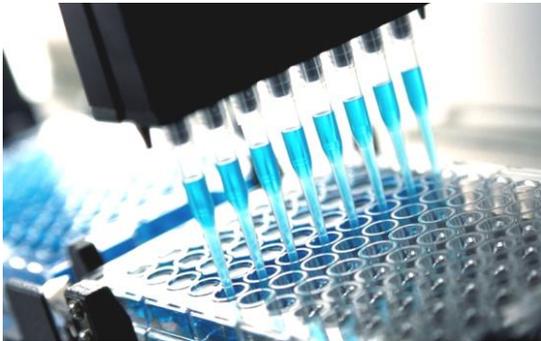


# 2014 Annual General Meeting: CEO Address

Dr Ross Macdonald, CEO, Cynata Therapeutics Limited

November, 2014



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# Cynata Therapeutics Ltd Key Facts

ASX:	<b>Resumed trading Nov 2013 as CYP</b> (prev ECQ)
Capital raised in Nov 2013:	<b>\$5m</b>
Market Cap (17 Nov 14):	<b>\$19.4m</b>
Shares on Issue*:	<b>55.0m</b>
Options (Dec 14, \$0.2):	<b>11.11m</b>
Cash (30 Sep 14):	<b>\$4.7m</b> (18 months runway)
Number of shareholders:	<b>~1150</b>
Business focus:	<b>Regenerative medicine: Cymerus™ stem cells</b>

\*includes 10m in escrow until 21 Nov 14

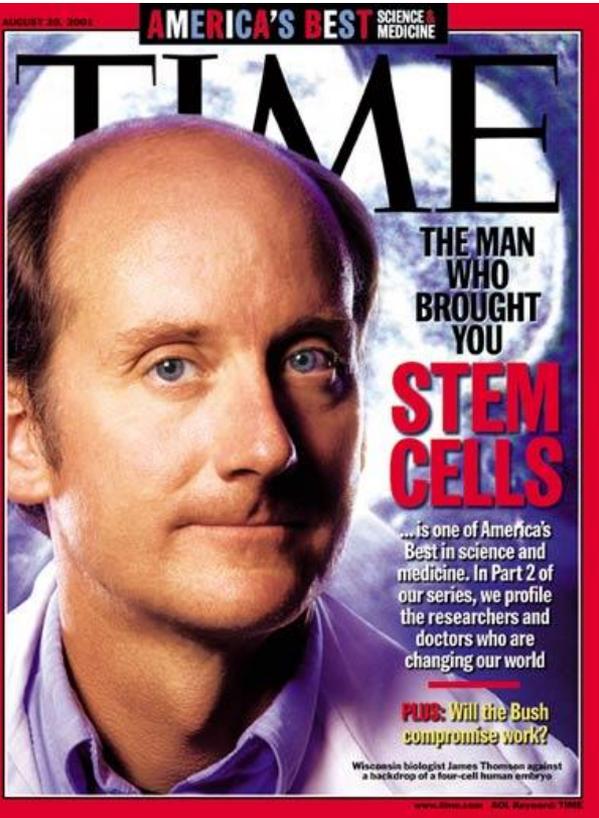
<b>Major holders:</b>	Mr Ian Dixon	4.34%
	Prof Igor Slukvin	4.34%
	Celtic Capital Pte Ltd	3.64%
	JK Nominees Pty Ltd	3.64%

2,500,000 27/9/18 unlisted \$0.40 restricted options issued to each of RM and SW, vesting upon attainment of performance hurdles

# Cynata's Cymerus™ : Outstanding Pedigree



THE UNIVERSITY  
of  
**WISCONSIN**  
MADISON



- Inventors include Dr James Thomson
  - In 1998 derived the first human embryonic stem cell line
  - 2007 derived human induced pluripotent stem cells
- Prof Igor Slukvin, co-founder and author of >70 publications in the stem cell field
- WARF: US\$2 billion endowment built from licensing and investment
- In-licensed intellectual property includes several issued US patents as well as a broad estate of issued and pending patents

# Why are Mesenchymal Stem Cells (MSCs) Important?

MSC therapies are here and now:

Spinal cord injury	Neurodegenerative diseases (eg MS)
Eye diseases (eg AMD)	Chronic wounds
Stroke	Myocardial infarction (heart attack)
Graft-versus-host disease (GvHD)	Bone fracture; cartilage repair
Osteoarthritis	++++

- Translating to ~280\* open clinical studies using MSCs to treat a variety of medical conditions
- Particular relevance to chronic diseases of ageing
- Major government initiatives to expedite stem cell therapies (eg Japan; California)

\*[www.clinicaltrials.gov](http://www.clinicaltrials.gov)

# Headlines.....

## The Telegraph

Home Video News World Sport Finance Com  
Politics Investigations Obits Education Earth  
Science News Space Night Sky Roger Highfield

HOME » SCIENCE » SCIENCE NEWS

### Cure for Type 1 diabetes imminent after Harvard stem-cell breakthrough

Harvard University has produced the vast quantities of insulin-producing cells

### Stem Cell Breakthrough Puts Type 1 Diabetes Cure In Reach

By Carl Engeling | October 10, 2014 1:35 pm

Stem-cell cure for Type 1 diabetes 'on par with discovery of antibiotics'

### Type 1 Diabetes Cure On The Horizon? Scientists Use Stem Cells To Produce Billions Of Insulin-Producing Beta Cells

By Science Staff | Oct 9, 2014 12:11 PM EDT

It's a condition that affects three million Americans, mostly children, and yet there has been little progress in developing medical interventions to cure type 1 diabetes. But a new study by Harvard stem cell researchers has generated great excitement among scientists working toward finding a cure for this



## STEM CELL THERAPY STARTS TO SHOW RESULTS

A heart patient can dance again, small steps in delivering on therapy's promise.

By KAREN WEDGECROFT  
New York Times

Edgar Irazoza was just 31 when his heart stopped beating in October 2008.

A Miami property manager, break-dancer and former high school wrestler, Irazoza had recently gained weight as his wife's third pregnancy progressed. "I kind of got pregnant, too," he said.

During a workout one day, he felt short of breath and insisted that friends rush him to the hospital. Minutes later, his pulse flattened.

He survived the heart attack, but the scar tissue that resulted cut his heart's pumping ability by a third. He couldn't pick up his children. He couldn't

Desperation motivated Irazoza to volunteer for an unusual medical research trial: getting stem cells injected directly into his heart. "I just trusted my doctors and the science behind it, and said, 'This is my only chance,'" he said recently.

Over the past five years, by studying stem cells in lab dishes, test animals and intrepid patients like Irazoza, researchers have brought vague, grandiose promises of stem cell therapies closer to reality.

Stem cells broke into the public consciousness in the early 1990s, offering the potential to help the body heal back diseases of degeneration like Alzheimer's, and to grow



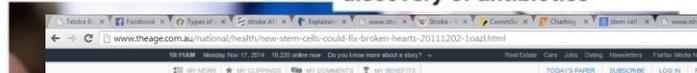
use and how to deliver them to the body — findings that are not singularly transformational, but progressive and pragmatic.

As many as 4,500 clinical trials involving stem cells are underway in the United States to treat patients with heart disease, blindness, Parkinson's, HIV, diabetes, blood cancers and spinal cord injuries, among other conditions.

against which other stem cells are measured. But the field is much less dependent on them.

Treatment for Irazoza, who received his own cells, began with the withdrawing of some of his bone marrow. Researchers took adult cells believed to be stem cells from the marrow and then inserted them through a catheter directly into Irazoza's heart.

About a third of his left ventricle had been destroyed by his attack, which was attributed to a hereditary cholesterol problem. It's impossible now to be sure whether the stem marrow cells descended because heart muscle is or if repairs were spared as other way, but today, his torso tells him his heart is one of the way back to normal. It's enough, Irazoza said, slow him to dance again to be the kind of father he wants to be: "My quality of life is night and day to before treatment." □



THE AGE National



### New stem cells could fix broken hearts

December 1, 2011

A rare type of stem cell could hold the key to mending a broken heart.

Australian scientists have discovered a new type of stem cell in mouse hearts which they believe plays a vital role in maintaining the muscle and its vessels.

They hope the cells could one day be used to regenerate and repair the literally broken hearts of people who have suffered a heart attack or heart disease.

The scientists from the Victor Chang Cardiac Research Institute in Sydney and University of NSW made the discovery during a seven-year study of heart stem cells in mice.

Lead researcher professor Richard Harvey said it appeared the heart stem cell's main role was to replace damaged vessels.

"In an injury situation where many of the vessels are killed and great slabs of tissue die, like in a heart attack, you need to replace muscle and vessels," he said.

"We think these cells are intimately involved in the regeneration of the heart and replacement of the old heart tissue as the organism ages."

Heart disease is the leading cause of death in Australia, accounting for 16 per cent of all deaths in 2009.

## THE STRAITS TIMES

### Stem cells may end diabetes jabs

Researchers in Australia have discovered a new type of stem cell in mouse hearts which they believe plays a vital role in maintaining the muscle and its vessels. They hope the cells could one day be used to regenerate and repair the literally broken hearts of people who have suffered a heart attack or heart disease.



Researchers in Australia have discovered a new type of stem cell in mouse hearts which they believe plays a vital role in maintaining the muscle and its vessels. They hope the cells could one day be used to regenerate and repair the literally broken hearts of people who have suffered a heart attack or heart disease.

## A stem cell jab to treat arthritis

An injection of stem cells extracted from the body but could one day help arthritis sufferers from their crippling discomforts, scientists have claimed. The treatment, which has been successfully trialed on animals, helps the body regrow tissue and cartilage that has been damaged by the degenerative condition.



According to the researchers, the 4-day period treatment takes three hours, during which time the surgeons remove some tissue of stomach for using. The stem cells are harvested and then injected back into the patient's knee.

Dr. Steven Robinson, from Sydney Spinal and Sports, who is one of the researchers, said the pain relieving effects were almost instantaneous, with improved knee function within 14 days. In some patients, knee pain has been almost completely eliminated after six months, he said, adding that knee improvement ranged from 38 to 50 per cent.

DRUG DISCOVERY & DEVELOPMENT

BRINGING Stem Cells to the Forefront

Wide ranges of cell lines and even tissues can now be purchased, allowing more time to explore therapeutic applications.

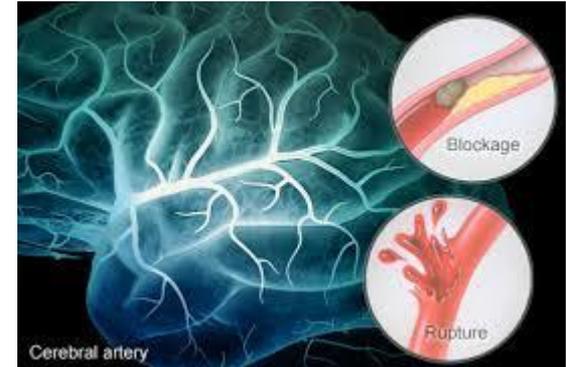
- July/August 2013
- Drug Safety: PREDICTING POTENTIAL CARDIAC EVENTS
- Pharmacology: DETECTING POTENTIAL TOXICITY IN MITOCHONDRIA
- Informatics: PUBLIC DATA SPURS PROFILING ADVANTAGE
- Clinical Trials: TAKING THE 505(b)(2) ROUTE
- DNA MICROARRAY TECHNOLOGY

NSW OFFSHORE ANALYSIS page 3



# Stroke: A Case Study

- Devastating affliction that strikes young and old alike
- I.V. MSCs could be a safe therapy for promoting neurovascular repair, consequently supporting better functional recovery: trials underway
- Strokes cost the US economy \$36.5b p.a. with 795,000 patients annually<sup>1</sup>
- Treatment of choice is thrombolysis: requires use <3 hours; overall benefit ~10%
- US market for stroke therapies estimated to approach \$1b by 2017<sup>2</sup>
- An effective MSC therapeutic could generate US sales in excess of \$1b p.a.<sup>3</sup> and result in substantial improvement in patient outcomes



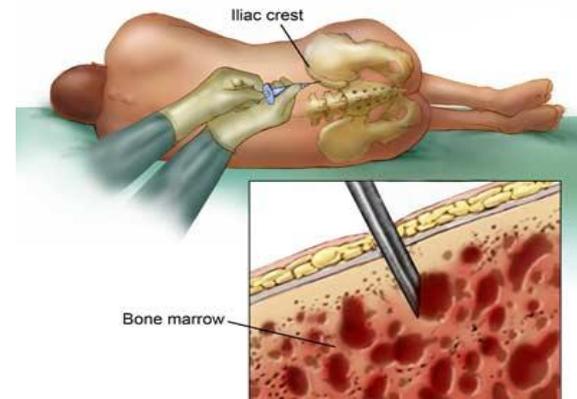
1. US Centre for Disease Control and Prevention  
2. GlobalData: Acute Ischaemic Stroke Market Value 2013  
3. Maxim research analysis May 2014

# Roadblock for MSC Medicines: Manufacture



# Current Manufacture of Stem Cell (MSC) Medicines

- Extract stem cells from human donor (eg bone marrow)
- MSCs represent a rare fraction of the cells in these tissues: a typical BM donation contains <20,000 MSCs
- BUT: A typical clinical **dose** is >100 million MSCs
- This means the donation needs to be *expanded* in the laboratory.....a lot!
- At commercial scale **hundreds of new donors** would be required each year, even if allowing for expansion



# Multiple Donors – Multiple Problems

- Recruitment and qualification of donors is costly, time consuming and is associated with logistical challenges
- May involve risk/discomfort to donor – especially with bone marrow or adipose tissue
- Intra- and inter- donor variability is likely to be significant
- Regulatory challenge:
  - Comparability studies will be required for each new donation, to demonstrate that change in starting material does not impact safety and/or efficacy of product
  - Analytical techniques not currently capable of demonstrating comparability, so *in vivo* efficacy data will likely be required

# This issue is attracting increasing attention

*Cytherapy*, 2013; 15: 2–8

International Society for Cellular Therapy  
ISCT 

## REVIEWS

**The mesenchymal stromal cells dilemma—does a negative phase III trial of random donor mesenchymal stromal cells in steroid-resistant graft-versus-host disease represent a death knell or a bump in the road?**

JACQUES GALIPEAU

*Departments of Hematology & Medical Oncology and Pediatrics, Emory University Winship Cancer Institute, Atlanta, Georgia, USA*

“the most egregious divergence between [commercial and academic MSC products] is the scale of product expansion. The industrialization of MSC manufacturing has favoured the production of large lots of 10,000 doses from each volunteer donor”

“the hypothesis that cells approaching replicative exhaustion are functionally distinct from manufactured MSCs devoid of such exhaustion ... may provide a mechanistically based rationale justifying use of modestly expanded MSCs for GvHD”

ASBMT  
American Society for Blood  
and Marrow Transplantation

## CLINICAL RESEARCH

### Long-Term Complications, Immunologic Effects, and Role of Passage for Outcome in Mesenchymal Stromal Cell Therapy

*Lena von Bahr, Berit Sundberg, Lena Lönnies, Birgitta Sander, Holger Karbach, Hans Hägglund, Per Ljungman, Britt Gustafsson, Helen Karlsson, Katarina Le Blanc,\* Olle Ringdén\**

“[lower] number of MSC expansion passages could be correlated to both better response and better survival”



**Democratizing Cell Technologies**

A RoosterBio Blog

Strategies, tools & technologies for simplifying the incorporation of living cells into tomorrow's products.

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July 7, 2014

**Best Practices in MSC Culture: Tracking and Reporting Cellular Age Using Population Doubling Level (PDL) and not Passage Number**

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“it is well documented that cell phenotype and function can be compromised the older a cell is”

“the regulators are going to ask that you define experimentally, backed up with data, the maximum PDL that will be used for clinical use. Lack of data in this area will likely not keep one out of a Phase 1 trial, but the further the product progresses in development and the clinical pipeline, this type of information is typically mandatory”

# Commercial Manufacture of MSC Therapies

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## THE SOLUTION:

Cynata's Cymerus™ technology facilitates commercial-scale manufacture of a consistent, reproducible product:

...”better, cheaper, faster”

# Path to Revenue

- Following two paths to monetise the Cymerus™ technology
  - Make our own stem cell medicines (GvHD and others progressing): confirm manufacturing process and efficacy;
  - Capital efficient license-driven strategy: partner with pharmaceutical companies and large biotech (in discussions); revenue through license fees, R&D payments and royalties; potential for M&A
- ***Cymerus™ = unlimited high quality stem cells for medicine***

# Cynata Therapeutics: The Past 12 Months

- Building a solid foundation for the future:
  - Timetable and budget consistent with October 2013 prospectus and market updates
  - Recruited VP, Product Development (ex MSB)
  - Product manufacturing and process development well advanced (Waisman)
  - Secured GMP-grade iPS cell line (CDI)
  - Further proof-of-concept study underway (following successful CLI study)
  - Completed regulatory review and roadmap: commenced interaction with regulators
  - Contracted pre-clinical program
  - Commenced planning for a Phase 1 clinical trial: Graft-versus-Host Disease
  - Engagement with potential partners (announced Grey Innovation)
  - Research coverage by both Baillieu Host and BBY: “buy” ratings

# Cynata: The Year Ahead

- Important Development Milestones and Value Catalysts:
  - Complete master cell bank (MCB)
  - Complete manufacturing scale-up: manufacture Cymerus™ GMP MSC's
  - Formal interaction with regulatory agencies (eg EMA, FDA)
  - Data from pre-clinical program and PoC study in GvHD model
  - Clinical trial jurisdiction and logistics (GvHD)
  - Continued engagement with potential partners
- Vigorous investor relations campaign
- Continued clinical success of MSC-based therapeutics

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Thank you for your attention

