

ASX ANNOUNCEMENT

18 March 2024

Cynata Presenting at Advanced Therapies Congress

Melbourne, Australia; 19 March 2024: Cynata Therapeutics Limited (ASX: “CYP”, “Cynata”, or the “Company”), a clinical-stage biotechnology company specialising in cell therapeutics, will participate by invitation in the Advanced Therapies Congress 2024 in London, UK.

At 3pm on Tuesday 19 March, Dr Kilian Kelly, Cynata’s Chief Executive Officer and Managing Director, will present on the clinical development of Cynata’s Cymerus™ off-the-shelf iPSC¹-derived MSC² products. A copy of the presentation is attached.

At 3:50 pm on the same day, Dr Kelly will take part in a panel discussion on “*Using pre-clinical models efficiently to avoid failure of clinical trials*”.

The Advanced Therapies Congress is Europe’s largest cell and gene therapy conference and exhibition, with over 2,500 attendees from across the entire value chain of cell and gene therapy development.

Further information on the event can be found at the following link:

<https://www.terrapinn.com/congress/advanced-therapies/index.stm>.

-ENDS-

Authorised for release by Dr Kilian Kelly, CEO & Managing Director

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About Cynata Therapeutics (ASX: CYP)

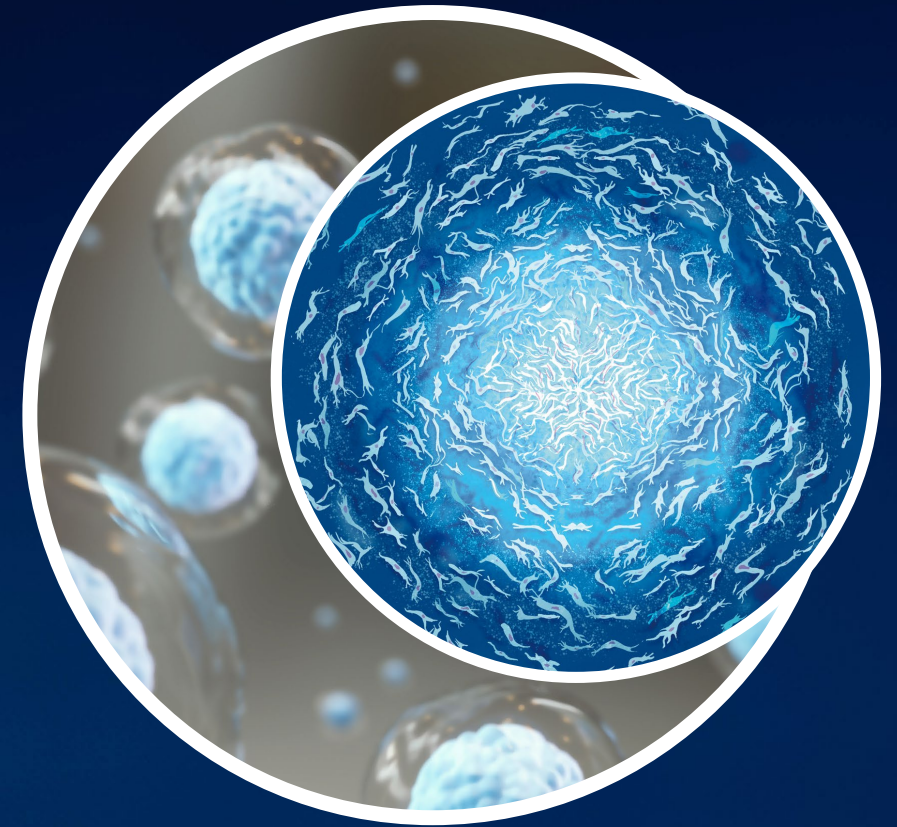
Cynata Therapeutics Limited (ASX: CYP) is an Australian clinical-stage stem cell and regenerative medicine company focused on the development of therapies based on Cymerus™, a proprietary therapeutic stem cell platform technology. Cymerus™ overcomes the challenges of other production methods by using 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. A Phase 2 clinical trial in GvHD under a cleared US FDA IND, as well as trials of Cymerus products in osteoarthritis (Phase 3) and diabetic foot ulcers (DFU) are currently ongoing, while a trial in renal transplant is expected to commence in the near future. In addition, Cynata has also demonstrated utility of its Cymerus technology in preclinical models of numerous diseases, including critical limb ischaemia, idiopathic pulmonary fibrosis, asthma, heart attack, sepsis, acute respiratory distress syndrome (ARDS) and cytokine release syndrome.

Cynata Therapeutics encourages all current investors to go paperless by registering their details with the designated registry service provider, Automic Group.

¹ iPSC = induced pluripotent stem cell

² MSC = mesenchymal stem (or stromal) cell



Clinical Development of iPSC-Derived MSCs

Advanced Therapies Congress
London, 19 March 2024

Kilian Kelly, PhD
CEO and Managing Director

ADVANCED
THERAPIES

Important information

Summary information

This Presentation contains summary information about Cynata Therapeutics Limited and its subsidiaries (CYP) which is current as at 14 March 2024. This Presentation should be read in conjunction with CYP's other periodic and continuous disclosure information lodged with the Australian Securities Exchange (ASX), which are available at www.asx.com.au.

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Financial data

All financial information in this Presentation is in Australian currency (A\$) unless otherwise stated. This Presentation contains historical financial information based on the Company's results for the half year to December 2023. This information is disclosed in the Appendix 4D report lodged with the ASX on 23 February 2024. Any discrepancies between totals and sums of components in tables and figures in this Presentation are due to rounding.

Forward-looking statements

This Presentation contains certain 'forward looking statements', which can generally be identified by the use of forward looking words such as 'expect', 'anticipate', 'likely', 'intend', 'should', 'could', 'may', 'predict', 'plan', 'propose', 'will', 'believe', 'forecast', 'estimate', 'target', 'outlook', 'guidance', 'potential' and other similar expressions. The forward looking statements contained in this Presentation are not guarantees or predictions of future performance and involve known and unknown risks and uncertainties and other factors, many of which are beyond the control of CYP, its directors and management, and may involve significant elements of subjective judgment and assumptions as to future events which may or may not be correct. There can be no assurance that actual outcomes will not differ materially from these forward looking statements. A number of important factors could cause actual results or performance to differ materially from the forward looking statements. No representation or warranty, express or implied, is made as to the accuracy, likelihood of achievement or reasonableness of any forecasts, prospects, returns or statements in relation to future matters contained in this Presentation. The forward looking statements are based on information available to CYP as at the date of this Presentation. Except as required by law or regulation (including the ASX Listing Rules), CYP and its directors, officers, employees, advisers, agents and intermediaries undertake no obligation to provide any additional or updated information whether as a result of new information, future events or results or otherwise. You are strongly cautioned not to place undue reliance on forward-looking statements, particularly in light of the current economic climate and the significant volatility, uncertainty and disruption caused by the outbreak of COVID-19.

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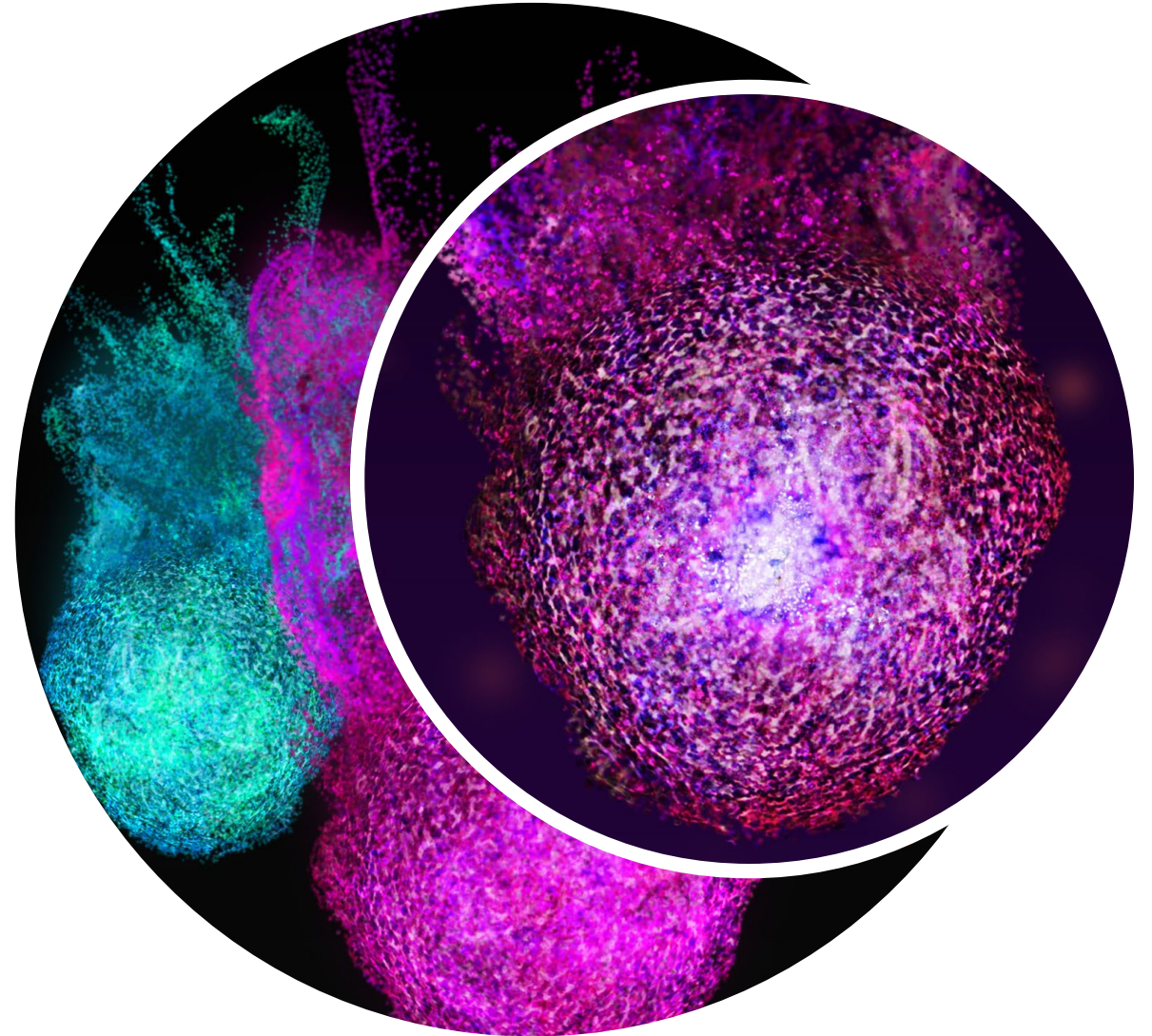
Certain market and industry data used in connection with this Presentation may have been obtained from research, surveys or studies conducted by third parties, including industry or general publications. Neither CYP nor its representatives have independently verified any such market or industry data provided by third parties or industry or general publications.

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About Cynata

- ASX-listed company (Ticker: **CYP**), based in Melbourne, Australia
- Exclusively focused on development of **Cymerus™** platform:
 - **iPSC**-based technology for scalable manufacture of consistent, allogeneic **MSC**-based therapeutic products
 - Developing therapies to treat a range of serious disorders with unmet needs
- Positive data in a range of indications
- Completed **world-first** iPSC clinical trial



Company highlights



Unique Manufacturing

Single donation from a single donor
iPSC strategy overcomes suboptimalities in conventional MSC manufacturing



Strong safety and efficacy

Positive pre-clinical and clinical data supporting versatility and efficacy of Cynata's MSCs; including in world-first iPSC trial in aGvHD Phase 1



Multiple clinical trials

Rich clinical pipeline:

- **aGvHD** (Phase 2)
- **DFU** (Phase 1)
- **Osteoarthritis** (Phase 3)
- **Renal** (Phase 1)



Large addressable market





Combined market opportunity of clinical trials underway and in planning is **~US\$28bn¹**



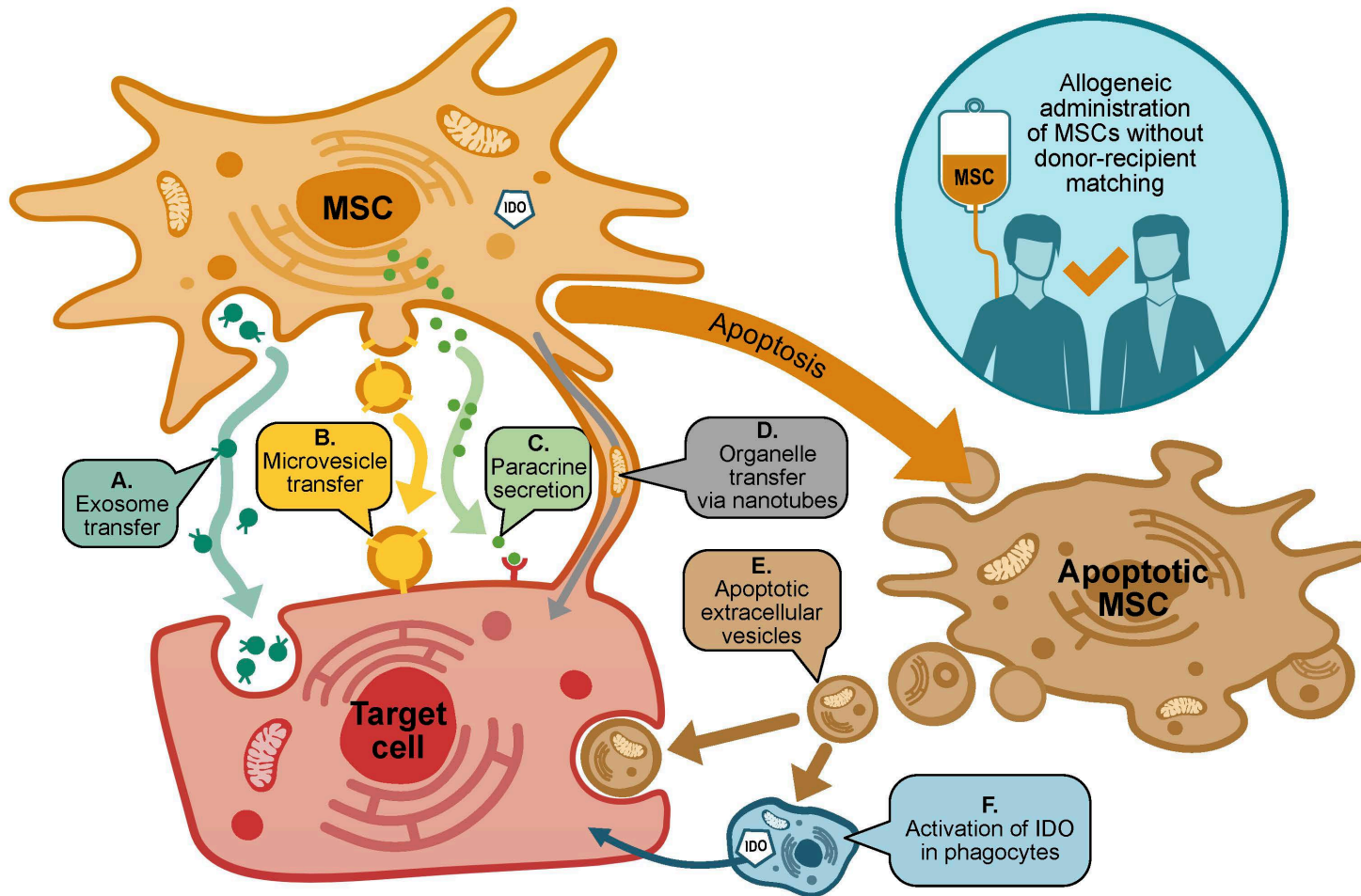
Solid funding position

~A\$11m in cash², and OA and renal trials funded by external partners

Advanced and diverse clinical pipeline

	Indication	Trial phase	Market opportunity
Cynata Sponsored	 Acute Graft vs Host Disease (aGvHD) CYP-001 <i>(FDA Orphan Designation)</i>	Phase 2 underway	US\$600m ¹
	 Diabetic Foot Ulcers (DFU) CYP-006TK	Phase 1 underway	US\$9.6bn ²
Partnered	 Osteoarthritis (OA) CYP-004 <i>(managed by USYD, funded by NHMRC)</i>	Phase 3 underway (recruitment complete)	US\$11.6bn ³
	 Renal Transplantation (Renal) CYP-001 <i>(managed and funded by LUMC)</i>	Phase 1 approved	US\$5.9bn ⁴

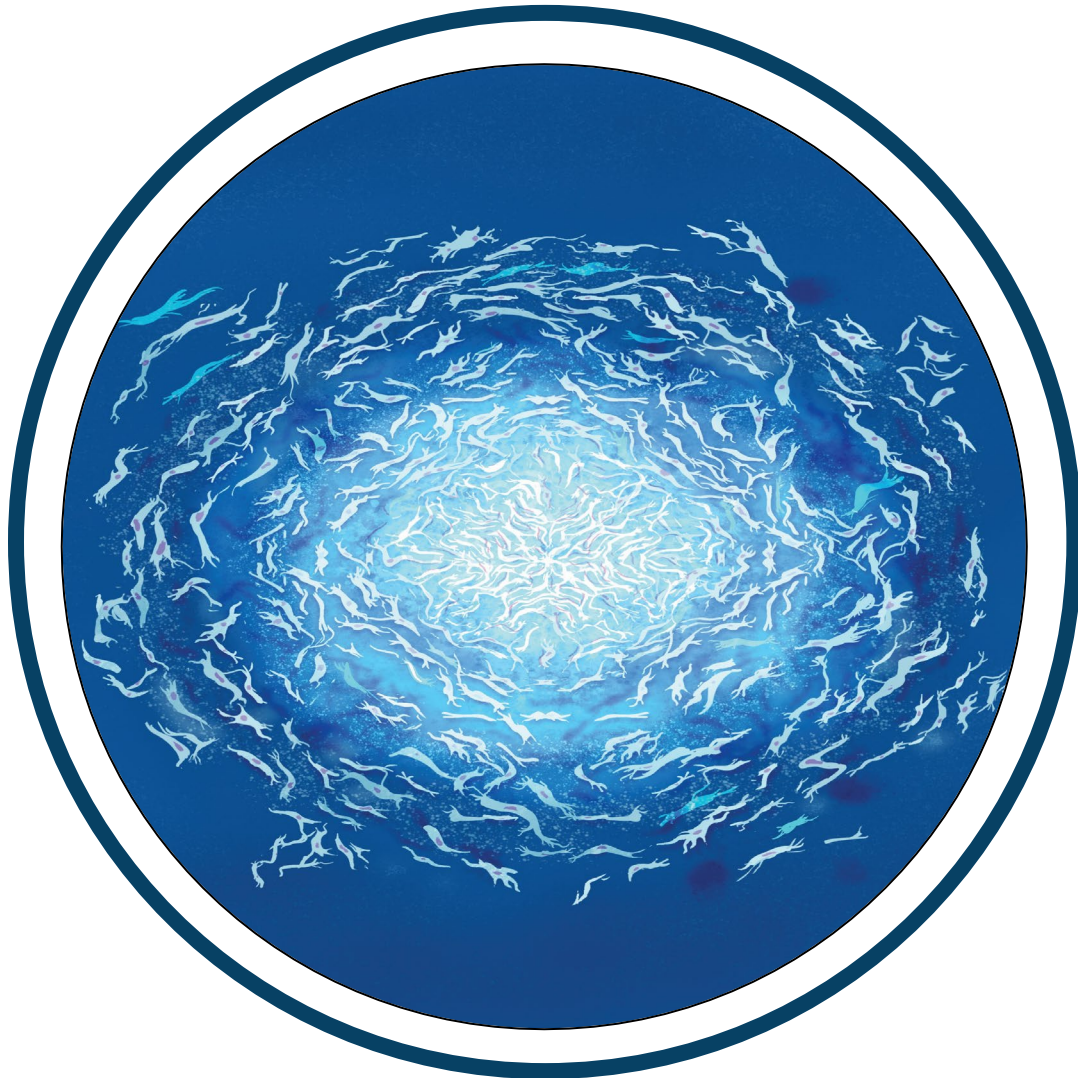
Why MSCs?



Mesenchymal stem (or stromal) cells (MSCs):

- promote an **immunomodulatory** environment via multifactorial mechanisms¹
- the “sensor and switcher of the immune system”²
- promote **tissue repair and regeneration**
- can be used **without** donor/recipient matching
- can be **engineered** to express other functional/therapeutic molecules

Why iPSCs?



Induced pluripotent stem cells (iPSCs):

- mature cells from adult donors, reprogrammed to become pluripotent
 - effectively limitless proliferation in cell culture
 - potential to differentiate into any adult cell type (including MSCs)
 - avoids ethical controversy associated with embryonic stem cells
- **ideal** starting material for large scale production of cellular products

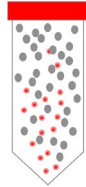
Conventional MSC process

Ongoing need
for new donors



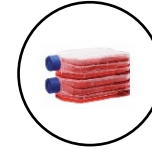
Substantial inter-donor **variability**

MSC isolation



Small number of MSCs
per donation

Culture expansion



Extensive MSC
culture expansion

Major challenges:

- inter-donor **variability**
- MSCs have **limited expansion potential**
- MSCs undergo **functional changes** during extensive culture expansion

Cymerus™ iPSC-based process

One donor,
one time

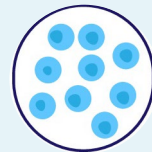


Avoids inter-donor
variability

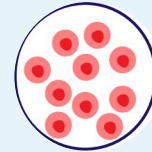
Reprogramming &
iPSC expansion



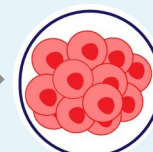
Effectively limitless
Expansion potential



Differentiation into MSCs
& culture expansion



Minimal MSC
culture expansion



Cymerus platform:

- Harnesses **effectively limitless** iPSC expansion potential
- **Avoids** inter-donor variability
- **Avoids** extensive MSC expansion

Strategic partnership with Fujifilm

- Fujifilm: one of largest conglomerates globally, with significant assets in biotechnology sector, bolstered by recent multi-billion dollar investments
- Fujifilm Cellular Dynamics Inc (FCDI: subsidiary of Fujifilm) developed the original iPSC line used in Cynata's Cymerus manufacturing process
- Parties now working towards establishing Cymerus manufacturing process at FCDI with Cynata's progress showcasing Fujifilm's iPSC platform
- Significant institutional shareholder; representing a 4.5% shareholding



Preclinical studies with Cymerus MSCs

Large body of data in wide range of preclinical models, in partnership with leading research groups worldwide:

- GvHD
- Diabetic wounds
- Critical limb ischaemia
- Organ transplant rejection
- Osteoarthritis
- Respiratory disorders (including asthma, pulmonary fibrosis, acute respiratory distress syndrome)
- Sepsis
- Cardiovascular disorders (including coronary artery disease, myocardial infarction)
- Cytokine release syndrome
- Glioblastoma



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MSC source affects properties

Comparative analysis of MSCs from various sources¹

- Source is primary driver of MSC heterogeneity
- Cymerus MSCs exhibit less batch-batch and intra-population variability than tissue-derived MSCs
- Cymerus MSCs successfully bypass much of the inherent variability that affects tissue-derived MSCs

Mouse model of diabetic wounds, using novel MSC-seeded dressing³

- Cymerus MSCs resulted in significantly greater re-epithelialisation (86%) compared with bone marrow MSCs (51%)
- Gingival fibroblast- and bone chip-derived MSCs produced similar results to Cymerus MSCs, but there are major challenges associated with producing clinical-grade cells from those sources

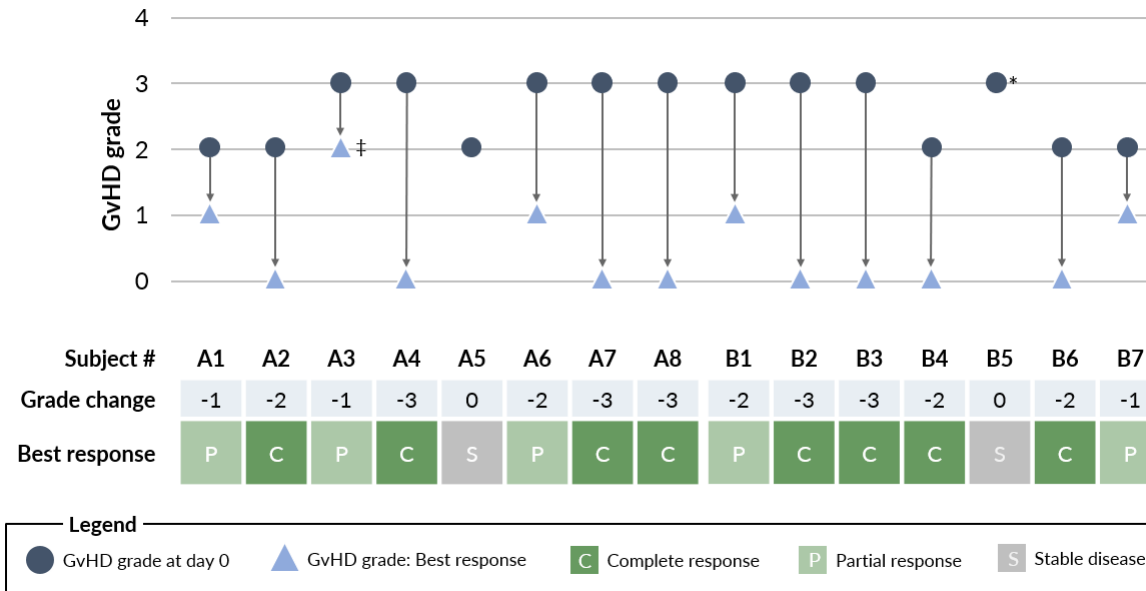
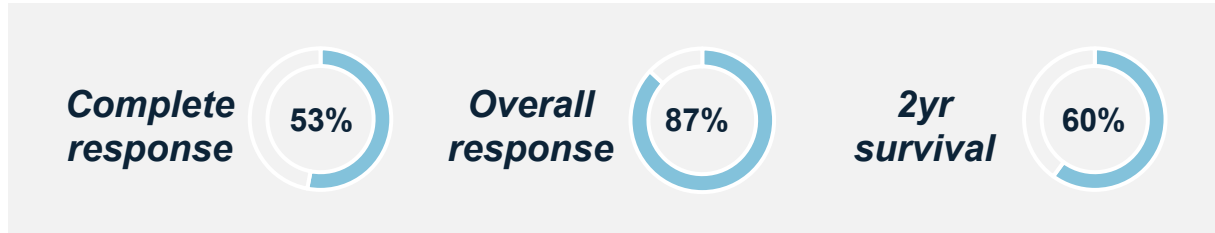
Pre-clinical rat model of myocardial ischemia-reperfusion²

Positive effects were observed with both Cymerus MSCs and bone marrow MSCs, but some different effects between MSC groups:

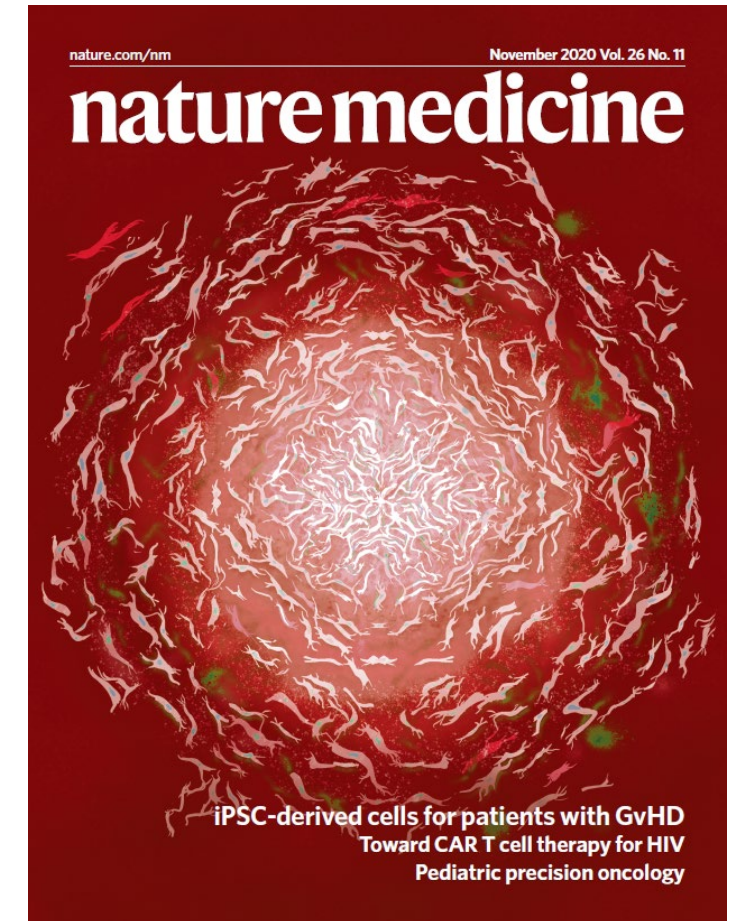
- Left ventricle function significantly improved in Cymerus MSC group (P=0.01) compared to placebo, but not in bone marrow MSC group (P=0.63)
- Arteriogenesis around infarct zone significantly improved in Cymerus MSC group compared to both placebo and bone marrow MSC group (P=0.01)
- Expression of a number of relevant cytokines by Cymerus MSCs was **2-4x higher** than by bone marrow MSCs

aGvHD | Phase 1 clinical trial

First completed clinical trial worldwide with any iPSC-derived product



Published in Nature Medicine¹



No treatment-related serious adverse events or safety concerns identified



- Subjects received 1×10^6 cells/kg (max 1×10^8 cells) or 2×10^6 cells/kg (max 2×10^8 cells) by IV infusion on D0 and D7

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

‡ 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

1. Bloor et al. 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. Nat Med 2020;26:1720-1725.

aGvHD | Phase 2 clinical trial

Product

CYP-001 (Cymerus™ iPSC-derived MSCs for intravenous infusion)

Indication

High risk acute graft versus host disease (aGvHD)¹

Study Design

- Randomised controlled trial in ~60 adults (steroids + CYP-001 vs steroids + placebo)
- Primary objective: to assess efficacy of CYP-001 based on Overall Response Rate at Day 28

Study Conduct

- Clinical sites in USA, Europe and Australia
- Regulatory/ethics approvals secured in Australia, USA and Turkey; EU regulatory process ongoing
- Numerous sites now open for recruitment, with remainder expected to open in 2024
- First patient enrolled – March 2024
- Aiming to complete recruitment by end of calendar year 2024

Results

Primary evaluation results expected in 2H CY 2025

DFU | Phase 1 clinical trial

Product

CYP-006TK (Novel silicone dressing seeded with Cymerus™ iPSC-derived MSCs)

Indication

Non-healing diabetic foot ulcers (DFU)

Study Design

- Randomised controlled trial in ~30 adults
- Patients randomised to receive either standard of care or CYP-006TK for 4 weeks, followed by standard of care
- Primary objective is safety; efficacy outcome measures include wound healing, pain & quality of life

Study Conduct

- Clinical sites in Australia (Adelaide and Perth)
- Recruitment ~85% complete – completion expected in near future

Results

- Positive initial results from first 16 patients – median reduction in wound surface area after 10 weeks was **87.6%** in CYP-006TK group compared to **51.1%** in controls (n=8 per group)
- Final results expected by end of calendar year 2024

OA | Phase 3 clinical trial¹

Product

CYP-004 (Cymerus™ iPSC-derived MSCs for intra-articular injection)

Indication

Osteoarthritis (OA) of the knee (Kellgren-Lawrence Grade 2-3)

Study Design

- Randomised, double-blind placebo-controlled trial in ~320 adults
- Each participant receives 3 injections over 12 months; follow-up of 24 months from first dose
- Co-primary endpoints: reduction of knee symptoms and measure of cartilage loss

Study Conduct

- Trial conducted by University of Sydney, funded by Australian Government NHMRC grant
- Clinical centres in Australia (Sydney and Hobart)
- Recruitment complete (commenced November 2020; completed in November 2023)
- Last patient last visit expected ~November 2025

Results

- Results expected in H1 CY 2026

Renal transplant | Phase 1 clinical trial

Product

CYP-001 (Cymerus™ iPSC-derived MSCs for intravenous infusion)

Indication

Prevention of kidney transplant rejection

Study Design

- ~16 patients to receive CYP-001 after kidney transplantation: cohort 1 (n=3); cohort 2 (n=3); cohort 3 (n=10)
- Trial will evaluate safety (all cohorts) and efficacy of MSCs in facilitating reduction of calcineurin inhibitors (anti-rejection medication; Cohort 3)

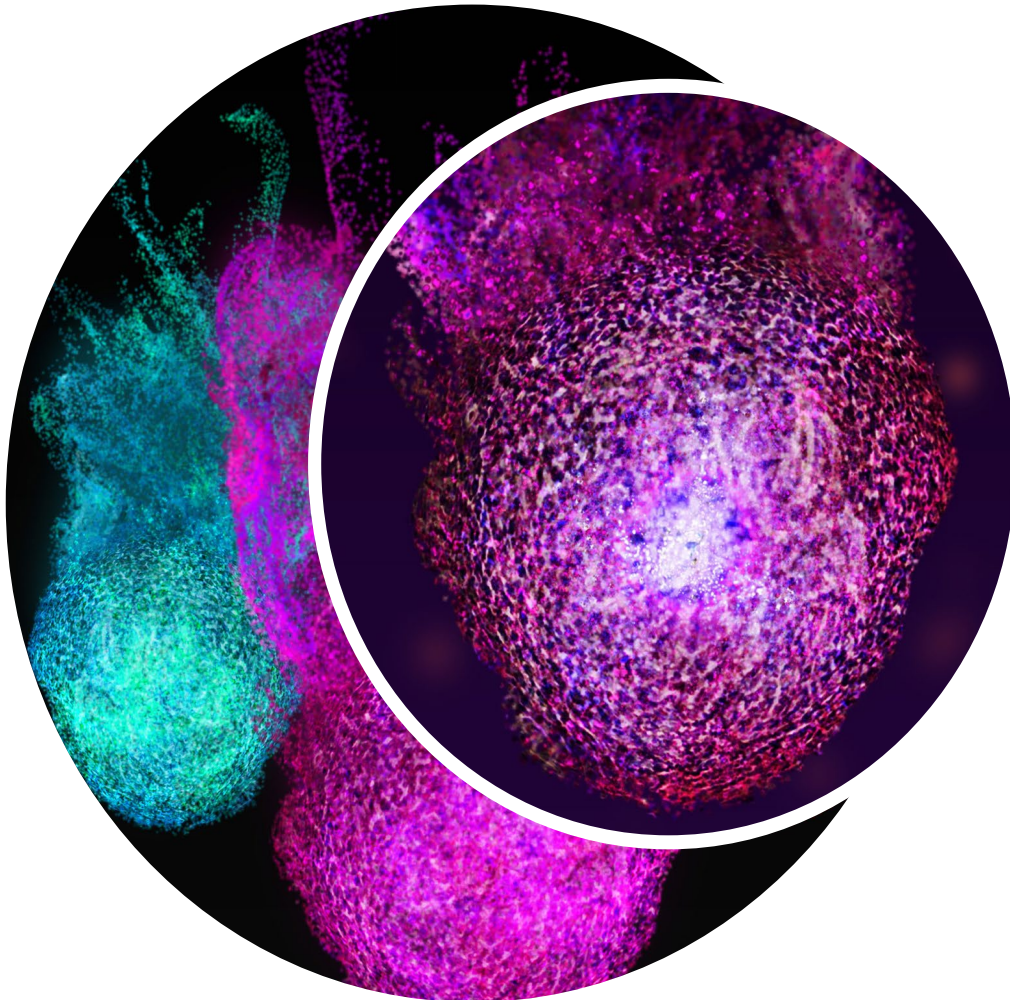
Study Conduct

- Trial to be conducted and funded by Leiden University Medical Center, Netherlands
- Regulatory and ethics approvals in place; final trial start-up activities ongoing
- Aiming to commence recruitment in Q1 2024
- Timing of further cohorts TBC

Results

Results of Cohort 1 anticipated in late 2024

Partnering



Cynata is pursuing a partnership-driven business model



Proactive outreach ongoing, aimed at development partners for existing clinical assets

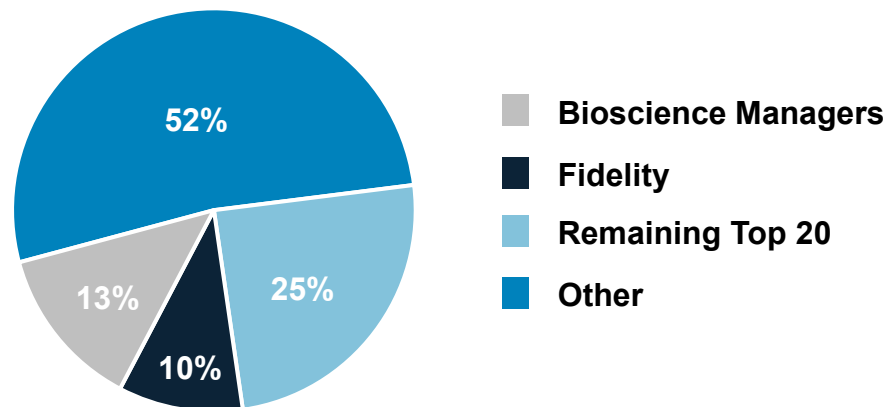


Cymerus platform also available for other indications and/or engineered MSC applications

Corporate overview

Cynata has been listed on the Australian Securities Exchange (ASX) since 2013 (Ticker: CYP)

Shareholder distribution



Financial information

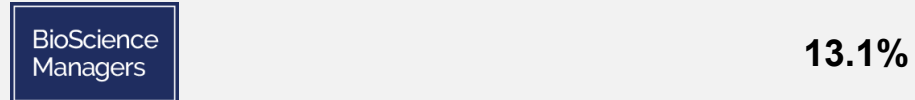
Share price (14 March 2024) A\$0.175

Shares on issue 179m

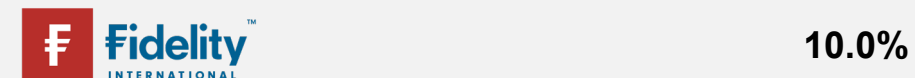
Market capitalisation ~A\$31.3m

Cash¹ ~A\$11m

Substantial shareholders (>5%)



BioScience Managers is an international healthcare investment firm headquarter in Melbourne that finances and enables innovative science and technology with the potential to transform healthcare.



Fidelity International is a world leading investment and asset management firm, responsible for total client assets of >US\$750 billion, from clients across Asia Pacific, Europe, the Middle East, South America and Canada.

Summary



Next generation stem cell company

- Leading platform technology in burgeoning stem cell sector
- Diverse and highly credentialed leadership team with proven clinical and commercial experience across a range of health sciences at leading institutions



Scalable manufacturing

- Patented Cymerus manufacturing technology enables scalable production of consistent MSCs from a single donation from a single donor, overcoming issues with conventional approaches



Successful clinical trial results

- Very encouraging safety and efficacy results from Phase 1 trial of Cymerus MSCs in aGvHD
- Highly encouraging initial DFU patient data



Robust and attractive pipeline

- Broad and diverse clinical stage MSC pipeline with active clinical programs in aGvHD, DFU, OA, and renal transplantation
- FDA cleared IND for Phase 2 aGvHD clinical trial; study underway



Significant growth potential

- Global estimated market opportunity across targeted indications of ~US\$28bn
- Continued focus on indications where there is significant unmet need
- Proactive B-2-B outreach to drive partnering strategy



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