

cynata
therapeutics



A Next Generation Stem Cell Company

Dr. Ross Macdonald, CEO
Cynata Therapeutics Limited

7-8 September, 2016

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About Cynata's Technology



Hyperlink to animation: ..\..\Business Development\Media\Cynata_V04.mp4



About Cynata

Cynata Therapeutics Ltd is an Australian stem cell and regenerative medicine company.

Competitive Strengths

- » Disruptive MSC platform technology: Cymerus™
- » Strong IP cover
- » Economical production of clinical grade product
- » Strategic collaborations with commercial and academic partners
- » Experienced Team
- » Ethically non-controversial
- » Low development risk
- » Phase 1 Clinical Trial

Key Facts



ASX CODE
CYP



COMMENCED OPERATIONS
November 2013



MARKET CAP (6 Sep 16)
AUD \$32m



SHARES ON ISSUE
72.7m



OPTIONS
10.5m¹



CASH (30 June 2016)
AUD \$4.9m (~ 8 months)



AVERAGE MONTHLY NET CASH BURN
AUD \$510k (gross)



NUMBER OF SHAREHOLDERS
~1900

¹ include 3.6m Jul 20 @ AUD \$1.00; plus 5m 27 Sep 18 unlisted AUD \$0.40 restricted options, 50% to each of Chairman and CEO

Recent Cynata Milestones

Partnership term sheet with FUJIFILM

Research coverage by
Rodman & Renshaw; Shaw
& Partners; CPS Capital

Executed license option
agreement (apceth GmbH &
Co)

Collaborations with leading
clinical research centres
worldwide, e.g. Harvard/MGH

Substantial progress in
product development, e.g.
GvHD model

Phase 1 clinical trial
application submitted to UK
MHRA July 2016 (GvHD)

2016

Partnership with FUJIFILM

- » Non-binding term sheet executed 5 September 2016
- » Anticipates finalisation of definitive agreement:
 - option to an exclusive, w/w licence to market and sell CYP-001 for prevention and treatment of graft-versus-host disease (GvHD)
 - + option to negotiate a licence for manufacturing CYP-001
 - + certain rights to Cynata's proprietary Cymerus™ technology for the prevention and treatment of other diseases
- » Strategic acquisition of CYP shares: US\$3m @ 35% premium to 6 month VWAP
- » Upfront + milestone payments + royalties on product sales
- » Major multinational with business in healthcare, graphic systems, functional materials, optical devices, digital imaging and document products
- » Significant and growing business in regenerative medicine: acquired Cellular Dynamics International, Inc in 2015 for \$US307m (also UW spinout)
- » Group revenue in 15-16: \$US22b; 79,000 employees; market cap ~\$US21b

Why Are Stem Cells Important?



Stem cells as therapies for disease: significant media interest.



Mesenchymal Stem Cells (MSCs) are specialised stem cells that can be used as therapeutics.

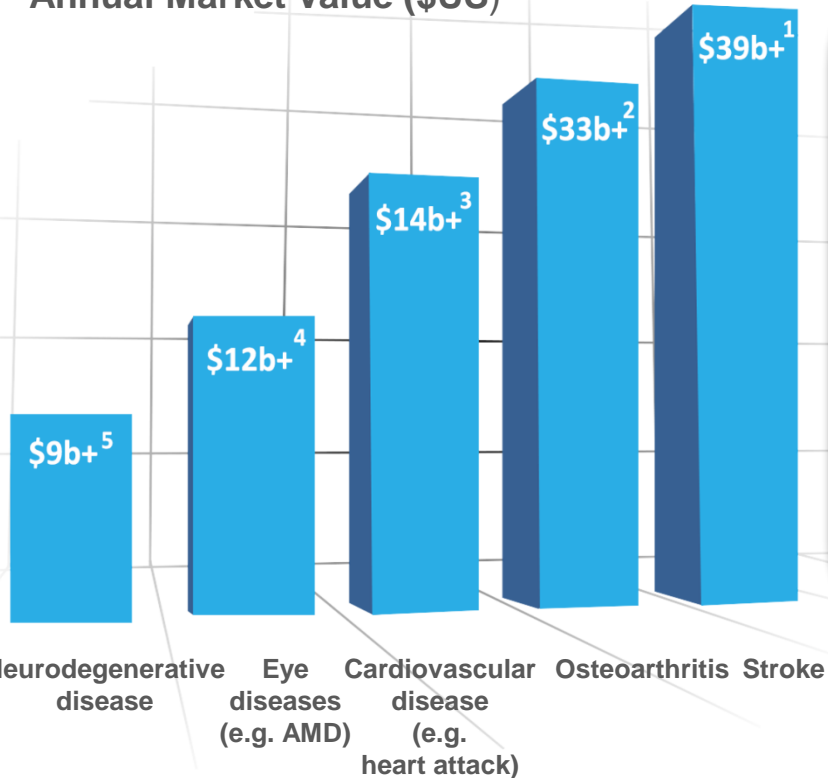


MSCs play a key role in modulating inflammation and co-ordinating repair: like an orchestra conductor.

Mesenchymal Stem Cell (MSC) Therapeutics

~652* open clinical studies using MSCs including:


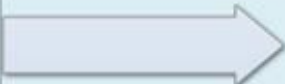

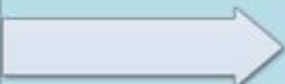



Annual Market Value (\$US)



- Particular relevance to chronic diseases of ageing
- Profound legislative changes to expedite stem cell therapies (Japan)
- Massive government investment e.g. California (CIRM): US\$3b
- Further potential applications: cell therapy in solid tumors

1. US Centre for Disease Control and Prevention
2. GBI Research
3. GBI Research
4. BCC Research
5. Research and Markets
*www.clinicaltrials.gov

Therapeutic Product Pipeline

Therapeutic Area	Indication	Preclinical	Phase 1	Phase 2
Immunological Disorders	Graft versus host disease			
	Organ transplant rejection			
Pulmonary Disorders	Pulmonary fibrosis			
	Asthma			
Circulatory Disorders	Critical limb ischaemia			
	Myocardial infarction (heart attack)			
Cancer	Glioblastoma (brain tumour)			



Graft vs Host Disease

What

Potentially fatal complication that can occur after a bone marrow transplant in cancer patients.

Market

Global GvHD market value estimated to increase from US\$295m in 2013 to US\$544m in 2023 ¹.

Reimbursed cost of MSC treatment (Japan)
\$US113k-US\$170k.

Why

Cynata has targeted GvHD in a Phase 1 clinical trial.

Speedy results with efficacy in GvHD:
→ further potential indications

¹ E.Vouvatsikou, 2015, Global Data



Roadblock for MSC Medicines: **Manufacture**



Major practical & regulatory challenges:



Issues with production scale-up



Inconsistent product quality

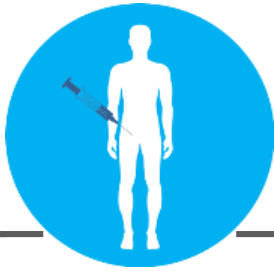


Reduced product efficacy



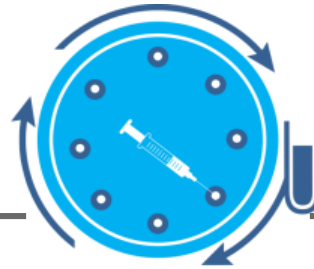
Donor variability

Current Manufacture of MSCs



Extraction

- Bone marrow extraction - risky & painful procedure
- Yields too few cells for a therapeutic dose:
“Solution”: massive expansion in culture & multiple donors



Expansion

- 20k cells per BM aspirate → 100m per dose (>12 population doublings)

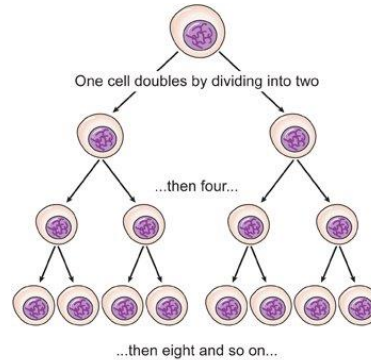
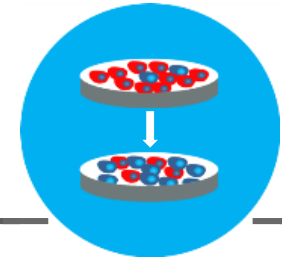


Diagram showing how cells reproduce
Copyright © CancerHelp UK

- MSCs **change** during expansion: altered phenotype, differentiation potential, gene expression profile, enter senescence



Efficacy?

- Modest expansion of MSCs in culture induces senescence
- This occurs after as few as 13 population doublings, equivalent to ~ 1.6 doses
- Reduced clinical efficacy has been reported at even low levels of expansion
- Commercial scale: hundreds of new donors required each year

Multiple Donors: Multiple Problems

- » Major practical & regulatory challenges
 - » Recruitment and qualification of donors is costly, time consuming and is associated with logistical challenges
 - » Significant intra- and inter- donor variability
 - » Regulatory challenges:
 - Comparability studies for each new donation: 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

Manufacturing Issues Attracting Global Attention

Cytotherapy, 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



Recent late stage trials are encouraging, e.g. TiGenix, JCR Pharma



BUT: initial spectacular successes in Phase 1, 2 not being confirmed



Leading many commentators to observe that manufacture is a problem

CLINICAL RESEARCH

ASBMT
American Society for Blood and Marrow Transplantation

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*

The Industry Solution



*New innovative platform technology for
the mass production of clinical grade
MSCs*

Competitor A

Production of
MSCs using
traditional
methods

Competitor B

Production of
MSCs using
traditional
methods



Industry Needs:

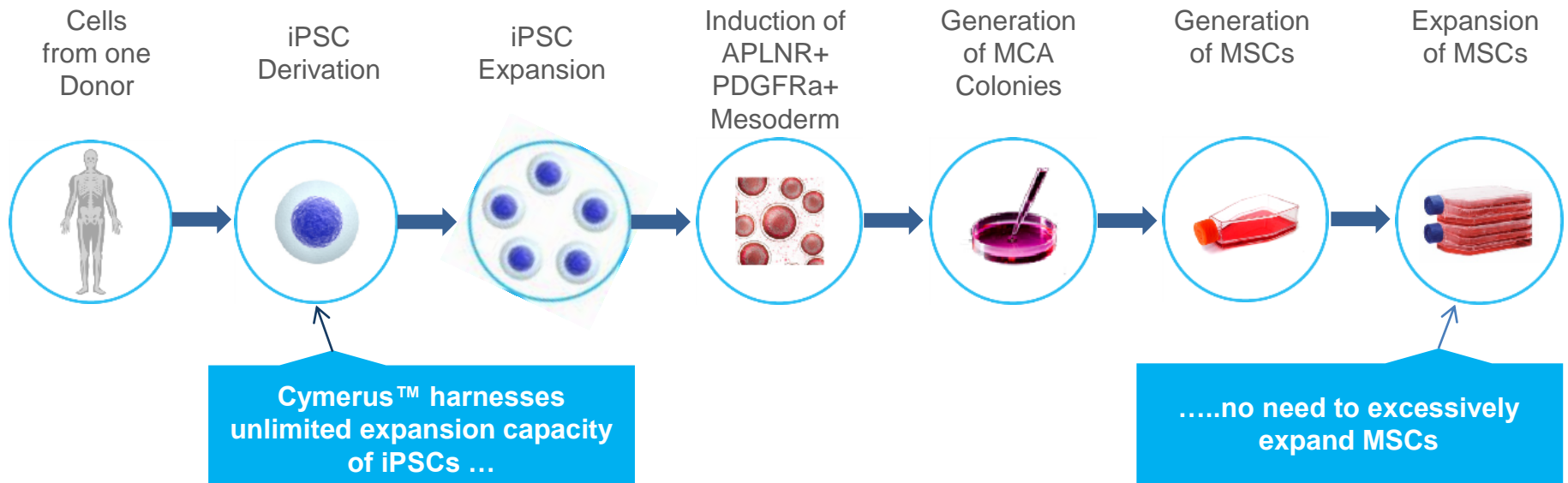
Cost effective, commercial production of MSCs, for use as therapeutics

Cynata's Cymerus™ Breakthrough

The Solution:

Cynata's Cymerus™ technology enables commercial-scale manufacture of a consistent, robust MSC product:

...*better, cheaper, faster*



Cynata's Cymerus™ Breakthrough



Modern innovative technology



Large scale production capacity



Efficient production process



Premier grade product



Cymerus™ MSC Characterization

Confirmation of MSC class characteristics / identity

- » Cell surface markers
- » Differentiation
- » Immunopotency
- » Genetic profiling
- » Successful in vivo model: critical limb ischaemia
(published) →
- » Further in vivo model (GvHD) ongoing

Cytherapy, 2016; 18: 219-228

International Society for Cellular Therapy
ISCT

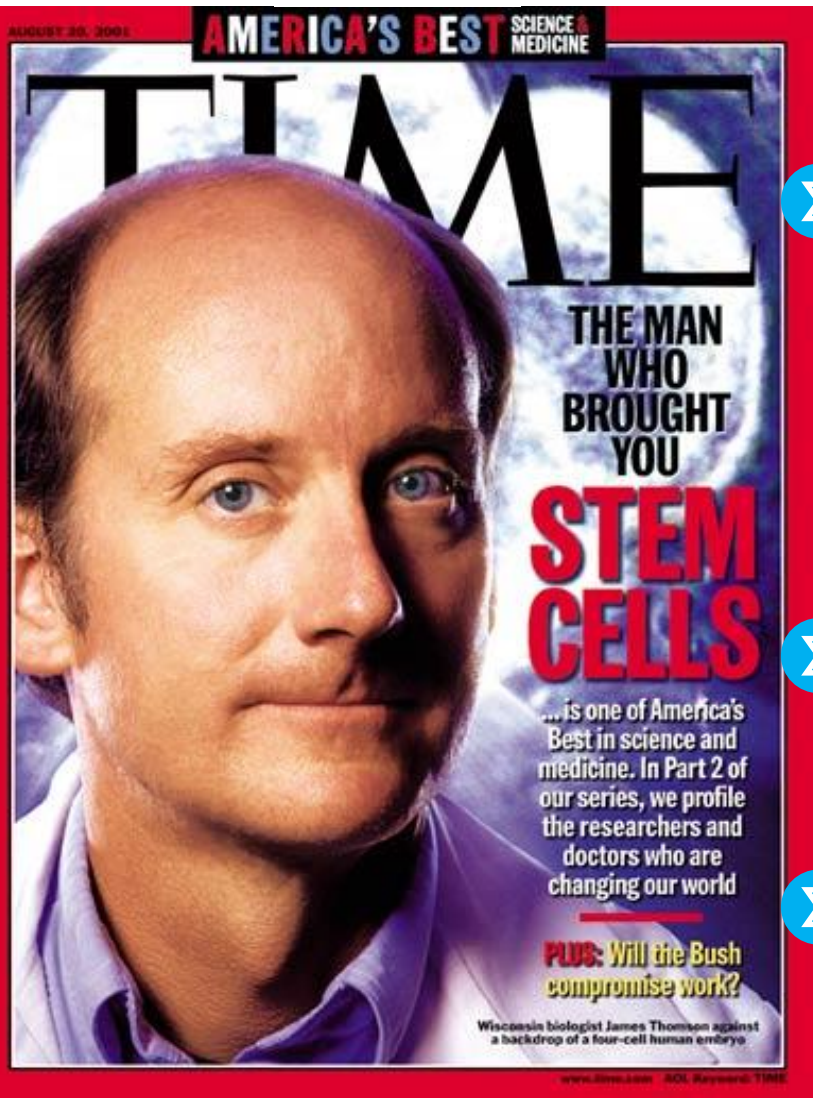


Mesenchymoangioblast-derived mesenchymal stromal cells inhibit cell damage, tissue damage and improve peripheral blood flow following hindlimb ischemic injury in mice

JILL M. KOCH¹, SARITHA S. D'SOUZA², DENISE J. SCHWAHN³, IAN DIXON⁴ & TIMOTHY A. HACKER⁵

¹Department of Medicine, University of Wisconsin-Madison, Madison, WI, USA, ²Wisconsin National Primate Research Center, University of Wisconsin-Madison, Madison, WI, USA, ³Research Animal Resources Center, University of Wisconsin-Madison, Madison, WI, USA, and ⁴Cynata Therapeutics Limited, Armadale, Victoria, Australia

Cynata's Cymerus™ : Outstanding Pedigree



Inventors include: Dr James Thomson

- In 1998 derived the first human embryonic stem cell line
- 2007 derived human induced pluripotent stem cells



...and Prof Igor Slukvin, co-founder and author of >70 publications in the stem cell field



In-licensed intellectual property includes several issued U.S. patents as well as a broad estate of issued and pending patents

Academic Partnerships



Universities

- University of Wisconsin
 - Technology spun out of university
- University of Massachusetts
 - GvHD model
- University of Sydney
 - Heart disease
- Harvard/MGH
 - Cancer
- University of Western Australia
 - Lung disease

- Cynata has commenced a collaboration with Dr Khalid Shah, of MGH/ Harvard Medical School and Harvard Stem Cell Institute
- Pioneers of technology to modify stem cells to secrete cancer-killing toxins
- Published studies of modified stem cells in an animal model of glioblastoma (brain tumours): treatment killed cancer cells and prolonged survival
- Dr Shah's group will now investigate similar modification of Cynata's Cymerus™ MSCs

BUSINESS MODEL: Commercial **Partnerships**



Companies

- apceth GmbH (Germany)
 - License option agreement
 - Upfronts, milestones and royalties
 - Opens new commercial opportunities for MSCs in cancer
- FUJIFILM
 - Non binding term sheet signed
 - Definitive agreement: equity, upfronts, milestones and royalties
 - Strategic investor; brings substantial resources

Development and commercialisation of the Cymerus™ technology:

- Capital efficient license-driven strategy: partner with leading pharma/big biotech
- **Near term revenues** through license fees, R&D payments; royalties
- Deal-experienced management team
- Vibrant and active transaction landscape: MSB, ICEL, ATHX, OCAT
- M&A potential

The Future Is Bright

What's Next?

FUJIFILM definitive agreement

Green light for Phase 1 clinical trial;
Formal interaction with FDA

Licence option agreement with apceth &
GmbH to bring in additional revenue

Continued success of MSC-based therapeutics

Develop opportunities in engineered MSCs



Now is the Right Time to Invest

EXISTING MARKET ISSUES

- Traditional production methods for MSCs limit their usage as effective therapies
- Competitors using existing, 1st generation production methods
- Growing demand for new therapies to cure disease
- Regulatory hurdles for current production methods



THE FUTURE OF MEDICINE

- Vibrant and expanding field of stem cell medicine
- Global demand for stem cell therapeutics (ageing population)
- Unique, innovative technology from prestigious centre
- Cymerus™ overcomes critical hurdle in industrialising stem cell production
- Licensing-driven business strategy with near term revenue
- Experienced management team
- Value-accretive news flow expected in near term

Thank you for your attention

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