

ASX ANNOUNCEMENT 18 September 2023

INVESTOR WEBINAR PRESENTATION

Melbourne, Australia; 18 September 2023: Cynata Therapeutics Limited (ASX:CYP) ("CYP", "Cynata" or "the Company") is pleased to invite shareholders to attend an investor webinar hosted by *The Watchlist*, to be held on Tuesday 19 September 2023, at 12:00pm AEST/ 10:00am AWST.

During the webinar, Dr Kilian Kelly (Cynata's CEO & MD) will provide an overview of the Company's strategic direction and clinical development pipeline.

Following the presentation, attendees will have the opportunity to ask questions during a moderated Q & A session.

Attendees are required to register in advance for the webinar – using the following link:

https://us02web.zoom.us/webinar/register/WN 2c9lxYzPRFWM9bkGTwmccQ

The event is free to attend. After registering, attendees will receive an email with login details. A recorded copy of the webinar will be made available following the event.

An updated version of the Company's Investor Presentation is attached to this announcement. The presentation delivered during the webinar will be an abbreviated version of this Investor Presentation.

-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) and diabetic foot ulcers (DFU) 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.



A Next Generation Stem Cell Therapeutics Company

Investor Presentation
September 2023



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











Single donation from a single donor iPSC strategy

overcomes suboptimalities in conventional MSC manufacturing Positive pre-clinical and clinical data

supporting versatility and efficacy of Cynata's MSCs; including in world-first iPSC trial in aGvHD Phase 1 Rich clinical pipeline:

- aGvHD (Phase 2)
- **DFU** (Phase 1)
- Osteoarthritis (Phase 3)
- Renal (Phase 1)

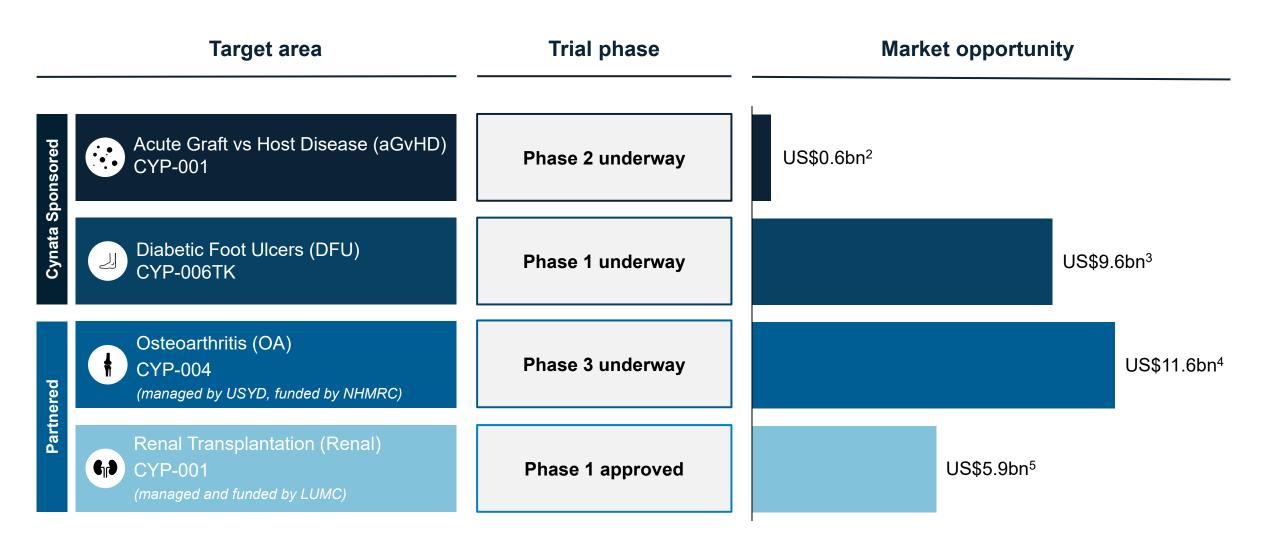
Combined market opportunity of clinical trials underway and in planning is ~US\$28bn¹

Well-funded to complete planned clinical trials with ~A\$16m in cash²

OA and renal trials fully funded by external partners



Cynata has an advanced and diverse clinical pipeline

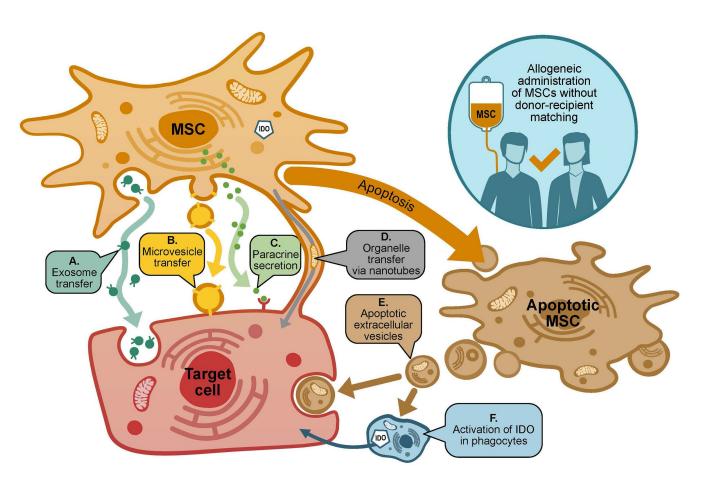




Why Mesenchymal Stem Cells (MSCs)?

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"

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



Medical Applications of Mesenchymal Stem Cells

MSCs are the subject of intense development worldwide

Promising potential as medical treatments

MSCs are being developed as potential therapeutic products for diseases including:

- ✓ Diabetes (type 1 and type 2)
- ✓ Heart disease; heart attack
- ✓ Circulatory disease
- ✓ Chronic skin wounds; skin burns
- ✓ Inflammatory joint disease, e.g., arthritis
- ✓ Respiratory disease
- ✓ Stroke
- ✓ Spinal cord injury
- ✓ Liver disease

Global interest in MSCs continues to grow

>1,200¹

Clinical trials of MSCs have been initiated in the past decade

Approved

MSC products are already marketed in **Asia** (including **Japan**) and **Europe**

This widespread interest brings into sharp focus the need for a robust, scalable and economic manufacturing process

Cynata's uniquely scalable and consistent process overcomes challenges associated with conventional methods of MSC production





Manufacturing



Cynata's process utilizes induced pluripotent stem cells (iPSCs)



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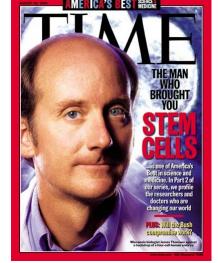
- iPSCs are mature cells from adult donors that are reprogrammed to be capable of:
 - effectively limitless proliferation in cell culture
 - differentiation into any adult cell type (including MSCs)

Thus an ideal starting material for cellular production processes



- iPSCs are derived from adult cells, avoiding ethical controversy associated with embryonic stem cells
- Cynata is the most advanced company worldwide developing iPSC-derived cell therapies
- Generation of human iPSCs first reported by two independent groups almost simultaneously:
 - Shinya Yamanaka, Kyoto University (awarded Nobel Prize in 2012)
 - James Thomson, University of Wisconsin-Madison





Cymerus™ iPSC-based manufacturing process

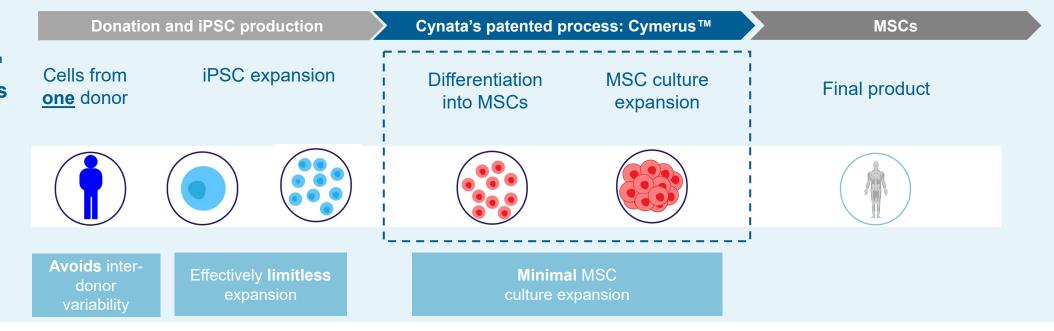
Conventional process

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

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

Cynata's Cymerus™ iPSC-based process

Avoids inter-donor variability and need for extensive MSC expansion





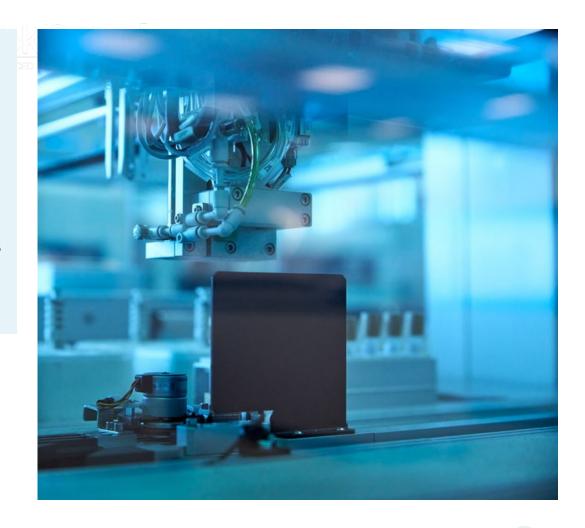
Strategic partnership with Fujifilm provides commercial benefits

Cynata executed a Strategic Partnership Agreement with Fujifilm, with Fujifilm involved in the path to market¹

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







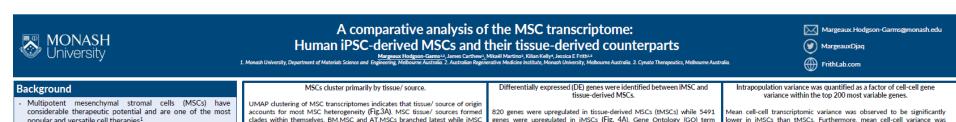


Preclinical Data



MSCs from different sources have different properties

and UC.MSCs branched earlier indicating comparatively less similarity (Fig.3B).



BM.MSC UC.MSC ATMSC

Key Findings include:

Source is the primary driver of MSC heterogeneity (variability)

Traditionally sourced from tissue donations, clinical translation

is affected by donor-dependence and significant batch-batch,

- 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 tissuederived MSCs, and significantly less intra-population variability

AT.MSC 1.

AT.MSC 2

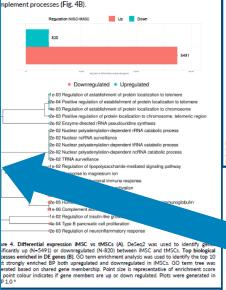
 Cymerus MSCs successfully bypass much of the inherent variability that affects tissue-derived MSCs

transcriptomes from 72,709 individual MSCs sequenced at a

depth of >100.000 reads/ cell.

genes were upregulated in iMSCs (Fig. 4A). Gene Ontology (GO) term enrichment analysis was used to query DE genes for enriched Biological Processes (BP). BP including telomere maintenance and RNA catabolism processes were enriched in genes upregulated in iMSCs, while genes

in regulated in iMSCs were enriched for humoral immune response and



gene markers driving separation of iMSCs.

1.16% of variation between MSC tissue/sources. PCA loading identified nd LIN28B was found to drive separation of iMSCs from tMSCs, with

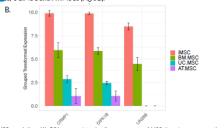
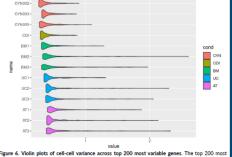


Figure 5. PCA of MSC populations (A). PCA was used to visualise components of MSC tissue/ source separation Populations are coloured by tissue/ source and marker shape indicates iMSC vs tMSC grouping. PCAtools Package was used to identify loading genes driving iMSC/ tMSC separation. Expression of major loading genes CRMP! DIPK1B, and LIN28B (B). Expression of loading genes is presented as bar plots with MSC tissue/ source indicated by

lower in iMSCs than tMSCs. Furthermore, mean cell-cell variance was comparable between iMSC populations while tMSC populations showed significant donor-donor differences.



variable genes were identified using DeSeq2. Gene-wise variance from the median was calculated for each cell and single-cell. Variance scores (x) are presented as a violin plot. Tissue/ source is indicated by colour. Plot was produced using Seurat.

Conclusions

Key Findings:

- 1) Tissue/ source is the primary driver of MSC heterogeneity.
- 2) iMSCs are most closely related to UC.MSCs, while BM.MSCs and MSCs are more closely related to each other.
- from tissue-derived MSCs by the upregulation of esses linked to telomere maintenance and RNA I the downregulation of humoral immune respons and comp
- 4) iMSCs exhibit less batch-batch heterogeneity than tissue-derived MSCs, furthermore they also exhibit significantly less intra-

transcriptomes at a single-cell level, allowing us to develop a better understanding of the sources of MSC heterogeneity and improve predictability of clinical outcomes. Moreover, this study confirms that iMSCs successfully bypass much of the inherent heterogeneity that affects the clinical application of tissue-derived MSCs, validating

References and Acknowledgments

- Wilson, A., Hodgson-Garms, vo., rive., between the repy. Front. Immunol. 10 (2019).
 Dominici, M. et al. 2006. Minial criteria for defining multipotent models of the results of the result Wilson, A., Hodgson-Garms, M., Frith, J. E. & Genever, P. Multiplicity of mesenchymal stromal cells: Finding the right route

Australian Govt. RTP Stipend

Monash University Dot, of Materials Science and Engineering







Efficacy of Cymerus MSCs vs conventional MSCs in AMI model

Key results from a pre-clinical study in rats illustrate that Cymerus MSCs provide better therapeutic effects compared with bone marrow MSCs derived via conventional manufacture

Context

- Pre-clinical rat model of myocardial ischemia-reperfusion (heart attack)
- Rats were randomly assigned to (i) Cymerus MSC group, (ii) Bone Marrow (BM) MSC group and (iii) control



	Cymerus MSCs	BM-MSCs (conventional MSCs)
Left Ventricle (LV) function (Measured by fractional shortening)	Significantly improved (P = 0.01)	Did not significantly improve (P = 0.63)
Number of capillaries in peri-infarct zone	High (compared to control) (P = 0.001)	High (compared to control) (P = 0.003)
Arteriogenesis in the peri-infarct zone (increase in the diameter of arterial vessels)	Enhanced arteriogenesis vs. controls and BM MSCs (P = 0.01)	Did not enhance arteriogenesis

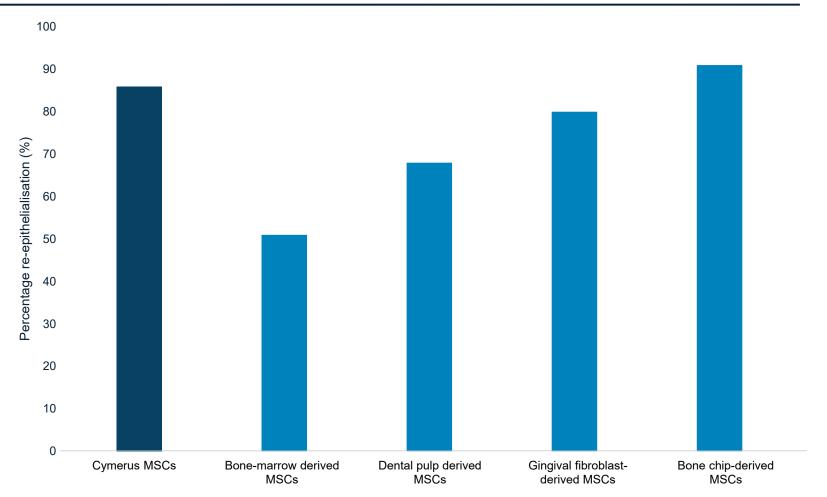
Explanation

- The beneficial effects of MSC transplantation are attributable to the capacity of MSCs to secrete a wide range of cytokines, chemokines and growth factors.
- The degree of expression of a number of relevant cytokines by Cymerus MSCs was **2-4x higher** than by BM-MSCs, which may explain the enhanced neovascularisation exhibited by Cymerus MSCs.



Efficacy of Cymerus MSCs vs conventional MSCs in DFU model

Preclinical model of Diabetic Wounds demonstrate efficacy of Cymerus MSCs



Key findings

- Primary outcome measure was the extent of re-epithelialisation (skin restoration) of the diabetic wound surface after 3 days, which is the speed of wound healing
- Comparator MSCs were derived using conventional manufacturing
- Cymerus MSCs resulted in significantly greater reepithelialisation (86%) compared with bone marrow MSCs (51%)
- Although gingival fibroblasts and bone chip MSCs produced similar results, there are major challenges associated with producing clinicalgrade cells from these sources at commercial scale



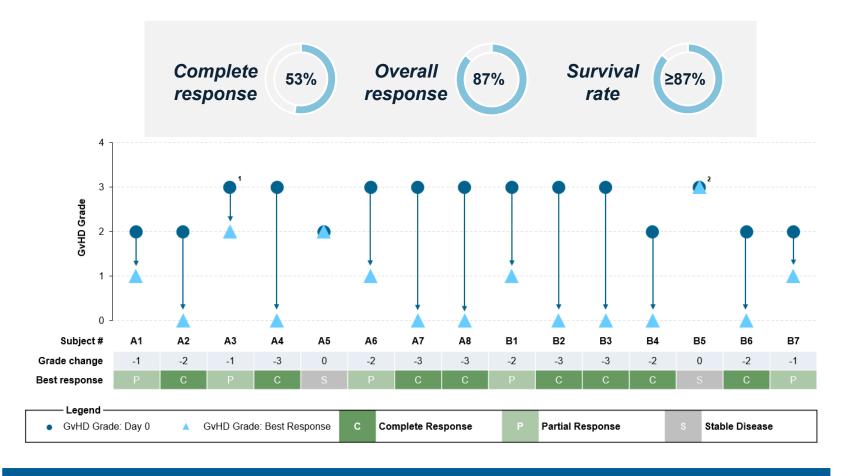


Clinical Trials



GvHD Phase 1: Primary Evaluation Period (up to Day 100)

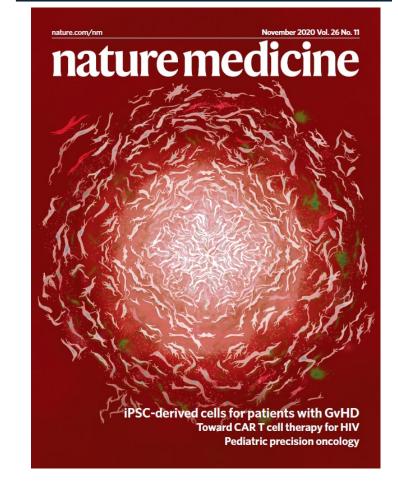
The first completed clinical trial of an iPSC-derived product



No treatment-related serious adverse events or safety concerns identified

- Subjects received 1x10⁶ cells/kg (max 1x10⁸ cells) or 2x10⁶ cells/kg (max 2x10⁸ 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)

Published in Nature Medicine³



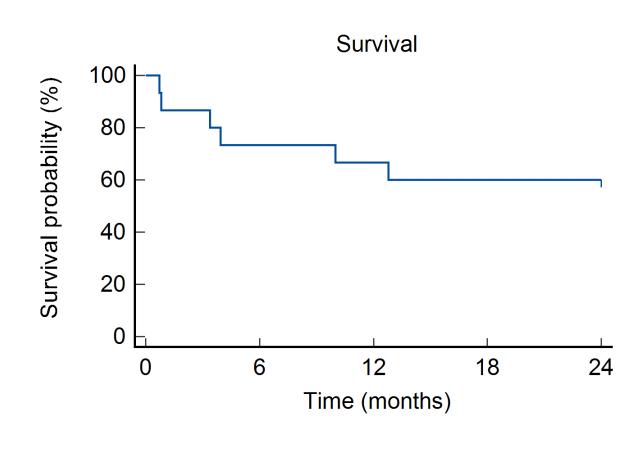
GvHD Phase 1: 2-Year Overall Survival

2-year overall survival (OS) rate in subjects treated with CYP-001 was 60% (9/15 subjects)

- Compares very favourably with previously reported outcomes in SR-aGvHD studies:
 - In the Ph 3 study of ruxolitinib OS at 18 months was just 38% in the ruxolitinib group and 36% in the "best available therapy" control group¹

(2-year OS was not evaluable; ruxolitinib is approved by FDA & EMA for SR-aGvHD)

 Several studies of MSCs from other sources in SR-aGvHD have reported 2-year OS rates ranging from 0-40%²⁻⁸





^{1.} Zeiser R, et al. N Engl J Med (2020) 382(19):1800–10.

^{2.} Introna M, et al. Biol Blood Marrow Transplant (2014) 20:375–81.

B. Prasad VK, et al. Biol Blood Marrow Transplant (2011) 17(4):534–41.

^{4.} Ringden O, et al. Transplantation (2006) 81:1390-7.

^{5.} Le Blanc K, et al. Lancet (2008) 371:1579–86.

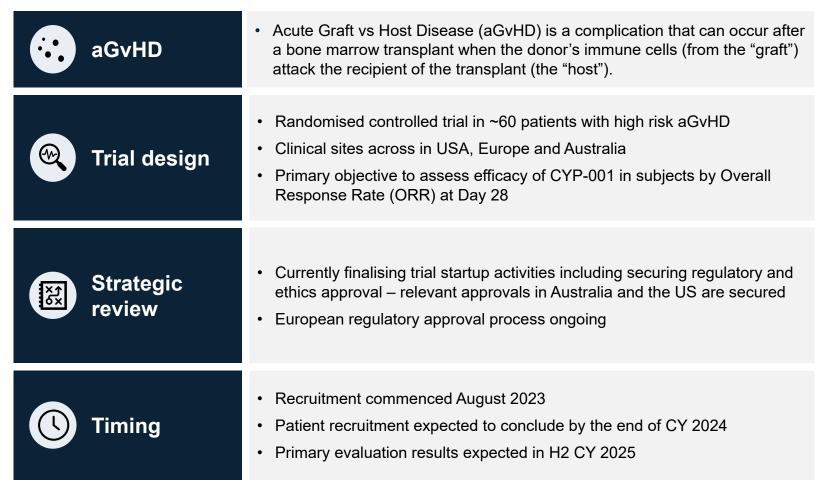
Arima N, et al. Cytotherapy (2010) 12:265–8.

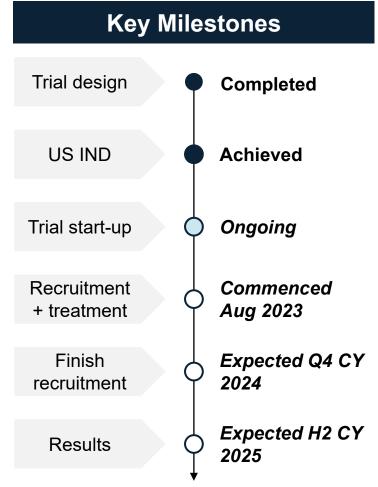
^{7.} Von Dalowski, et al. Stem Cells (2016) 34:357–66.

^{8.} Dotoli GM, et al. Bone Marrow Transplant (2017) 52:859–62.

aGvHD | Phase 2 clinical trial

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

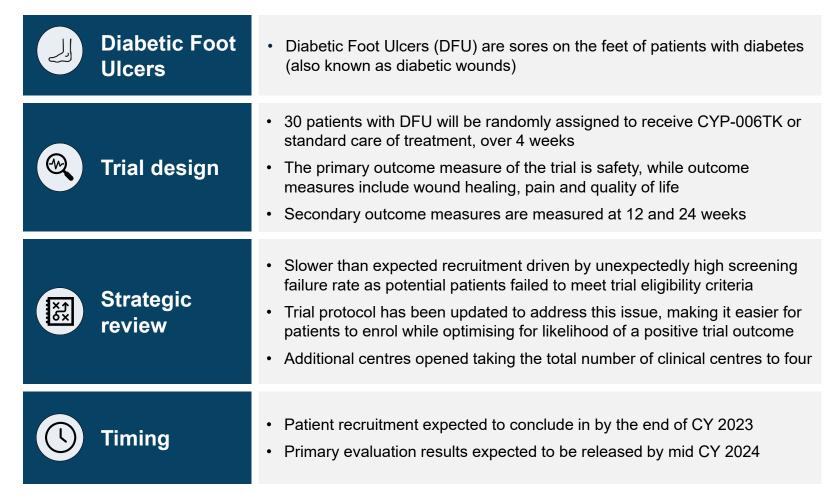






DFU | Phase 1 clinical trial

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







DFU | Initial clinical update

A review has been conducted of the first 6 patients who have completed at least the 28 day follow-up



- Three patients were randomised to Group 1 and were treated with CYP-006TK dressings for 4 weeks (dressings changed twice a week) and then reverted to standard care (SoC)
- Three patients were randomised to Group 2 and were treated with SoC throughout the study



- Clinical assessment of ulcers
- Collection of 3-dimensional clinical photographs utilizing a stereovision camera and image management software to conduct 3D surface area calculations followed by blinded, independent quantitative assessments of the data by QuantifiCare. This is more sensitive and appropriate than 2D assessment *
- Monitoring of tolerability and adverse events



- Average ulcer size notably decreased in the three patients treated with CYP-006TK compared with patients receiving SoC
- Average rate of ulcer healing was faster in patients treated with CYP-006TK compared with patients receiving SoC
- The study treatment was well tolerated and safe
- Full trial has not yet completed and final results may vary

Initial results are encouraging; suggestive of safety and efficacy of CYP-006TK in chronic wounds



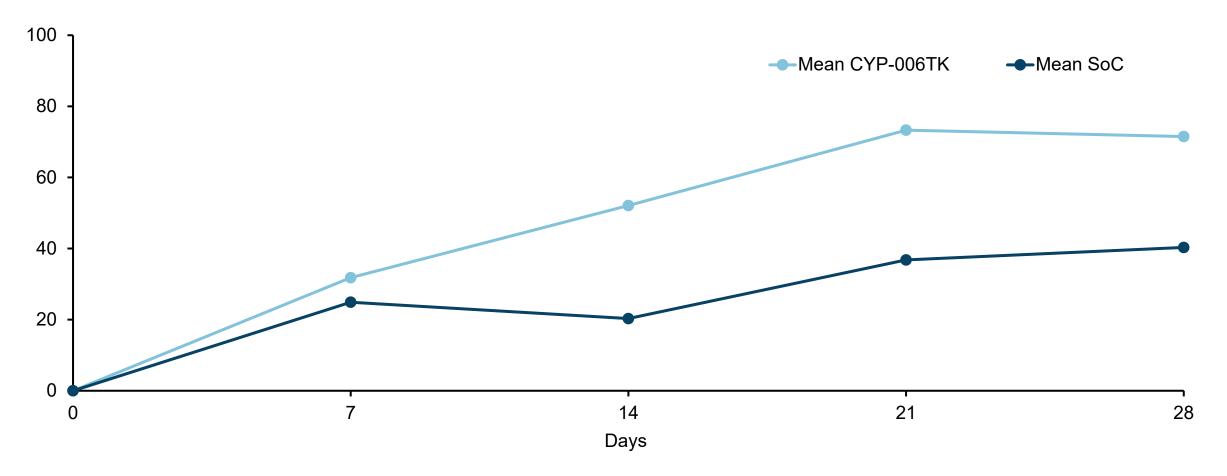
DFU | Largest ulcer at baseline from each group



DFU | CYP-006TK treatment data

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

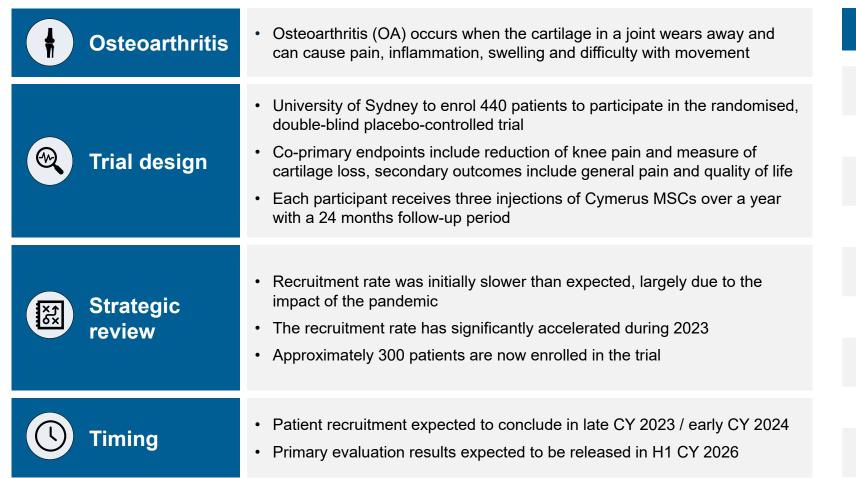
Mean % ulcer surface area healed over time (%)1; n=6





OA | Phase 3 clinical trial¹

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

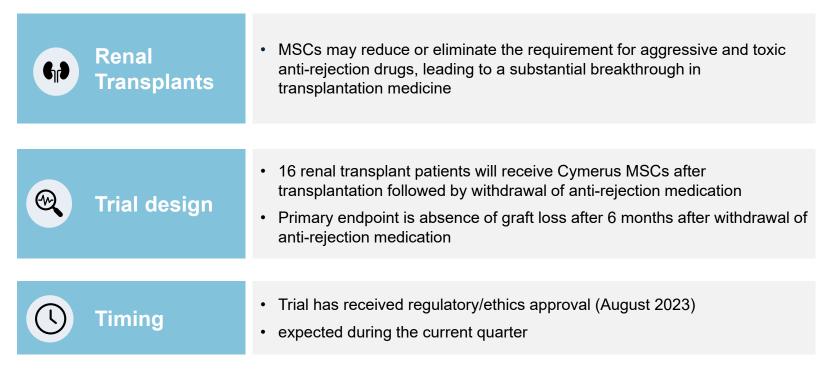


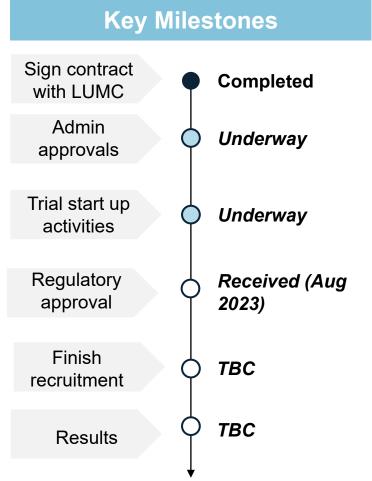




Renal | Phase 1 clinical trial

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









Corporate Information



Board & Senior Management

Highly skilled and experienced senior leadership team with decades of experience



Dr Kilian KellyChief Executive Officer &
Managing Director

- 20+ years' experience in biopharma R&D
- Previous roles at Biota Pharmaceuticals, Mesoblast, Amgen & AstraZeneca



Dr Geoff BrookeIndependent Non-Executive Chairman

- 30+ years' experience in the healthcare investment industry
- Founder and MD of Medvest Inc and GBS Venture Partners



Dr Paul WottonIndependent Non-Executive Director

- 30+ years' experience in senior positions of life sciences companies
- Previously President and CEO of Ocata Therapeutics, Inc



Ms Janine Rolfe
Independent Non-Executive Director

- 20+ years legal, governance and management experience across multiple sectors
- Founder of Company Matters



Dr Darryl MaherIndependent Non-Executive Director

- Former Vice President, R&D and Medical Affairs at CSL Behring
- Former President of Australian
 Pharmaceutical Physicians Association
 and Director of Vaccine Solutions



Dr David AtkinsNon-Executive Director

- 25+ years' leadership experience in broad range of businesses including Johnson & Johnson and Danaher
- Managing Partner at BioScience Managers



Dr Jolanta Airey
Chief Medical Officer

- 25+ years' experience in respiratory, rheumatology, dermatology, biologicals and listed companies
- Previously Director, Translational Development at CSL



Mr Peter Webse Company Secretary

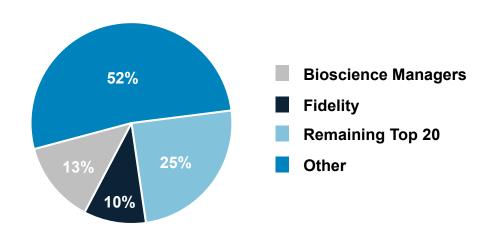
- 25+ years company secretarial experience
- MD of Platinum Corporate Secretariat Pty Ltd



Corporate overview

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

Shareholder distribution



Financial information

Share price (14 September 2023)	A\$0.13
Shares on issue	179m
Market capitalisation	~A\$23m
Cash ¹	~A\$16m

Substantial shareholders (>5%)



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.



10.0%

Fidelity International is a world leading investment and asset management firm that invests A\$556.7 billion globally on behalf of clients in Asia-Pacific, UK, Europe, the Middle East and South America.



Investment summary

Next generation stemcell 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



Important information

Summary information

This Presentation contains summary information about Cynata Therapeutics Limited and its subsidiaries (CYP) which is current as at 14 September 2023. 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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Financial data

All financial information in this Presentation is in Australian currency (A\$) unless otherwise stated. This Presentation contains historical financial information based on the Company's results for the quarter year to June 2023. This information is disclosed in the 4C report lodged with ASX on 26 July 2022. Any discrepancies between totals and sums of components in tables and figures in this Presentation are due to rounding.

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This Presentation contains certain 'forward looking statements', which can generally be identified by the use of forward looking words such as 'expect', 'anticipate', 'likely', 'intend', 'should', 'could', 'may', 'predict', 'plan',

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