - Physical reconstruction of tissue (or causing it to happen)
  - **Immune modulation, i.e. anti-inflammatory**

# Cynata's Cymerus™ Stem Cell Technology

- Cynata has exclusive therapeutic rights to certain WARF patents, including:
  - a unique type of precursor stem cell, the mesenchymoangioblast (MCA)
  - methods of manufacture of pure mesenchymal stem/stromal cells (MSC's) from MCAs
  - patent protection to 2028
- Outstanding pedigree: inventors on the WARF i.p. include James Thomson who derived the first human embryonic stem (ES) cell line in 1998 and human induced pluripotent stem cells (iPSCs) in 2007
- Cymerus™ technology:
  - Specific clinical uses: to derive MSCs from MCAs for therapeutic applications
  - Platform Technology: proprietary method of commercial-scale manufacture from a single ES or iPS cell, providing a significant competitive advantage



# Cymerus™ Pedigree: Stem Cell Pioneers

Cell  
PRESS

Cell Stem Cell  
Article

## A Mesoderm-Derived Precursor for Mesenchymal Stem and Endothelial Cells

Maxim A. Vodyanik,<sup>1</sup> Junying Yu,<sup>1</sup> Xin Zhang,<sup>2</sup> Shulan Tian,<sup>3</sup> Ron Stewart,<sup>3</sup> James A. Thomson,<sup>1,3</sup> and Igor I. Slukvin<sup>1,4,\*</sup>

<sup>1</sup>National Primate Research Center, University of Wisconsin Graduate School, 4220 Capitol Court, Madison, WI 53715, USA

<sup>2</sup>WiCell Research Institute, Madison, WI 53726, USA

<sup>3</sup>Morgridge Institute for Research, The Genetics and Biotechnology Building, 425 Henry Mall Madison, WI 53706, USA

<sup>4</sup>Department of Pathology and Laboratory Medicine, University of Wisconsin Medical School, 600 Highland Avenue, Madison, WI 53792, USA

\*Correspondence: islukvin@wisc.edu

DOI 10.1016/j.stem.2010.11.011

### James Thomson

- First to successfully isolate ES cells.
- Developed technique to manufacture iPSCs from differentiated cells.
- Scientific founder of Cellular Dynamics International (CDI)

### Igor Slukvin

- Inventor of MCAs
- Scientific founder of Cynata
- Cofounder of CDI with James Thomson
- Published almost 70 peer reviewed papers in highly respected journals

Selected by Faculty of 1,000, placing it in top 2% of Biology/Medicine publications

# Eco Quest Board and Management

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Executive Chairman: **Dr Stewart Washer**

Managing Director & CEO: **Dr Ross Macdonald**

Non-executive Director  
and Company Secretary: **Mr Peter Webse**

Executive Director: **Mr Howard Digby**

- A tight team with extensive industry and public company experience plus a track record of commercialising therapeutic products
- Additional resources to be considered as product development progresses



# Eco Quest Current Cap Structure

ASX:	<b>ECQ</b>
Market Cap (13 Sept 13):	<b>\$15.9m</b>
Shares on Issue:	<b>636m</b>
Options (31/12/14, \$0.01):	<b>235m</b>
Cash (13 Sept 13):	<b>\$1.826m</b>
Number of shareholders:	<b>869</b>



<b>Major holders:</b>	Celtic Capital Pty Ltd	6.5%
	JK Nominees Pty Ltd	6.27%
	Denlin Nominees Pty Ltd	6.27%
	Tisia Nominees Pty Ltd	6.21%

50,000,000 unlisted \$0.02 options to be issued to each of RM and SW, subject to shareholder approval, vesting upon attainment of performance hurdles





# Why stem cells?

SAFE

PLATFORM TECHNOLOGY

VALUATIONS

GOLDRUSH EFFECT

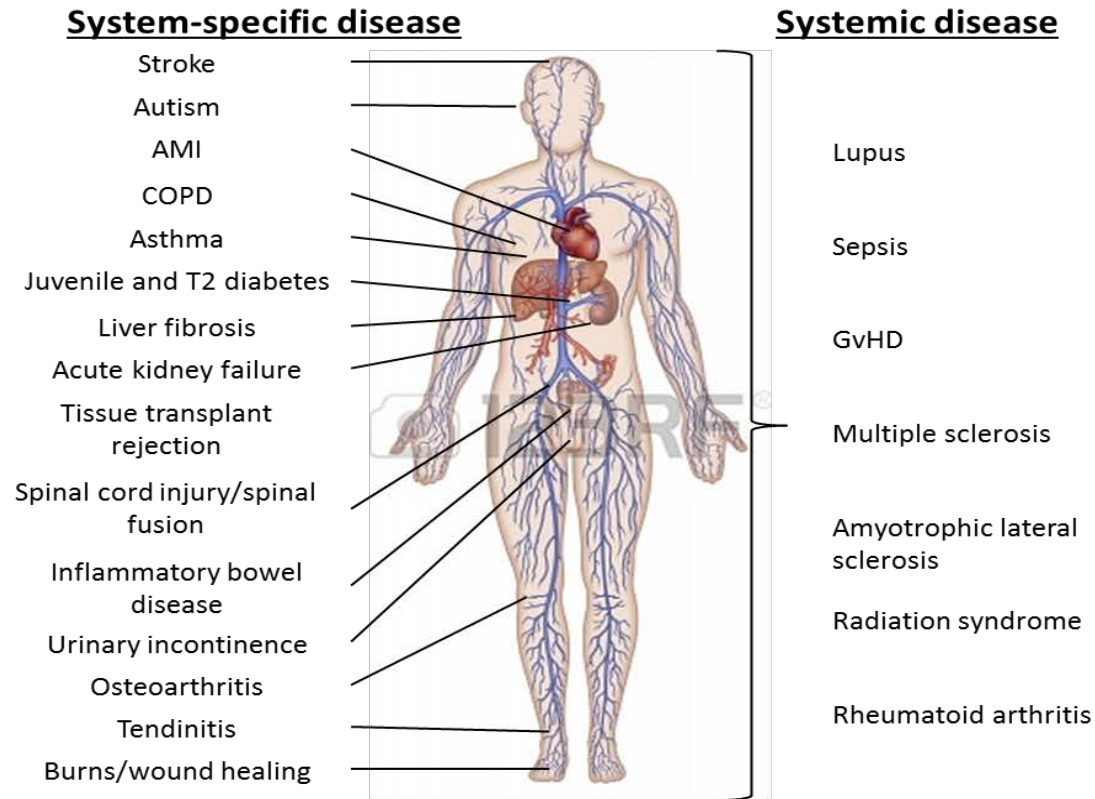


# Safety of Stem Cell Products

- Meta-analysis shows MSCs are safe: review of 1,012 patients in 36 MSC clinical studies<sup>1</sup>:
  - *“However, aside from <transient> fever, the published clinical trials suggest that the administration of MSCs is safe”.*
  - *“Although malignant transformation is a theoretical risk, ... found no association between MSCs and tumour formation”.*

<sup>1</sup>Lalu *et al* (2012): Safety of Cell Therapy with Mesenchymal Stromal Cells: A Systematic Review and Meta-analysis of Clinical Trials. PLOS One 7(10): e47559

# Stem cells: the ultimate platform?



“... the MSCs serve as site-regulated, multidrug dispensaries or “drugstores” to promote and support the natural regeneration of focal injuries”

*“... all of these disorders and conditions appear to be muted or cured by the injected or infused MSCs based upon two generalisable therapeutic activities: immunomodulation and trophic activities.”*

Adapted from Caplan and Correa (2011): The MSC: An Injury Drugstore. Cell Stem Cell 9,11-15

# Stem Cell Field is Emerging

- Analogous to monoclonal antibody enabling technologies in '80s and '90s; therapeutic market value now in excess of US\$44.6b<sup>1</sup>
- Commercial stem cell products are entering the market:
  - Prochymal (GvHD) – Osiris (USA)
  - Cartistem (Osteoarthritis) – Medipost/Dong-A (Korea)
- Most stem cell companies attractively priced based on forward estimates
- Multiple products in Phase 2 and 3
  - Sector news flow
  - Creates opportunities for Cynata
- Big pharma partnering/M&A:
  - Teva/Mesoblast
  - Pfizer/Athersys
  - United Therapeutics/Pluristem
  - Novartis/Regenerex

<sup>1</sup>BCC Research, 2011 global market estimate of therapeutic monoclonals



# Stem Cell Company Market Valuations

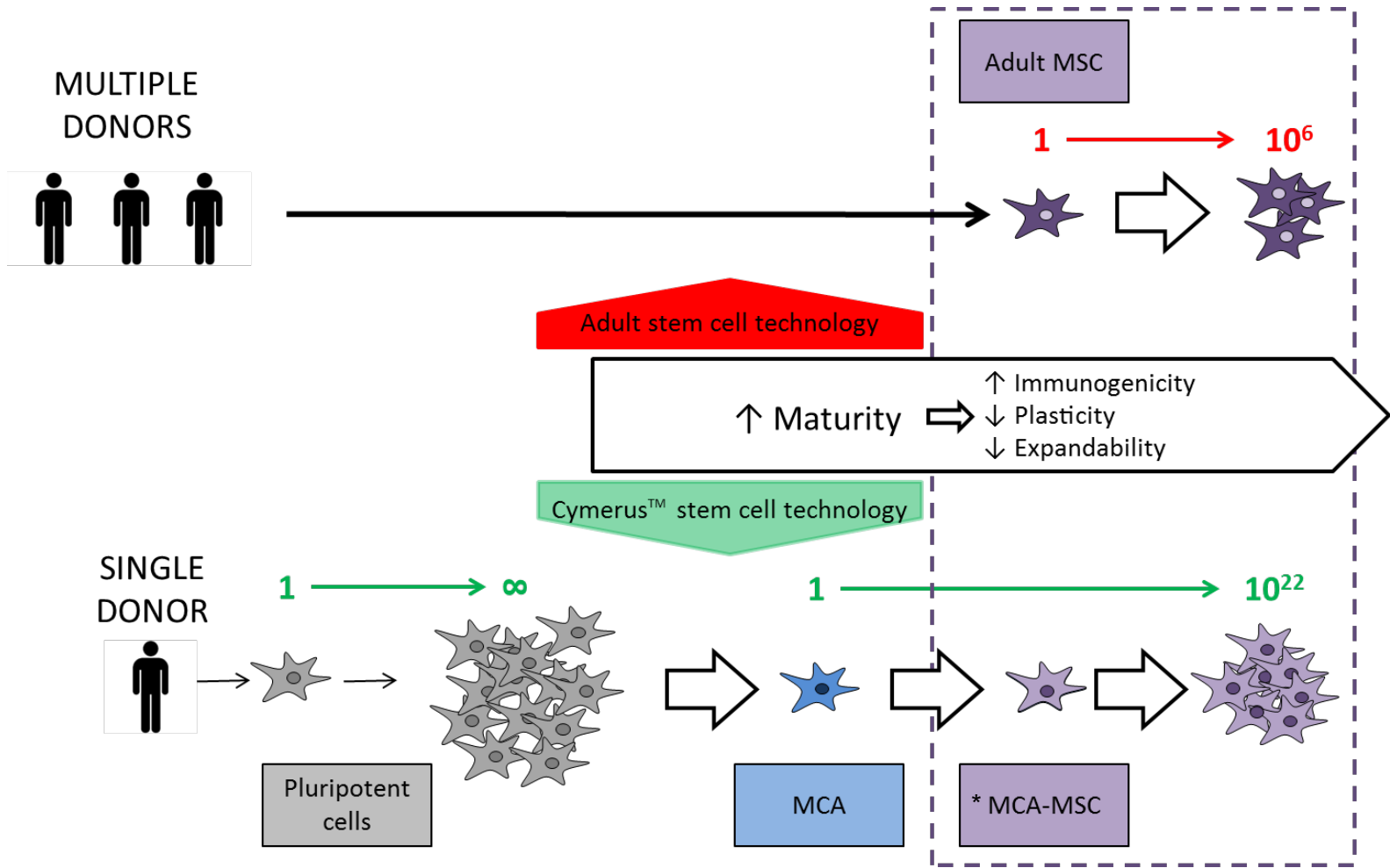
Company	Mkt cap	Development stage	Partners	Cash
Mesoblast (Aus)	\$1.8b	6 x Ph2 1 x Ph3	Teva (CHF)	\$178M
Medipost (S. Korea)	\$407m	Cartistem on sale 2 x Ph1	N/A	-
Osiris (USA)	US\$562m*	Prochymal on sale 3 x Ph3 3 x Ph2	N/A	\$37m
Biotime (USA)	US\$219m	1 x Ph1	Teva (AMD)	\$20M
ACT (USA)	\$161m	2 x Ph1		\$40M
Pluristem (Israel)	\$189m	2 x Ph1 2 x Ph2	United Therapeutics (Pulmonary HT)	\$65M
Athersys (USA)	\$99m	2 x Ph2	Pfizer (IBD)	\$21M

As at 13 September 13

\*Nearly trebled in Aug on news of overwhelming efficacy in diabetic foot ulcers



# Cymerus™ : manufacturing scalability



\*Potential opportunity to provide cell bank

# Potential Benefits of Cynata's MCSs vs Adult MSCs

VERSATILITY



• MSCs →

IMMUNOSUPPRESSION  
REVASCULARISATION  
BONE/CARTILAGE

MANUFACTURING  
SCALEABILITY



• POTENTIALLY INFINITE EXPANSION FROM A SINGLE DONOR

MANUFACTURING COST &  
COMPLEXITY



• ELIMINATION OF REPEATED SOURCING AND SCREENING OF DONORS  
• REDUCED BATCH/BATCH VARIABILITY ISSUES

EFFICACY



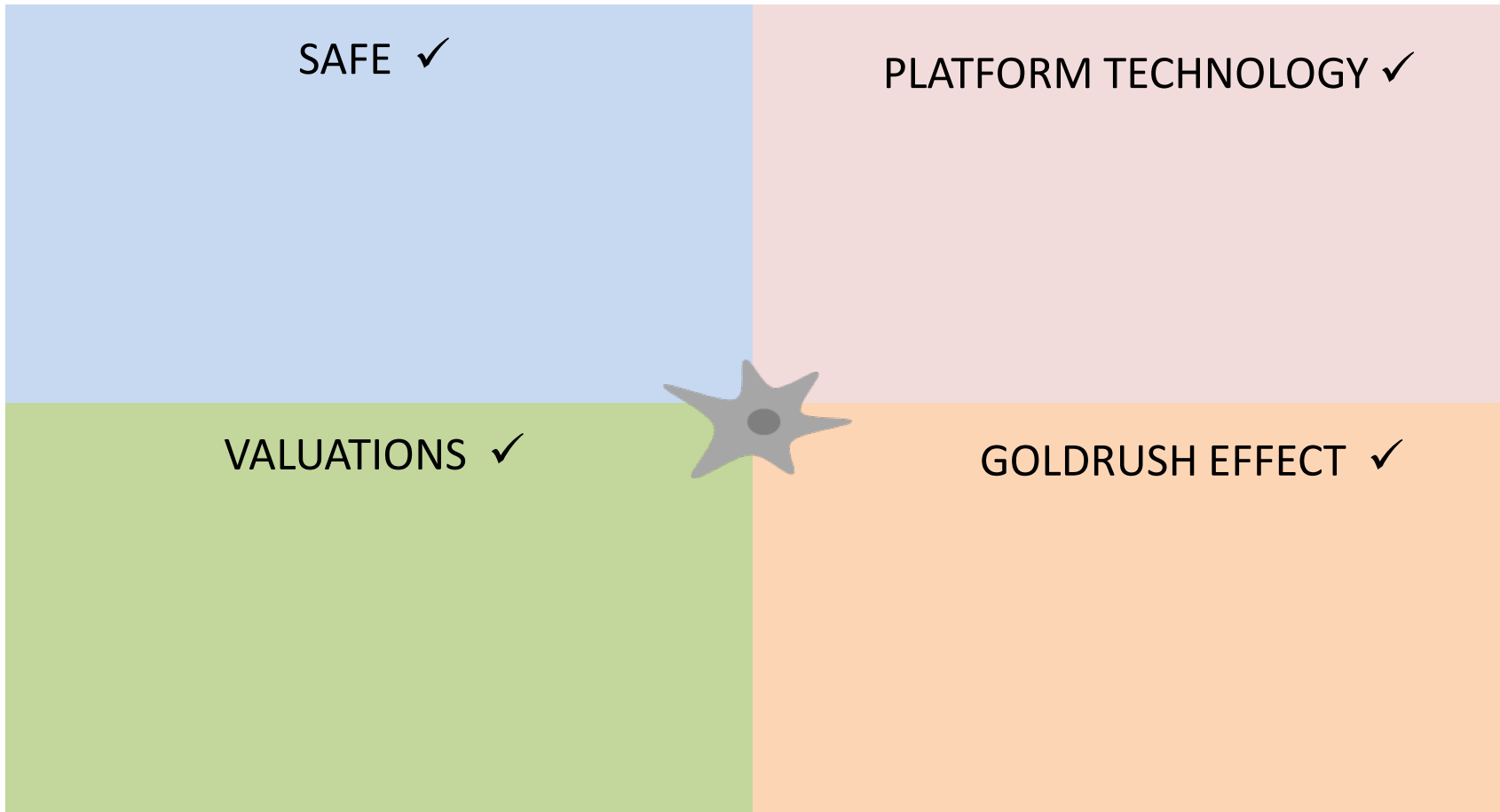
• GREATER BATCH/BATCH REPRODUCIBILITY MAY INCREASE CLINICAL PREDICTABILITY

SIDE EFFECTS



• MANY OBSERVED AE'S IN CLINICAL TRIALS THOUGHT TO BE DUE TO CELL IMPURITIES

# Why stem cells?





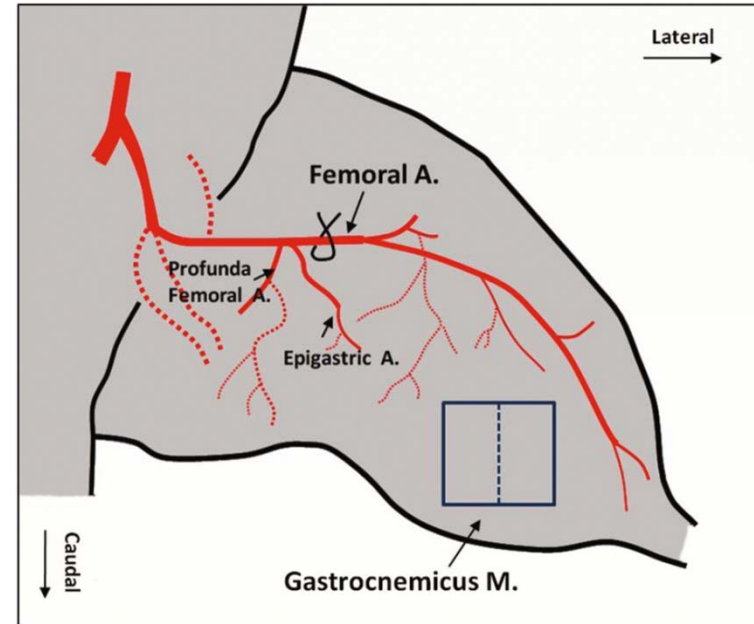
# PoC Indication: Critical Limb Ischaemia

- Dangerously diminished tissue perfusion:
  - Occluded arteries reduces blood flow to extremities.
  - Tissue necrosis, ulceration, gangrene.
- Poor prognosis. Within 1 year of CLI diagnosis:
  - 40-50% patients undergo amputation
  - 30-40% patients will die
- 3 million CLI cases in the USA - 60% are diabetics
  - Annual cost of treatment \$10-20 billion
  - Market opportunity \$3 billion
  - Insurance: \$30-40K – amputations  
\$25-75K – prosthetics  
\$75K annually - rehabilitation
- Current management
  - Revascularisation via angioplasty or stent placement
  - Amputation where revascularisation unavailable



# PoC Pre-clinical Study Details

- Total excision of femoral artery in 20 mice
- 10 mice:  $5 \times 10^6$  Cymerus™ MSCs IM;  
10 mice: Vehicle
- Recovery monitored:  
Days 0, 3, 7, 14, 21, 28
  - Laser Doppler blood flow
  - Form and function of hind limb
- Post-mortem histology of gastrocnemius



# PoC Pre-clinical Study Conclusions

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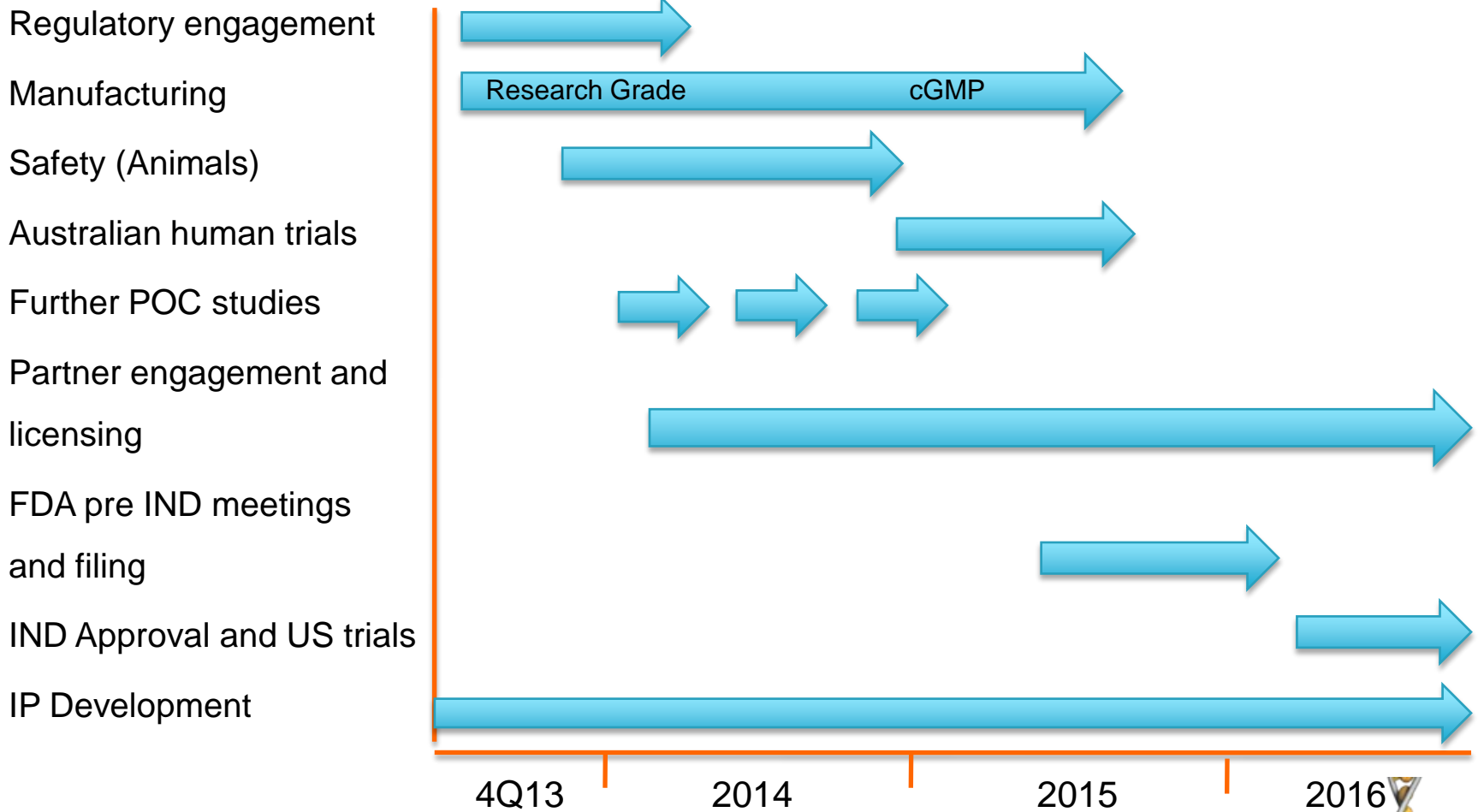
- Recovery of animals in Cynata MSC treatment group was significantly better as measured by:
  - Recovery of hind-limb blood flow
  - Reduction of toe necrosis/loss
  - Prevention of hind-limb muscle atrophy
- Promising potential treatment using Cynata MSC's in a range of circulatory/vascular diseases including chronic limb ischaemia

# Cymerus™ Development Strategy

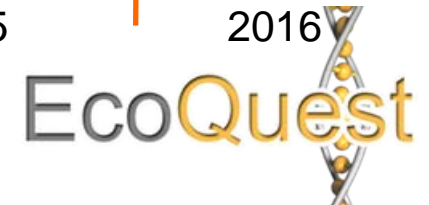
- **REGULATORY:** confirmation of regulatory strategy to assist in pre-clinical requirements and facilitate first-in-man Phase 1 study
- **MANUFACTURE:** manufacture of Cymerus™ product for pre-clinical program; commence development of manufacturing scale-up
- **CLINICAL:** aim to commence Phase 1 clinical study during 2H14 or 2015 (dependent upon regulatory path)
  - Selection of lead indication during 4Q13: short study, clear endpoints
  - Identify most attractive & feasible indication and study center(s)
  - Support with appropriate pre-clinical and further PoC studies
- Expect value inflection points coincident with this program and with partnering activity



# Cynata Timeline



Subject to completion of potential ECQ acquisition



# Commercial Strategy

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- Commercial opportunities from two sources:
  - Licensor of enabling technology to other stem cell companies/big pharma
  - Development of specific therapeutic products
- Partnering activities will be initiated upon completion of roll-up

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Thank you for your attention

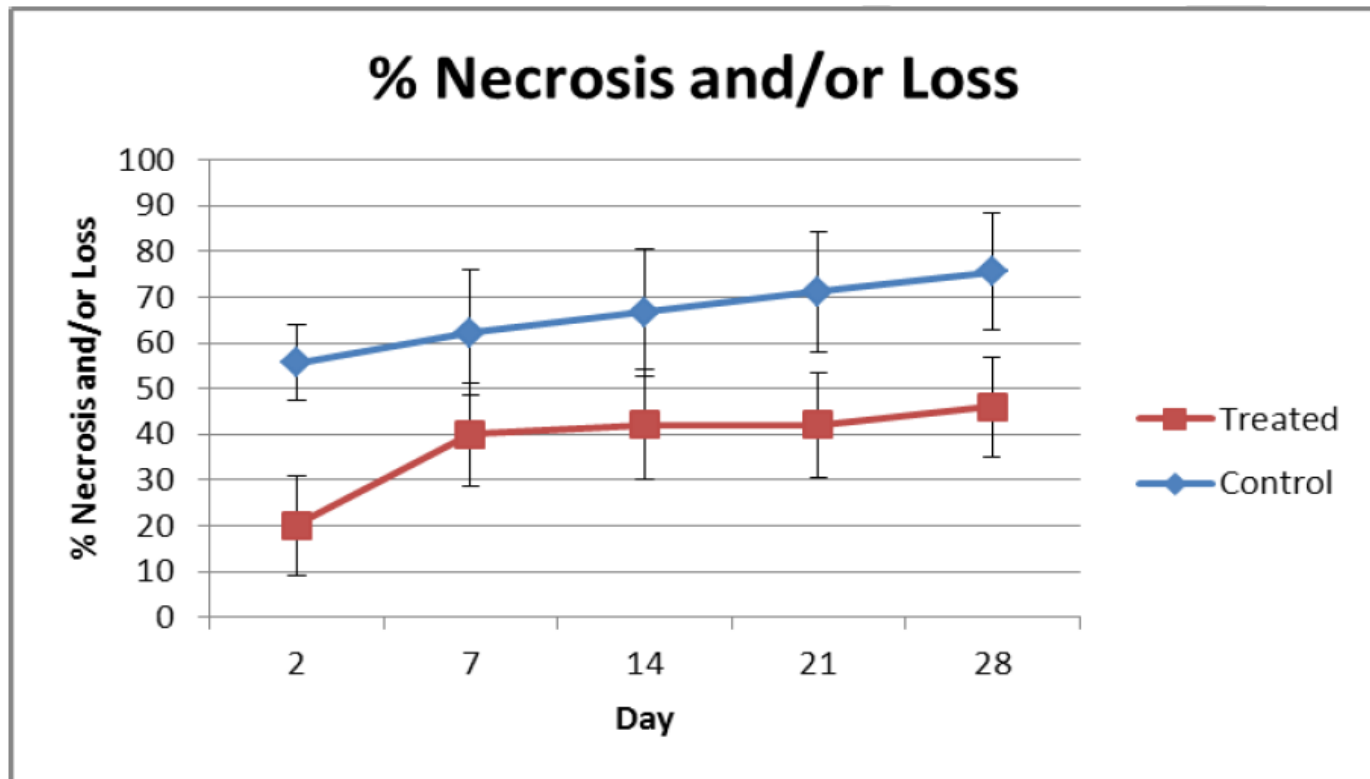


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## Appendix: PoC Study in CLI

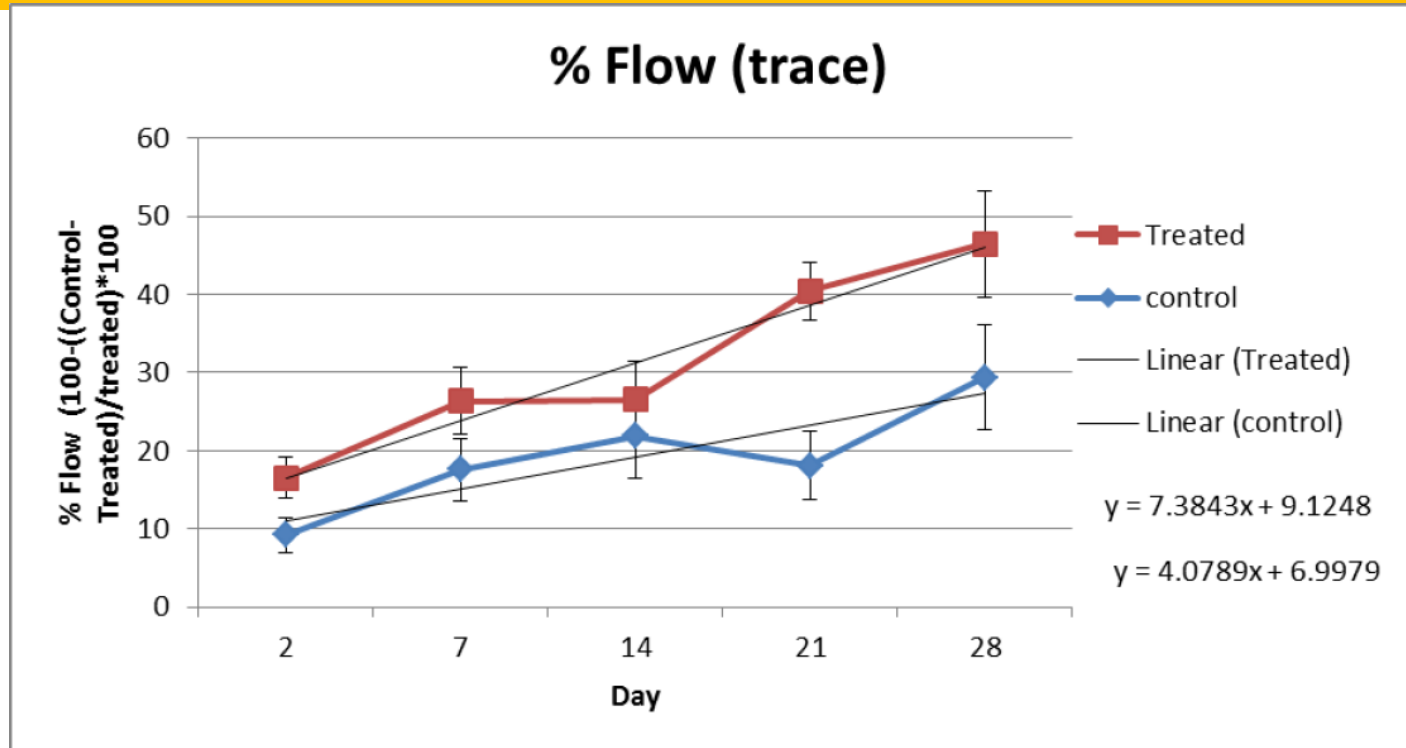


# Results 1: Tissue necrosis and/or loss



- Toe loss on any given day greater in the control mice ( $P < 0.001$ )

# Results 2: Return of blood flow



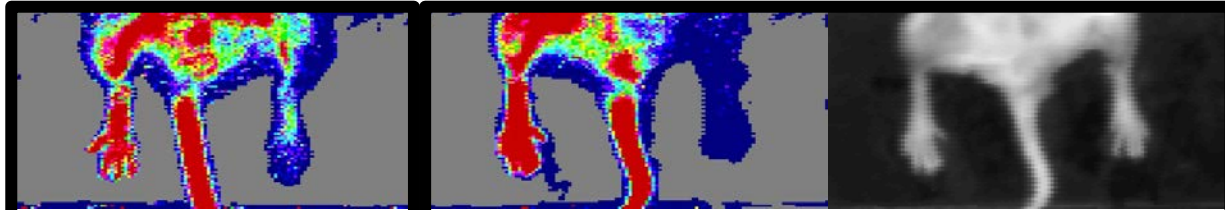
- Blood flow in treated animals is higher on each assessment day ( $P < 0.05$ )
- Blood flow recovery is faster in treated animals ( $P < 0.001$ )

# Pictorial: Return of blood flow

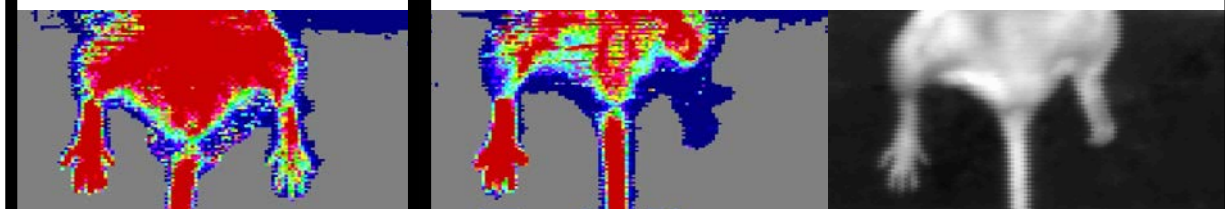
*Cymerus™ cells*

*Vehicle*

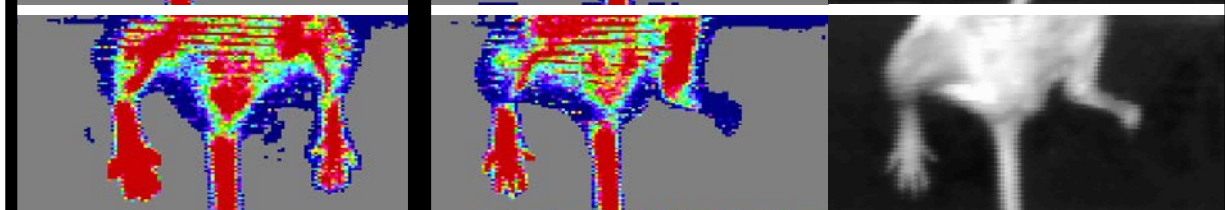
Day 2



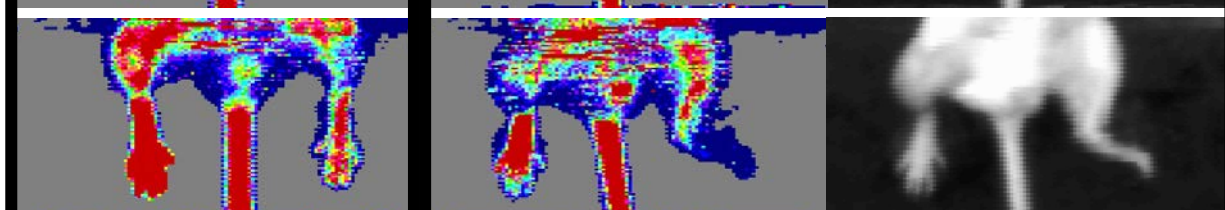
Day 7



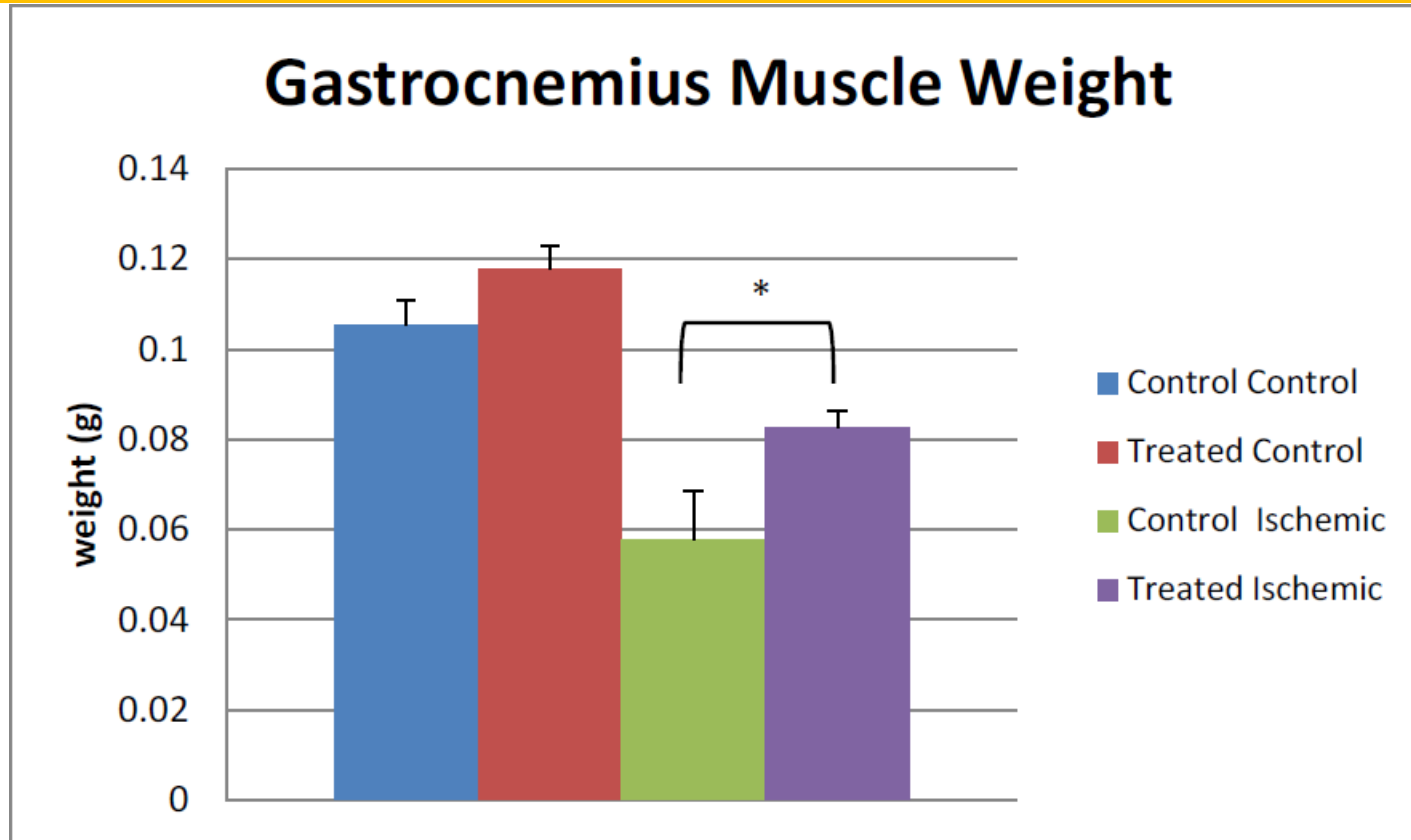
Day 14



Day 21



# Results 3: Gastrocnemius muscle weight



- MCA treatment resulted in trend to heavier gastrocnemius (P=0.051)