

ASX ANNOUNCEMENT

8 October 2024

Cynata to Present at Alliance for Regenerative Medicine Meeting

Melbourne, Australia; 8 October 2024: Cynata Therapeutics Limited (ASX: “CYP”, “Cynata”, or the “Company”), a clinical-stage biotechnology company specialising in cell therapeutics, is participating in the *Cell and Gene Meeting on the Mesa* in Phoenix, Arizona.

This annual conference is run by the Alliance for Regenerative Medicine (ARM), which represents more than 400 members across 25 countries, including emerging and established biotechnology companies, academic and medical research institutions, and patient organisations.

The conference program features expert-led panels, extensive partnering capabilities, exclusive networking opportunities, and 100+ dedicated presentations by the leading publicly traded and privately held companies in the space. The conference attracts more than 2,000 attendees from over 150 companies.

At 10:45am local time today (8 October 2024), Dr Kilian Kelly, Cynata’s Chief Executive Officer and Managing Director, will present on the Company’s Cymerus™ iPSC¹-derived MSC² technology and clinical development programs. Cynata will also be participating in partnering meetings throughout the conference.

A copy of the 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’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 – patient enrolment completed) and diabetic foot ulcers (DFU – patient enrolment completed) 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.

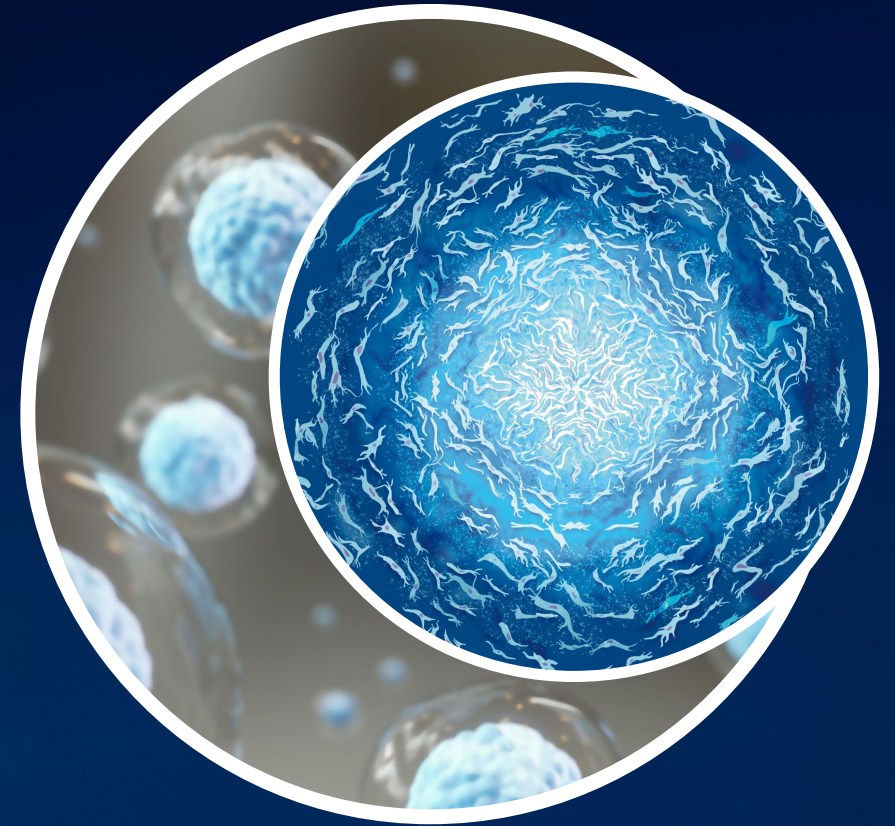
Cynata Therapeutics encourages all current investors to go paperless by registering their details with the designated registry service provider, Automic Group.

¹ iPSC = induced pluripotent stem cell

² MSC = mesenchymal stem (or stromal) cell



A Clinical Stage Next Generation Stem Cell Therapeutics Company



CELL  GENE

M E E T I N G O N T H E M E S A

Phoenix, Arizona, 8 October 2024

Important information

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Company highlights

Revolutionary Cymerus™ manufacturing platform

- Mesenchymal stem cells (**MSCs**)¹ have shown potential to treat a wide range of illnesses²
- However, standard manufacture requires ongoing supply of donors and extensive MSC culture expansion → challenges with consistency, potency and scale
- The induced pluripotent stem cell (**iPSC**)-based Cymerus™ platform overcomes these challenges by enabling production of an **effectively limitless** number of **consistent** MSC doses **from a single blood donation**

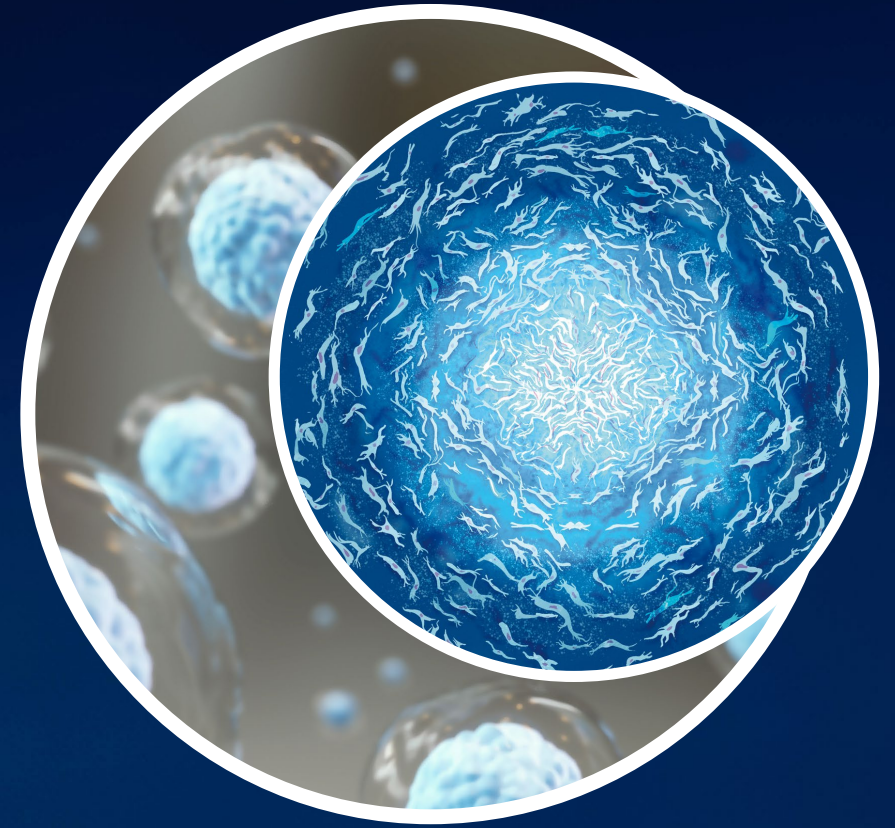
Cynata leads the burgeoning iPSC-derived therapy field

- **First completed iPSC clinical trial** worldwide
- **US FDA Orphan Drug Designation**³ and cleared **IND**⁴
- Compelling clinical data in **acute graft versus host disease (aGvHD)**⁵ and **diabetic foot ulcer (DFU)**⁶
- **Four active clinical programs** (including ongoing **Phase 2** and **Phase 3** trials)
- **Three randomised controlled clinical trial readouts** upcoming between **late 2024** and **early 2026**

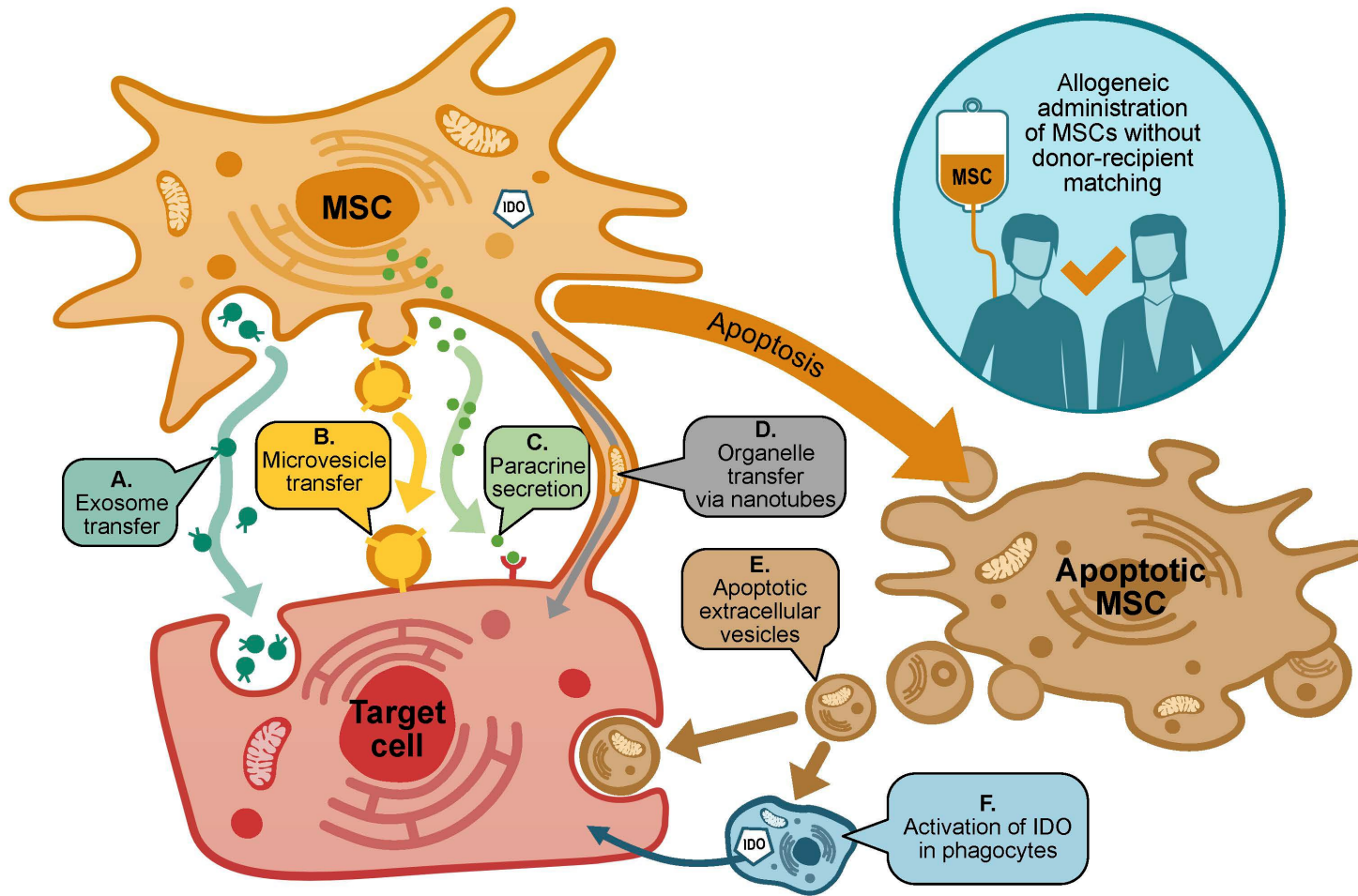
Advanced and diverse clinical pipeline

	Indication	Trial phase	Upcoming catalysts*	Market opportunity
Cynata Sponsored	 Acute Graft vs Host Disease (aGvHD) CYP-001 FDA Orphan Designation	Phase 2 ongoing	Enrolment completion – Q4 2024 Results – 2H 2025	US\$600m ¹
	 Diabetic Foot Ulcers (DFU) CYP-006TK	Phase 1 ongoing (enrolment complete)	Results – Q4 2024/Q1 2025	US\$9.6bn ²
Partnered	 Osteoarthritis (OA) CYP-004 <i>(managed by USYD, funded by NHMRC)</i>	Phase 3 ongoing (enrolment complete)	Results – 1H 2026	US\$11.6bn ³
	 Kidney Transplantation CYP-001 <i>(managed and funded by LUMC)</i>	Phase 1/2 approved	Enrolment start – Q4 2024 Cohort 1 results – Q1 2025	US\$5.9bn ⁴

Revolutionary iPSC-based Cymerus™ Manufacturing Platform



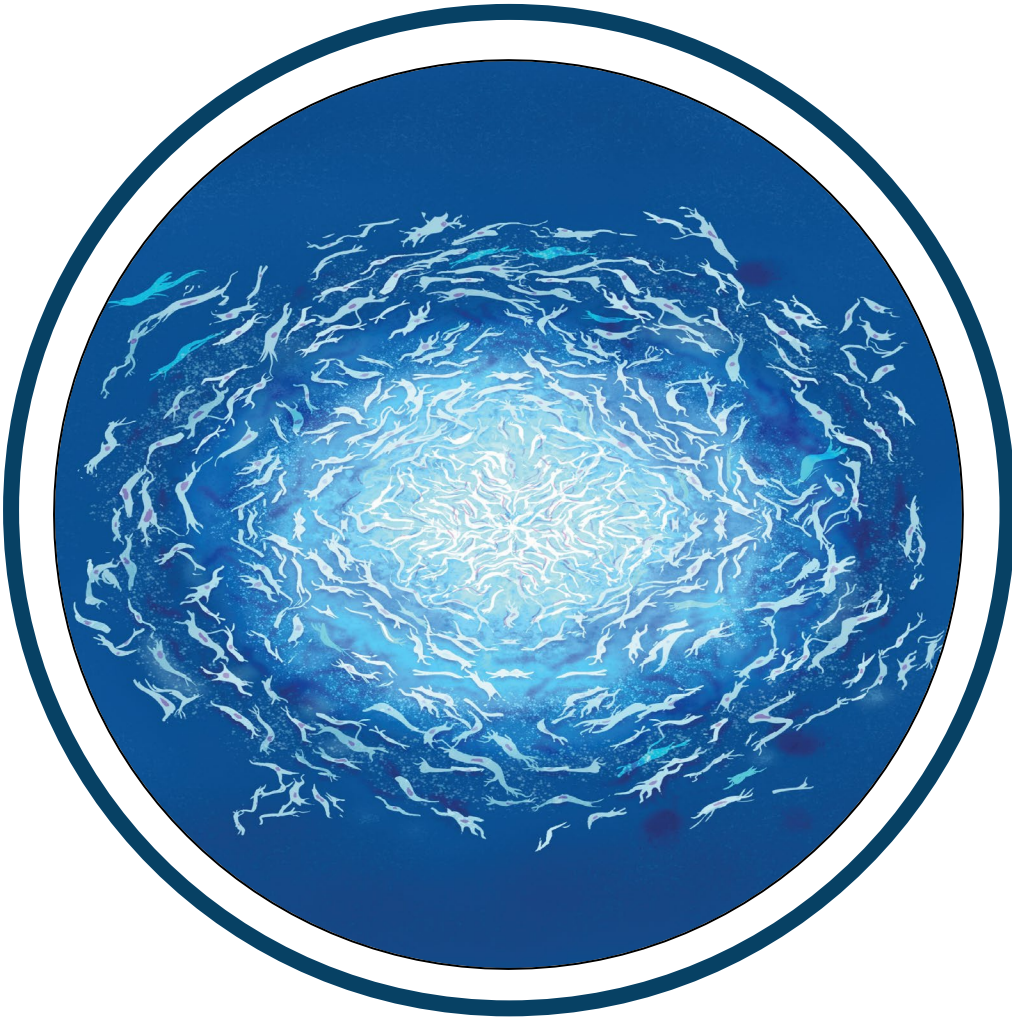
Therapeutic potential of MSCs



Mesenchymal stem cells¹ (MSCs):

- Promote an **immunomodulatory** environment²
- The “sensor and switcher of the immune system”³
- Promote **tissue repair** and **regeneration**
- Can be used **without** matching donors to recipients
- Can be **engineered** to express other functional/therapeutic molecules
- However, with conventional manufacturing methods, there are consistency, potency and scalability challenges

Advantages of iPSC-based platform



Induced pluripotent stem cells (iPSCs):

- Mature **adult** cells **reprogrammed** to become **pluripotent**, which means:
 - Effectively **limitless** proliferation capacity
 - Potential to differentiate into any adult cell type (including MSCs)
 - Similar properties to embryonic stem cells ... but iPSCs are derived from **adult donors**, so they **avoid** ethical controversy associated with embryonic stem cells
- iPSCs are **ideal** starting material for commercial production of cellular products

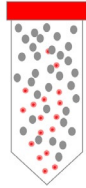
Conventional MSC process

Ongoing need
for new donors



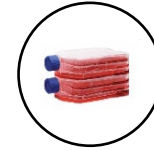
Substantial inter-donor **variability**

MSC isolation



Small number of MSCs
per donation

Culture expansion



Extensive MSC culture
expansion required

Major challenges:

- MSCs undergo **functional changes** and **loss of potency** during extensive culture expansion
- Continuously finding and testing new donors is **logistically challenging**
- Inter-donor **variability** – **inconsistent** activity in MSCs from different donors

Cymerus™ iPSC-based process

**One donor,
one time**

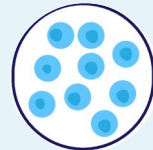


Avoids inter-donor
variability

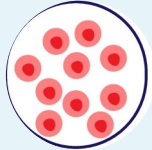
Reprogramming &
iPSC expansion



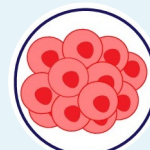
Effectively limitless
expansion potential



Differentiation into MSCs
& culture expansion



Minimal MSC
culture expansion

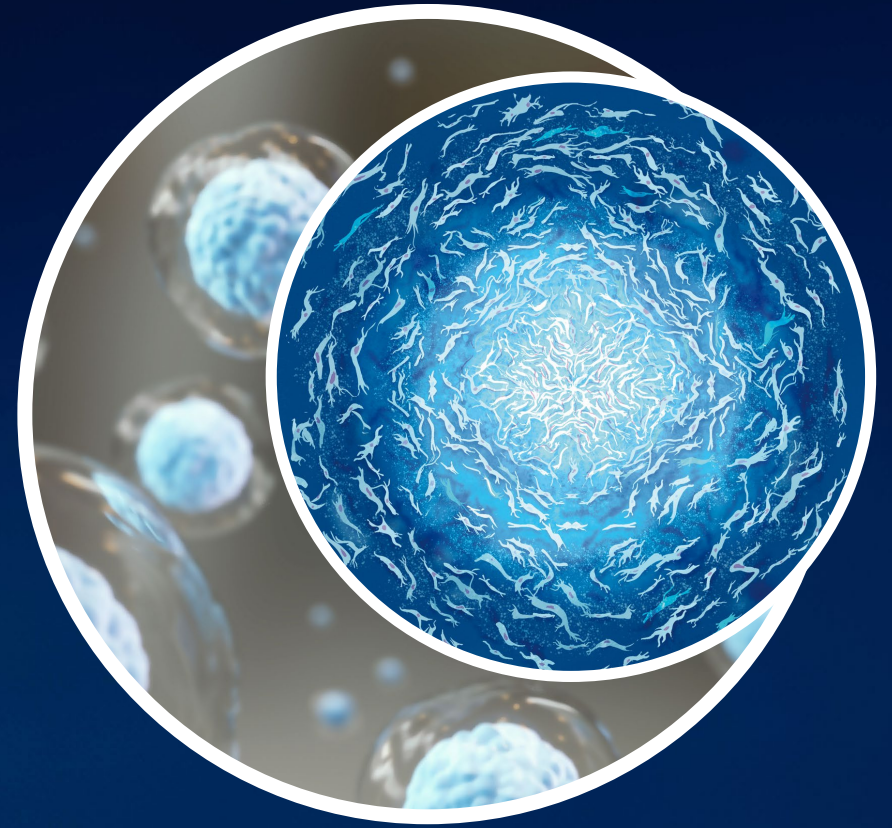


Robust patent protection

Advantages of Cymerus™ platform:

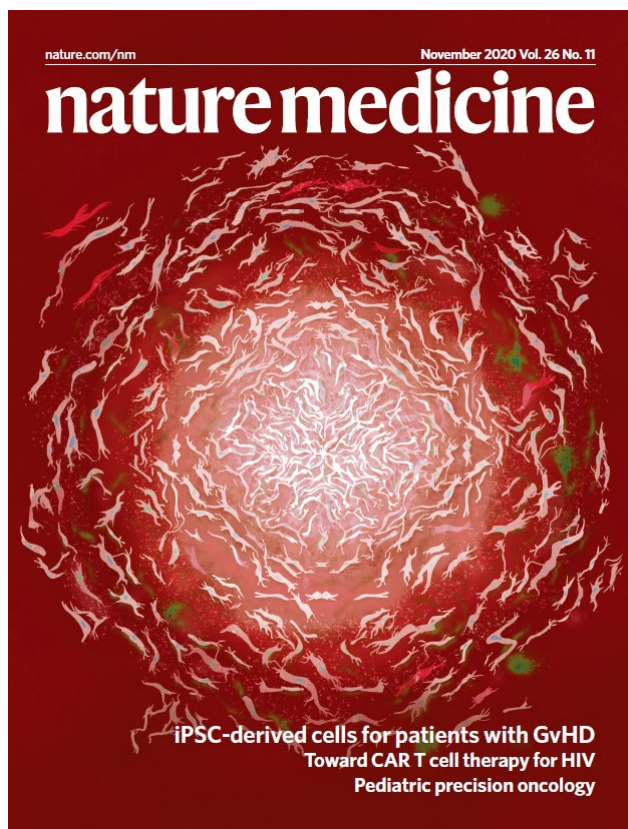
- **Effectively limitless** iPSC expansion potential
- **Avoids** need for new donors
- **Avoids** inter-donor variability
- **Avoids** extensive MSC culture expansion
- High level of **potency, consistency** and **scalability**

Compelling Clinical Data



CYP-001: Two *Nature Medicine* publications

- CYP-001 has been granted **Orphan Drug Designation** by the US FDA for the treatment of GvHD
- Phase 1 trial of CYP-001 was the first completed clinical trial worldwide with **any iPSC-derived product**



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 Patel¹, James E. Griffin³, Maria H. Gilleece⁴, Rohini Radia⁵, David T. Yeung^{6,7}, Diana Drier⁸, Laurie S. Larson⁸, Gene I. Uenishi⁹, Derek Hei¹⁰, Kilian Kelly¹¹, Igor Slukvin⁹ 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>

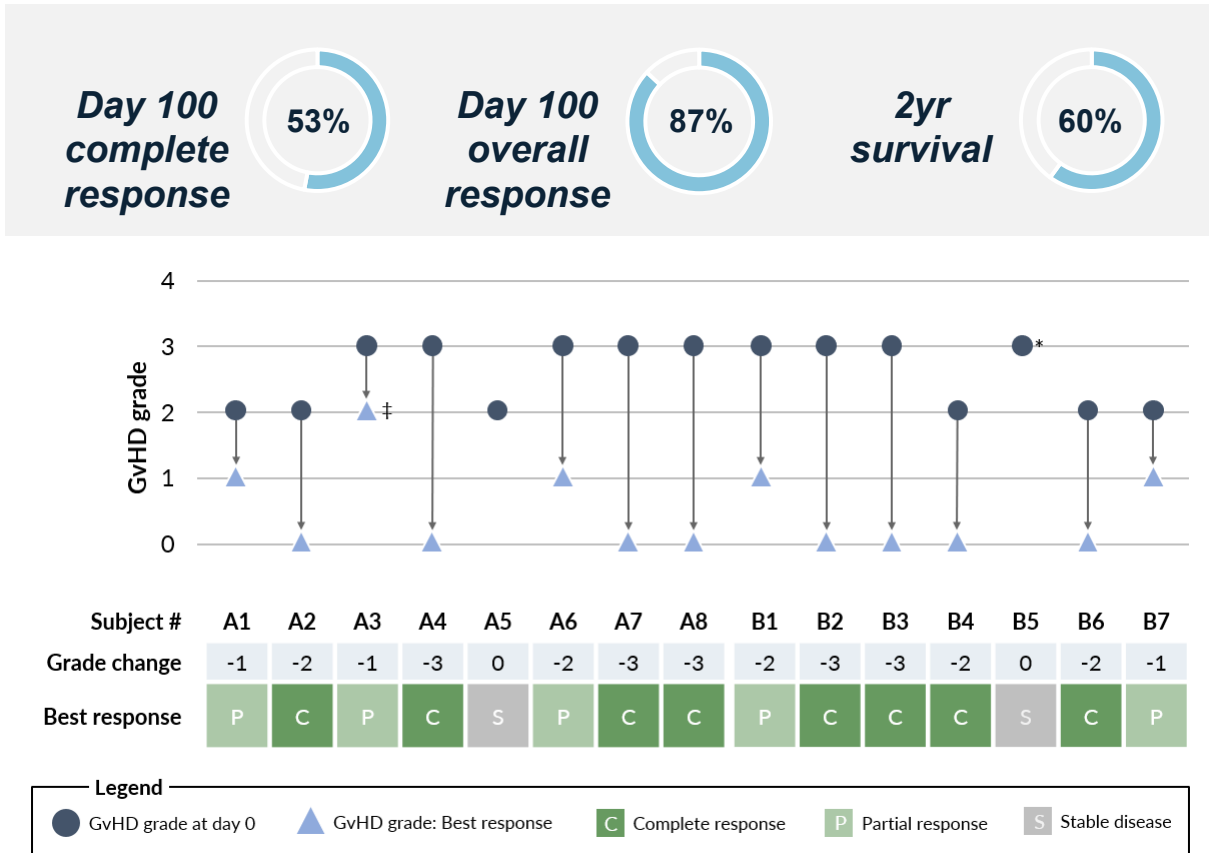
Two-year safety outcomes of iPS cell-derived mesenchymal stromal cells in acute steroid-resistant graft-versus-host disease

Kilian Kelly¹, Adrian J. C. Bloor², James E. Griffin³, Rohini Radia⁴, David T. Yeung^{5,6} & John E. J. Rasko^{7,8,9}

aGvHD | Phase 1 clinical trial - results

Product: CYP-001 (Cymerus™ MSCs for intravenous infusion)

Trial conducted in 15 patients with **steroid-resistant aGvHD (SR-aGvHD)**



- CYP-001 was shown to be **safe and well tolerated**, with **sustained outcomes up to 2 years** after the first infusion
- **No serious adverse events or other safety concerns related to CYP-001**
- **Very encouraging response rates and overall survival**

Ph1 SR-aGvHD results compared to other therapies

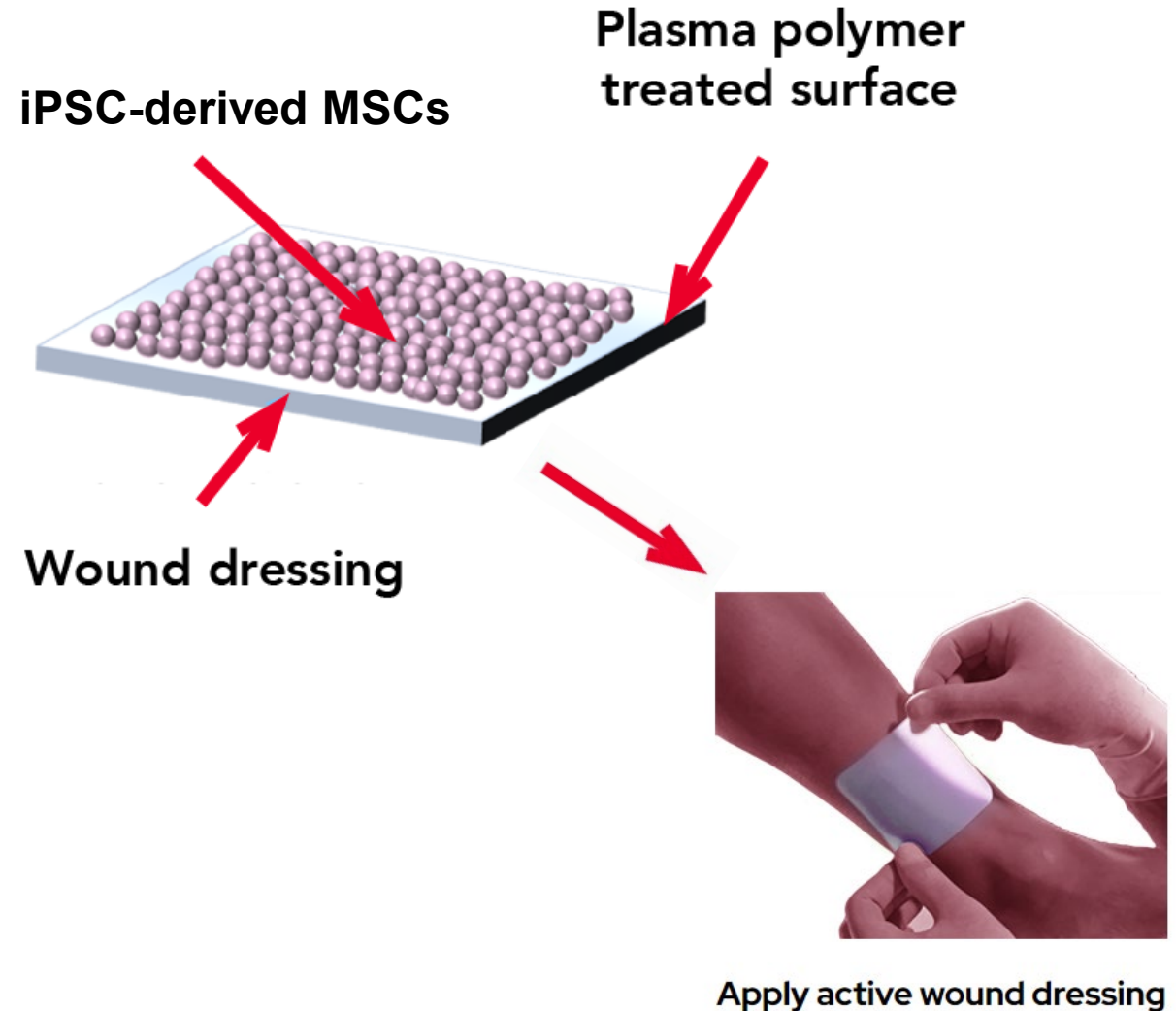
	CYP-001 (Ph 1)	Ruxolitinib (Ph 3)	“Best available therapy” controls (Ph 3)
Day 28 Overall Response	67%	62%	39%
Day 56-60* Overall Response	73%	40%	22%
Overall Survival	60% after <u>2 years</u>	38% after <u>18 months</u>	36% after <u>18 months</u>
Safety	No safety concerns related to CYP-001 identified	Serious adverse reactions to ruxolitinib are common	Several other agents investigated for GvHD have poor safety profiles

Notes:

- Ruxolitinib is approved for treatment of SR-aGvHD in most jurisdictions
- 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/D56-60 time points used for response rate comparison as D28/D56 were the only response rate time points reported in the ruxolitinib/best available therapy clinical trial (NCT02913261); Overall Response at Day 56-60 refers to Day 56 response for ruxolitinib and best available therapy, and Day 60 response for CYP-001.

CYP-006TK – a novel topical MSC product

- CYP-006TK utilises a proprietary surface-coating, optimised for the delivery of MSCs directly to the wound bed
- Technology exclusively licenced to Cynata by Tekcyte Limited (agreement for Cynata to acquire this IP outright announced 1 July 2024)



DFU | Phase 1 clinical trial – initial data

Product: CYP-006TK (topical Cymerus™ MSC wound dressing)

- Ongoing trial in non-healing diabetic foot ulcer (DFU)
- Patients randomised to receive standard of care (SoC) or CYP-006TK for 4 weeks, followed by SoC
- In the first 16 patients enrolled in the trial (8 per group), after 10 weeks' follow-up, the median reduction in wound surface area was:
 - **87.6%** in the active CYP-006TK group
 - compared to **51.1%** in SoC group

Example of ulcer healing in patient treated with CYP-006TK:

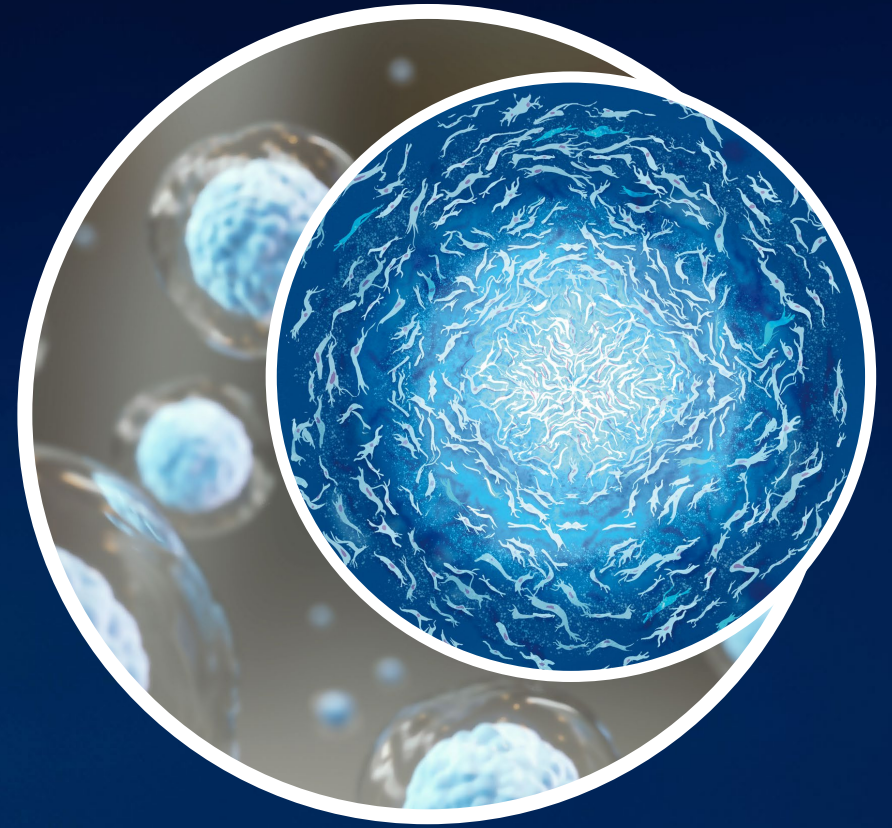
Day 0



Day 28

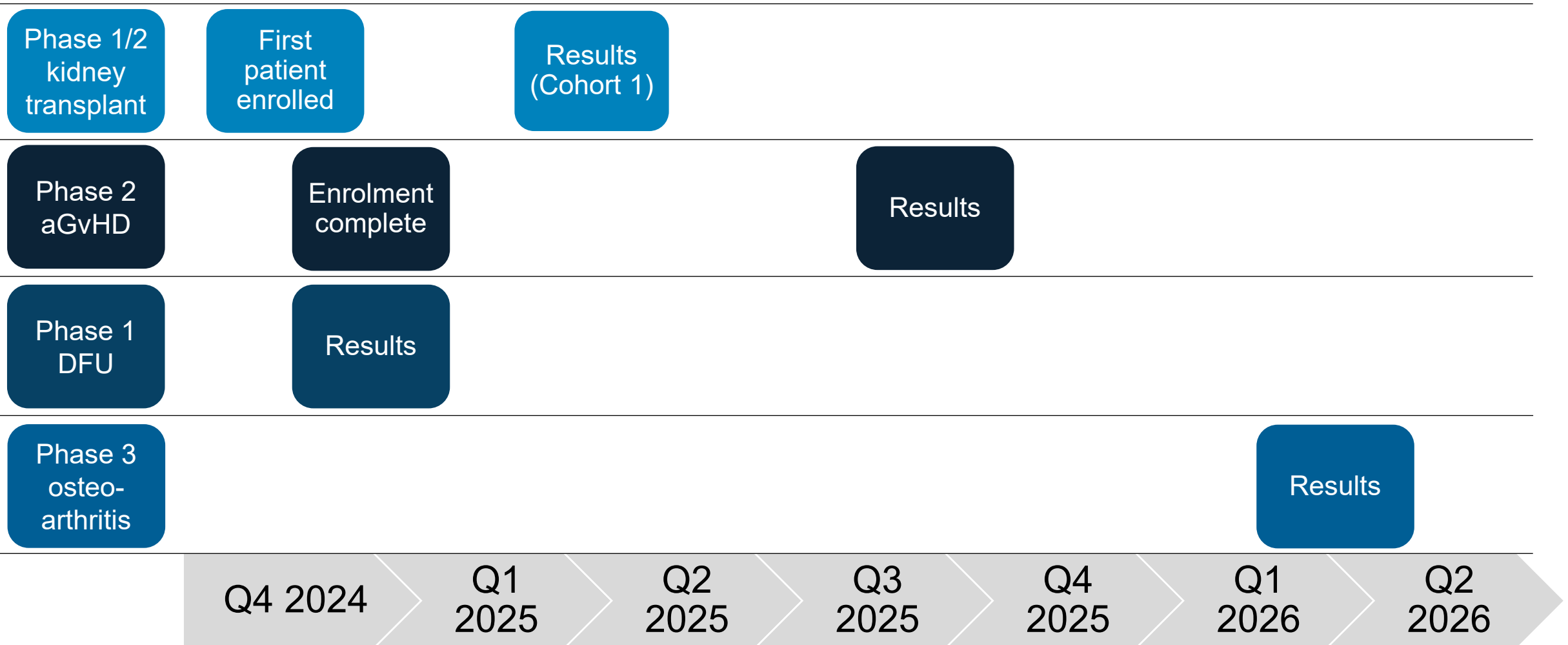


Outlook



Upcoming catalysts*

Results of three randomised controlled clinical trials expected between late 2024 and early 2026



Summary

 Next generation stem cell company	• Leading platform technology in burgeoning stem cell sector • Diverse and highly credentialed leadership team with proven experience
 Scalable manufacturing	• Cymerus™ manufacturing technology protected by robust patent portfolio • Enables scalable production of consistent MSCs from a single donation from a single donor, overcoming major challenges with conventional approaches
 Compelling clinical data	• Very encouraging safety and efficacy results from aGvHD clinical trial (CYP-001) • Promising initial data from ongoing DFU clinical trial (CYP-006TK)
 Rich clinical pipeline	• Broad pipeline with four active clinical programs • FDA orphan drug designation & cleared IND for ongoing Phase 2 aGvHD clinical trial • Patient enrolment complete in DFU & OA clinical trials • Commencement of kidney transplantation clinical trial imminent
 Significant growth potential	• Global estimated market opportunity across targeted indications of ~US\$28bn¹ • Focus on indications with significant unmet need • Proactive B-2-B outreach to drive partnering strategy



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