ASX ANNOUNCEMENT 29 October 2020

# AusBiotech Conference Presentation

**Melbourne, Australia; 29 October 2020:** Cynata Therapeutics Limited (ASX: CYP), a clinical-stage biotechnology company specialising in cell therapeutics, is pleased to release a presentation that was given by Dr. Kilian Kelly at the AusBiotech + Invest 2020 conference on 28 October 2020.

The AusBiotech + Invest 2020 conference attracts industry leaders within the biotech space and is Australia's largest life science conference. Dr. Kelly presented as part of the regenerative medicine session, which provided an opportunity for Cynata to highlight the unique advantages of its Cymerus™ therapeutic mesenchymal stem cell (MSC) platform technology to industry leaders and investors.

The conference presentation is attached to this release and provides an overview of the Company, the benefits of the Cymerus iPSC-derived MSC process and Cynata's key clinical programs.

**Dr. Kilian Kelly, Cynata's COO, said:**
*"The AusBiotech + Invest conference was a valuable opportunity for Cynata to engage with industry leaders and investors as interest in regenerative medicine continues to grow. Our Cymerus technology is a unique MSC manufacturing platform and we look forward to generating further data on our MSC products in the upcoming clinical trials."*

**-ENDS-**

**Authorised for release by Dr Ross Macdonald, Managing Director & CEO**

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## About Cynata Therapeutics (ASX: CYP)

Cynata Therapeutics Limited (ASX: CYP) is an Australian clinical-stage stem cell and regenerative medicine company focused on the development of therapies based on Cymerus™, a proprietary therapeutic stem cell platform technology. Cymerus™ overcomes the challenges of other production methods by using induced pluripotent stem cells (iPSCs) and a precursor cell known as mesenchymoangioblast (MCA) to achieve economic manufacture of cell therapy products, including mesenchymal stem cells (MSCs), at commercial scale without the limitation of multiple donors.

Cynata's lead product candidate CYP-001 met all clinical endpoints and demonstrated positive safety and efficacy data for the treatment of steroid-resistant acute graft-versus-host disease (GvHD) in a Phase 1 trial. Cynata plans to advance its Cymerus™ MSCs into Phase 2 trials for severe complications arising from COVID-19, GvHD, critical limb ischemia and into a Phase 3 trial for osteoarthritis. In addition, Cynata has demonstrated utility of its Cymerus™ MSC technology in preclinical models of asthma, diabetic wounds, heart attack, sepsis, acute respiratory distress syndrome (ARDS) and cytokine release syndrome.

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**A Next Generation Stem Cell Therapeutics Company**

Kilian Kelly, PhD
Chief Operating Officer, Cynata Therapeutics Limited

AusBiotech +Invest2020

Engage, your way

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# Cynata Therapeutics is a clinical stage biotech with a highly scalable, proprietary platform for developing stem cell therapeutics

## Our focus

Utilise our proprietary Cymerus™ platform technology to develop commercially scalable mesenchymal stem cell (MSC) therapeutic products to treat serious disorders

## About us

- Stem cell and regenerative medicine company
- Induced pluripotent stem cell (iPSC)-based technology from University of Wisconsin-Madison
- Addresses a critical shortcoming in existing methods of MSC production – the ability to achieve economic manufacture at commercial scale
- First product, CYP-001, licensed to Fujifilm for graft-versus-host-disease (GvHD)
- Multiple further products in pipeline

## Financial information

| | |
|---|---|
| Share price (26-Oct-20) | A$0.81 |
| Shares on issue | 117m |
| **Market capitalisation** | **A$95m** |
| Cash[1] | A$13.6m |
| Debt | - |
| **Enterprise value** | **A$81.4m** |

## Top shareholders

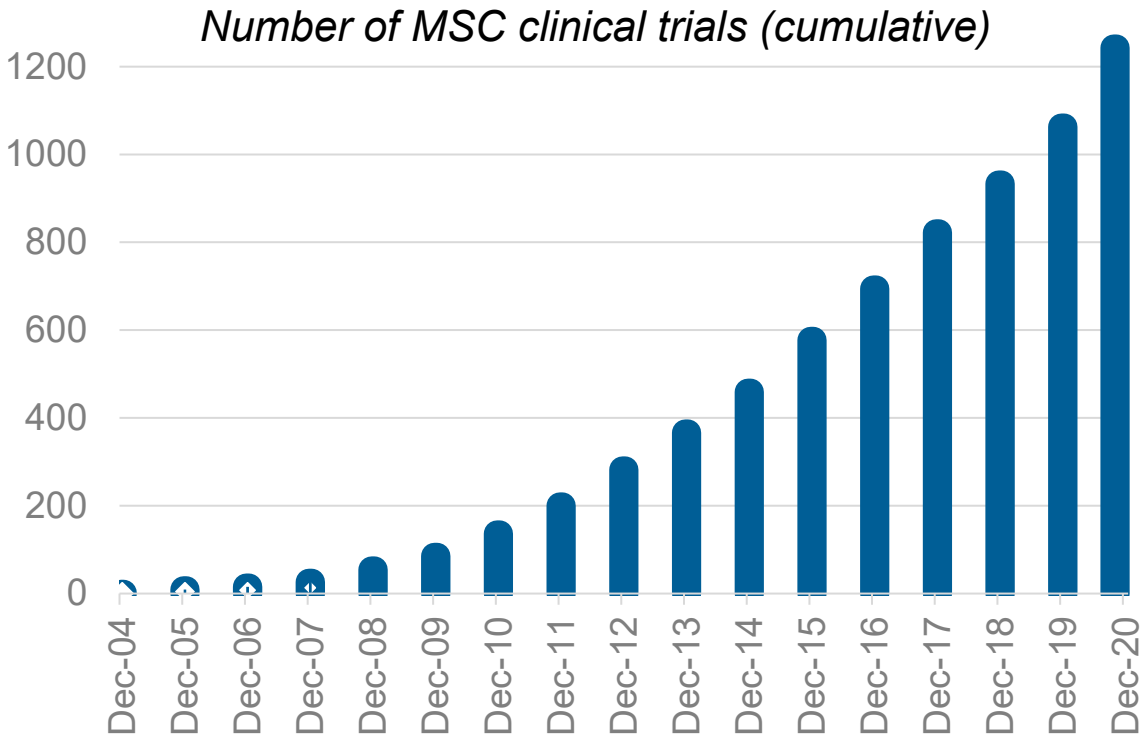
| | |
|---|---|
| Fidelity INTERNATIONAL | 9.9% |
| FUJIFILM | 6.9% |
| Board and management | 5.8% |



1. Cash as at 30 June 2020

# Mesenchymal stem (or stromal) cells (MSCs)

## Over **1,200** clinical trials of MSCs have been initiated[1]




Growing body of evidence for the therapeutic role of MSCs in wide range of conditions:

- ✓ Modulate the immune system
- ✓ Regenerate damaged tissue
- ✓ Accelerate recovery from the effects of disease or injury

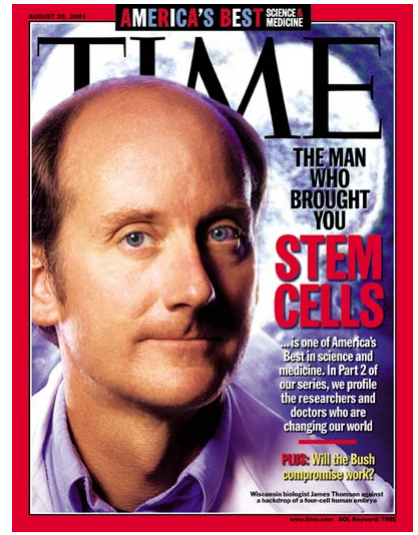
However: major challenges associated with consistent and scalable manufacture of primary, donor-derived MSCs

1. www.clinicaltrials.gov (as at October 2020)

# Induced Pluripotent Stem Cells (iPSCs)


- Murine iPSCs first generated by **Shinya Yamanaka, Kyoto University** in 2006[1]
- Generation of human iPSCs first reported by two independent groups almost simultaneously in November 2007:
  - **Shinya Yamanaka[2] (awarded Nobel Prize in 2012)**
  - **James Thomson, University of Wisconsin-Madison[3]**
- iPSCs are mature cells reprogrammed to behave like embryonic stem cells (ESCs):
  - Indefinite replication capacity
  - Capacity to differentiate into any adult cell type
  - Because iPSCs are sourced from adult cells, ethical controversy associated with ESCs is avoided

→ iPSCs represent **an ideal starting material** for cellular production processes





1. Takahashi K, Yamanaka S. ***Cell***. 2006;126(4):663-76.
2. Takahashi K, Tanabe K, Ohnuki M, *et al*. ***Cell***. 2007;131(5):861-72.
3. Yu J, Vodyanik MA, Smuga-Otto K, *et al*. ***Science***. 2007;318(5858):1917-20.

# Conventional MSC processes

Cells from donors

MSC isolation

**Extensive** MSC culture expansion

Substantial variability between donors

Low numbers → e.g. 20,000 MSCs per bone marrow donation

May require **1 billion+** cells/patient → **Very high** levels of culture expansion required

**MSCs change when excessively expanded (loss of potency, senescence, decreased efficacy)**

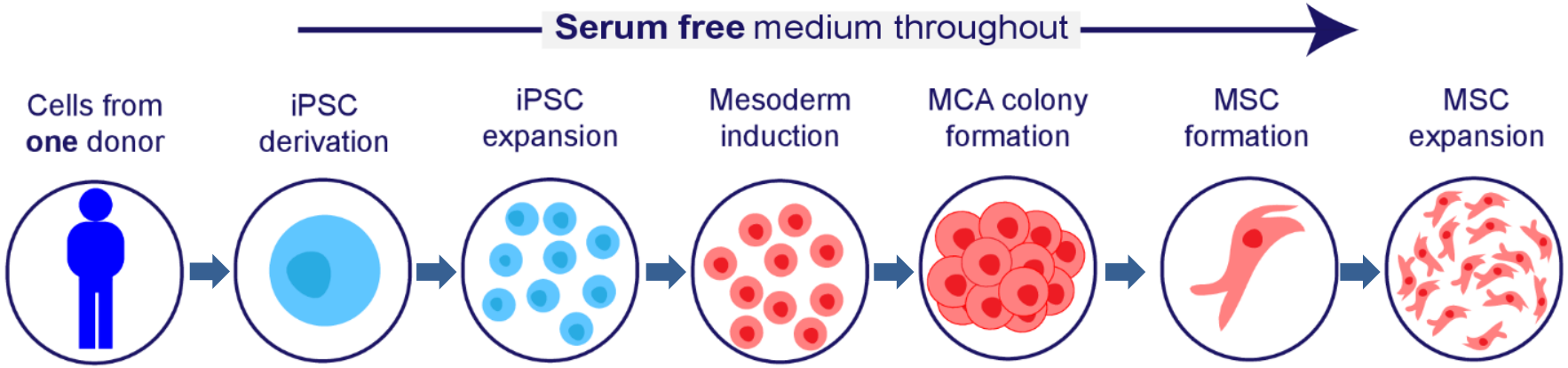
→ limited number of doses per donation

→ new donors required more frequently

→ more variability

# Cymerus™ iPSC-derived MSC process

**Serum free** medium throughout




Avoids inter-donor variability

Effectively limitless numbers

Minimal MSC culture expansion

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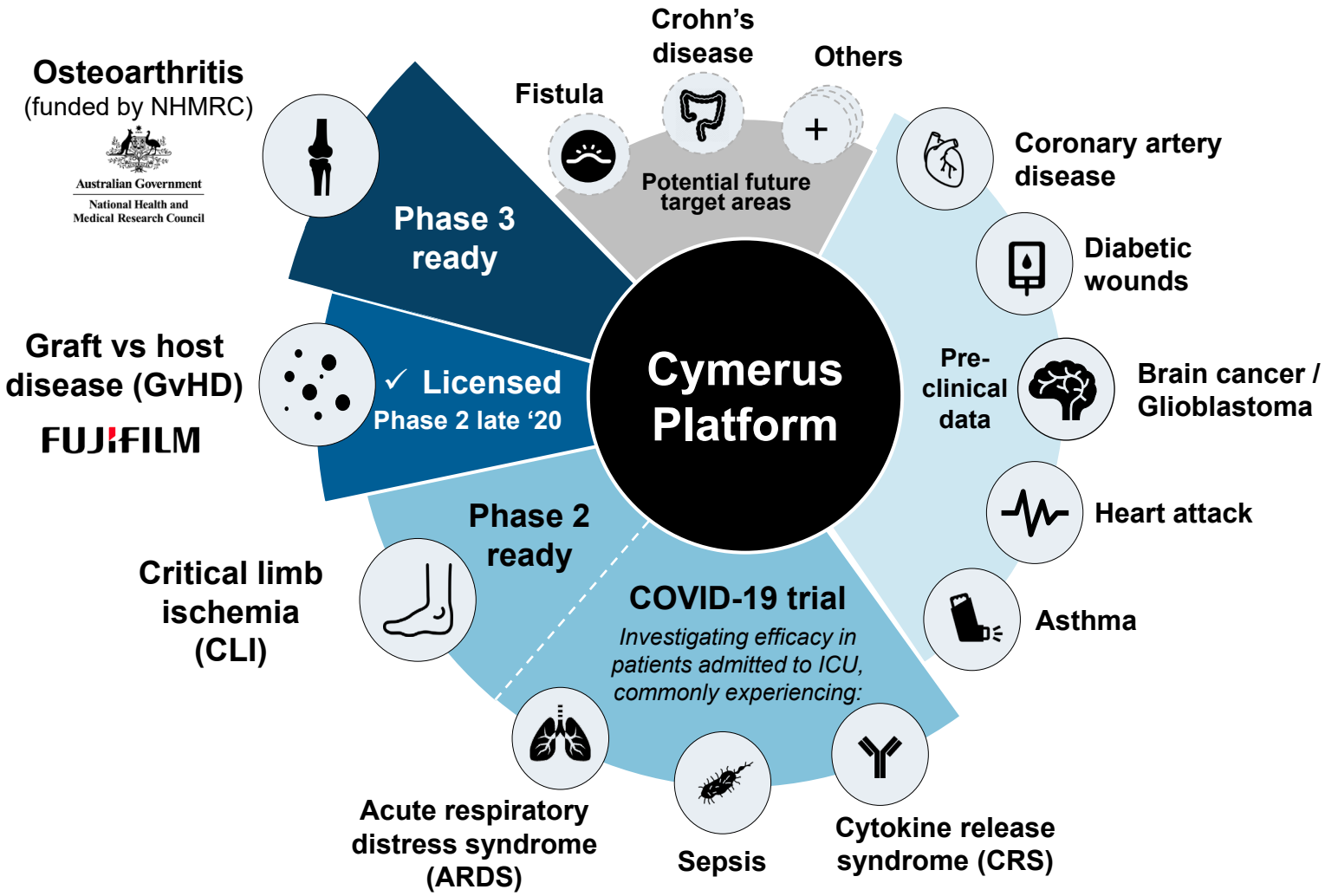
# Cymerus platform: potential applications



# CYP-001 Phase 1 Clinical Trial in GvHD

nature medicine

LETTERS

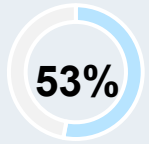
https://doi.org/10.1038/s41591-020-1050-x

## Production, safety and efficacy of iPSC-derived mesenchymal stromal cells in acute steroid-resistant graft versus host disease: a phase I, multicenter, open-label, dose-escalation study

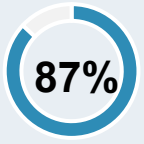
Adrian J. C. Bloor[1,2] ✉, Amit Patel[1], James E. Griffin[3], Maria H. Gilleece[4], Rohini Radia[5], David T. Yeung[6,7], Diana Drier[8], Laurie S. Larson[8], Gene I. Uenishi[9], Derek Hei[10], Kilian Kelly[11], Igor Slukvin[9] and John E. J. Rasko[12,13,14] ✉

## Key clinical trial results (primary evaluation at Day 100)

**All endpoints met**



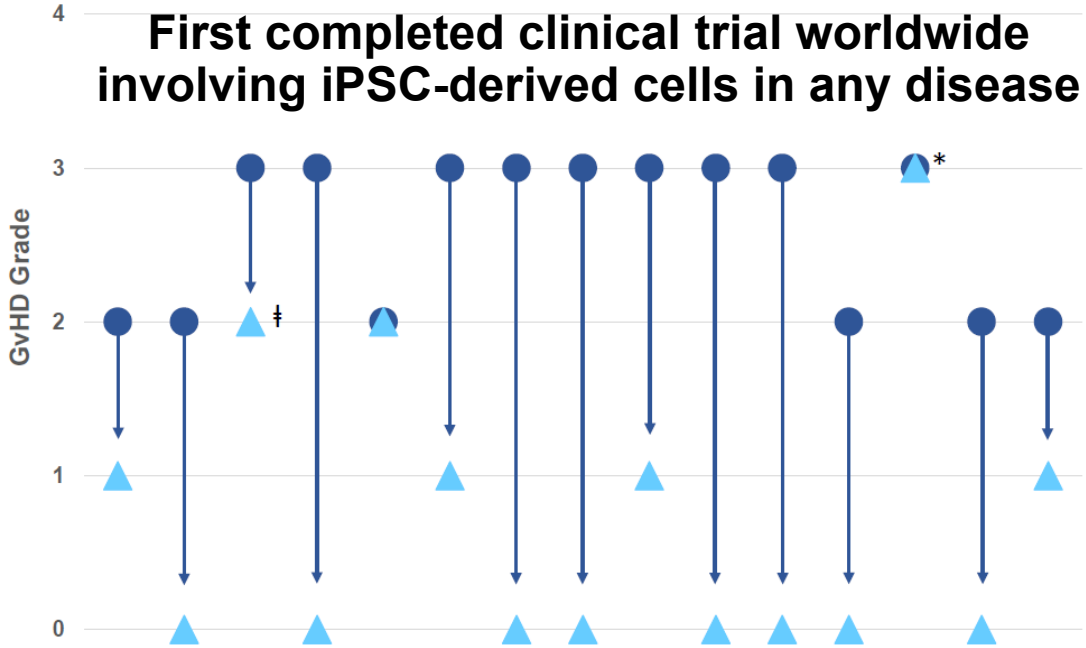

*Complete response*




*Overall response*


*Survival rate*

## First completed clinical trial worldwide involving iPSC-derived cells in any disease




| Subject # | A1 | A2 | A3 | A4 | A5 | A6 | A7 | A8 | B1 | B2 | B3 | B4 | B5 | B6 | B7 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Grade change | -1 | -2 | -1 | -3 | 0 | -2 | -3 | -3 | -2 | -3 | -3 | -2 | 0 | -2 | -1 |
| Best response | P | C | P | C | S | P | C | C | P | C | C | C | S | C | P |

**Legend**

GvHD Grade: Day 0 | GvHD Grade: Best Response | C Complete Response | P Partial Response | S Stable Disease

ǂ Subject A3 showed a PR at Days 14 and 21 but died due to pneumonia on Day 28

* Subject B5 withdrew from the trial on Day 22 to commence palliative care

Eight subjects were enrolled in each cohort, but one subject in Cohort B withdrew prior to infusion of CYP-001

**No treatment-related serious adverse events or safety concerns were identified**

# The MEND trial

## (The MEseNchymal coviD-19 trial)

**Target population**

- **24 adult patients** admitted to intensive care with **COVID-19 and respiratory distress** (compromised lung function), demonstrating symptoms which could include ARDS and other common hallmarks of serious infection (sepsis, CRS)

**Rationale for selection**

- Respiratory distress, CRS & sepsis also **represent significant unmet needs** beyond COVID-19
- **Strong pre-clinical results** in indications that can arise from a severe case of COVID-19

**Clinical trial design**

- In collaboration with the Cerebral Palsy Alliance Research Institute and the COVID-19 Stem Cell Treatment Group
- Open-label, randomised controlled clinical trial: Cymerus MSC infusions plus standard care (n=12) or standard care only (n=12)
- **Primary endpoints:** change in $PaO_2/FiO_2$ ratio by Day 7, and safety & tolerability
- **Secondary endpoints:** include clinical improvement scale; CRP levels; ventilator-free days; other physiological indices of respiratory function

# **Osteoarthritis** | New Phase 3 program

Funded by National Health and Medical Research Council

Australian Government
National Health and Medical Research Council

THE UNIVERSITY OF SYDNEY

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## Estimated market size

**30,000,000**
People in the USA affected by osteoarthritis

**~US$11.6B[1]**
Forecast global market opportunity by 2025

### Osteoarthritis

- Assess the effect of Cymerus MSCs on clinical outcomes and knee joint structures of patients with osteoarthritis of the knee (compared to a placebo)

### Rationale for selection

- Preclinical research showed MSCs can exert a number of important effects, including release of cytokines and growth factors that reduce inflammation and promote tissue repair, new blood vessel formation, and regeneration of compromised cartilage which may result in improved outcomes for patients

### Clinical trial design

- 440-patient trial sponsored by the University of Sydney and funded by NHMRC/in-kind contributions from participating institutions (no cash contribution from Cynata)
- Cynata to supply Cymerus MSCs for use in the trial[2] and will retain full commercial rights to the use of Cymerus MSCs in osteoarthritis

### Key milestones

- Phase 3 clinical trial expected to commence in 2H2020



1. Persistence Market Research 2018 research report: "Osteoarthritis Treatment Market: Global Industry Analysis (2012-2016) and Forecast (2017-2025)."
2. Subject to finalisation of trial start-up activities

# Thank you for your attention

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