ASX ANNOUNCEMENT **18 March 2025**

Cynata Presenting at Advanced Therapies Congress

Melbourne, Australia; 18 March 2025: Cynata Therapeutics Limited (ASX: **"CYP"**, **"Cynata"**, or the **"Company"**), a clinical-stage biotechnology company specialising in cell therapeutics, is participating in the Advanced Therapies Congress 2025.

The congress, which is taking place at the ExCel Centre in London, is Europe's largest commercial cell and gene therapy conference and exhibition. It attracts over 2,500 attendees including senior biopharmaceutical executives, clinicians, academics, payers and regulators.

Dr Mathias Kroll (Cynata's Chief Business Officer) will present on the Company's clinical development programs at 13:40 GMT today, and participate in partnering meetings during the conference. A copy of Dr Kroll's presentation is attached.

-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 has demonstrated positive safety and efficacy data for its Cymerus™ product candidates CYP-001 and CYP-006TK, in Phase 1 clinical trials in steroid-resistant acute graft versus host disease (GvHD), and diabetic foot ulcers (DFU), respectively. Further clinical trials are now ongoing: a Phase 2 trial of CYP-001 in GvHD under a cleared US FDA IND; a Phase 1/2 trial of CYP-001 in patients undergoing kidney transplant; and a Phase 3 trial of CYP-004 in osteoarthritis. In addition, Cynata has demonstrated utility of its Cymerus™ technology in preclinical models of numerous other 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.

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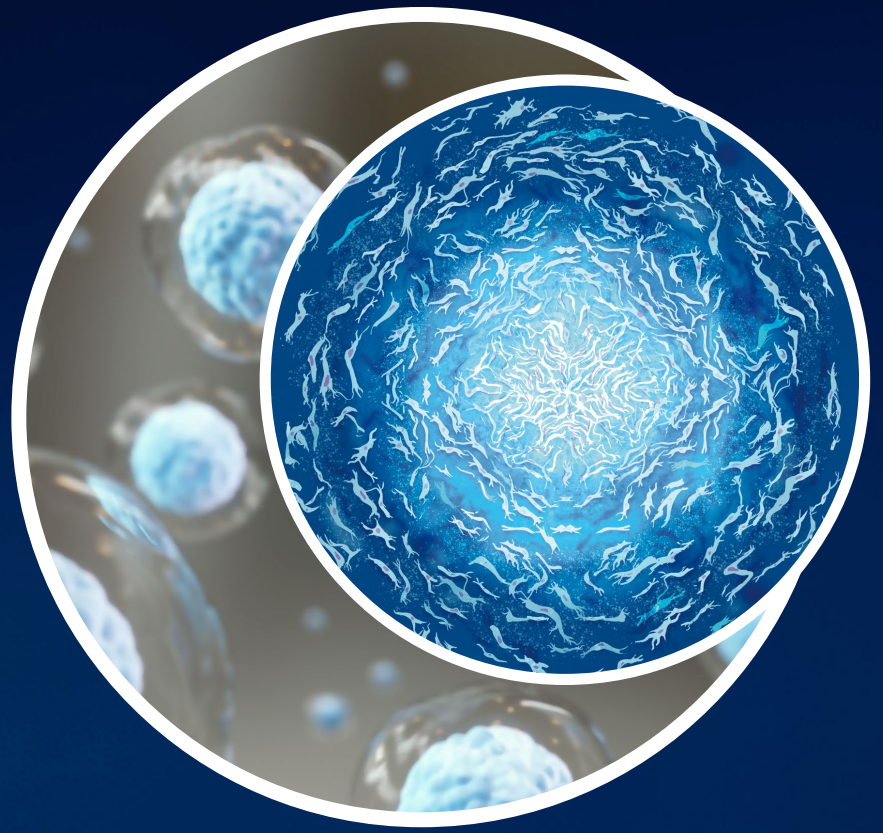

Pioneering more powerful MSCs

Advanced Therapies, London ExCel
18 March 2025

Mathias Kroll, Chief Business Officer

Important information

Summary information

This Presentation contains summary information about Cynata Therapeutics Limited and its subsidiaries (**CYP**, or **Cynata**) which is current as at 17 March 2025. 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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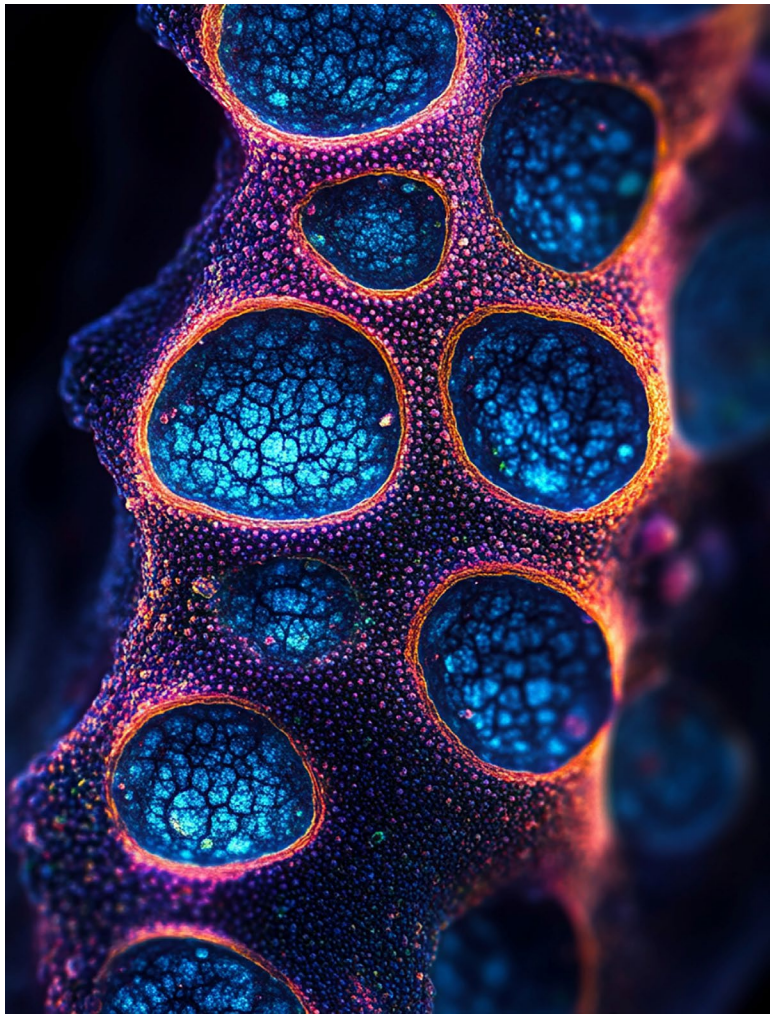
Introduction to MSCs

What are MSCs?

- **Mesenchymal stem cells**
  (also known as **mesenchymal stromal cells** or **medicinal signalling cells**)
- These cells occur naturally in **small numbers** in the human body
- Key MSC properties[1]:
  - **Immunomodulatory** effects – they help balance the immune system
  - **Anti-inflammatory** effects
  - Promote **tissue repair** and **regeneration**

MSC-based therapy:

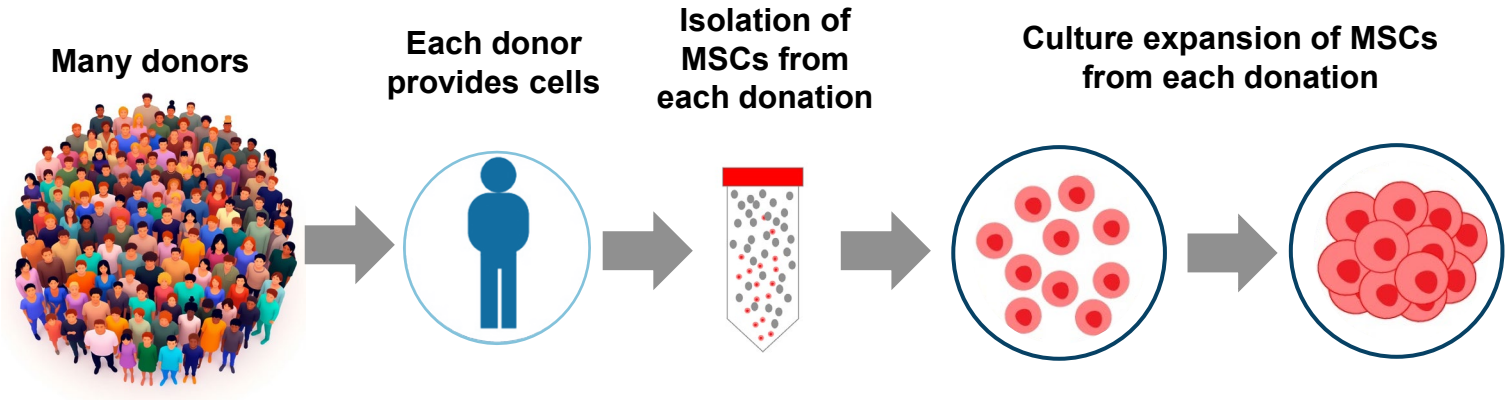
- Involves administration of much **larger numbers** of MSCs than exist within the body naturally, to treat/prevent disease
- First investigated in 2004, in a 9-year old boy with graft versus host disease[2]
- Since then, more than 1,700 clinical trials have been initiated, to investigate MSC therapy for many different diseases[3]



1. Spees et al, Stem Cell Res Ther 7:125 (2016)
2. Le Blanc et al, Lancet. 363: 1439–41 (2004)
3. Clinicaltrials.gov

Conventional MSC manufacturing process

Standard Process[1]



New donors must be identified on regular basis; donors must consent to **surgical extraction**	MSCs must be **isolated** from **mixture of cells** from **each** donation – producing only **small number** of MSCs per donation	**Extensive** culture expansion required (growing cells) – **large number** of MSCs required	Different batches of MSCs come from **different donors**

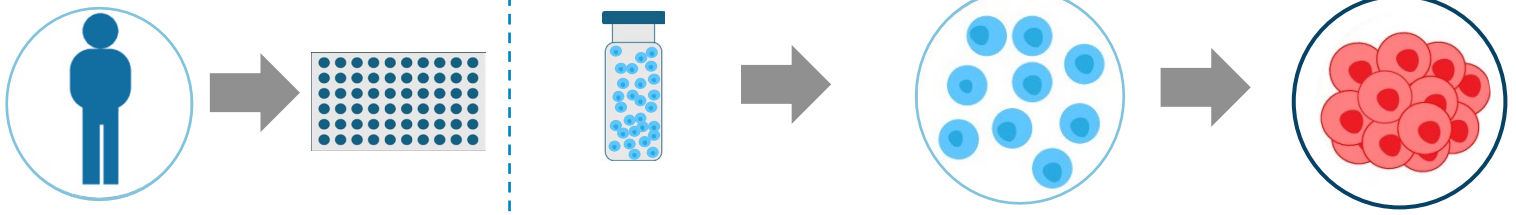
Major Challenges

Different donors = **Variable** starting material = **Inconsistent** product	**Small number** of MSCs retrieved per donation = **Extensive** MSC culture expansion required	**Extensive MSC culture expansion** = **Functional changes** = **Loss of potency**	MSCs from **different donors** are administered to **different patients** = **Inconsistent results**

This is a representative, high-level summary of a typical process to produce donor-derived MSCs. Some manufacturing processes may differ.

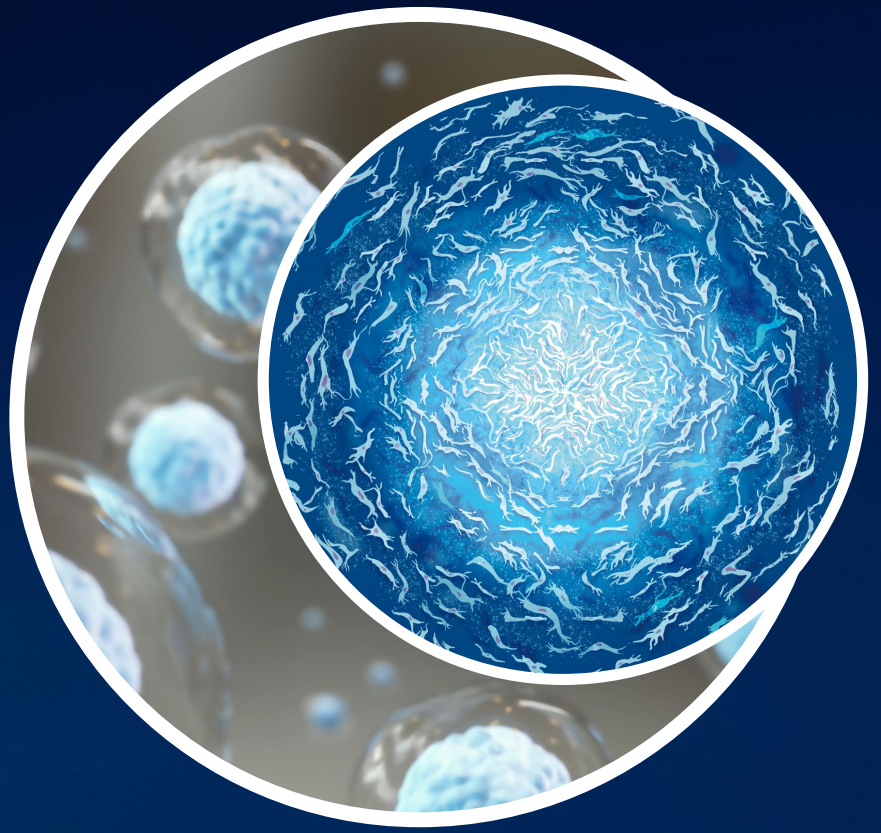
The solution: the Cymerus™ process

	One donor → iPSC bank	Vial of iPSCs from bank	iPSC expansion and differentiation	Formation of MSCs	Patients
Cymerus™ Process	Blood donation from a **single donor** was used to produce a high-quality **iPSC**[1] **bank**	Cells from **same** iPSC bank are used to make **every batch** of Cymerus™ MSCs	iPSCs are culture expanded, then **turned into MSCs** using **patented** Cymerus™ process		**All** batches of Cymerus™ MSCs come from the **same donor**
Major Benefits	iPSCs have effectively **limitless** expansion capacity = **Scalability**	Starting material for **all** batches is **the same** = **Consistent** MSC product	**Minimal** MSC culture expansion required = MSCs **retain potency**		**All** patients receive MSCs from the **same donor** = **Avoids variability**



1. iPSCs are induced pluripotent stem cells (iPSCs). Mature adult cells reprogrammed to become pluripotent, which means they have effectively limitless proliferation capacity and potential to differentiate into any adult cell type (including MSCs). iPSCs are the ideal starting material for commercial production of cellular products.

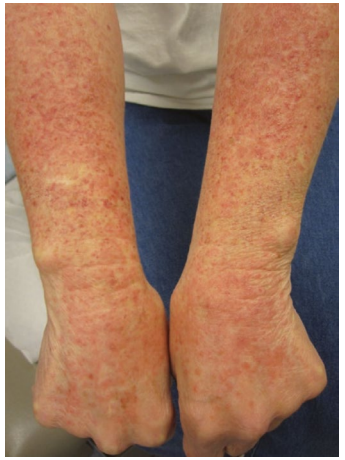
Acute Graft versus Host Disease (aGvHD)

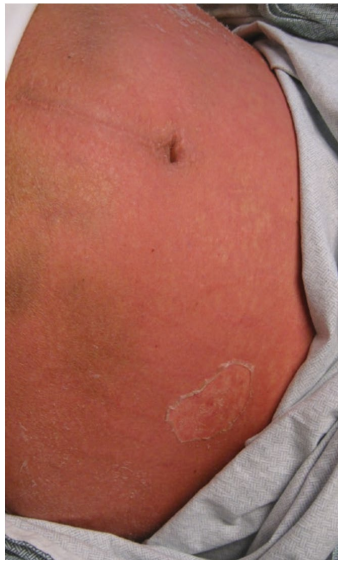


Bone marrow transplants & GvHD

Bone marrow transplant (also known as blood stem cell transplant)

- The procedure replaces blood stem cells in people whose bone marrow has been destroyed by large doses of chemotherapy or radiotherapy
- Bone marrow transplants can be curative for blood cancers (e.g. lymphoma & leukaemia)
- However, these procedures, if they use third party donors (“allogeneic”), can result in graft versus host disease (GvHD)





Graft versus host disease

- GvHD is where the transplanted cells recognise the recipient’s cells as “foreign”
- This results in the transplant (the “graft”) attacking the recipient’s (the “host’s”) tissues and organs
- First-line treatment for acute GvHD (aGvHD) is corticosteroids, but ~50% of patients develop what’s known as steroid-resistant acute GvHD (SR-aGvHD)
- In steroid-resistant patients, 2-year survival rate is less than 20%[1]

1. Westin JR et al. Adv Hematol. 2011:601953 (2011)

Images from: A Cotliar, Atlas of Graft-versus-Host Disease, 2016

Acute graft versus host disease (aGvHD)

>38,000 allogeneic transplants* **per year**[1]

~35-50% develop aGvHD[2,3]

Almost all receive steroids

<50% respond to steroids[4]

Up to **9,500** steroid-resistant cases **per year**

2-year survival rate in SR-aGvHD: **<20%**[5]

* "Allogeneic" means cells come from someone else (a donor) rather than the recipient; "transplant" refers to blood stem cell transplants

Current treatments for steroid-resistant aGvHD (SR-aGvHD):

- **Ruxolitinib**
  - Good initial response rates but no apparent increase in longer-term survival rates (18 months +) compared to controls[6]
  - Serious/life threatening adverse reactions are common in patients who receive Ruxolitinib (e.g. infections, blood disorders)[7]
  - Ruxolitinib is priced at ~US$18k per month, and typically requires at least 6 months treatment for GvHD (i.e. >US$100k per patient), and has forecast sales of US$4.5b in 2024 across all indications[8]
- **Other investigational agents**
  - Sometimes referred to as "Best Available Therapy (BAT)" in clinical trials
  - Most have shown limited efficacy and/or poor safety profiles

Safer and more effective treatments are desperately needed for aGvHD

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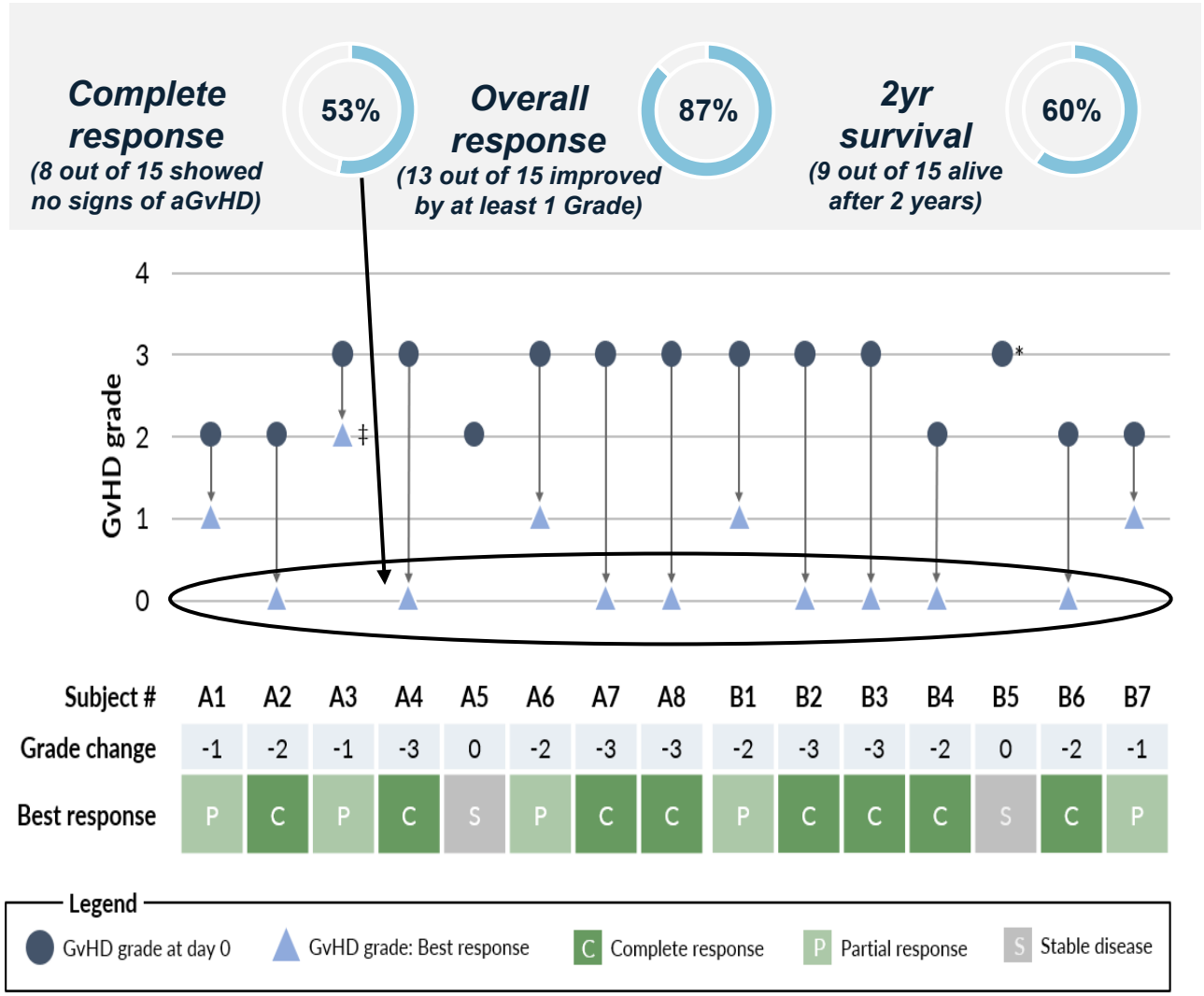
1. Malard et al, Nature Reviews Disease Primers 9: 27 (2023).
2. Reshef et al, J Clin Oncol. 39(17):1878-1887 (2021).
3. Akahoshi et al, Blood Adv. 7(16):4479-4491 (2023).
4. Major-Monfried et al, Blood.131(25):2846-2855 (2018).
5. Westin JR et al, Adv Hematol. 2011:601953 (2011).
6. Zeiser et al, N Engl J Med 2020;382:1800-1810 (2020).
7. JAKAFI® (ruxolitinib) tablets, for oral use, US FDA approved Prescribing Information, September 2021.
8. Sales figures relate to all approved indications, including myelofibrosis, polycythemia vera, and GvHD.

SR-aGvHD | Phase 1 clinical trial – results



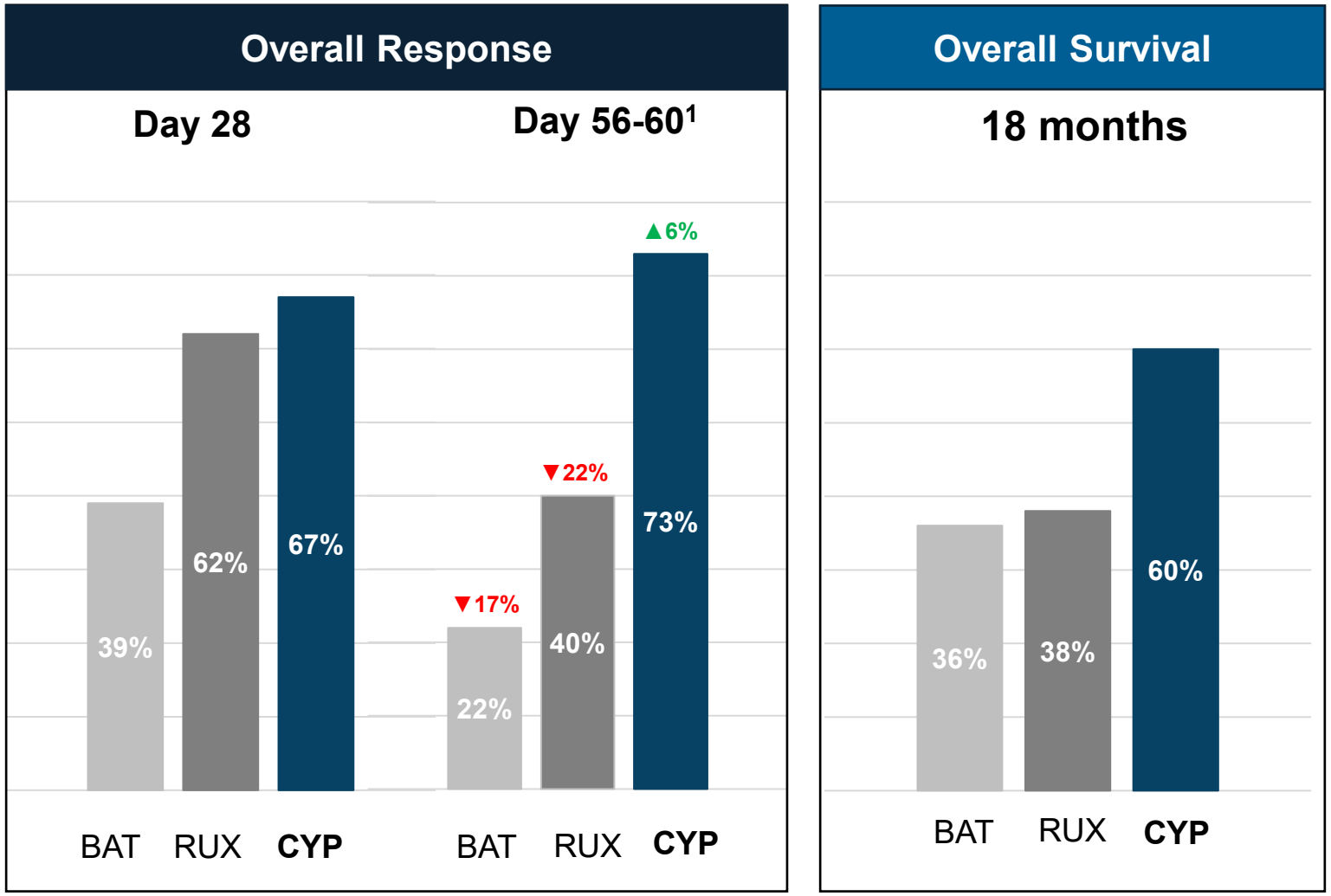
- Outstanding **response rates** and **overall survival**
- **Sustained outcomes achieved up to 2 years** after the first infusion
- **Importantly:** CYP-001 was shown to be **safe and well tolerated**
- **No serious adverse events or other safety concerns related to CYP-001**

Trial conducted in 15 patients with steroid-resistant aGvHD (SR-aGvHD)
Product: CYP-001 (Cymerus™ MSCs for intravenous infusion)

- Subjects received $1x10^6$ cells/kg (max $1x10^8$ cells) or $2x10^6$ cells/kg (max $2x10^8$ 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
For further information: https://clinicaltrials.gov/study/NCT02923375

CYP-001 vs other treatments in SR-aGvHD



CYP = CYP-001 in Phase 1 trial (NCT02923375). **Rux** = ruxolitinib in Phase 3 trial (NCT02913261) (ruxolitinib is now approved for SR-aGvHD). **BAT** = "best available therapy" control arm in ruxolitinib Phase 3 trial (NCT02913261)

Overall Response

- Between Day 28 and Day 56-60, the Overall Response Rate (ORR) for both RUX and BAT **decreased** markedly, while the ORR for CYP-001 marginally **increased**

Overall Survival

- CYP also reported **60% survival at 24 months** (not shown on graph, as 18 months was the latest timepoint reported in RUX/BAT trial)

Safety

- No serious adverse events or safety concerns for CYP-001

Note: comparisons are for illustrative purposes only; data taken from different clinical trials with different sample sizes (BAT: n=155; Rux: n=154; CYP-001: n=15).
D28/D56 time points used for response rate comparison as D28/D56 were the only response rate time points reported in the BAT/Rux clinical trial (NCT02913261; Zeiser et al. N Engl J Med 382:1800-1810 [2020]).
1. Overall Response at Day 56-60 refers to Day 56 response for BAT & Rux, and Day 60 response for CYP-001

Scientific and regulatory recognition

Scientific: Publications

- Cynata was published in two editions of the highly prestigious *Nature Medicine* journal following its Phase I trial results

Cynata featured on front-page of Nature Medicine

nature medicine
LETTERS
https://doi.org/10.1038/s41591-020-1050-x
Nature Medicine 26, 1720–1725 (2020)

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]

nature medicine
Nature Medicine 30, 1556–1558 (2024)
https://doi.org/10.1038/s41591-024-02990-z

Two-year safety outcomes of iPS cell-derived mesenchymal stromal cells in acute steroid-resistant graft-versus-host disease

Kilian Kelly[1], Adrian J. C. Bloor[2], James E. Griffin[3], Rohini Radia[4], David T. Yeung[5,6] & John E. J. Rasko[7,8,9]

Regulatory: Orphan Drug Designation

- CYP-001 has been granted Orphan Drug Designation by the US FDA for the treatment of GvHD

FDA U.S. FOOD & DRUG ADMINISTRATION

Benefits include:

- Tax credits for qualified clinical trials
- Exemption from user fees
- Potential seven years of market exclusivity after approval

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1. CYP-001 is Cynata's Cymerus iPSC-derived MSC product candidate for intravenous infusion

aGvHD | Phase 2 clinical trial

Indication	High risk acute graft versus host disease (aGvHD)[1]
Product	CYP-001 (Cymerus™ iPSC-derived MSCs for intravenous infusion)
Study Design	• Randomised, double-blind, placebo-controlled trial • ~60 adults (steroids + CYP-001 vs steroids + placebo) • Primary objective is to assess efficacy of CYP-001 based on Overall Response Rate at Day 28
Study Conduct	• Conducted under IND from US FDA • Clinical sites in USA, Europe and Australia • First patient enrolled in March 2024; enrolment >40% complete[2] • Aiming to complete patient enrolment in H1 2025
Results	Results anticipated in H2 2025 (primary evaluation)

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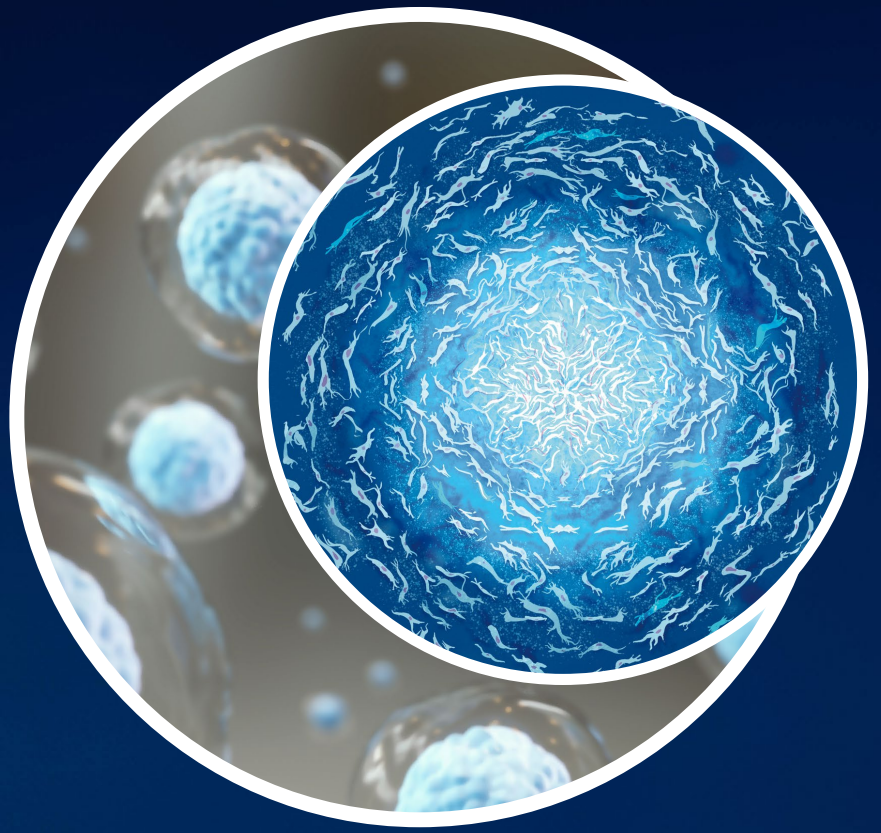
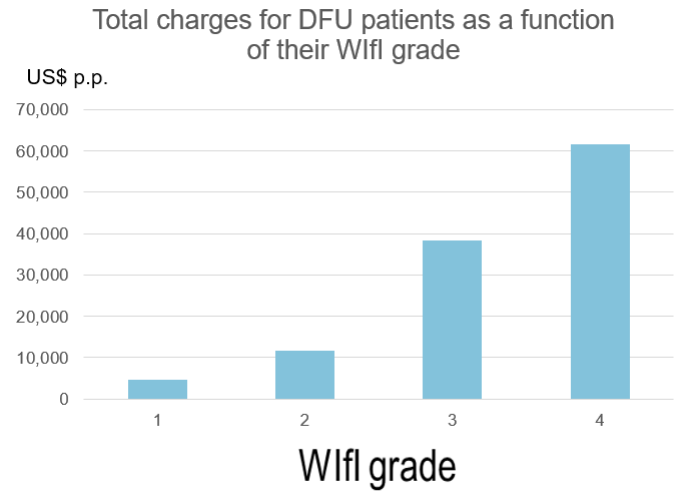
1. Trial is recruiting patients with High Risk newly diagnosed aGvHD (risk assessed based on refined Minnesota criteria), which means patients are not yet eligible to receive ruxolitinib. This is earlier in treatment pathway than completed Phase 1 trial, which was conducted in patients with steroid-resistant aGvHD. For further information see: https://clinicaltrials.gov/study/NCT05643638
2. As of December 2024 Quarterly Activity Report, released to ASX on 30 January 2025

CYP-006TK for Diabetic Foot Ulcers



Diabetic foot ulcers (DFU)

- Open sore or wound that develops in patients with diabetes
- Very difficult to heal, which can lead to serious complications such as serious infection
- 20% of patients who develop DFU will require an amputation[1]
- Multi-disciplinary team can be required to treat: GP, endocrinologist, podiatrist, wound care nurse, vascular surgeon and infectious disease specialist
- Cost to treat DFU in the US can exceed US$60,000 per patient (depending on severity)[2]
- Annual costs to US public and private payers estimated to be US$9 – 13 billion per year[2]



WIfI = Wound, Ischemia, and foot Infection[3]

Diabetes is the **fastest growing** public health concern worldwide[4]

~38 million Americans have diabetes[5]

Up to 34% of those with diabetes will develop a foot ulcer[1]

20% of patients with DFU will require **amputation** of the foot or limb[1]

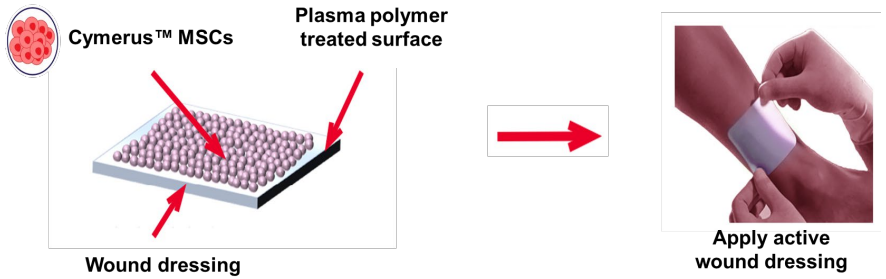
150,000+ amputations **per year** in the US due to **DFU**[6]

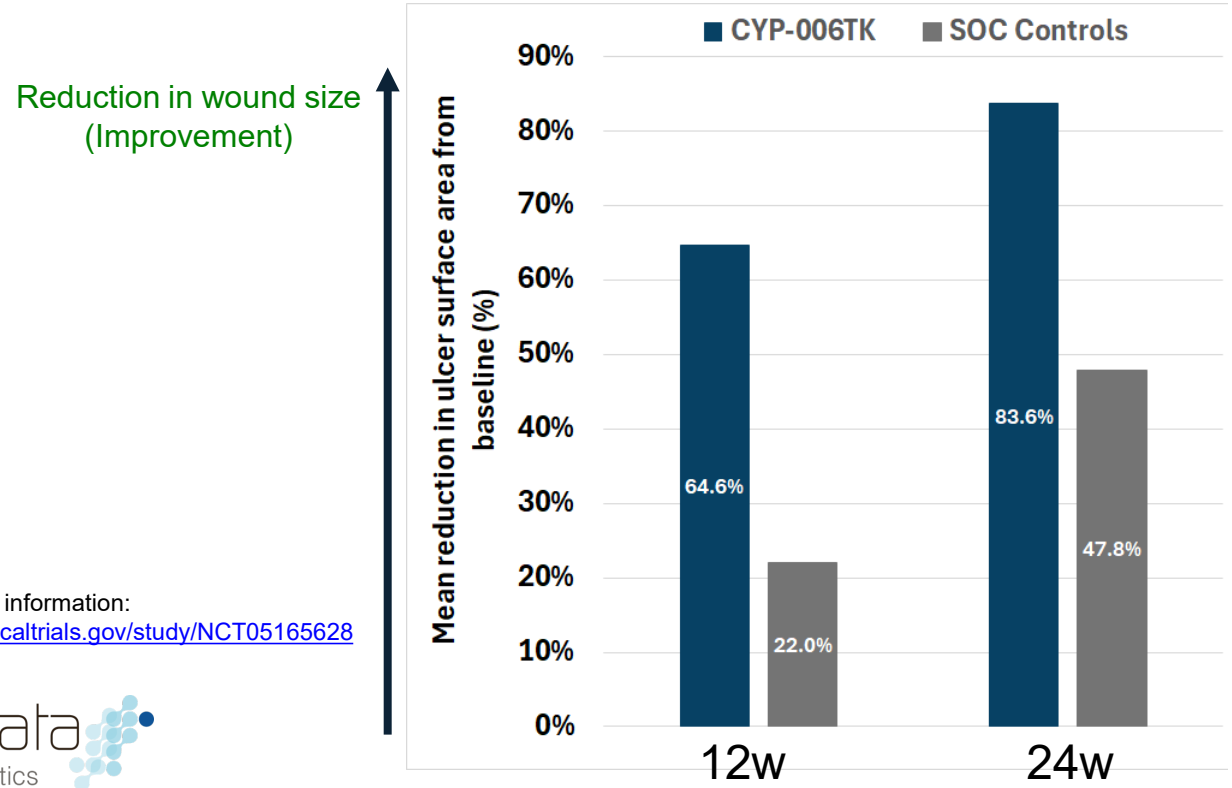
Estimated costs to US public and private payers **US$9–13 billion** per year[2]

1. McDermott et al. Diabetes Care. 46:209–221 (2023).
2. Raghav et al. Ther Adv Endocrinol Metab. 9(1) 29-31 (2018).
3. Hicks et al. J Vasc Surg. 67:1455-62 (2018).
4. Hossain et al. Health Sci Rep. 7(3):e2004 (2024).
5. American Diabetes Association: https://diabetes.org/about-diabetes/statistics/about-diabetes
6. American Diabetes Association: https://diabetes.org/advocacy/amputation-prevention-alliance

Positive clinical results in DFU phase 1

- Indication: Non-healing diabetic foot ulcers (DFU)
- Investigational product: CYP-006TK (novel silicone dressing seeded with Cymerus™ iPSC-derived MSCs)
- Randomised controlled trial in 30 adults receiving either standard of care (SOC) or CYP-006TK for 4 weeks, followed by SOC
- Primary objective was safety; efficacy measures included wound healing, pain and quality of life





- Wound surface reduction was substantially greater in treatment group than in standard of care group at both 12 and 24 weeks
- The treatment effect was even greater in large wounds measuring >200 mm^2 at baseline
- Also consistent with an even larger effect size in larger wounds, mean absolute wound surface area reduced dramatically in treatment group but increased in standard of care group

For further information:
https://clinicaltrials.gov/study/NCT05165628

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Safety and tolerability

Primary Objective

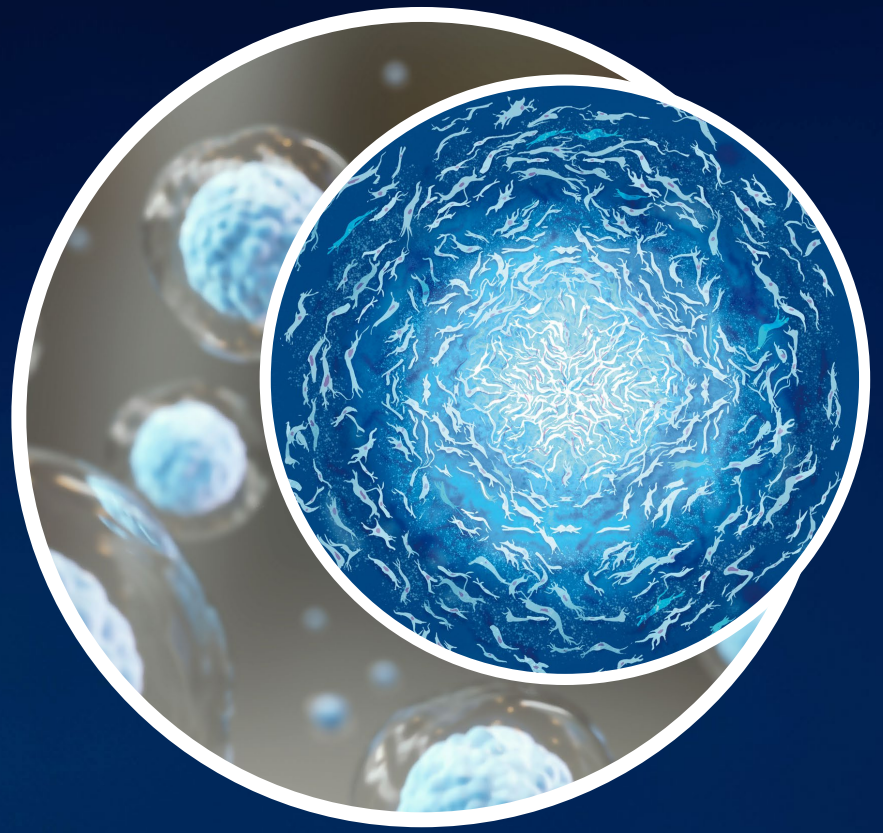
Phase 1 clinical trial of CYP-006TK in DFU **successfully achieved** its primary objective:

– safe and well-tolerated

– no participants withdrew from the trial due to adverse events

– no suspected serious adverse reactions were reported

Leveraging the unique potential of Cymerus MSCs



OA | Phase 3 clinical trial

Indication	Osteoarthritis (OA) of the knee (Kellgren-Lawrence Grade 2-3)
Product	CYP-004 (Cymerus™ iPSC-derived MSCs for intra-articular injection)
Study Design	• Randomised, double-blind placebo-controlled trial in ~320 adults[1] • Each participant receives 3 injections over 12 months; follow-up of 24 months from first dose • Co-primary endpoints are reduction of knee symptoms and measure of cartilage loss
Study Conduct	• Trial conducted by University of Sydney, funded by Australian Government NHMRC grant, while Cynata retains commercial rights • Clinical centres in Australia (Sydney and Hobart) • Patient enrolment complete (November 2023) • Last patient last visit expected ~November 2025
Results	• Results anticipated in H1 2026

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1. Clinical trial entitled Stem Cells as a symptom – and strUcture-modifying Treatment for medial tibiofemoral OsteoaRthritis: a randomised placebo-controlled trial (SCUlpTOR). NHMRC: National Health and Medical Research Council
For further information: https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=379726&isReview=true

Kidney transplant | Phase 1/2 clinical trial

Indication	Prevention of kidney transplant rejection
Product	CYP-001 (Cymerus™ iPSC-derived MSCs for intravenous infusion)
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 conducted and funded by Leiden University Medical Center (LUMC), Netherlands, while Cynata retains commercial rights • Patient enrolment commenced in Q4 2024, with first patient treatment completed in Dec 2024
Results	Outcome of Cohort 1 anticipated in H1 2025

Research partnerships

PLATFORM POTENTIAL OF CYNATA

Large body of positive preclinical data generated via R&D partnerships:

- 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

Several of these studies have been published in peer-reviewed journals – see cynata.com/science_publications

Studies conducted in partnership with leading research groups worldwide

Comparison of MSCs from different sources

npj | regenerative medicine Article

Published in partnership with the Australian Regenerative Medicine Institute

https://doi.org/10.1038/s41536-024-00382-y

Proteomic profiling of iPSC and tissue-derived MSC secretomes reveal a global signature of inflammatory licensing

Margeaux Hodgson-Garms[1,2], Matthew J. Moore[1], Mikaël M. Martino[3,4], Kilian Kelly[2] & Jessica E. Frith[1,3]

Background

- Effects of MSCs depend largely on “secretome” – proteins and other molecules released by cells
- This study assessed similarities/differences between secretomes of MSCs derived from either iPSCs or a donor tissue source (bone marrow, adipose tissue or umbilical cord), under different conditions
- Important to assess MSCs under different conditions because MSCs respond to their environment, which changes their effects
- Notably, MSCs are often exposed to inflammatory conditions after administration to patients

Key Highlights

- Substantial differences between MSCs from different sources
- Substantially less variability between batches of iPSC-derived MSCs than between batches of MSCs derived from donor tissue, especially bone marrow
- iPSC-derived MSCs released many more unique proteins than donor tissue-derived MSCs: indicates iPSC-derived MSCs could have additional effects compared to donor tissue-derived MSCs
- iPSC-derived and umbilical cord-derived MSCs displayed features consistent with “younger” cells, suggesting sustained ability to avoid ageing (“senescence”)
- Strong regenerative potential of iPSC-derived and umbilical cord-derived MSCs (but not bone marrow or adipose tissue-derived MSCs) maintained under both resting and inflammatory conditions
- *In vitro* studies of MSC secretomes found:
  - iPSC-derived and umbilical cord-derived MSCs resulted in significantly faster wound closure than bone marrow or adipose tissue-derived MSCs
  - iPSC-derived MSCs showed greater immunomodulatory effects than MSCs derived from any donor tissue source

cynata therapeutics

Commercial Attractiveness

Proprietary Platform Technology	• Ability to produce MSCs consistently and at scale allows for MSCs to be used in multiple indications = Platform Technology appeal
Platform Technology	• Platform Technology allows CYP to target multiple multi-billion dollar indications
Multiple Multi-Billion Dollar Indications	• Four clinical indications currently targeted have total combined market opportunities of ~US$27.7 billion • All indications capable of being out-licensed / partnered
Commercial interest	• In 2019 (post Phase I results in GvHD), the Company received a non-binding indicative offer to acquire all shares in Cynata for $2 per share (The parties subsequently withdrew from discussions as a result of being unable to reach agreement on satisfactory terms) • Cynata anticipates significant commercial interest following any positive read-outs • Three further read-outs expected by H1 CY2026
Seeking Partnership Opportunities	• Following the successful DFU results, Cynata will now continue discussions with potential commercial partners and engage with regulatory agencies (including FDA) as part of its strategy for further clinical development

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