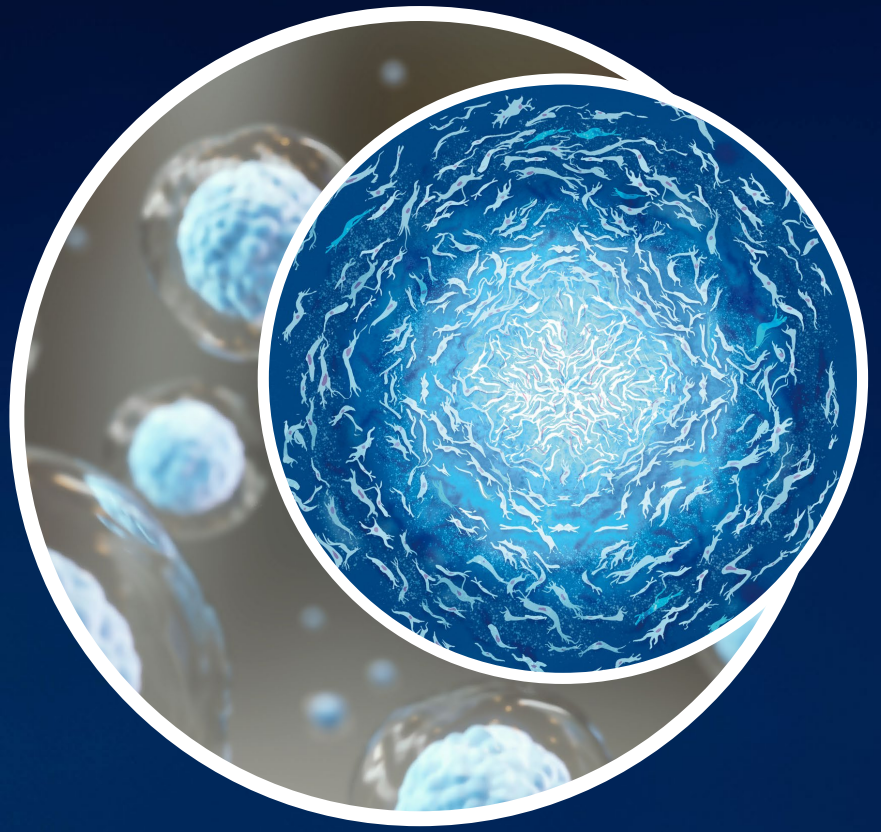
cynata therapeutics



Clinical Development of iPSC-Derived MSCs

Advanced Therapies Congress
London, 19 March 2024

Kilian Kelly, PhD
CEO and Managing Director

ADVANCED THERAPIES 2024

Important information

Summary information

This Presentation contains summary information about Cynata Therapeutics Limited and its subsidiaries (**CYP**) which is current as at 14 March 2024. 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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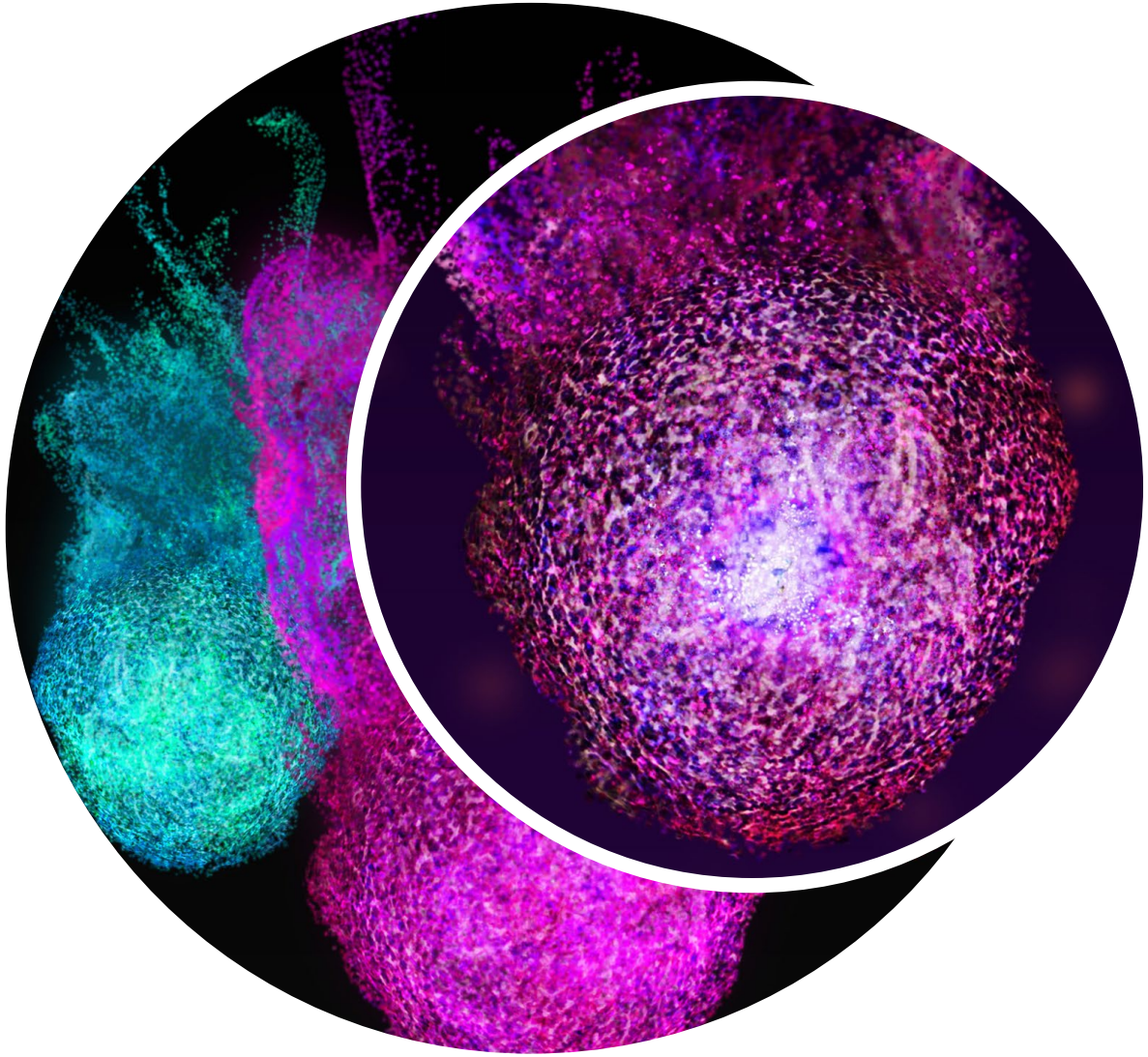
About Cynata

- ASX-listed company (Ticker: **CYP**), based in Melbourne, Australia
- Exclusively focused on development of **Cymerus™** platform:
  - **iPSC**-based technology for scalable manufacture of consistent, allogeneic **MSC**-based therapeutic products
  - Developing therapies to treat a range of serious disorders with unmet needs
- Positive data in a range of indications
- Completed **world-first** iPSC clinical trial



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ASX: Australian Securities Exchange
iPSC: induced Pluripotent Stem Cell
MSC: Mesenchymal Stem (or Stromal) Cell

Company highlights

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]

Solid funding position

~A$11m in cash[2], and OA and renal trials **funded by external partners**

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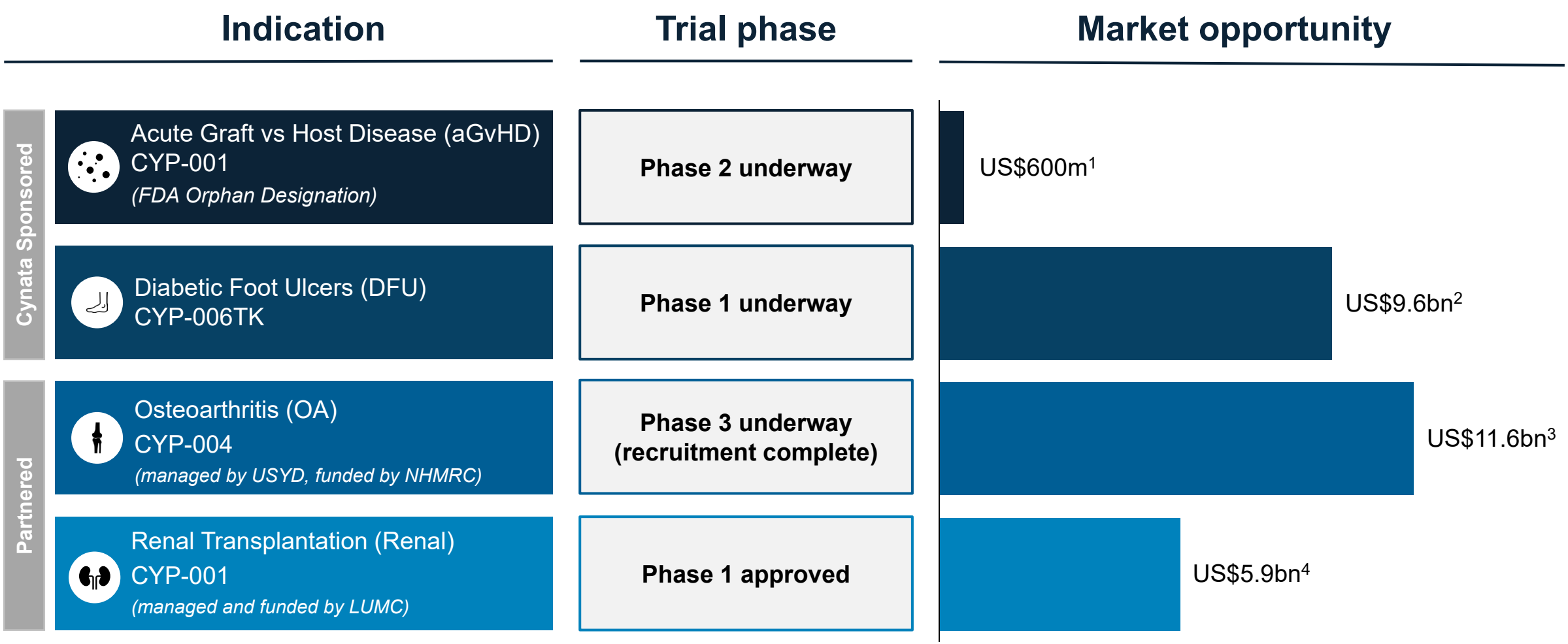
1. Refer to next slide
2. Cash as at 31 December 2023

Advanced and diverse clinical pipeline



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

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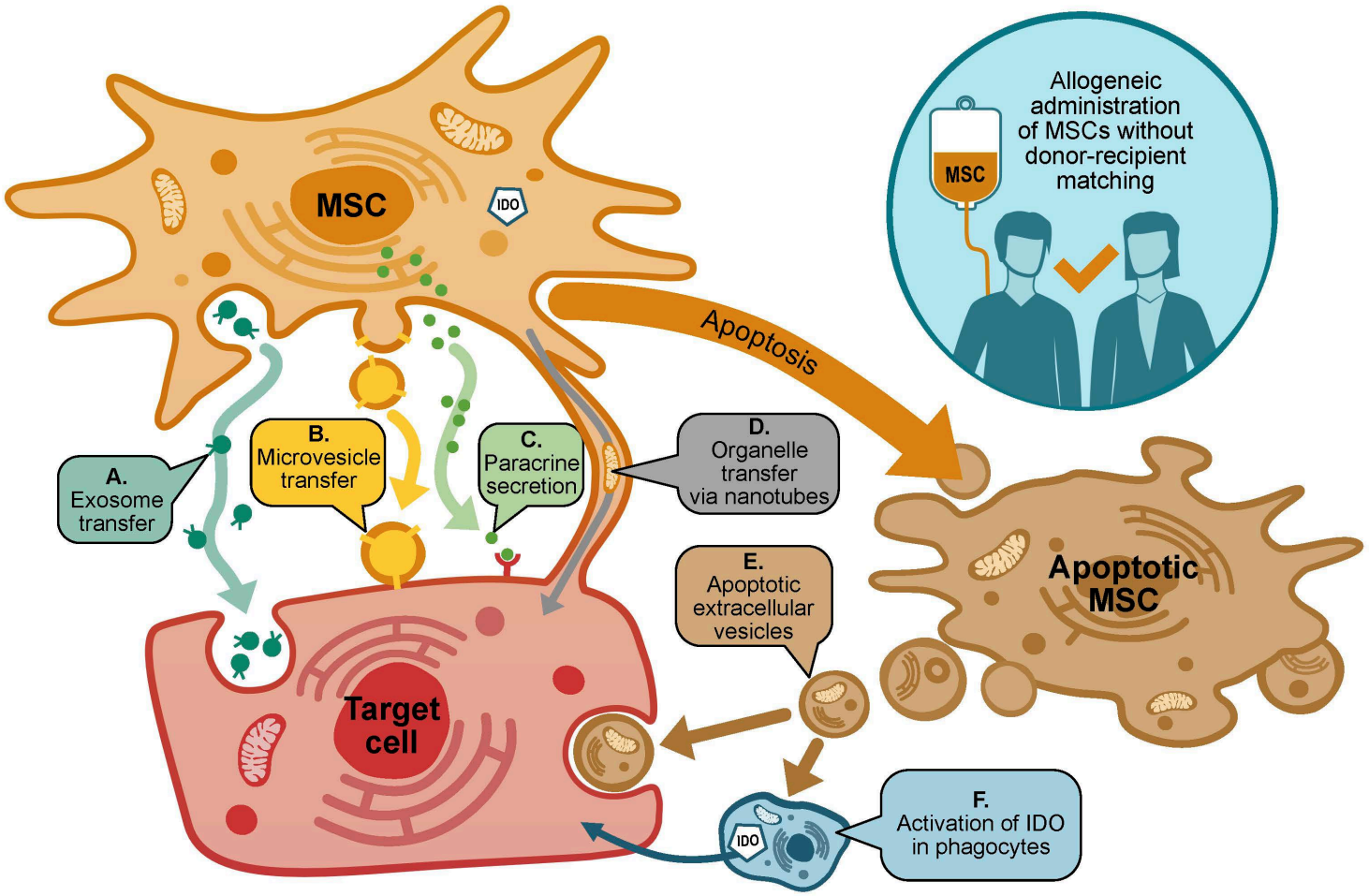
Why MSCs?



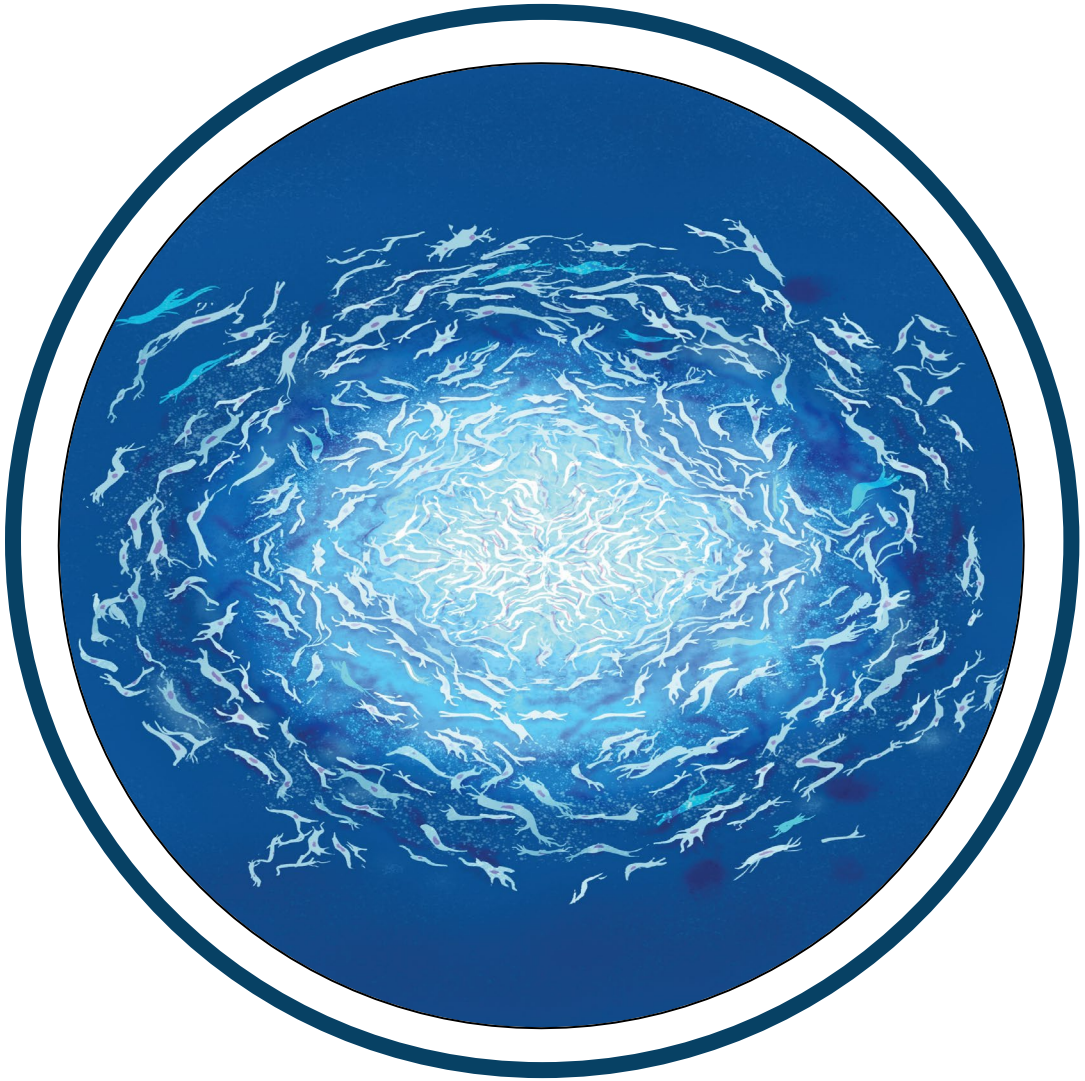
Mesenchymal stem (or stromal) cells (MSCs):

- promote an **immunomodulatory** environment via multifactorial mechanisms[1]
- the "sensor and switcher of the immune system"[2]
- promote **tissue repair** and **regeneration**
- can be used **without** donor/recipient matching
- can be **engineered** to express other functional/therapeutic molecules

1. Kelly and Rasko, Front. Immunol. 12:761616.
2. Sarsenova et al, Front. Immunol.13:1010399.

Illustration from ref #1.

Why iPSCs?



Induced pluripotent stem cells (iPSCs):

- mature cells from adult donors, reprogrammed to become pluripotent
- effectively limitless proliferation in cell culture
- potential to differentiate into any adult cell type (including MSCs)
- avoids ethical controversy associated with embryonic stem cells

→ **ideal** starting material for large scale production of cellular products

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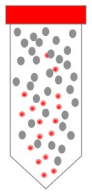
Conventional MSC process

Ongoing need for new donors

Substantial inter-donor **variability**

MSC isolation



Small number of MSCs per donation

Culture expansion

Extensive MSC culture expansion

Major challenges:

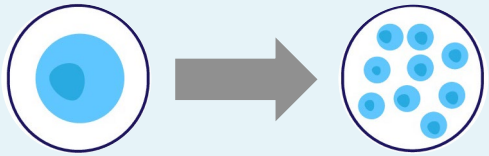
- inter-donor **variability**
- MSCs have **limited expansion potential**
- MSCs undergo **functional changes** during extensive culture expansion

Cymerus™ iPSC-based process

One donor, one time

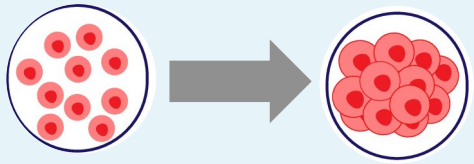
Avoids inter-donor variability

Reprogramming & iPSC expansion



Effectively **limitless** Expansion potential

Differentiation into MSCs & culture expansion



Minimal MSC culture expansion

Cymerus platform:

- Harnesses **effectively limitless** iPSC expansion potential
- **Avoids** inter-donor variability
- **Avoids** extensive MSC expansion

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Strategic partnership with Fujifilm

- Fujifilm: one of largest conglomerates globally, with significant assets in biotechnology sector, bolstered by recent multi-billion dollar investments
- 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

Preclinical studies with Cymerus MSCs

Large body of data in wide range of preclinical models, in partnership with leading research groups worldwide:

- 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

MSC source affects properties

Comparative analysis of MSCs from various sources[1]

- Source is primary driver of MSC heterogeneity
- Cymerus MSCs exhibit less batch-batch and intra-population variability than tissue-derived MSCs
- Cymerus MSCs successfully bypass much of the inherent variability that affects tissue-derived MSCs

Mouse model of diabetic wounds, using novel MSC-seeded dressing[3]

- Cymerus MSCs resulted in significantly greater re-epithelialisation (86%) compared with bone marrow MSCs (51%)
- Gingival fibroblast- and bone chip-derived MSCs produced similar results to Cymerus MSCs, but there are major challenges associated with producing clinical-grade cells from those sources

Pre-clinical rat model of myocardial ischemia-reperfusion[2]

Positive effects were observed with both Cymerus MSCs and bone marrow MSCs, but some different effects between MSC groups:

- Left ventricle function significantly improved in Cymerus MSC group (P=0.01) compared to placebo, but not in bone marrow MSC group (P=0.63)
- Arteriogenesis around infarct zone significantly improved in Cymerus MSC group compared to both placebo and bone marrow MSC group (P=0.01)
- Expression of a number of relevant cytokines by Cymerus MSCs was **2-4x higher** than by bone marrow MSCs

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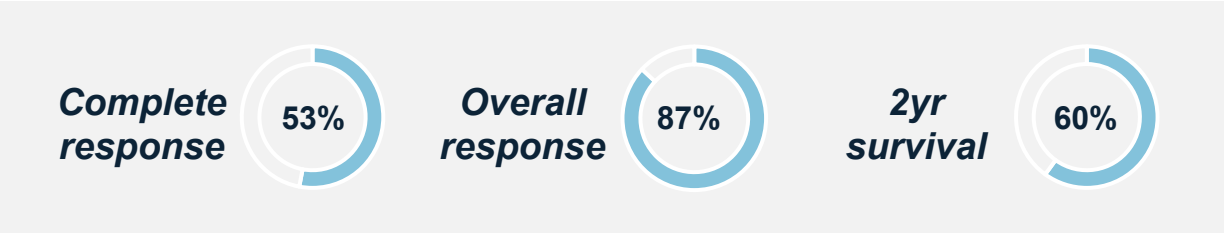
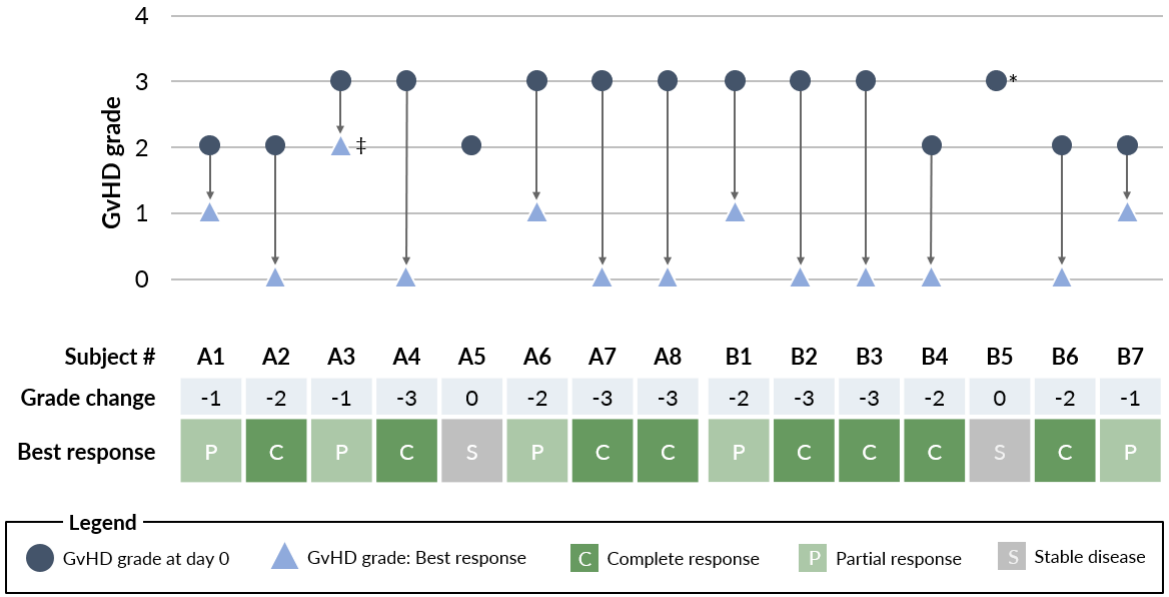
1. https://files.cynata.com/675/22.11-Monash-Poster-Margeaux-Hodgson-Garms-ASSCR-2022_221109_191955.pdf
2. Thavapalachandran et al. Cytotherapy 2021;23(12):1074-1084
3. https://tekcyte.com/cypatch/

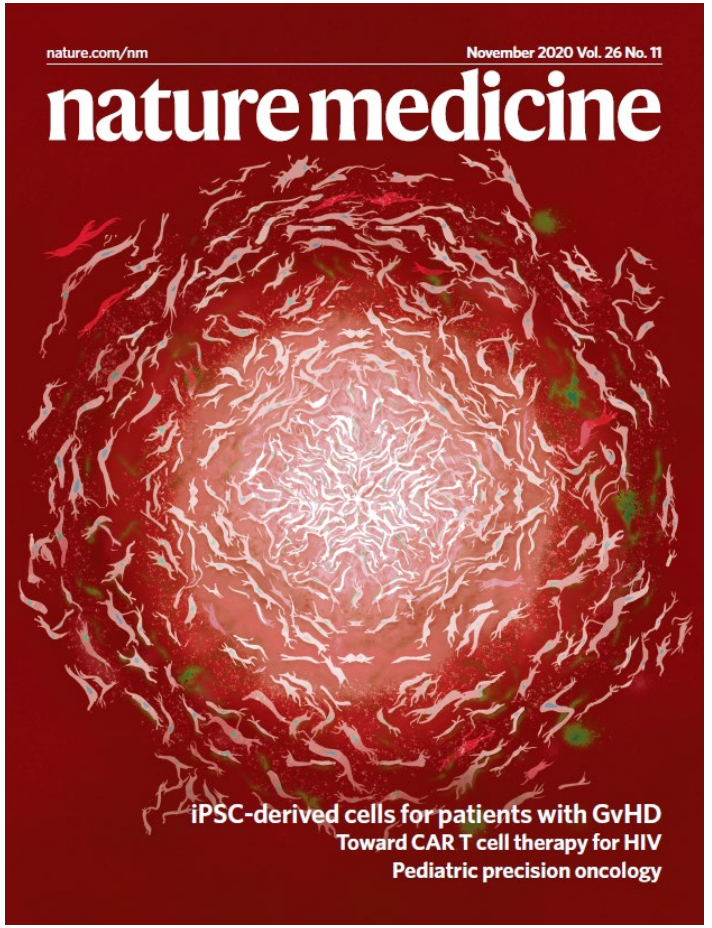
aGvHD | Phase 1 clinical trial

First completed clinical trial worldwide with any iPSC-derived product





Published in Nature Medicine[1]



No treatment-related serious adverse events or safety concerns identified

- 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

1. Bloor et al. 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. Nat Med 2020;26:1720-1725.

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aGvHD | Phase 2 clinical trial

Product	CYP-001 (Cymerus™ iPSC-derived MSCs for intravenous infusion)
Indication	High risk acute graft versus host disease (aGvHD)[1]
Study Design	• Randomised controlled trial in ~60 adults (steroids + CYP-001 vs steroids + placebo) • Primary objective: to assess efficacy of CYP-001 based on Overall Response Rate at Day 28
Study Conduct	• Clinical sites in USA, Europe and Australia • Regulatory/ethics approvals secured in Australia, USA and Turkey; EU regulatory process ongoing • Numerous sites now open for recruitment, with remainder expected to open in 2024 • First patient enrolled – March 2024 • Aiming to complete recruitment by end of calendar year 2024
Results	Primary evaluation results expected in 2H CY 2025

1. aGvHD may occur after bone marrow transplantation/similar procedures, due to donor immune cells (from the “graft”) attacking the transplant recipient (the “host”).

DFU | Phase 1 clinical trial

Product	CYP-006TK (Novel silicone dressing seeded with Cymerus™ iPSC-derived MSCs)
Indication	Non-healing diabetic foot ulcers (DFU)
Study Design	• Randomised controlled trial in ~30 adults • Patients randomised to receive either standard of care or CYP-006TK for 4 weeks, followed by standard of care • Primary objective is safety; efficacy outcome measures include wound healing, pain & quality of life
Study Conduct	• Clinical sites in Australia (Adelaide and Perth) • Recruitment ~85% complete – completion expected in near future
Results	• Positive initial results from first 16 patients – median reduction in wound surface area after 10 weeks was **87.6%** in CYP-006TK group compared to **51.1%** in controls (n=8 per group) • Final results expected by end of calendar year 2024

OA | Phase 3 clinical trial[1]

Product	CYP-004 (Cymerus™ iPSC-derived MSCs for intra-articular injection)
Indication	Osteoarthritis (OA) of the knee (Kellgren-Lawrence Grade 2-3)
Study Design	• Randomised, double-blind placebo-controlled trial in ~320 adults • Each participant receives 3 injections over 12 months; follow-up of 24 months from first dose • Co-primary endpoints: reduction of knee symptoms and measure of cartilage loss
Study Conduct	• Trial conducted by University of Sydney, funded by Australian Government NHMRC grant • Clinical centres in Australia (Sydney and Hobart) • Recruitment complete (commenced November 2020; completed in November 2023) • Last patient last visit expected ~November 2025
Results	• Results expected in H1 CY 2026

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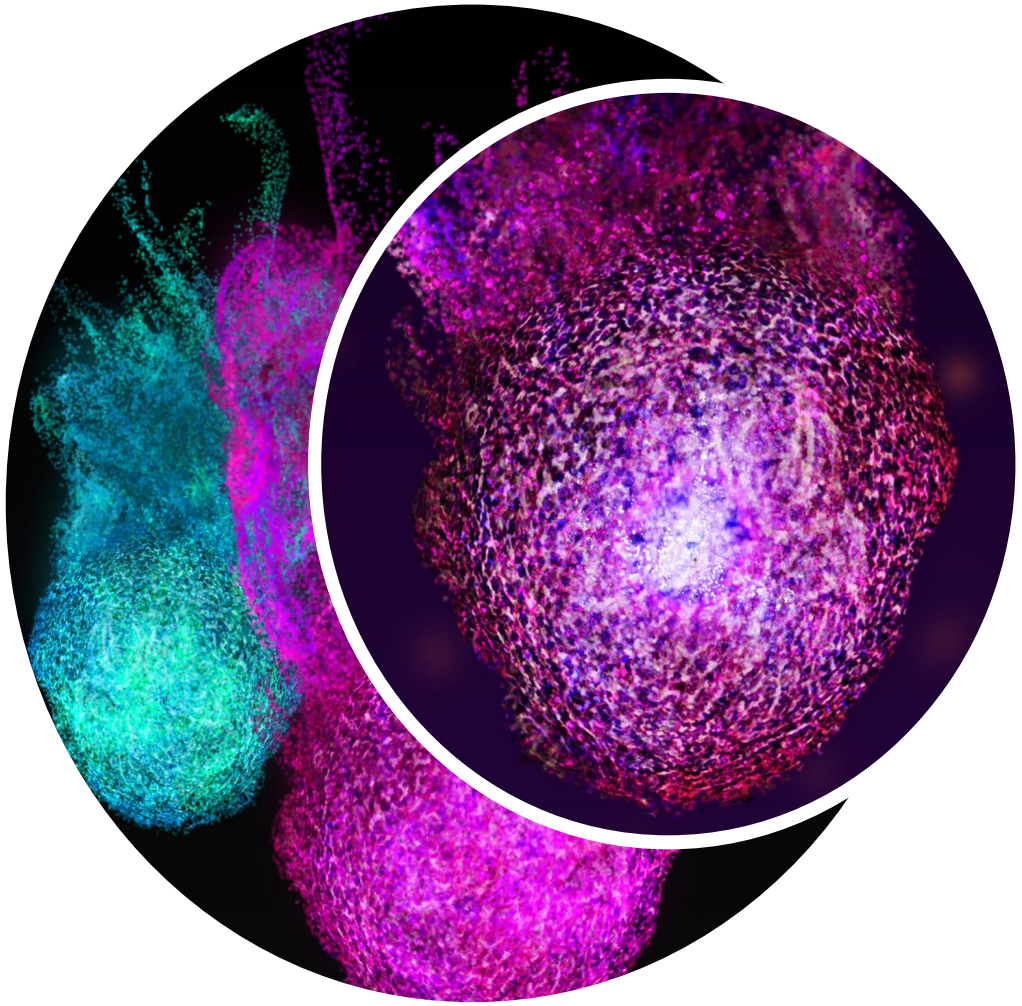
1. Clinical trial entitled Stem Cells as a symptom – and strUcture-modifying Treatment for medial tibiofemoral OsteoaRthritis: a randomised placebo-controlled trial (SCUlpTOR). NHMRC: National Health and Medical Research Council

Renal transplant | Phase 1 clinical trial

Product	CYP-001 (Cymerus™ iPSC-derived MSCs for intravenous infusion)
Indication	Prevention of kidney transplant rejection
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 to be conducted and funded by Leiden University Medical Center, Netherlands • Regulatory and ethics approvals in place; final trial start-up activities ongoing • Aiming to commence recruitment in Q1 2024 • Timing of further cohorts TBC
Results	Results of Cohort 1 anticipated in late 2024

Partnering



- Cynata is pursuing a partnership-driven business model
- Proactive outreach ongoing, aimed at development partners for existing clinical assets
- Cymerus platform also available for other indications and/or engineered MSC applications

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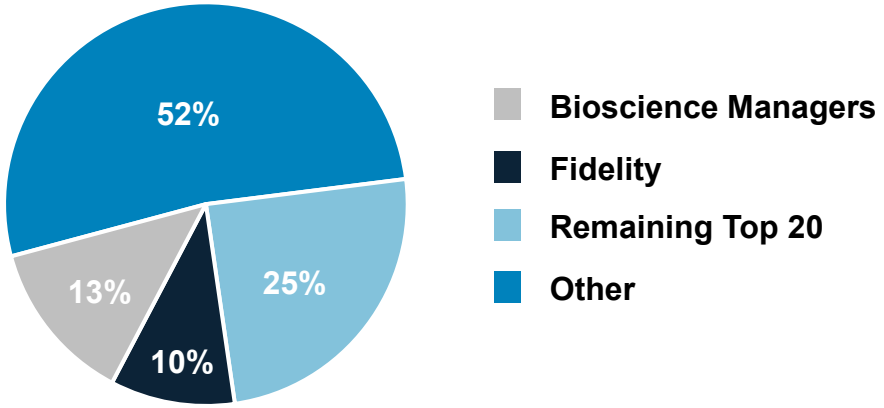
Corporate overview

Cynata has been listed on the Australian Securities Exchange (ASX) since 2013 (Ticker: CYP)

Shareholder distribution



Financial information

Share price (14 March 2024)	A$0.175
Shares on issue	179m
Market capitalisation	**~A$31.3m**
Cash[1]	~A$11m

Substantial shareholders (>5%)

BioScience Managers — **13.1%**

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 — **10.0%**

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.

Source: IRESS
1. As at 31 December 2023

Summary

Next generation stem cell company	• Leading platform technology 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	• Patented Cymerus manufacturing technology enables scalable production of consistent MSCs from a single donation from a single donor, overcoming issues with conventional approaches
Successful clinical trial results	• Very encouraging safety and efficacy results from Phase 1 trial of Cymerus MSCs in aGvHD • Highly encouraging initial DFU patient data
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 for Phase 2 aGvHD clinical trial; study underway
Significant growth potential	• 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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