cynata therapeutics

A Next Generation Stem Cell Therapeutics Company

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10 October 2023

CELL GENE

MEETING ON THE MESA

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Company highlights

Cynata is a clinical stage biotech developing its proprietary Cymerus platform technology for the scalable manufacture of mesenchymal stem cell (MSC) therapeutic products to treat serious disorders

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$28bn**[1]

Well funded

Well-funded to complete planned clinical trials with **~A$16m in cash**[2]

OA and renal trials **fully funded by external partners**

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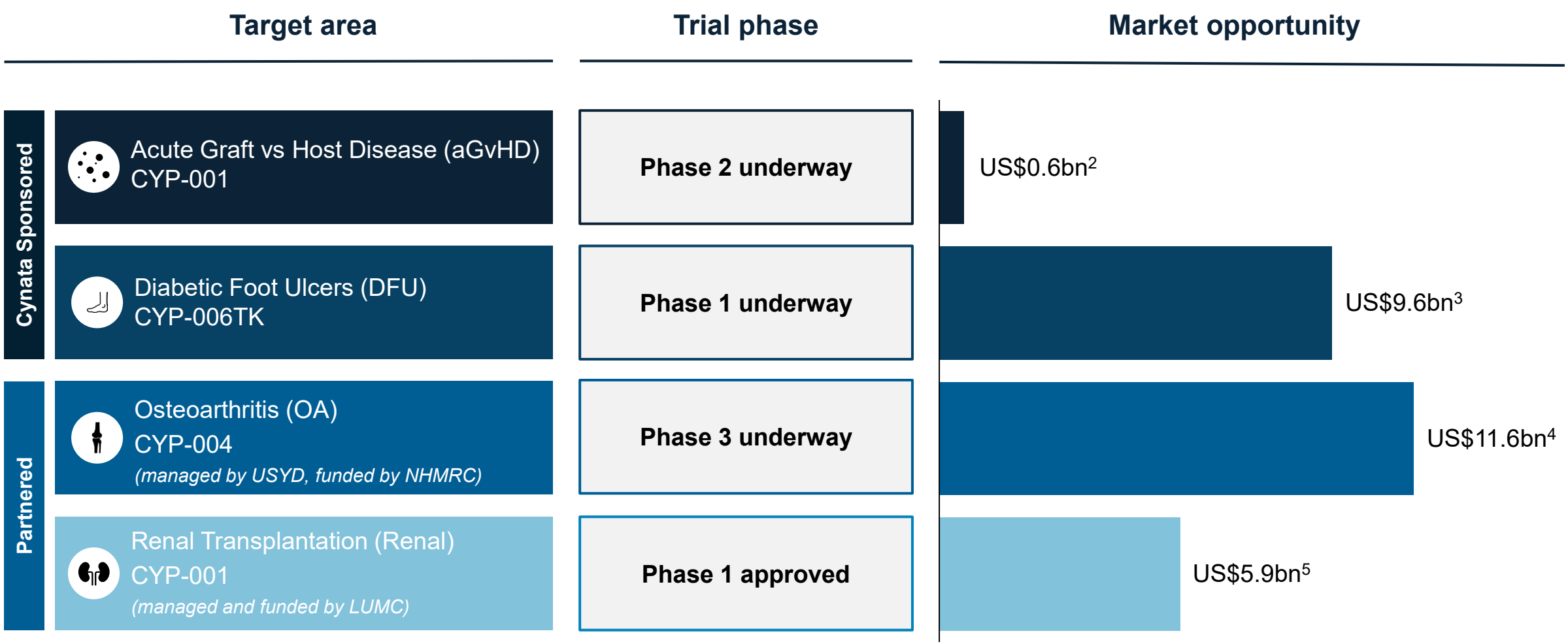
1. Refer to slide #3
2. Cash as at 30 June 2023

Cynata has an advanced and diverse clinical pipeline

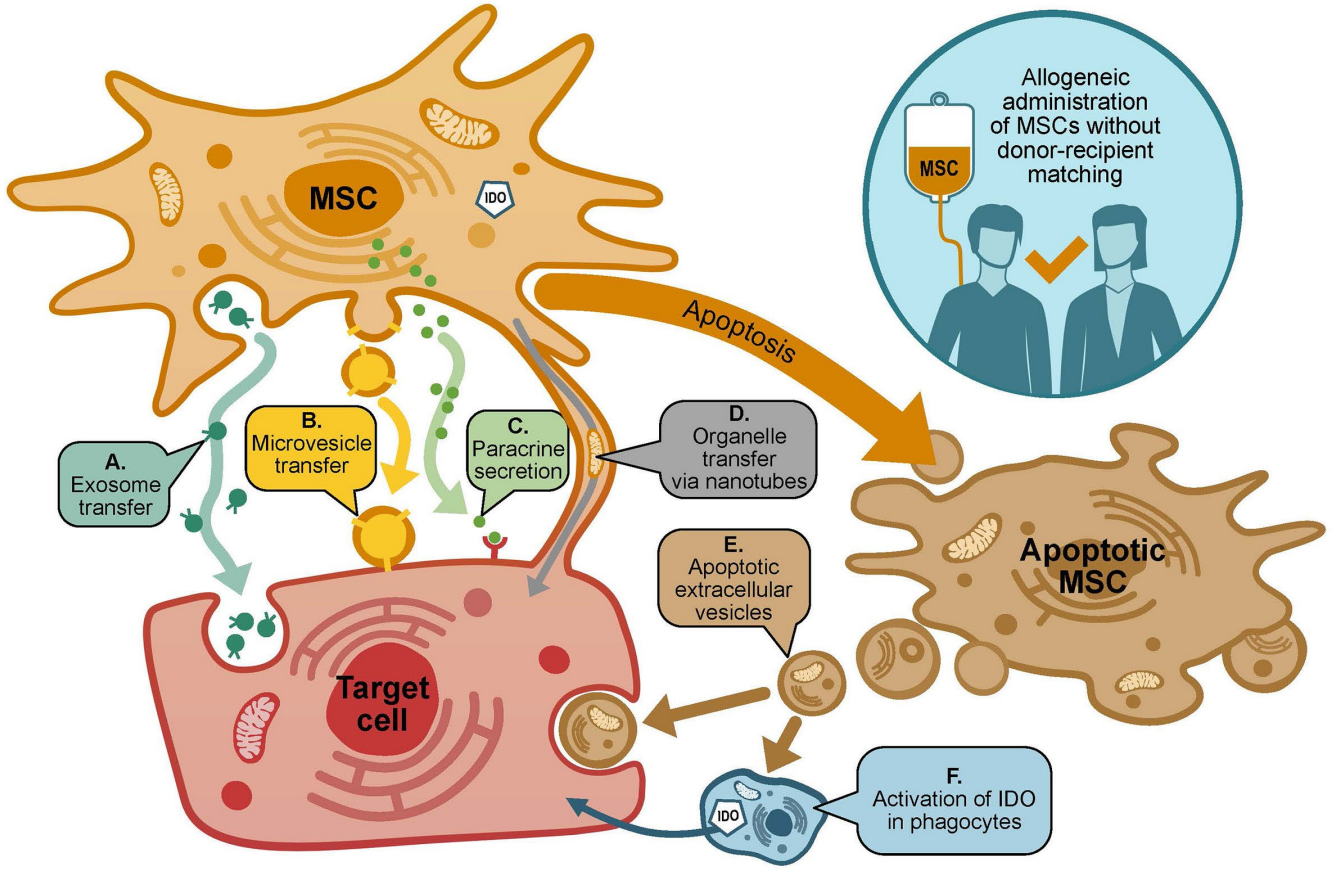


1.Investigational New Drug approval received from the US Food and Drug Administration to commence a Phase 2 GvHD trial; 2. Global Graft versus Host Disease Market 2019-2029 (Reflects forecast market in 2026); 3. Zion Market Research, 2019 (represents global treatment market in 2025); 4. Persistence Market Research 2018 research report: "Osteoarthritis Treatment Market: Global Industry Analysis (2012-2016) and Forecast (2017-2025) (Reflect OA market by 2025); 5. 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

Why Mesenchymal Stem Cells (MSCs)?

MSCs play a central co-ordinating role in many of the body's mechanisms of defence, repair and regeneration: the "sensor and switcher of the immune system"[1]

They are able to be used therapeutically without matching the donor and the recipient



*MSCs promote an **imunomodulatory** and **immunoregulatory** environment via multifactorial mechanisms, including secretion of proteins / peptides / hormones; transfer of mitochondria; and transfer of exosomes or microvesicles containing RNA and other molecules*

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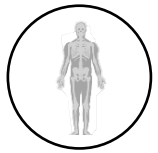
1. Aggarwal S, et al. Blood. 2005;105(4):1815-1822
2. Illustration from: Kelly K and Rasko J. Frontiers in Immunology. 12 October 2021

Cymerus™ iPSC-based manufacturing process

Conventional process

Major challenges include inter-donor variability and functional changes during MSC expansion

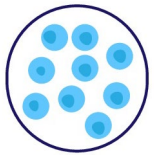
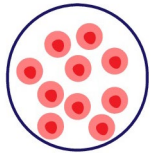
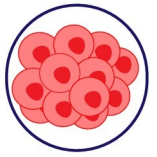
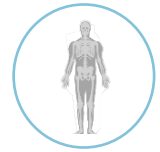
Cells donated → **Conventional process** → **MSCs**

Cells from multiple donors	MSC isolation	MSC culture expansion	Final product
			
Substantial variability in starting material	**Limited quantity** of MSCs obtained per donation	Large number of MSCs required – **extensive** culture expansion	

Cynata's Cymerus™ iPSC-based process

Avoids inter-donor variability and need for extensive MSC expansion

Donation and iPSC production → **Cynata's patented process: Cymerus™** → **MSCs**

Cells from **one** donor	iPSC expansion	Differentiation into MSCs	MSC culture expansion	Final product
					

Avoids inter-donor variability

Effectively **limitless** expansion

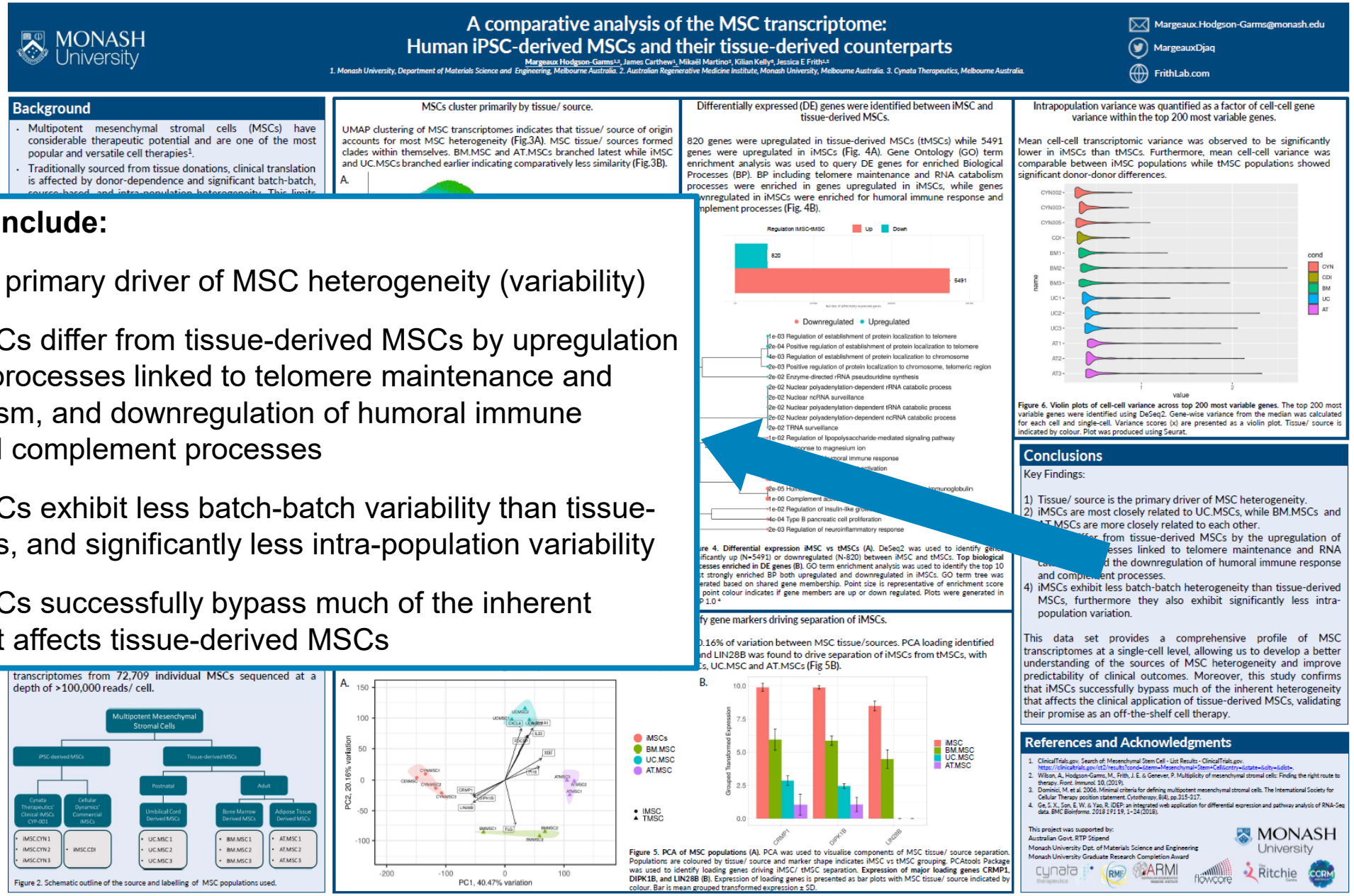
Minimal MSC culture expansion

iPSC: Induced Pluripotent Stem Cells. iPSC's derived directly from adult cells and can propagate indefinitely.

MSCs from different sources have different properties

Key Findings include:

- Source is the primary driver of MSC heterogeneity (variability)
- Cymerus MSCs differ from tissue-derived MSCs by upregulation of biological processes linked to telomere maintenance and RNA catabolism, and downregulation of humoral immune response and complement processes
- Cymerus MSCs exhibit less batch-batch variability than tissue-derived MSCs, and significantly less intra-population variability
- Cymerus MSCs successfully bypass much of the inherent variability that affects tissue-derived MSCs



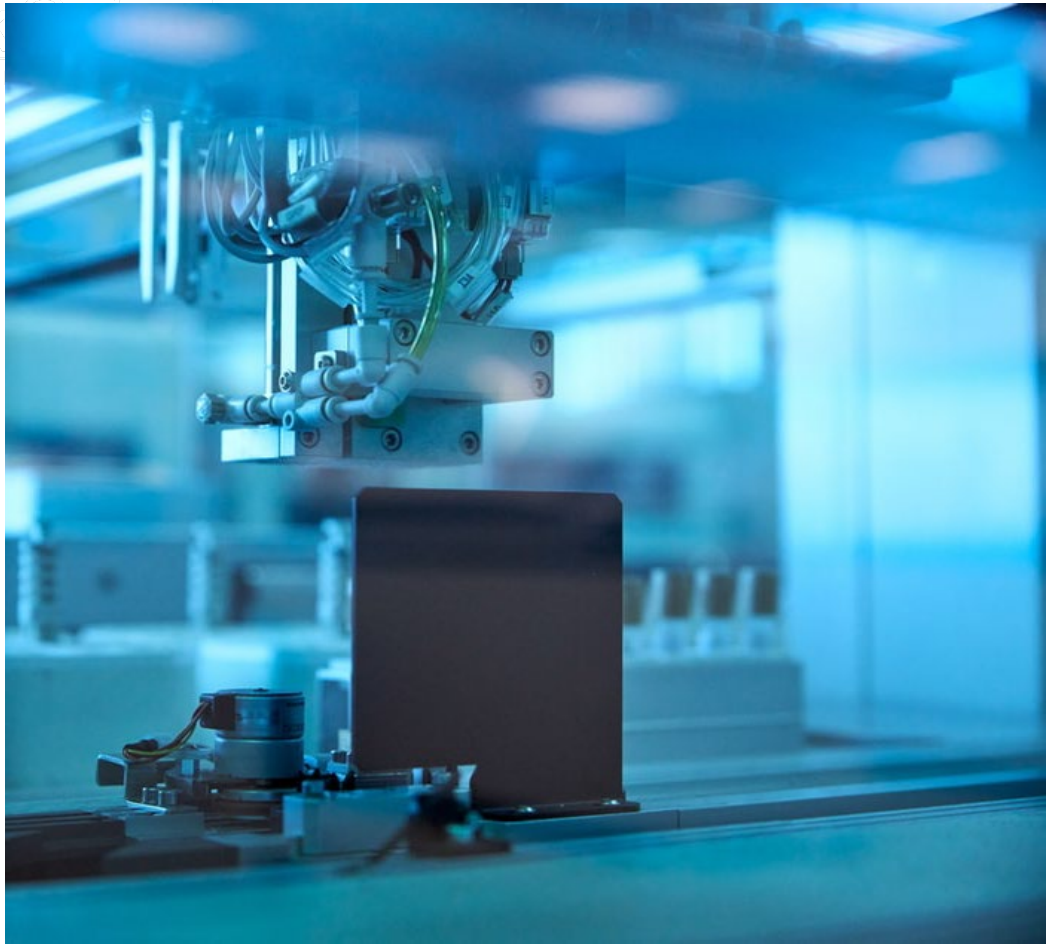
Strategic partnership with Fujifilm provides commercial benefits

Cynata executed a Strategic Partnership Agreement with Fujifilm, with Fujifilm involved in the path to market[1]

Strategic benefits for Cynata

- ✓ Fujifilm is one of the largest conglomerates in the world with a significant network and assets in the biotechnology space and recent multi-billion dollar investments in expanding its business as a comprehensive healthcare company
- ✓ 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

FUJIFILM
Value from Innovation

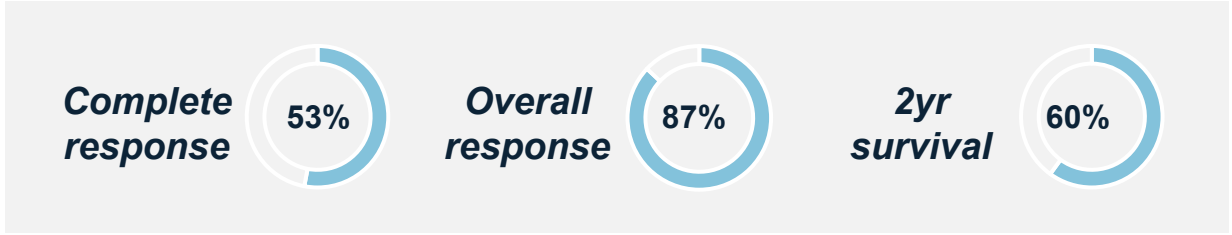


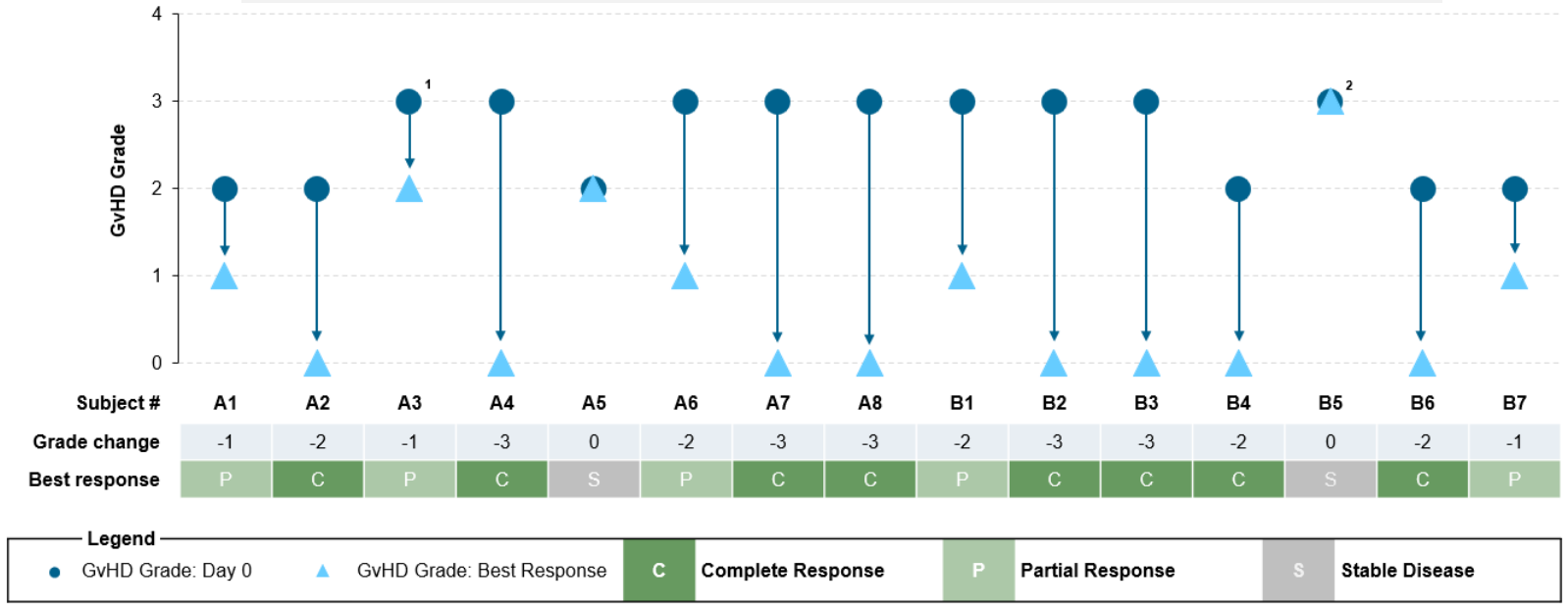
SPA: Strategic Partnership Agreement

1. Refer to announcement on 30 September 2021 "Cynata Enters into a New Strategic Partnership with Fujifilm".

aGvHD | Phase 1 clinical trial (completed)

The first completed clinical trial of an iPSC-derived product





No treatment-related serious adverse events or safety concerns identified

Published in Nature Medicine[3]

- 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

1. Subject A3 showed a PR at Days 14 and 21 but died due to pneumonia on Day 28
2. Subject B5 withdrew from the trial on Day 22 to commence palliative care
3. Bloor AJC, et al, Nat Med 26, 1720-1725 (2020)

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aGvHD | Phase 2 clinical trial

Cynata plans to commence recruitment during the current quarter, with results expected H2 CY 2025

aGvHD

- Acute Graft vs Host Disease (aGvHD) is a complication that can occur after a bone marrow transplant when the donor's immune cells (from the "graft") attack the recipient of the transplant (the "host").

Trial design

- Randomised controlled trial in ~60 patients with high risk aGvHD
- Clinical sites across in USA, Europe and Australia
- Primary objective to assess efficacy of CYP-001 in subjects by Overall Response Rate (ORR) at Day 28

Strategic review

- Currently finalising trial startup activities including securing regulatory and ethics approval – relevant approvals in Australia and the US are secured
- European regulatory approval process ongoing

Timing

- Recruitment commenced August 2023
- Patient recruitment expected to conclude by the end of CY 2024
- Primary evaluation results expected in H2 CY 2025

Key Milestones

Trial design	**Completed**
US IND	**Achieved**
Trial start-up	***Ongoing***
Recruitment + treatment	***Commenced Aug 2023***
Finish recruitment	***Expected Q4 CY 2024***
Results	***Expected H2 CY 2025***

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DFU | Phase 1 clinical trial

High screening failure rate has resulted in slower than expected recruitment, Cynata has undertaken steps to accelerate recruitment rate with enrolment expected to be completed by the end of CY 2023

Diabetic Foot Ulcers

- Diabetic Foot Ulcers (DFU) are sores on the feet of patients with diabetes (also known as diabetic wounds)

Trial design

- 30 patients with DFU will be randomly assigned to receive CYP-006TK or standard care of treatment, over 4 weeks
- The primary outcome measure of the trial is safety, while outcome measures include wound healing, pain and quality of life
- Secondary outcome measures are measured at 12 and 24 weeks

Strategic review

- Slower than expected recruitment driven by unexpectedly high screening failure rate as potential patients failed to meet trial eligibility criteria
- Trial protocol has been updated to address this issue, making it easier for patients to enrol while optimising for likelihood of a positive trial outcome
- Additional centres opened taking the total number of clinical centres to four

Timing

- Patient recruitment expected to conclude in by the end of CY 2023
- Primary evaluation results expected to be released by mid CY 2024

Key Milestones

Sign licence with TekCyte	**Completed**
Ethics approval	**Completed**
Trial start up	**Completed**
Recruitment + treatment	***Underway***
Finish recruitment	***Expected by Q4 CY 2023***
Results	***Expected by mid CY 2024***

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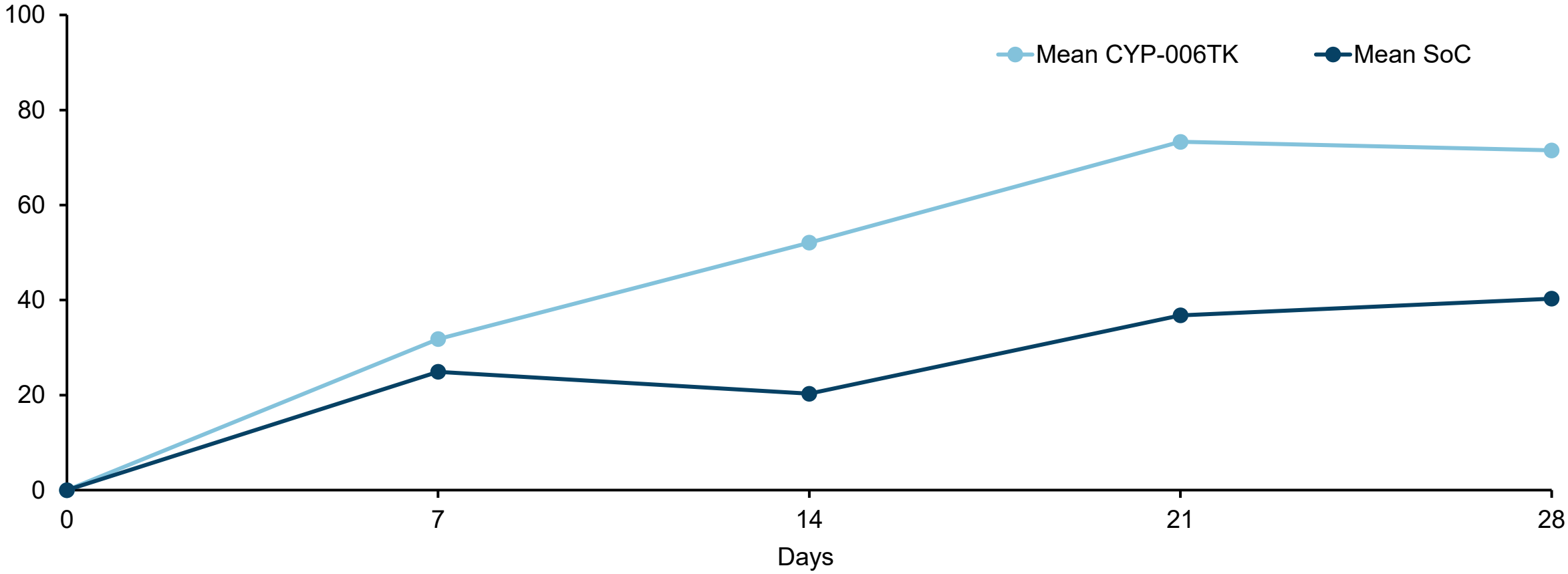
DFU | Initial clinical update

CYP-006TK has healed more ulcer surface area than standard of care (SoC) at every timepoint of the trial so far

Mean % ulcer surface area healed over time (%)[1]; n=6



1. Mean defined as average ulcer surface area healed for participants in each trial group

OA | Phase 3 clinical trial[1]

Recruitment accelerating and expected to be completed by the end of CY 2023, with evaluation results expected to be released in CY 2026

Osteoarthritis

- Osteoarthritis (OA) occurs when the cartilage in a joint wears away and can cause pain, inflammation, swelling and difficulty with movement

Trial design

- University of Sydney to enrol 440 patients to participate in the randomised, double-blind placebo-controlled trial
- Co-primary endpoints include reduction of knee pain and measure of cartilage loss, secondary outcomes include general pain and quality of life
- Each participant receives three injections of Cymerus MSCs over a year with a 24 months follow-up period

Strategic review

- Recruitment rate was initially slower than expected, largely due to the impact of the pandemic
- The recruitment rate has significantly accelerated during 2023
- Approximately 300 patients are now enrolled in the trial

Timing

- Patient recruitment expected to conclude in late CY 2023 / early CY 2024
- Primary evaluation results expected to be released in H1 CY 2026

Key Milestones

Initial safety follow-up	**Completed**
Recruitment + treatment	***Ongoing***
Finish recruitment	***Expected Q4 CY 2023 / Q1 CY 2024***
Final follow-up (24 months)	***Expected Q4 CY 2025 / Q1 CY 2026***
Results	***Expected H1 CY 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).

Renal | Phase 1 clinical trial

Clinical trial start up activities with partner Leiden University Medical Center (LUMC) underway, with outcome from regulatory approval process expected during the current quarter

Renal Transplants

- MSCs may reduce or eliminate the requirement for aggressive and toxic anti-rejection drugs, leading to a substantial breakthrough in transplantation medicine

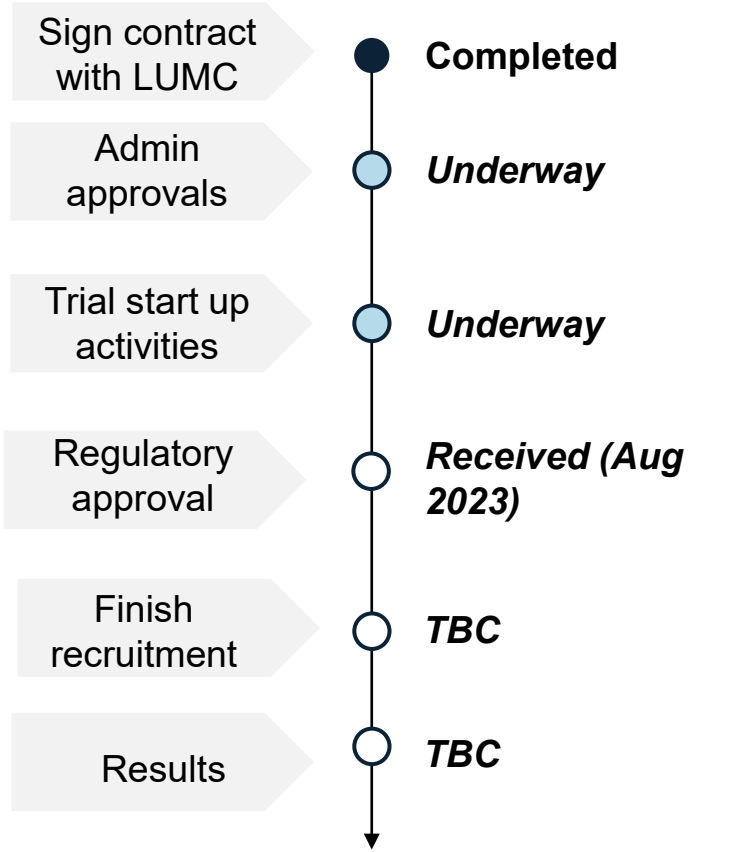
Trial design

- 16 renal transplant patients will receive Cymerus MSCs after transplantation
- Trial will evaluate safety and efficacy of reduction of anti-rejection medication

Timing

- Trial has received regulatory/ethics approval (August 2023)
- Final trial start-up activities ongoing

Key Milestones



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Investment summary

Next generation stem cell company	• Market leader 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 process	• Patented Cymerus manufacturing technology enables commercial-scale production of MSCs from a single donation from a single donor, overcoming multiple issues with today's on-market solutions • Cymerus MSCs have demonstrated higher potency versus conventionally manufactured MSCs
Successful clinical trial results	• All clinical endpoints achieved in Phase 1 trial of Cymerus MSCs in aGvHD, with no safety concerns identified and highly encouraging efficacy data • Highly encouraging initial DFU patient data in chronic wounds
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 application for Phase 2 aGvHD clinical trial; study open for recruitment
Significant growth potential	• Pipeline has significant commercial opportunities: 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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