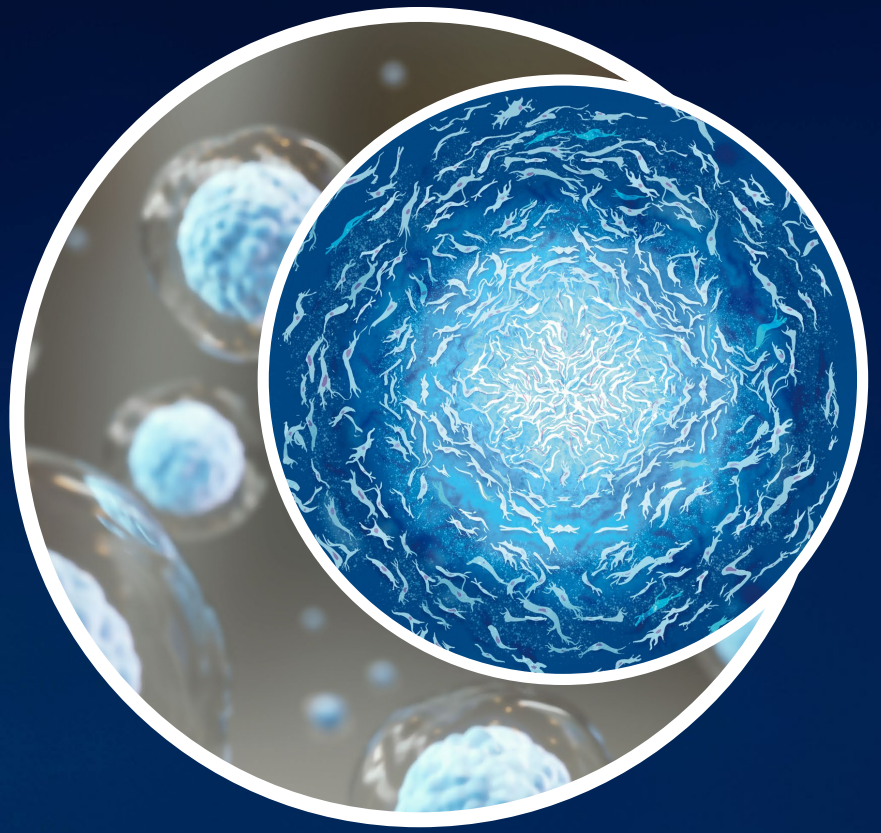
cynata therapeutics



A Clinical Stage Next Generation Stem Cell Therapeutics Company

CELL GENE MEETING ON THE MESA

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 illnesses[2]
- 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**

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1. Also known as mesenchymal stromal cells
2. Zhou J, Shi Y. Cell Mol Immunol 20, 555–557 (2023)
3. CYP-001 granted Orphan Drug Designation for treatment of aGvHD – qualifies Cynata for incentives including extended marketing exclusivity, tax credits and fee waivers
4. IND = Investigational New Drug application – the clearance required from FDA to conduct clinical trials
5. Completed Phase 1 clinical trial in steroid-resistant aGvHD;
6. Initial data in first 16 patients (n=8 per group) after 10 weeks; final results in all 30 patients expected in Q4 2024/Q1 2025

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]
Cynata Sponsored	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 *(managed by USYD, funded by NHMRC)*	**Phase 3 ongoing** **(enrolment complete)**	**Results – 1H 2026**	US$11.6bn[3]
Partnered	Kidney Transplantation CYP-001 *(managed and funded by LUMC)*	**Phase 1/2 approved**	**Enrolment start – Q4 2024** **Cohort 1 results – Q1 2025**	US$5.9bn[4]

1. Global Graft versus Host Disease Market 2019-2029 (Reflects forecast market in 2026); 2. Zion Market Research, 2019 (represents global treatment market in 2025); 3. Persistence Market Research 2018 research report: "Osteoarthritis Treatment Market: Global Industry Analysis (2012-2016) and Forecast (2017-2025) (Reflect OA market by 2025); 4. Organ Transplant Immunosuppressant Drugs Market in 2026, Grand View Research, Inc.,2019

USYD = University of Sydney; NHMRC = National Health and Medical Research Council; LUMC = Leiden University Medical Center
* Timing of events is approximate, based on the Company's information as at the date of this presentation, and subject to change

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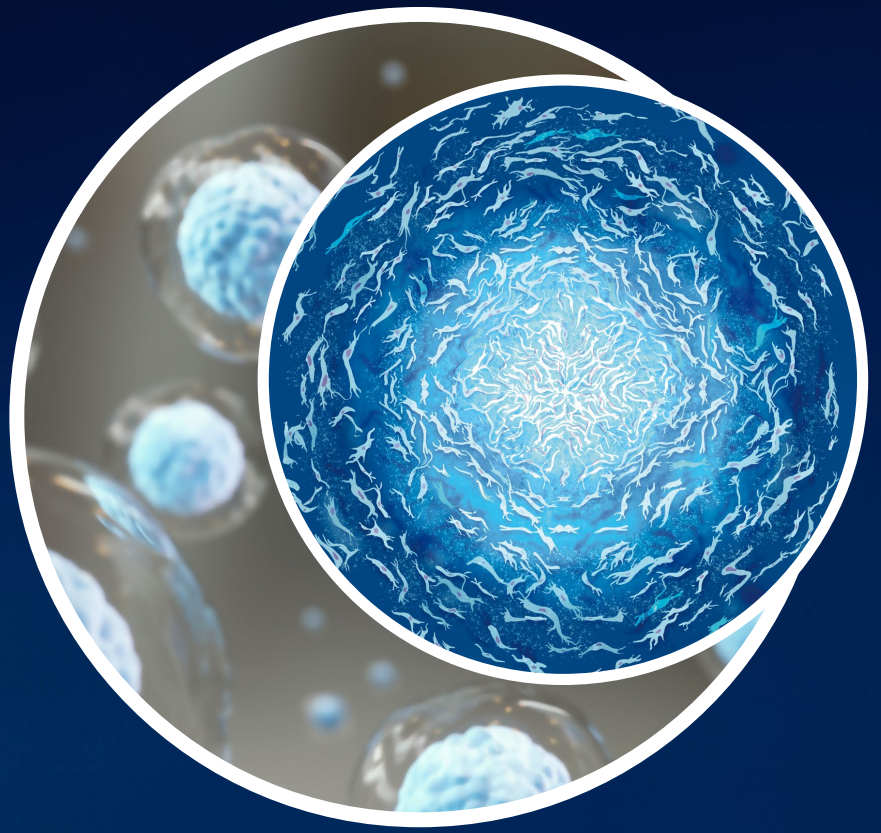
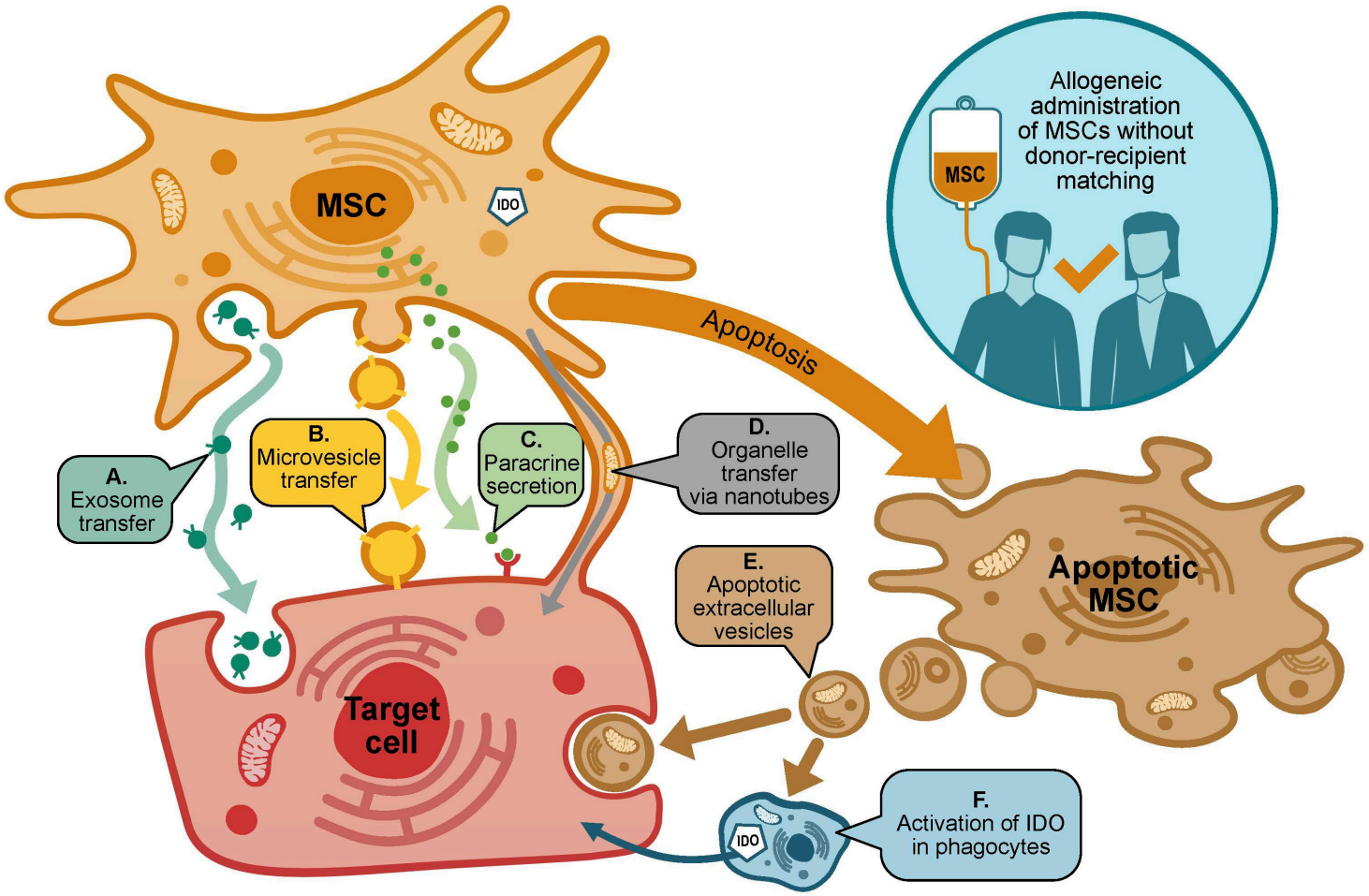
Revolutionary iPSC-based Cymerus™ Manufacturing Platform



Therapeutic potential of MSCs



Mesenchymal stem cells[1] (MSCs):

- Promote an **immunomodulatory** environment[2]
- 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

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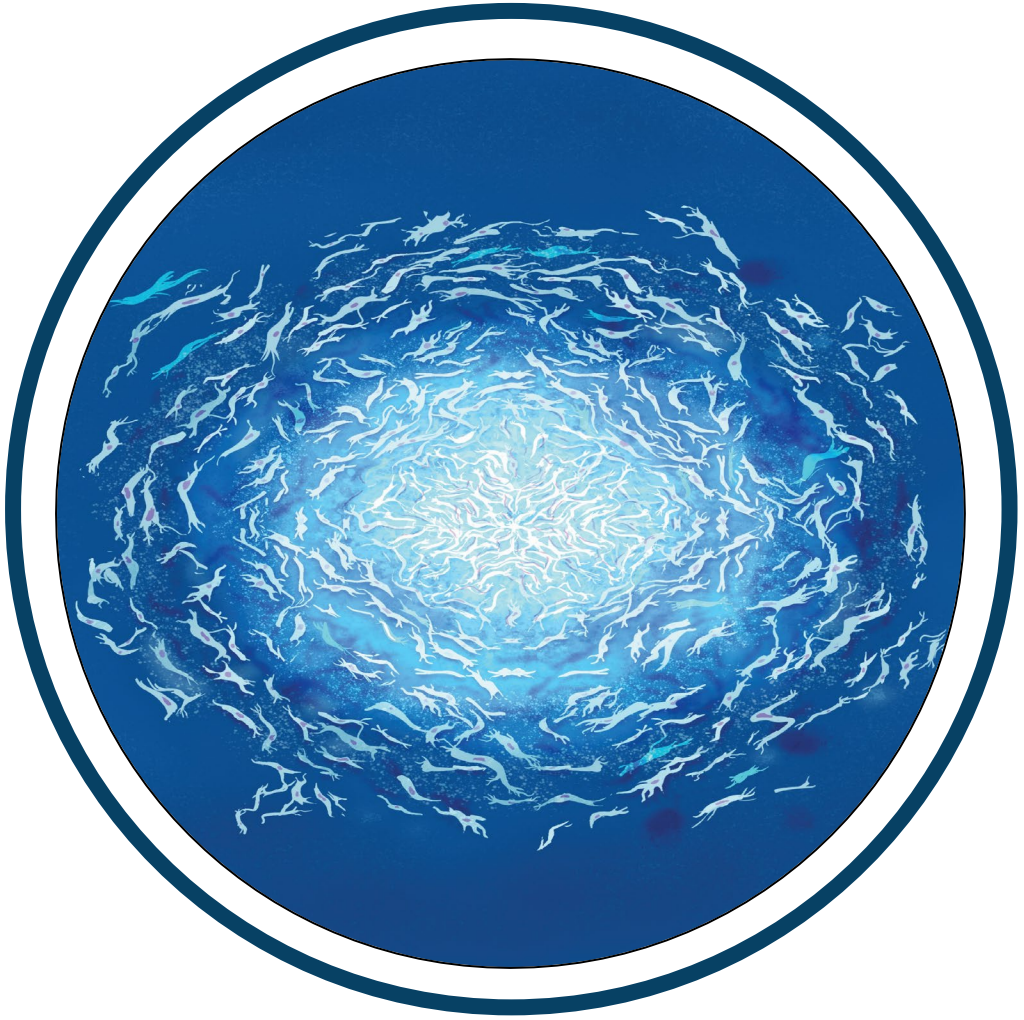
1. Also known as mesenchymal stromal cells
2. Kelly and Rasko, Front. Immunol. 12:761616 (2021)
3. Sarsenova et al, Front. Immunol.13:1010399 (2022)

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

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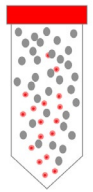
Conventional MSC process

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:

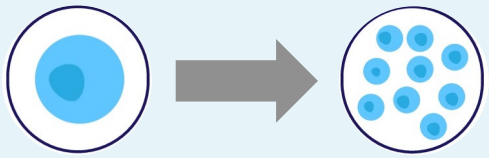
- MSCs undergo **functional changes** and **loss of potency** during extensive culture expansion
- Continuously finding and testing new donors is **logistically challenging**
- Inter-donor **variability** – **inconsistent** activity in MSCs from different donors

Cymerus™ iPSC-based process

One donor, one time

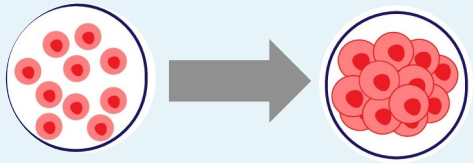
Avoids inter-donor variability

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**

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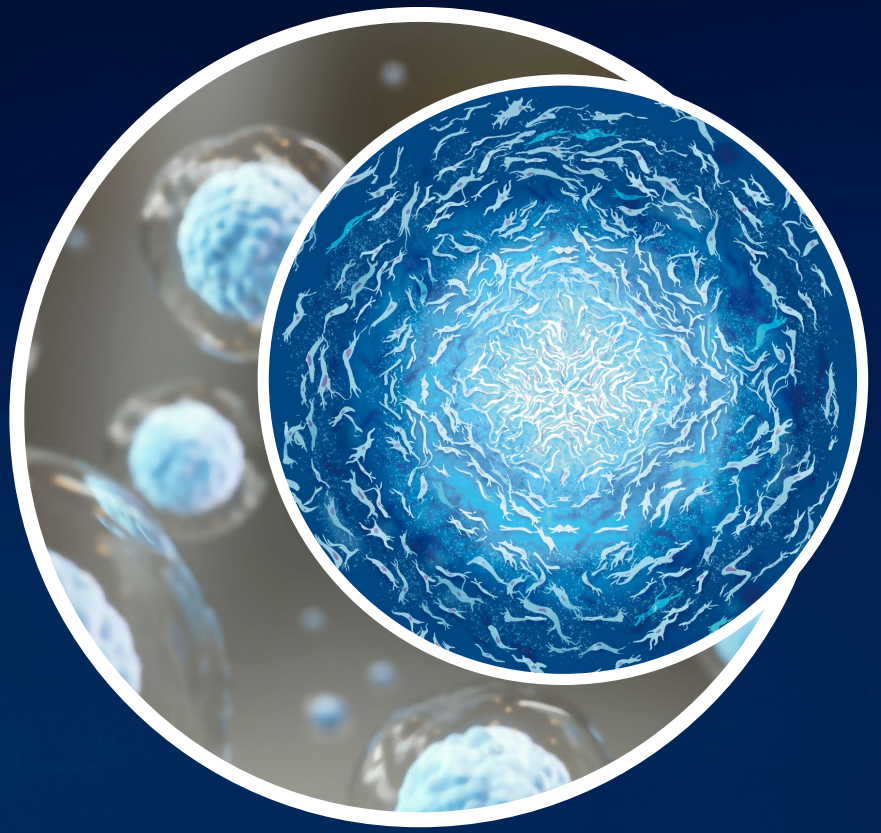
Compelling Clinical Data



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
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] ✉

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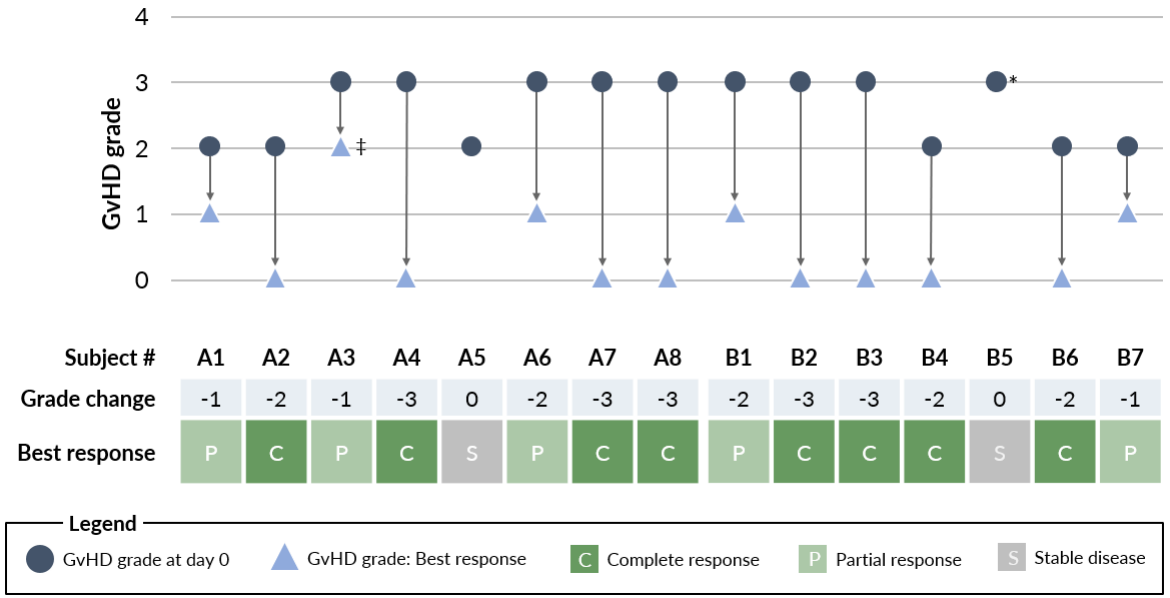
1. CYP-001 is Cynata's Cymerus iPSC-derived MSC product candidate for intravenous infusion

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**

- 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

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 2 years	38% after 18 months	36% after 18 months
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

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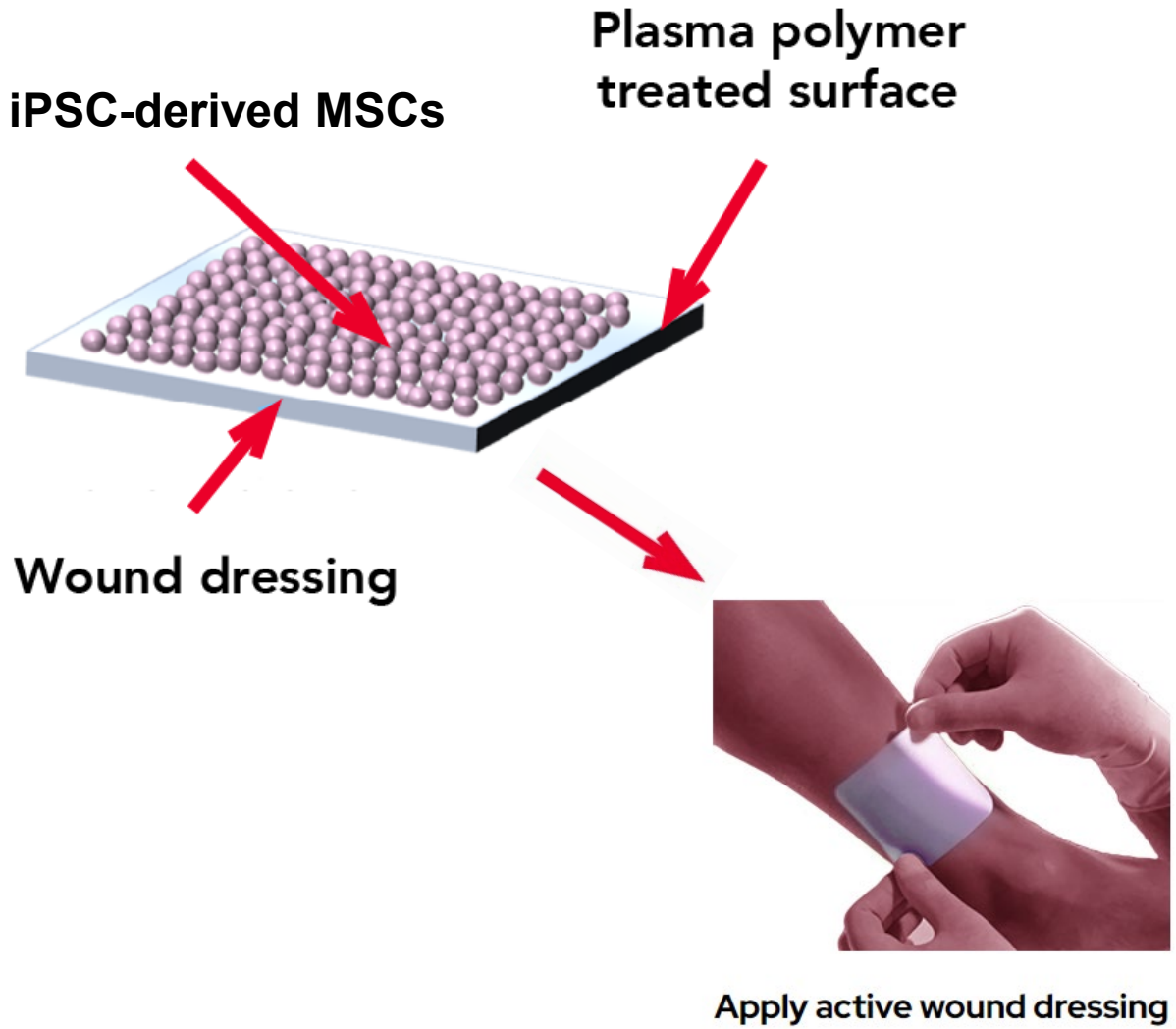
Notes:
- Ruxolitinib is approved for treatment of SR-aGvHD in most jurisdictions
- Comparisons are for illustrative purposes only; data taken from different clinical trials with different sample sizes (BAT: n=155; Rux: n=154; CYP-001: n=15)
- D28/D56-60 time points used for response rate comparison as 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)



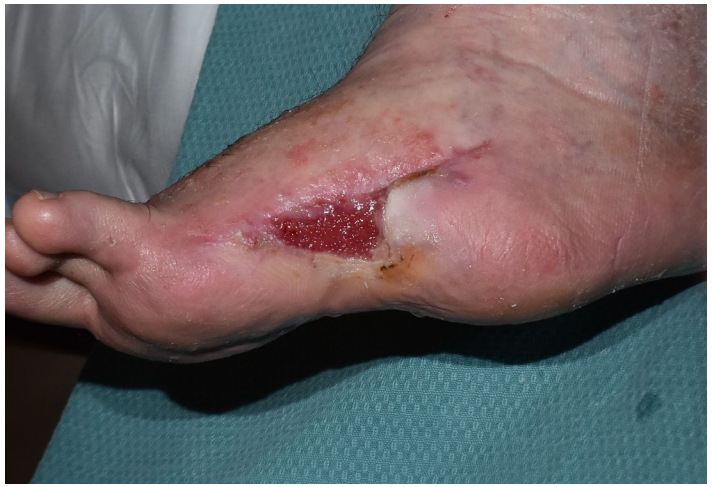
DFU | Phase 1 clinical trial – initial data

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

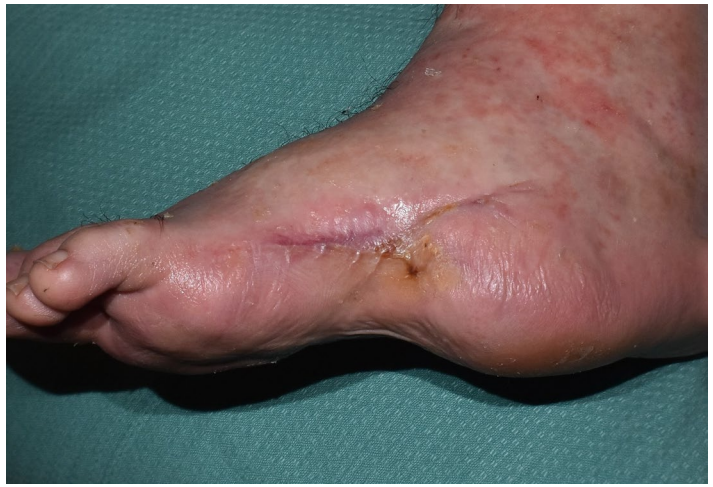
- Ongoing trial in non-healing diabetic foot ulcer (DFU)
- Patients randomised to receive standard of care (SoC) or CYP-006TK for 4 weeks, followed by SoC
- In the first 16 patients enrolled in the trial (8 per group), after 10 weeks' follow-up, the median reduction in wound surface area was:
  - **87.6%**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



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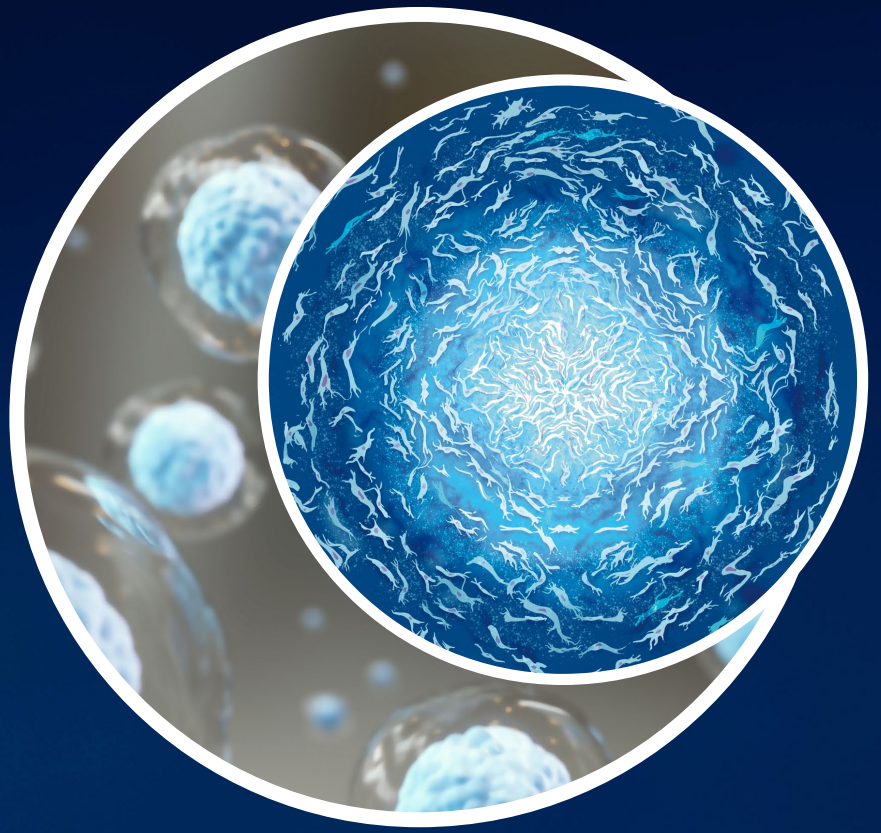
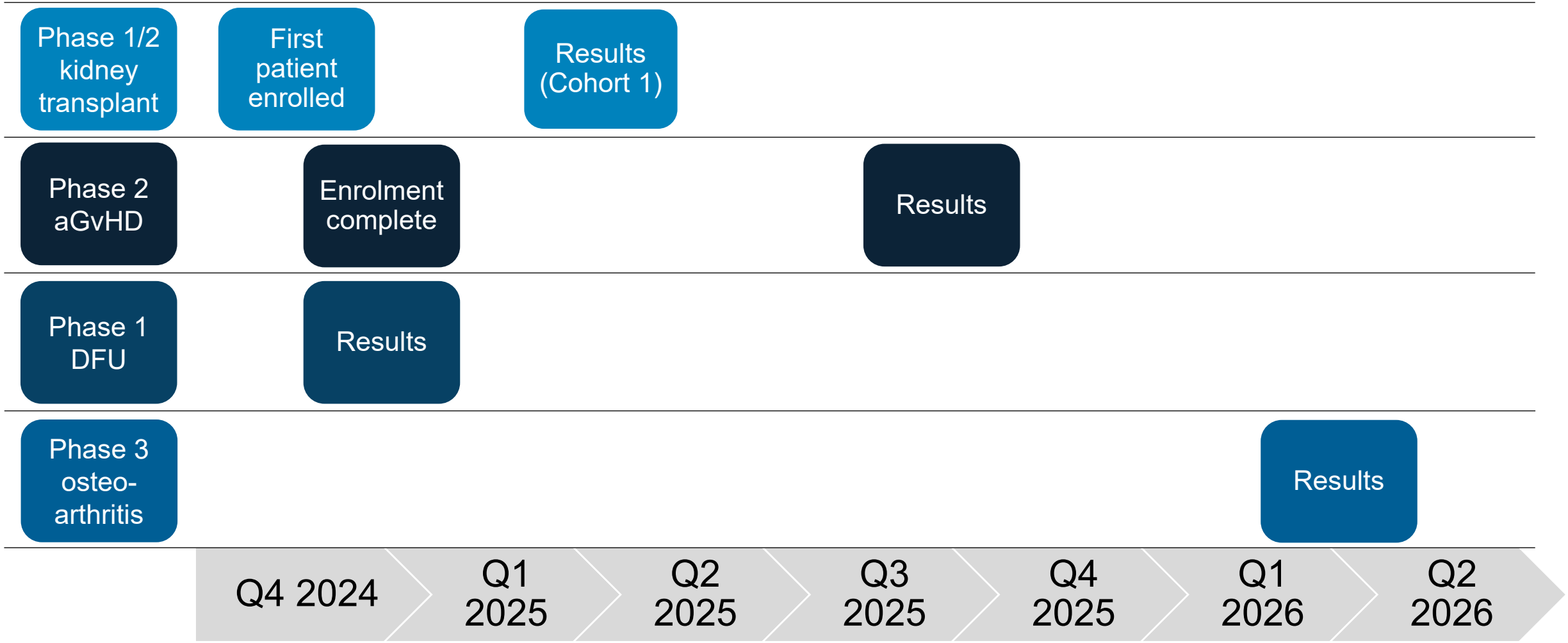
For further information: https://clinicaltrials.gov/study/NCT05165628

Outlook



Upcoming catalysts*

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



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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$28bn[1] • Focus on indications with significant unmet need • Proactive B-2-B outreach to drive partnering strategy

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1. Global Graft versus Host Disease Market 2019-2029 (Reflects forecast market in 2026); 2. Zion Market Research, 2019 (represents global treatment market in 2025); 3. Persistence Market Research 2018 research report: "Osteoarthritis Treatment Market: Global Industry Analysis (2012-2016) and Forecast (2017-2025) (Reflect OA market by 2025); 4. Organ Transplant Immunosuppressant Drugs Market in 2026, Grand View Research, Inc.,2019

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