cynata therapeutics

# A Next Generation Stem Cell Company

**Dr. Ross Macdonald, CEO**
**Cynata Therapeutics Limited**

**7-8 September, 2016**

# Important Information

This presentation has been prepared by Cynata Therapeutics Limited. ("Cynata" or the "Company") based on information available to it as at the date of this presentation. The information in this presentation is provided in summary form and does not contain all information necessary to make an investment decision.

This presentation does not constitute an offer, invitation, solicitation or recommendation with respect to the purchase or sale of any security in Cynata Therapeutics , nor does it constitute financial product advice or take into account any individual's investment objectives, taxation situation, financial situation or needs. An investor must not act on the basis of any matter contained in this presentation but must make its own assessment of Cynata Therapeutics and conduct its own investigations. Before making an investment decision, investors should consider the appropriateness of the information having regard to their own objectives, financial situation and needs, and seek legal, taxation and financial advice appropriate to their jurisdiction and circumstances. Cynata Therapeutics is not licensed to provide financial product advice in respect of its securities or any other financial products. Cooling off rights do not apply to the acquisition of Cynata Therapeutics securities.

Although reasonable care has been taken to ensure that the facts stated in this presentation are accurate and that the opinions expressed are fair and reasonable, no representation or warranty, express or implied, is made as to the fairness, accuracy, completeness or correctness of the information, opinions and conclusions contained in this presentation. To the maximum extent permitted by law, none of Cynata Therapeutics, its officers, directors, employees and agents, nor any other person, accepts any responsibility and liability for the content of this presentation including, without limitation, any liability arising from fault or negligence, for any loss arising from the use of or reliance on any of the information contained in this presentation or otherwise arising in connection with it.

The information presented in this presentation is subject to change without notice and Cynata Therapeutics does not have any responsibility or obligation to inform you of any matter arising or coming to their notice, after the date of this presentation, which may affect any matter referred to in this presentation.

The distribution of this presentation may be restricted by law and you should observe any such restrictions.

**Forward looking statements**

This presentation contains certain forward looking statements that are based on the Company's management's beliefs, assumptions and expectations and on information currently available to management. Such forward looking statements involve known and unknown risks, uncertainties, and other factors which may cause the actual results or performance of Cynata to be materially different from the results or performance expressed or implied by such forward looking statements. Such forward looking statements are based on numerous assumptions regarding the Company's present and future business strategies and the political and economic environment in which Cynata will operate in the future, which are subject to change without notice. Past performance is not necessarily a guide to future performance and no representation or warranty is made as to the likelihood of achievement or reasonableness of any forward looking statements or other forecast. To the full extent permitted by law, Cynata and its directors, officers, employees, advisers, agents and intermediaries disclaim any obligation or undertaking to release any updates or revisions to information to reflect any change in any of the information contained in this presentation (including, but not limited to, any assumptions or expectations set out in the presentation).

# 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**
10.5m[1]

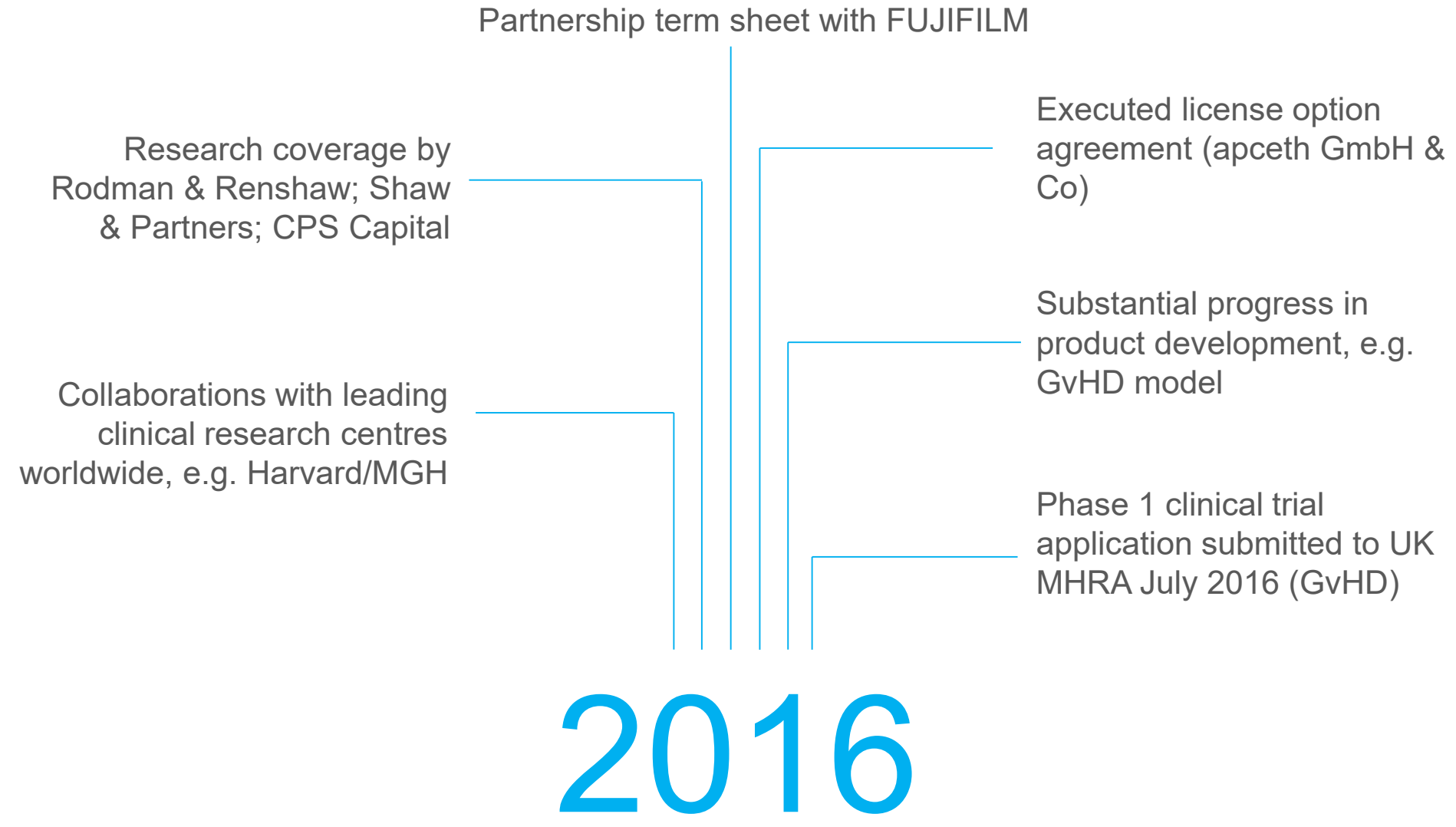
**CASH (30 June 2016)**
AUD $4.9m (~ 8 months)

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

**NUMBER OF SHAREHOLDERS**
~1900

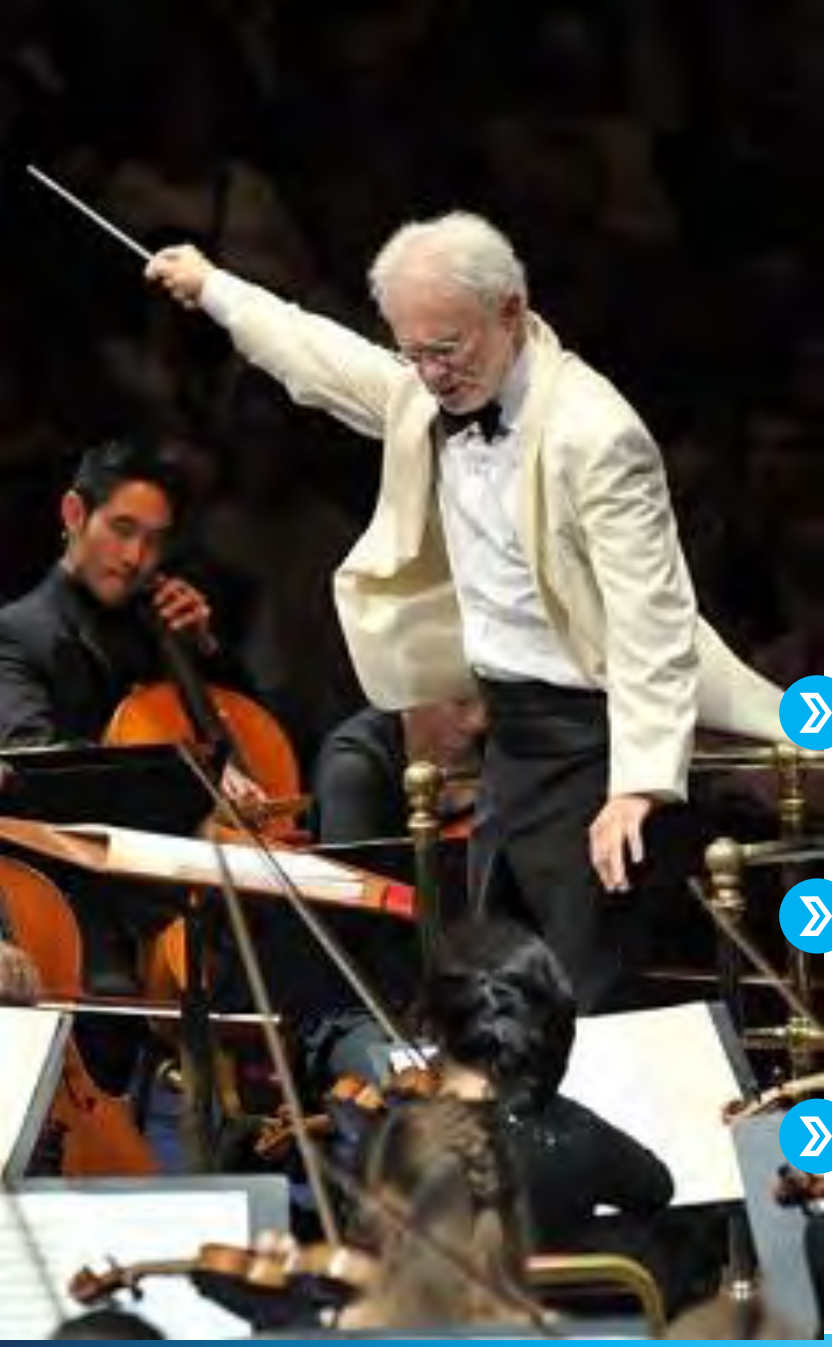
[1] include 3.6m Jul 20 @ AUD $1.00; plus 5m 27 Sep 18 unlisted AUD $0.40 restricted options, 50% to each of Chairman and CEO

# Recent Cynata Milestones



# Partnership 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

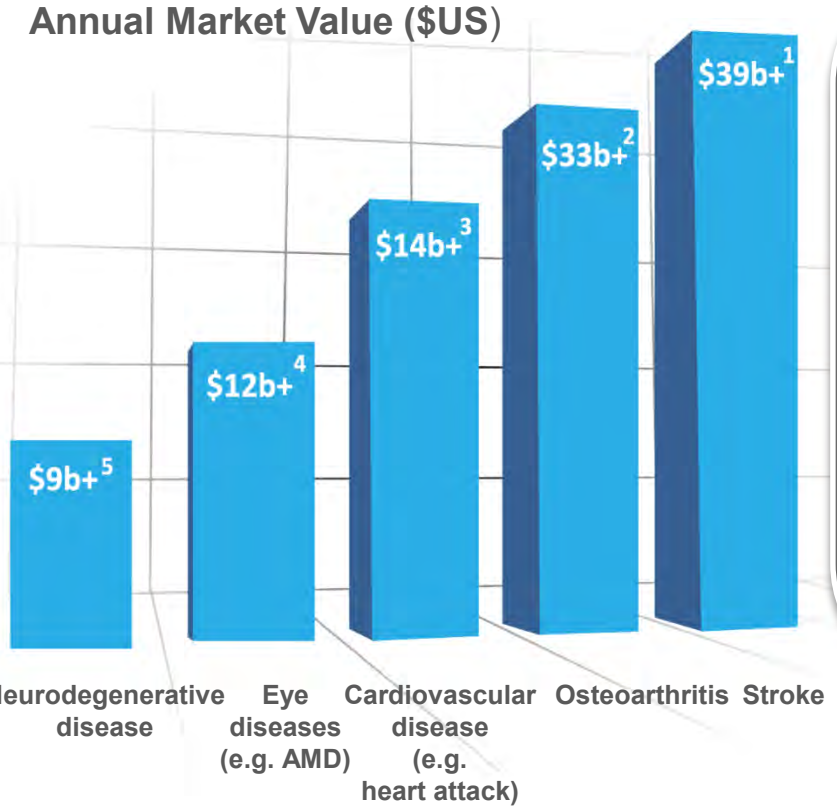


# Why Are Stem Cells Important?


- 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:




- 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.

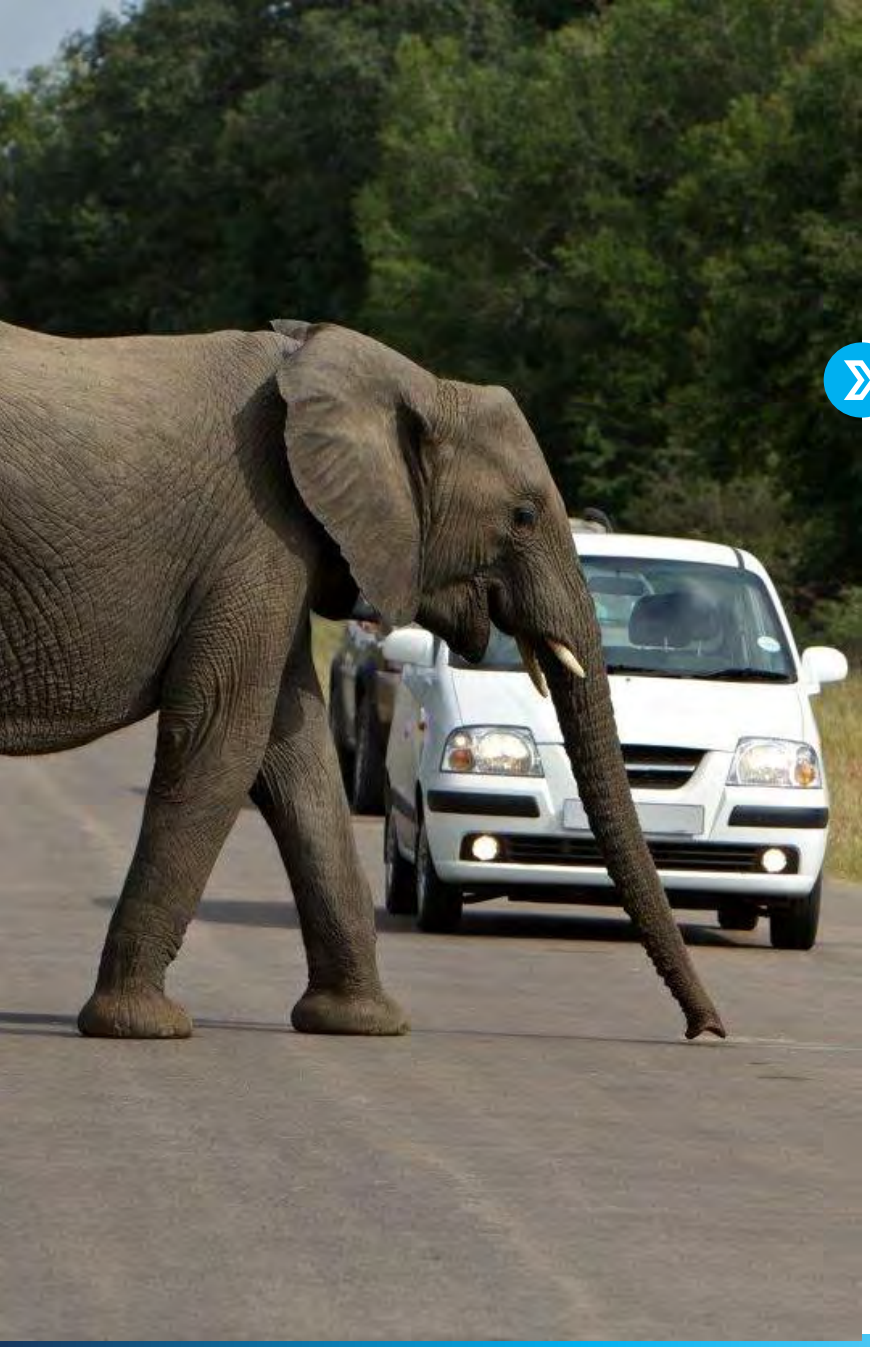
**Why**

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



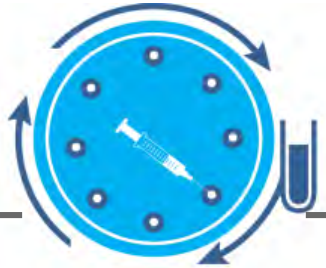
# Roadblock for MSC Medicines: Manufacture

- Major practical & regulatory challenges:
  - Issues with production scale-up
  - Inconsistent product quality
  - Reduced product efficacy
  - Donor variability

# Current Manufacture of MSCs

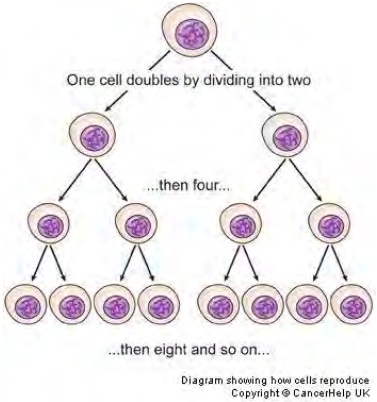
## Extraction

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

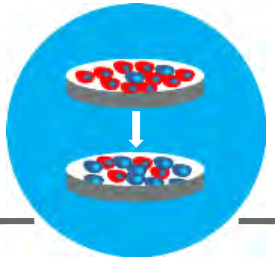


## Expansion

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




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



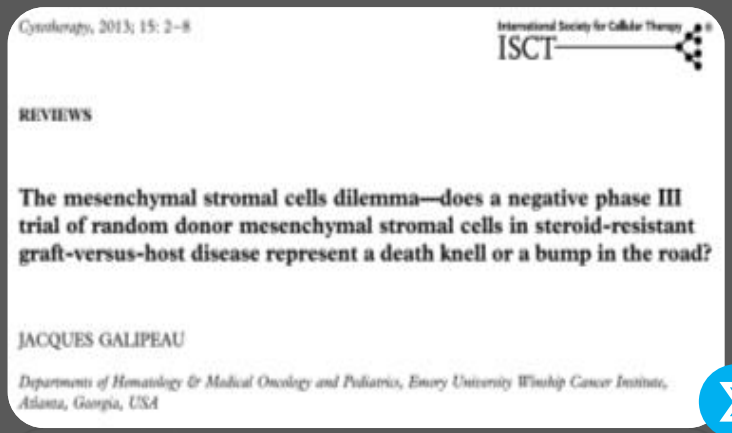
## Efficacy?

- 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

ASBMT

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**

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

- Leading many commentators to observe that manufacture is a problem

# The Industry Solution

cynata therapeutics

***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:**

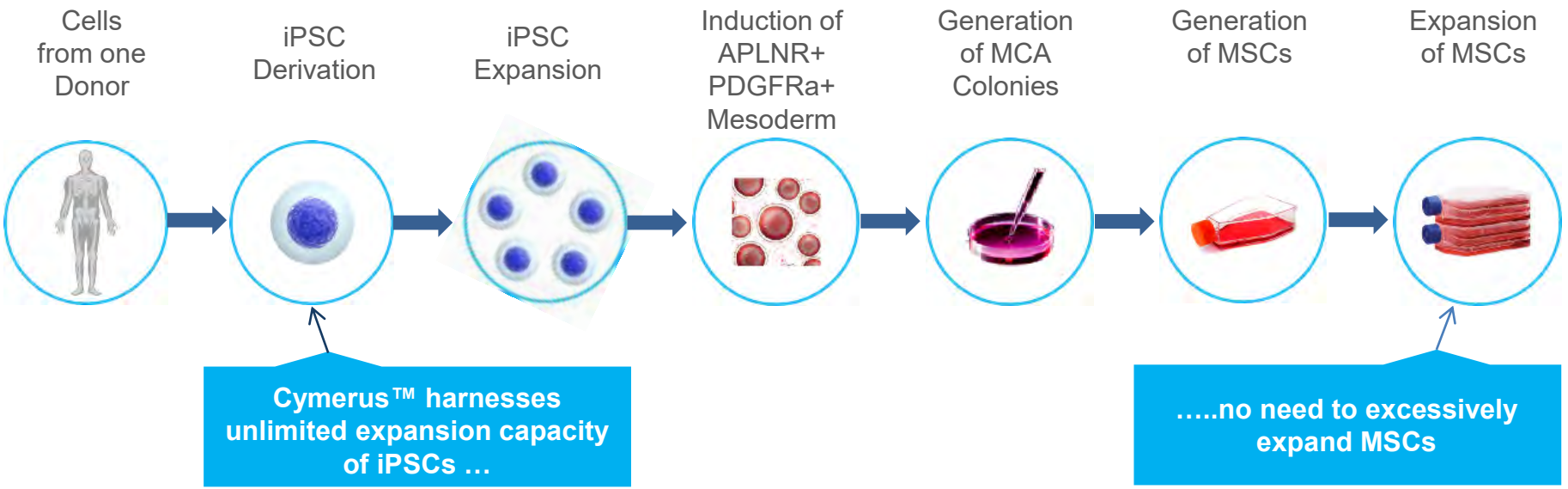
**Cost effective, commercial production of MSCs, for use as therapeutics**

# 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)

*Cytotherapy*, 2016; 18: 219–228

International Society for Cellular Therapy ISCT

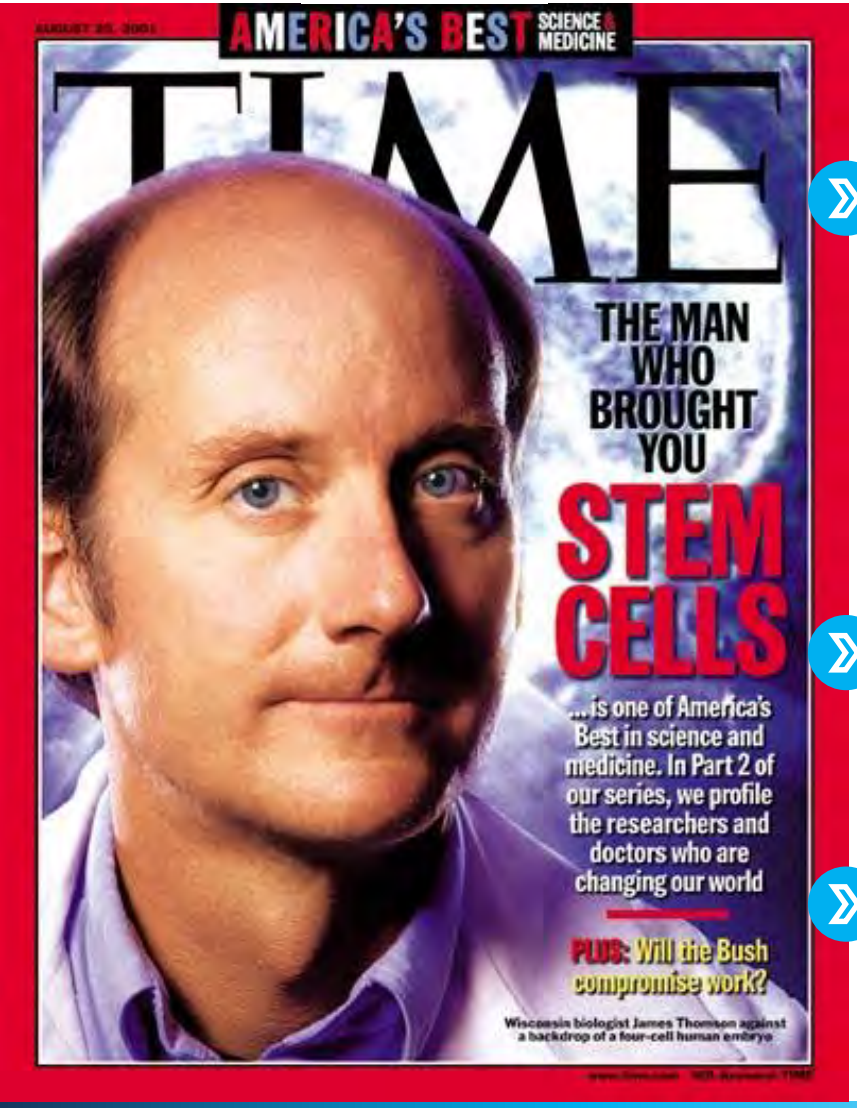
**Mesenchymoangioblast-derived mesenchymal stromal cells inhibit cell damage, tissue damage and improve peripheral blood flow following hindlimb ischemic injury in mice**

JILL M. KOCH[1], SARITHA S. D'SOUZA[2], DENISE J. SCHWAHN[3], IAN DIXON[4] & TIMOTHY A. HACKER[1]

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

- Further in vivo model (GvHD) ongoing

# 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

cynata therapeutics

## 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

Cynata Therapeutics Limited
Suite 1,
1233 High Street,
Armadale, Victoria 3143


Contact details:
ross.macdonald@cynata.com
+61 (0) 412 119343
www.cynata.com