

Cynata to Present at Euroz Hartleys Healthcare Forum

Melbourne, Australia; 4 February 2025: Cynata Therapeutics Limited (ASX: “CYP”, “Cynata”, or the “Company”), a clinical-stage biotechnology company specialising in cell therapeutics, will present at the 2025 Euroz Hartleys Healthcare Forum.

Dr Kilian Kelly (Chief Executive Officer & Managing Director) will present on the Company’s Cymerus™ iPSC¹-derived MSC² technology and clinical development programs. The presentation will take place at 9:50am AWST today. 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 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.

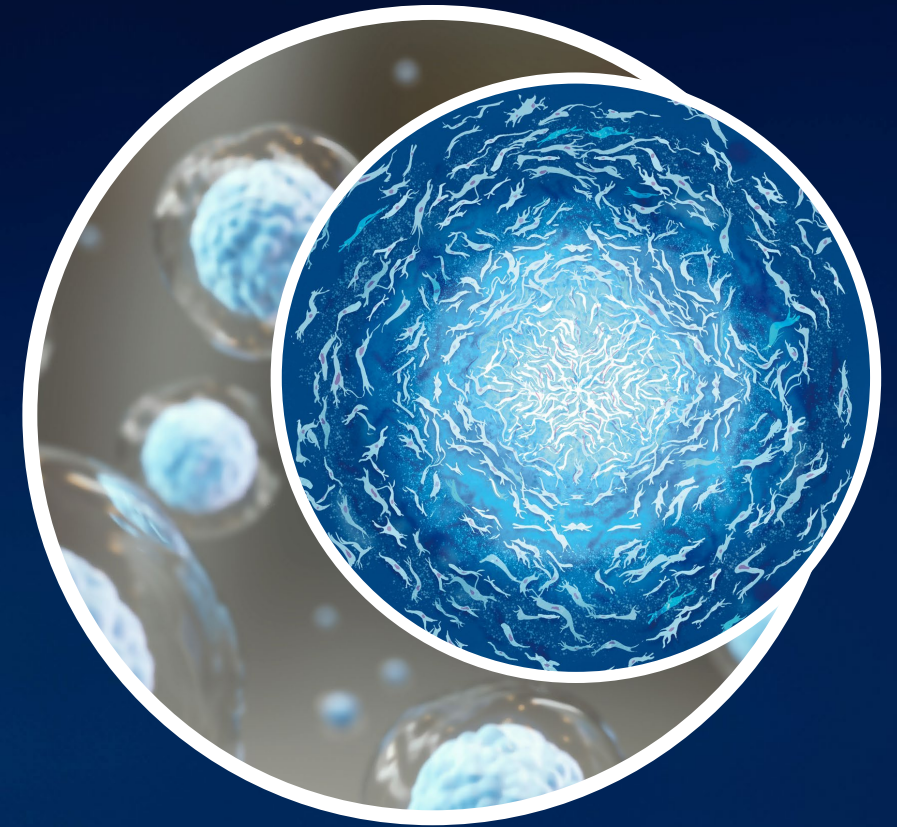
Cynata Therapeutics encourages all current investors to go paperless by registering their details with the designated registry service provider, Automic Group.

¹ iPSC = induced pluripotent stem cell

² MSC = mesenchymal stem (or stromal) cell



A Clinical Stage Company Pioneering the
Next Generation of Cellular Therapies



Euroz Hartleys Healthcare Forum

Dr Kilian Kelly – Chief Executive Officer and Managing Director

4 February 2025

Important information

Summary information

This Presentation contains summary information about Cynata Therapeutics Limited and its subsidiaries (**CYP**, or **Cynata**) which is current as at 3 February 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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Corporate overview

Cynata is an ASX-listed company (ticker **CYP**), founded to commercialise the novel iPSC-based Cymerus™ platform, for the scalable and consistent production of mesenchymal stem cell (MSC)-based therapies

Financial information

Share price (3 February 2025)	A\$0.227
Shares on issue	~225m
Market capitalisation	~A\$51m

Share price – calendar year 2024



Largest shareholders

BioScience
Managers

10.5%

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

10%

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.





FUJIFILM

3.6%

Fujifilm is a Japanese multinational conglomerate. Cynata has a strategic manufacturing partnership with Fujifilm.

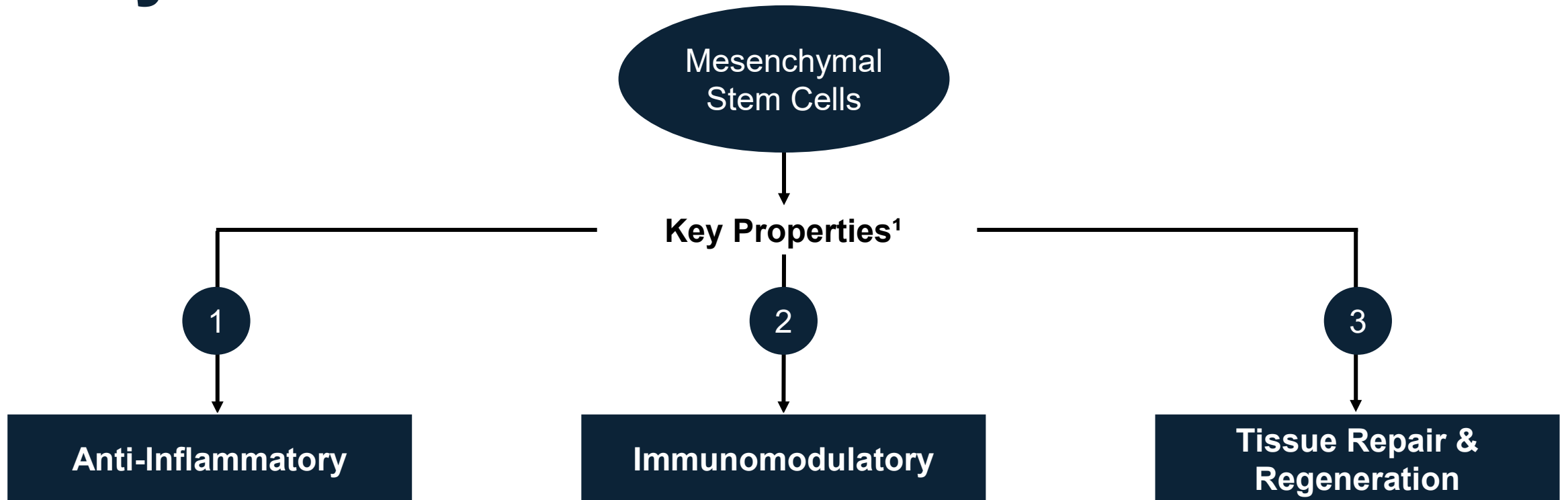
Top 20 shareholders hold ~47% of shares on issue

Target indications

Indication		Trial phase	Upcoming catalysts*	Market opportunity
 Acute Graft vs Host Disease (aGvHD) FDA Orphan Designation	Cynata Funded & Managed	Phase 2 ongoing	Enrolment completion – H1 2025 Results – H2 2025	US\$600m ¹
 Diabetic Foot Ulcers (DFU)		Phase 1 complete	Results released Dec 2024	US\$9.6bn ²
 Osteoarthritis (OA) <i>(managed by USYD, funded by NHMRC)</i>	Partner Funded & Managed	Phase 3 ongoing (enrolment complete)	Results – H1 2026	US\$11.6bn ³
 Kidney Transplantation <i>(managed and funded by LUMC)</i>		Phase 1/2 ongoing	Results (Cohort 1) – H1 2025	US\$5.9bn ⁴

Note: Cynata retains commercial rights for both of the partner funded & managed programs

Why MSCs?



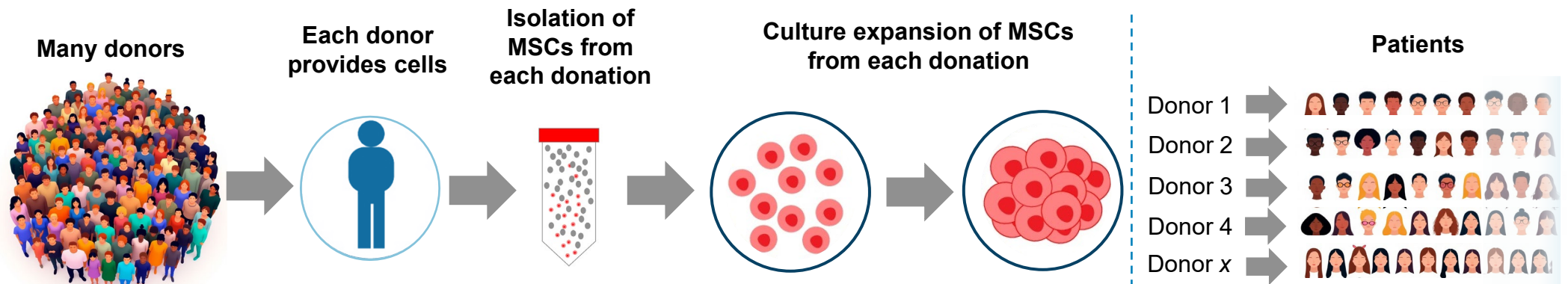
Importance:

Inflammation and inappropriate immune responses contribute to many diseases/medical disorders, and often lead to tissue damage. Consequently, the anti-inflammatory and immunomodulatory properties of MSCs, as well their ability to promote tissue repair and regeneration, can play an important role in treating many diseases.

Unlike many other cell therapies where patients have to be matched to donors, MSCs can be used without matching donors to recipients

Conventional MSC manufacturing process

Standard Process¹



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

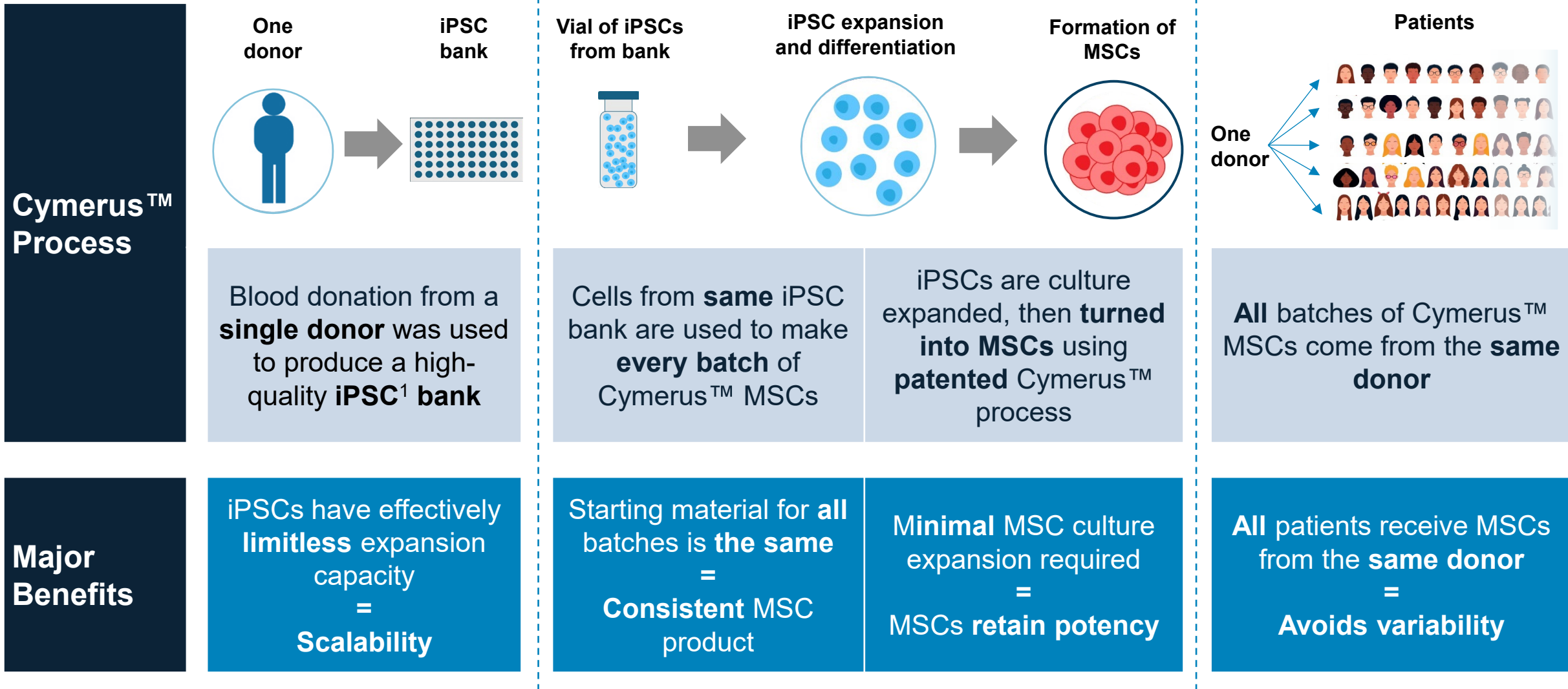
Different donors
= Variable starting material
= **Inconsistent product**

Small number of MSCs retrieved per donation
= **Extensive** MSC culture expansion required

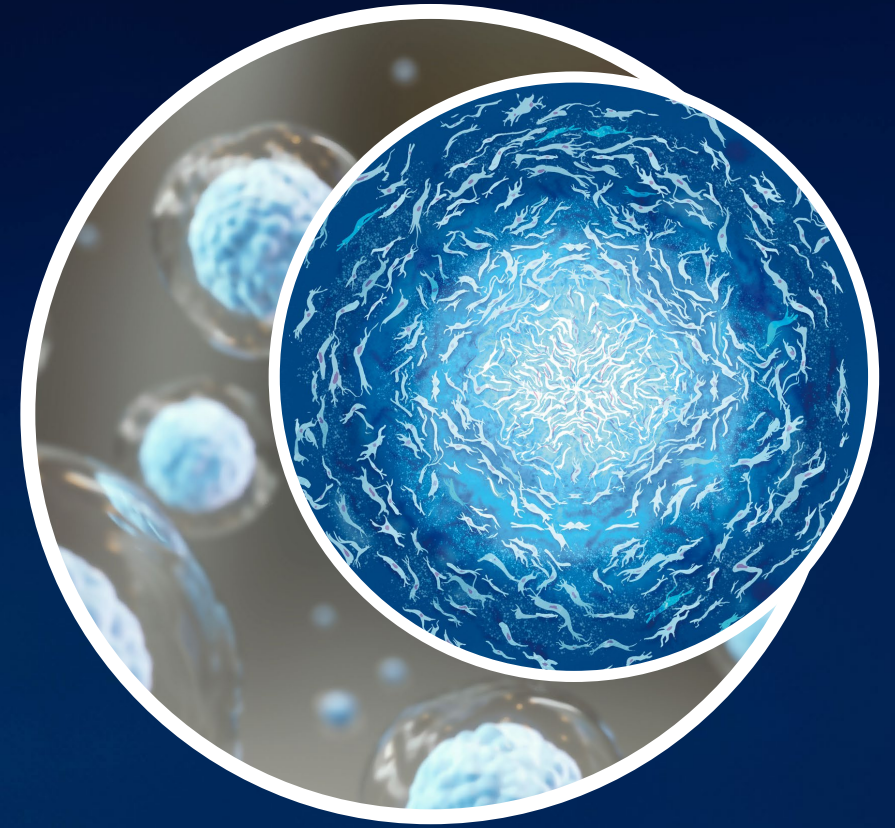
Extensive MSC culture expansion
= **Functional changes**
= **Loss of potency**

MSCs from **different donors** are administered to **different patients**
= **Inconsistent results**

The solution: the Cymerus™ process

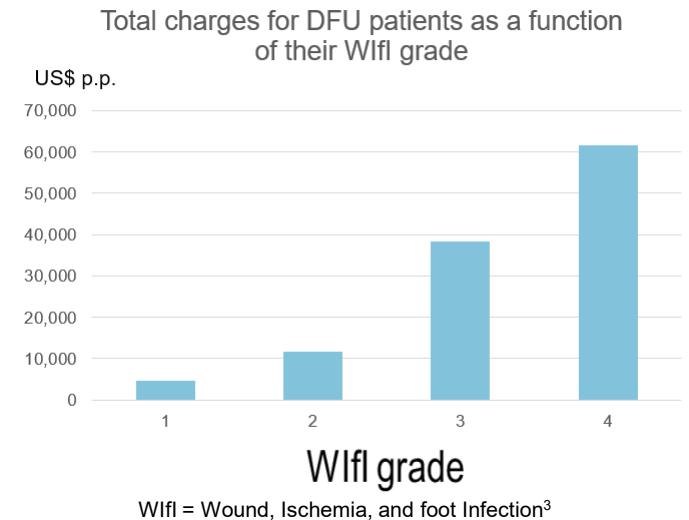


CYP-006TK for Diabetic Foot Ulcers



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 amputation¹
- 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 year²



Diabetes is the **fastest growing** public health concern worldwide⁴

~38 million Americans have diabetes⁵

Up to 34% of those with diabetes will develop a foot ulcer¹

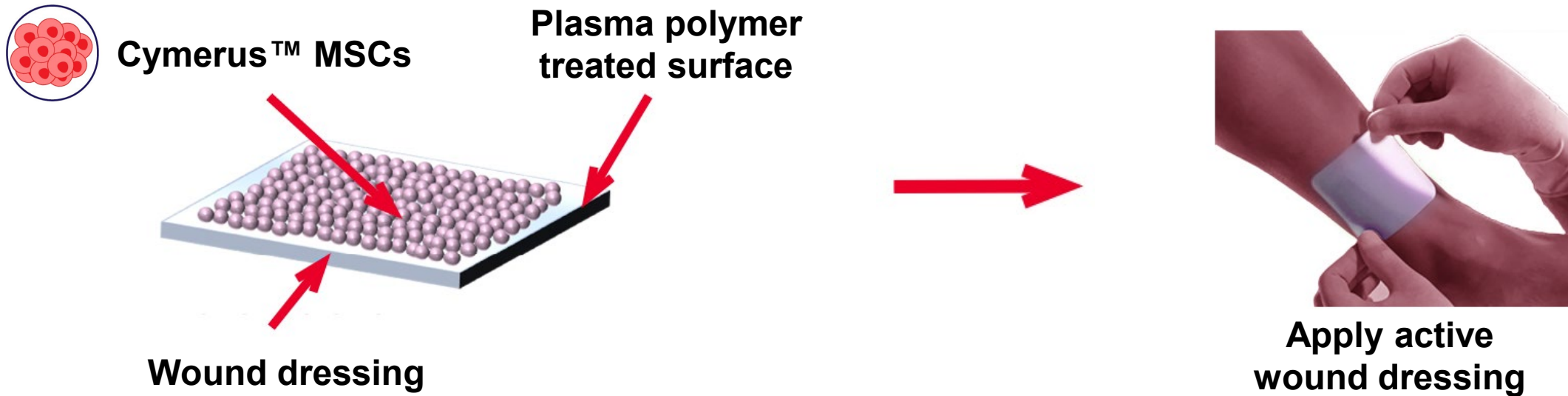
20% of patients with DFU will require **amputation** of the foot or limb¹

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 year²

Cynata's MSC product for DFU

- Cynata has developed a proprietary wound dressing using MSCs ("CYP-006TK")
- CYP-006TK utilises a proprietary surface-coating, optimised for the delivery of MSCs directly to the wound



DFU | Phase 1 clinical trial

Indication

Non-healing diabetic foot ulcers (DFU)

Product

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

Study Design

- Randomised controlled trial in ~30 adults
- Patients randomised to receive either standard of care (SOC) or CYP-006TK for 4 weeks, followed by SOC
- SOC treatment = current best practice as determined by investigator (e.g. conventional wound dressings etc)
- Primary objective was safety; efficacy measures included wound healing, pain and quality of life
- Clinical sites in Australia (Adelaide and Perth)

Study Conduct

- Patient enrolment complete (April 2024)
- All patient visits complete (September 2024)

Results

Final results released in December 2024

DFU | Phase 1 clinical trial – key results

Primary Objective

CYP-006TK **successfully achieves** its primary objective:

- safe and well-tolerated (primary objective)
- no participants withdrew from the trial due to adverse events
- no suspected serious adverse reactions were reported

Mean change in wound surface area from baseline (mm²)*

Time	CYP-006TK	Standard of Care
12 weeks	Decreased by 181 mm ²	Increased by 355 mm ²
24 weeks	Decreased by 261 mm ²	Increased by 62 mm ²

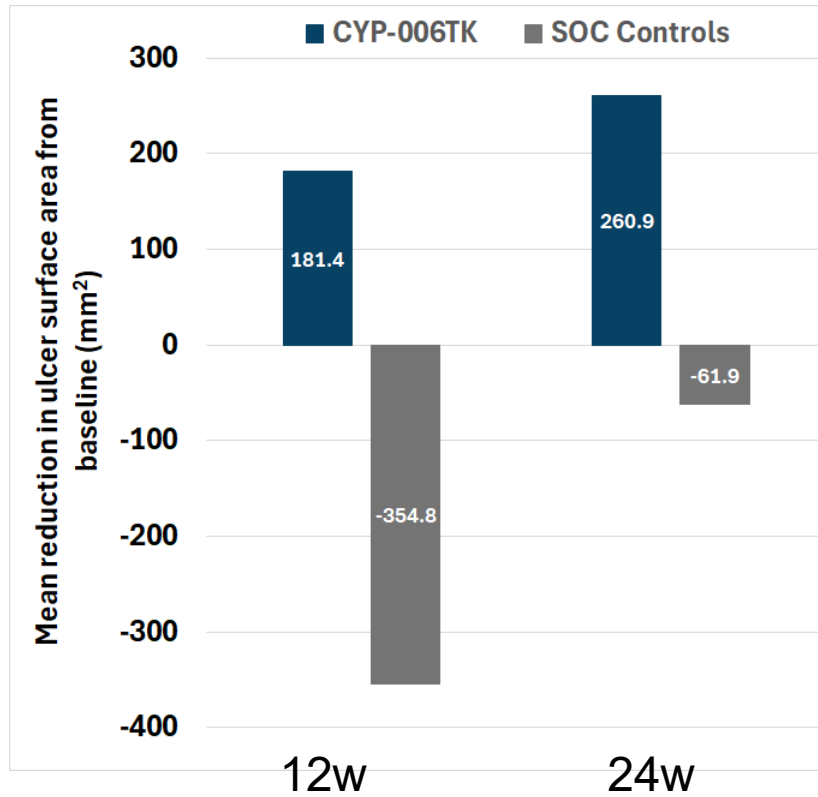
Mean change in wound surface area from baseline (%)

12 weeks	Decreased by 64.6%	Decreased by 22.0%
24 weeks	Decreased by 83.6%	Decreased By 47.8%

N=15

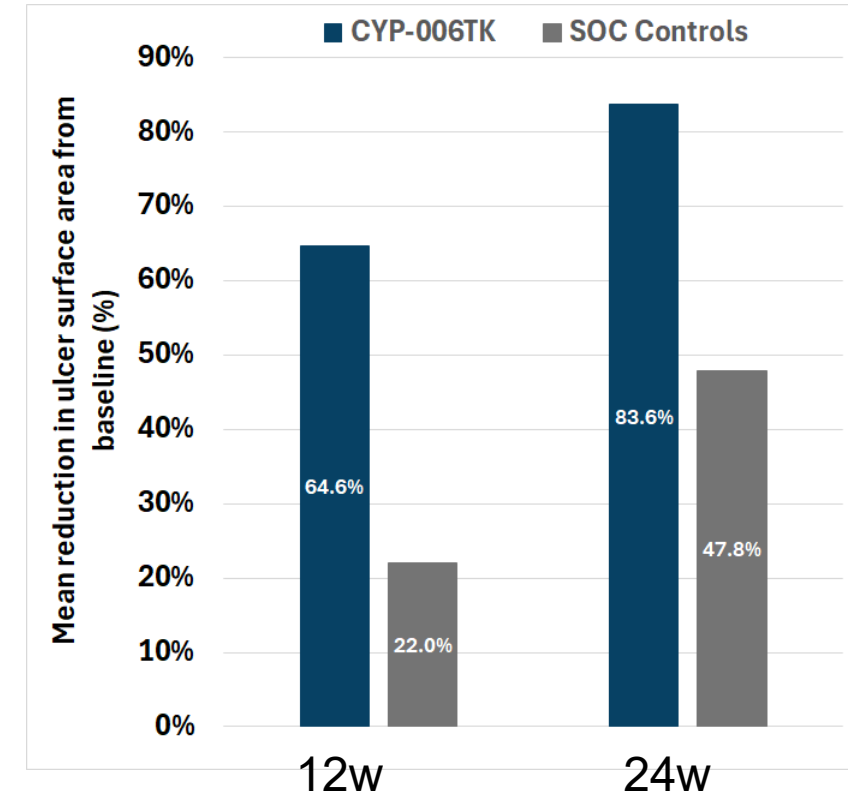
N=15

Change in wound surface area



Reduction in wound size
(Improvement)

Increase in wound size
(Deterioration)



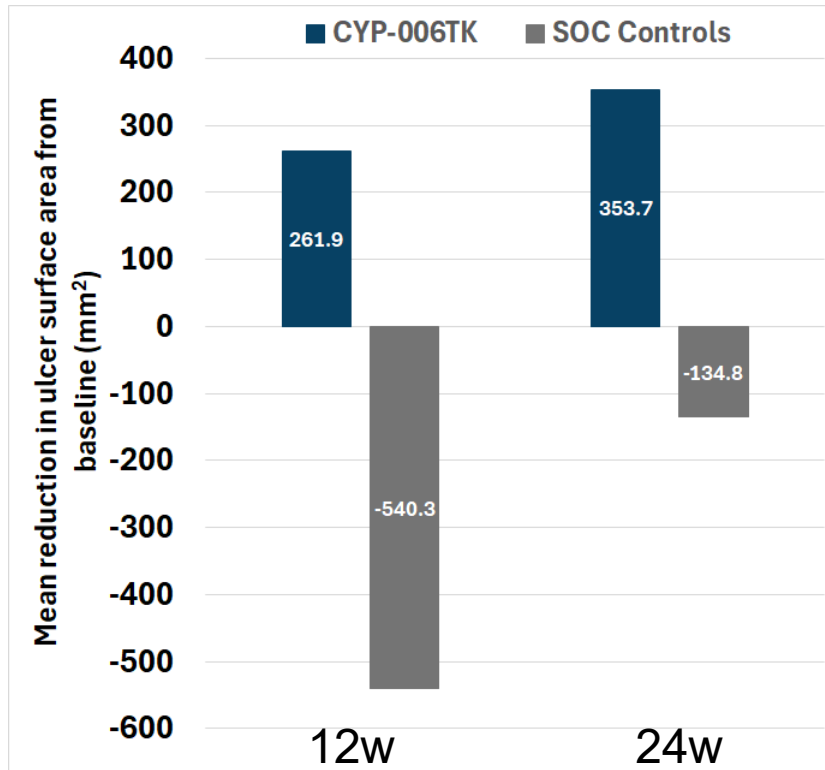
CYP-006TK

- Substantial mean reduction (improvement) in wound surface area at both 12 & 24 weeks, in both mm² and percentage terms

Standard of Care

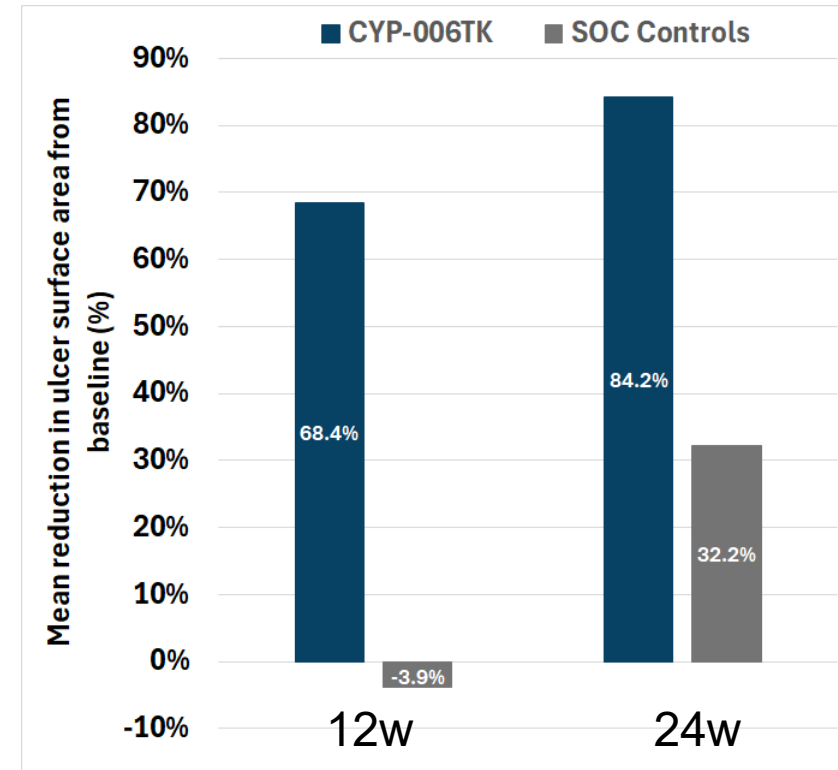
- Mean increase (deterioration) in wound surface area at both 12 & 24 weeks, in mm² terms
- Increase in mm² terms combined with moderate reduction in percentage terms indicates that **larger wounds were less likely to heal**

Larger wounds* (measuring >200 mm²)



Reduction in wound size
(Improvement)

Increase in wound size
(Deterioration)



CYP-006TK

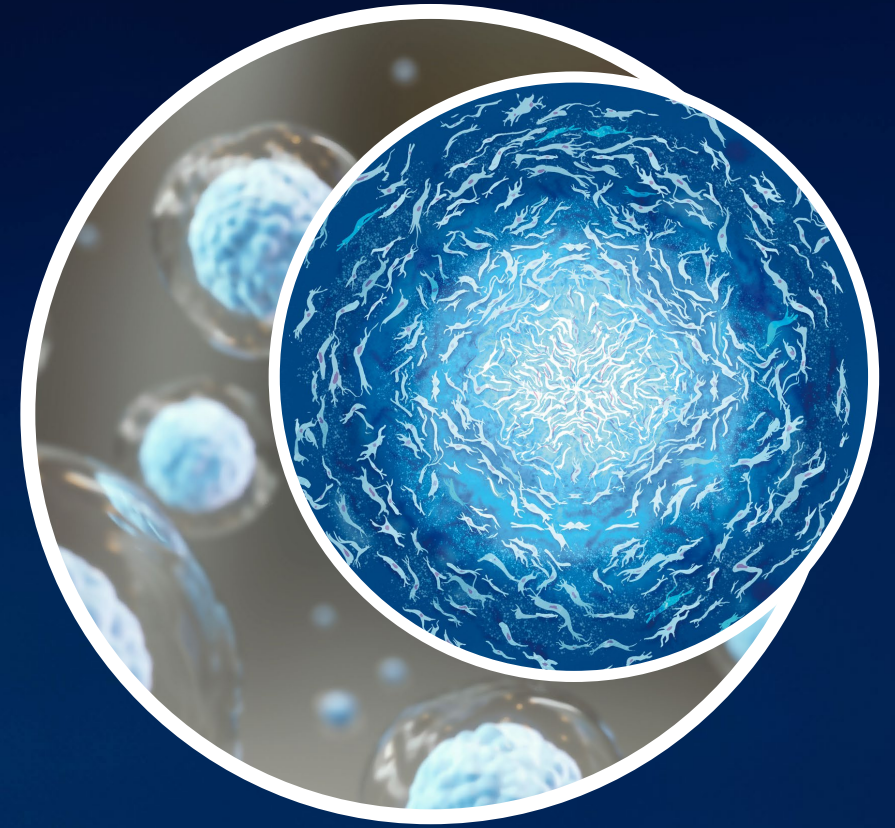
- Mean reduction in wound surface area was similar in larger wounds to when all wounds were included
- Substantial improvement in large wounds is especially encouraging as larger DFU are more likely to lead to an amputation¹

Standard of Care

- Extent of mean increase (deterioration) was greater in larger wounds than when all wounds were included
- Mean change by percentage was markedly worse in larger wounds than in all wounds

Acute Graft versus Host Disease (aGvHD)

An opportunity based on
compelling clinical data



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



Acute graft versus host disease (aGvHD)

>38,000
allogeneic
transplants*
per year¹

~35-50%
develop
aGvHD^{2,3}

Almost all
receive
steroids

<50% respond
to steroids⁴

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**

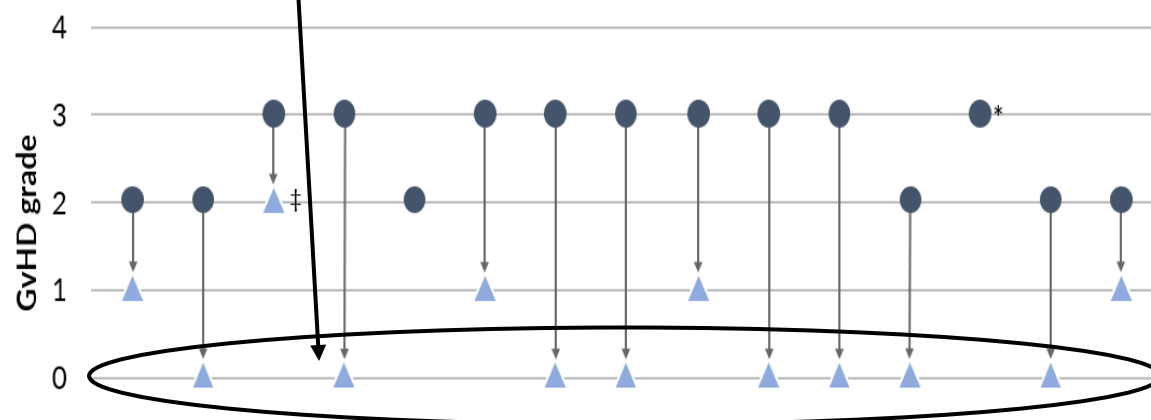
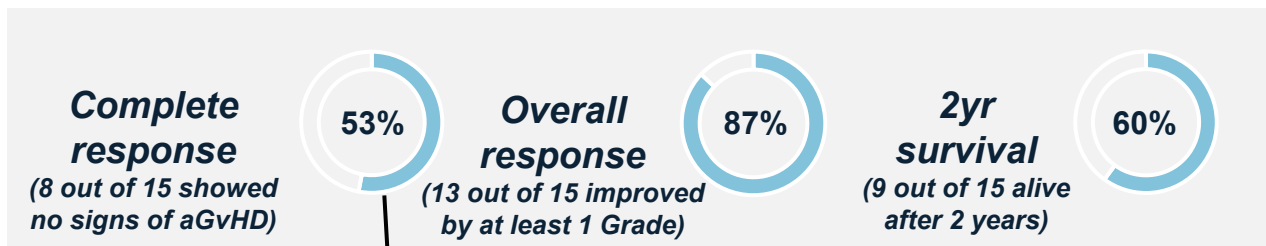
- Good initial response rates but no apparent increase in longer-term survival rates (18 months +) compared to controls⁶
- Serious/life threatening adverse reactions are common in patients who receive Ruxolitinib (e.g. infections, blood disorders)⁷
- Ruxolitinib is priced at ~US\$18k per month, and typically 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 indications⁸

- **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

SR-aGvHD | Phase 1 clinical trial – results



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 at day 0
- ▲ GvHD grade: Best response
- C Complete response
- P Partial response
- S Stable disease

✓ Outstanding response rates and overall survival

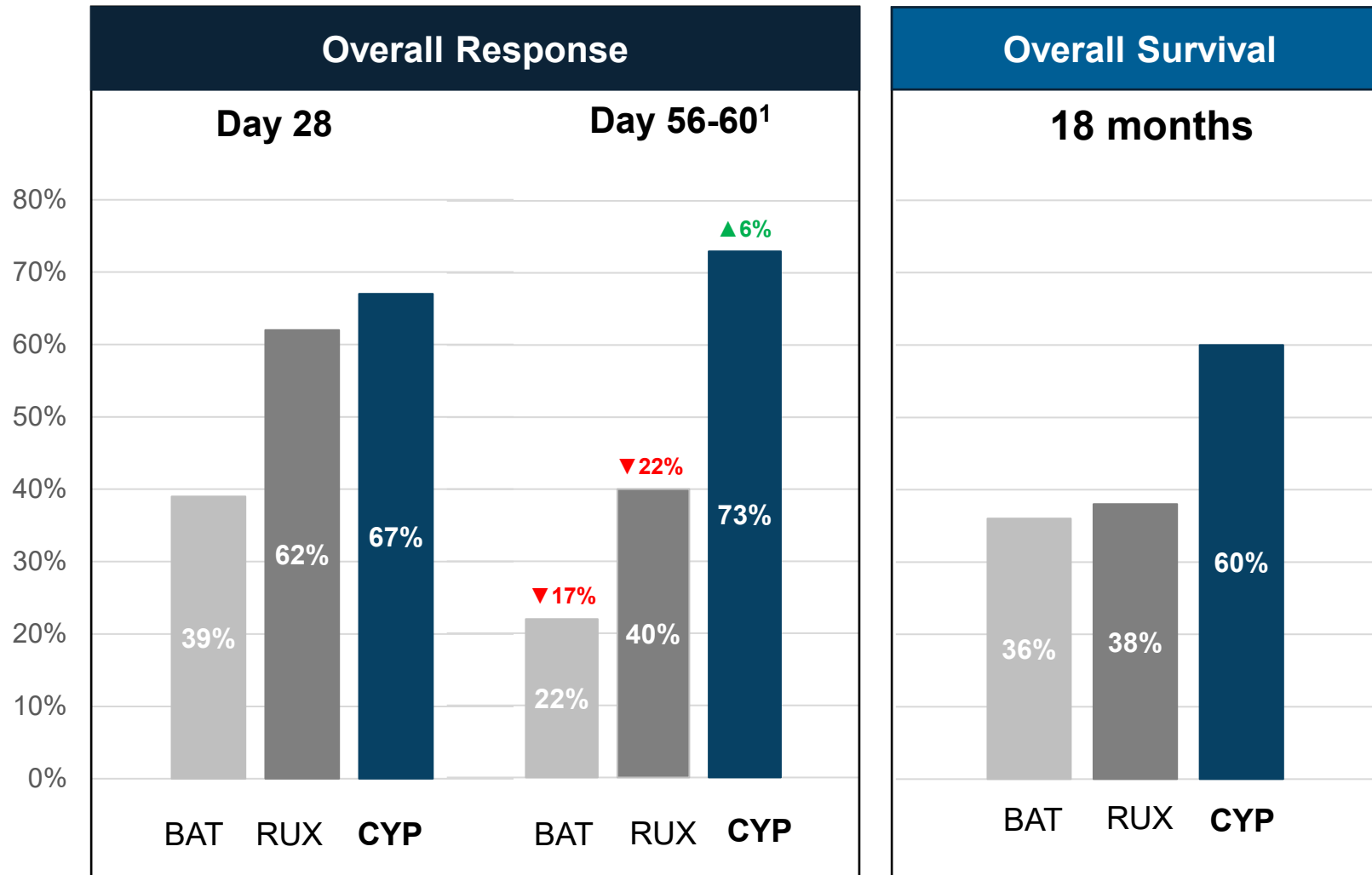
✓ Sustained outcomes achieved up to 2 years after the first infusion

✓ 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)

CYP-001 vs other treatments in SR-aGvHD



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

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)

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

Regulatory: Orphan Drug Designation

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



Benefits include:

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

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

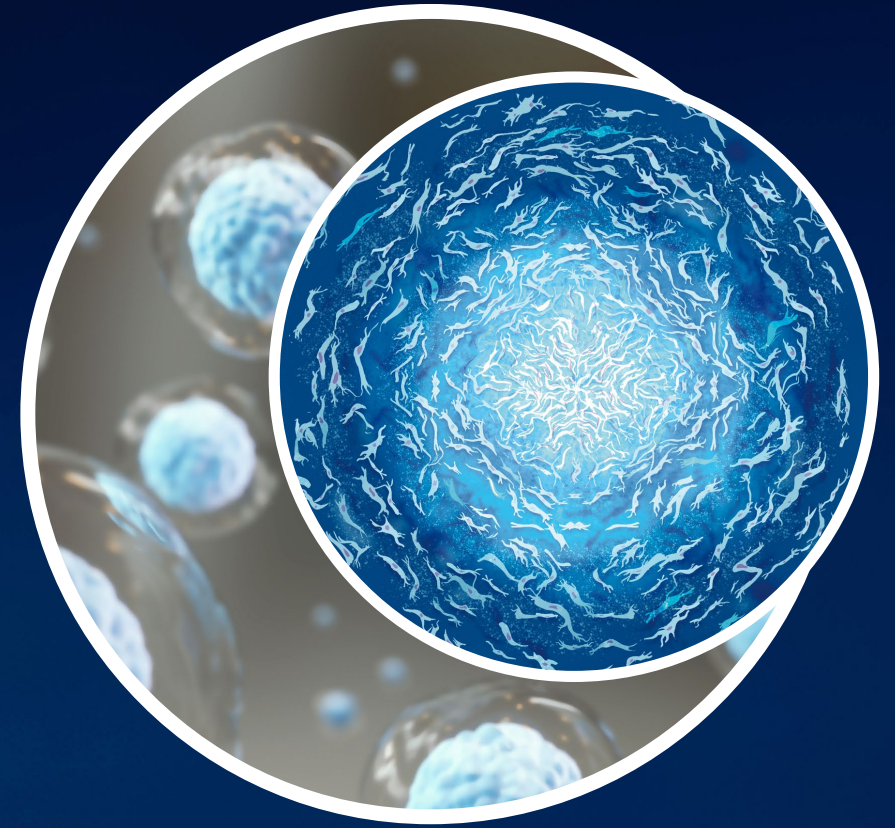
Study Conduct

- Conducted under IND from US FDA
- Clinical sites in USA, Europe and Australia
- First patient enrolled in March 2024; enrolment ~20% complete²
- Aiming to complete patient enrolment in H1 2025

Results

Results anticipated in H2 2025 (primary evaluation)

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 adults¹
- 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

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](https://www.cynata.com/science_publications)

Studies conducted in partnership with leading research groups worldwide



MONASH University



THE UNIVERSITY
of
WISCONSIN
MADISON



THE UNIVERSITY OF
SYDNEY



UNSW
SYDNEY



RCSI



University of
Massachusetts
Amherst



**Cell Therapy
Manufacturing**
Cooperative Research Centre

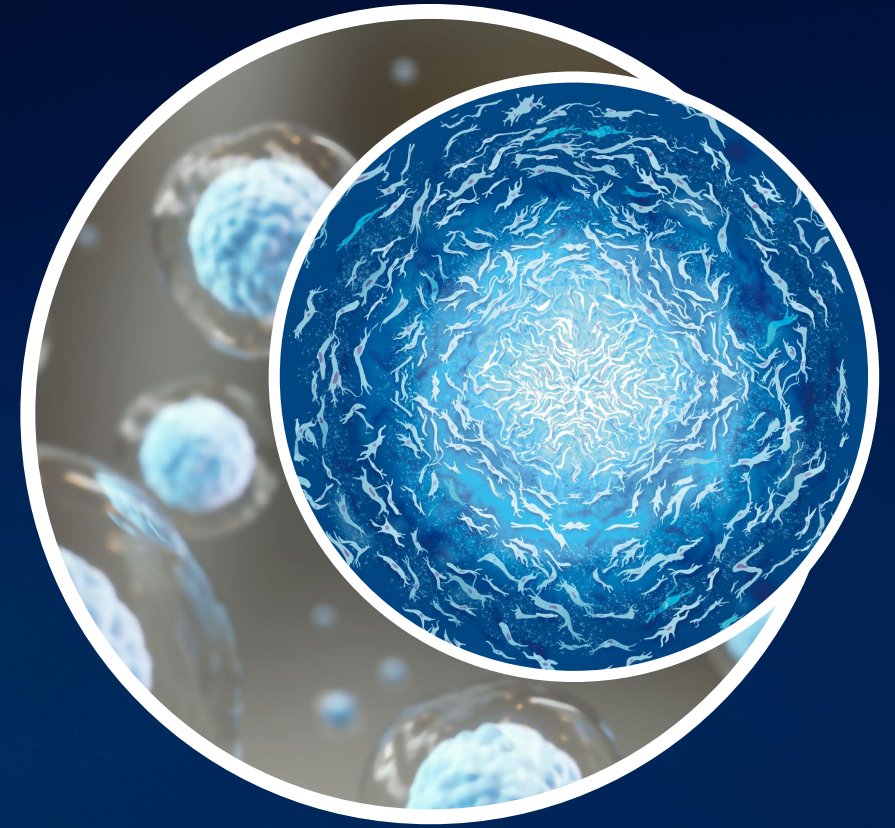


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criticalcare
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SVI
St Vincent's Institute
MEDICAL RESEARCH

Outlook and commercial potential



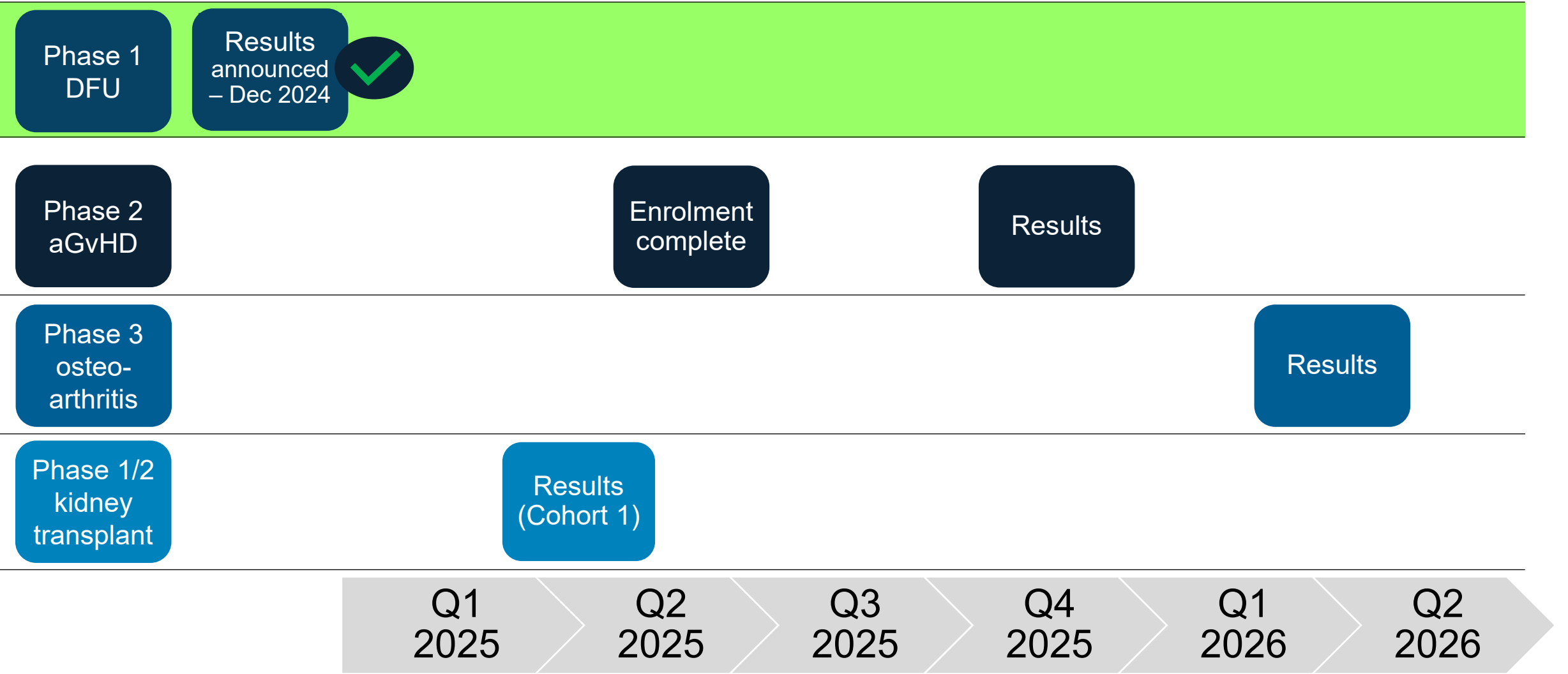
Commercial Attractiveness



 Proprietary Platform Technology	<ul style="list-style-type: none">• Ability to produce MSCs consistently and at scale allows for MSCs to be used in multiple indications = Platform Technology appeal
 Platform Technology	<ul style="list-style-type: none">• Platform Technology allows CYP to target multiple multi-billion dollar indications
 Multiple Multi-Billion Dollar Indications	<ul style="list-style-type: none">• 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	<ul style="list-style-type: none">• 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	<ul style="list-style-type: none">• 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

Upcoming catalysts*

DFU results announced Dec 2024; results from THREE further trials expected by 1H 2026





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