

ASX ANNOUNCEMENT 22 November 2022

#### Chairman's 2022 AGM Address

Good morning and welcome to this year's Annual General Meeting of Cynata Therapeutics Ltd. I am Geoff Brooke, the Non-Executive Chairman, and I am joined today by Dr Ross Macdonald, the Managing Director and Chief Executive Officer of Cynata; and the Cynata Non-Executive Directors including Drs Paul Wotton, Stewart Washer, Darryl Maher, and Ms Janine Rolfe. I would also like to acknowledge our Chief Operating Officer, Dr Kilian Kelly, Chief Medical Officer, Dr Jolanta Airey, and Company Secretary, Peter Webse, who are also present with us today.

It is my pleasure to address you all today and provide an overview of Cynata's progress over the last twelve months. Following my address, I will invite Ross, Kilian, and Jolanta to provide a detailed overview of Cynata's clinical program and outlook.

The financial year was marked by unique challenges with rising interest rates, supply chain issues, and conflict in Ukraine leading to increased market volatility and risk aversion from investors, particularly impacting the biotechnology sector. Despite weakness in the equity markets, Cynata continued to advance its position and made strong progress towards its clinical and commercial goals. Highlights for the financial year include:

- 1. We are actively recruiting and treating patients in two clinical trials: a phase Ib in diabetic foot ulcers; and a phase 3 trial in osteoarthritis;
- 2. We signed a Strategic Partnership Agreement and Manufacturing Services Agreement with Fujifilm and received a US\$5m payment under that new agreement;
- 3. We regained development and commercialisation rights for CYP-001 for GvHD;
- 4. We received clearance from the US FDA for an IND application for a phase 2 trial in acute Graft Verus Host Disease, otherwise known as aGvHD;
- 5. We strengthened our team with the strategic hire of Dr Jolanta Airey as our Chief Medical Officer; and
- 6. We continued to strengthen our broad portfolio of patents and patent applications through the grant of several important patents in key jurisdictions such as the United States.

The commercial opportunity for mesenchymal stem cell (MSC) products is compelling, with a growing body of evidence substantiating their use as a therapeutic modality across a broad range of diseases representing major medical challenges. Regulatory bodies in major global markets are becoming more comfortable with cell therapies, and our own experience with the USA FDA is an example of that.

Cynata is uniquely positioned to capitalise on the advancement of MSC therapies through our proprietary Cymerus™ platform - the most advanced single donor derived MSC manufacturing technology globally. Our Cymerus technology overcomes inherent challenges associated with conventional methods of manufacturing MSCs by leveraging Nobel Prize winning induced pluripotent stem cells, or iPSCs, as a starting material. The iPSCs are used as part of the Cymerus™ MSC manufacturing process to produce virtually unlimited quantities of consistent, potent MSCs from a single donor and single donation.

In September 2021, Cynata signed a new Strategic Partnership Agreement and Manufacturing Services Agreement with Fujifilm. The new partnership allows Cynata to leverage Fujifilm's world-leading production capabilities to



produce MSC products, eventually at a commercial scale, while allowing Cynata to retain the commercial and developmental rights to our CYP-001 product for acute GvHD. Cynata also received a US\$5m payment as part of the new partnership. In light of this, we made the decision to divert resources towards pursuing a US development strategy and conducting a phase 2 trial in aGvHD in the US.

We are extremely proud that Cynata's Investigational New Drug, or IND, application for a proposed Phase 2 trial in acute GvHD was cleared by the US Food and Drug Administration, or FDA. This important achievement is a milestone for Cynata as it confirms the quality of our data package and provides a gateway into the US, which is the world's largest healthcare market.

The upcoming GvHD trial contributes to Cynata's strong clinical portfolio which includes the ongoing clinical trials in osteoarthritis, which is a phase 3 study, and trial in diabetic foot ulcers. Cynata is also progressing several other indications through partnering opportunities which exhibit large market potential and are backed by supportive preclinical data. One example of this is our recently announced collaboration with the Leiden University Medical centre for a new clinical trial investigating Cymerus MSCs as a treatment for renal graft rejection. The Leiden University is funding the conduct of the trial, providing Cynata shareholders with an additional clinical target.

We have continued to strengthen our management team with the strategic hire of Dr Jolanta Airey as Chief Medical Officer earlier in the financial year. Dr Airey brings to the role over 25 years of experience in companies such as CSL and will help drive Cynata's clinical development and commercialisation strategy. Dr Airey has already made a significant contribution in her short time with Cynata, and we look forward to continuing to leverage her insights and knowledge to monetise our portfolio.

Further, we were delighted to appoint Ms Janine Rolfe to the Cynata Board as an independent Non-Executive Director subsequent to the financial year. Ms Rolfe's extensive experience in M&A, governance and growth businesses will provide added depth to the Company at a very exciting time in our maturation.

Cynata is well placed to progress development across existing clinical programs and to drive shareholder value, with approximately \$18m in cash at the end of the most recent quarter.

On behalf of the Board, I would like to thank my fellow directors and extend my gratitude to our staff for their commitment to our Company. Our achievements this year are a testament to our exceptional team, and I am confident that they will continue to execute on our organisational goals in the coming financial year.

I would like to thank Ross and the management team for their exceptional leadership which has allowed us to make impressive operational progress despite a tumultuous market backdrop.

Finally, I would like to thank all our shareholders for their support as we continue to advance our Cymerus technology and develop scalable cellular therapeutic products to treat serious and debilitating diseases.

**Dr Geoff Brooke** 

**Cynata Chairman** 

-ENDS-

Authorised for release by Dr Ross Macdonald, Managing Director & CEO

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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<sup>™</sup>, a proprietary therapeutic stem cell platform technology. Cymerus<sup>™</sup> 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. Planning for a Phase 2 clinical trial in GvHD under a cleared US FDA IND is presently underway. Clinical trials of Cymerus products in osteoarthritis (Phase 3) and diabetic foot ulcers (DFU) are currently ongoing. In addition, Cynata has demonstrated utility of its Cymerus technology in preclinical models of numerous diseases, including the clinical targets mentioned above, as well as 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

**AGM Presentation** 22 November 2022



## **Key Highlights: FY22**

#### **Clinical & Pre-clinical**











Progress toward partnering clinical pipeline opportunities









- 1. aGvHD: Acute Graft vs Host Disease
- 2. Post FY22 event, LUMC: Leiden University Medical Centre
- 3. IPF: idiopathic pulmonary fibrosis

## **Key Highlights: FY22**

### **Commercial & Corporate**



Signed a Strategic
Partnership
Agreement (SPA) and
Manufacturing
Services Agreement
with Fujifilm: tech
transfer advancing
well



Regained
development and
commercialisation
rights to CYP-001 for
GvHD



Received payment of US\$5m as part of the SPA



Strengthened IP portfolio, with patents granted in the US, Canada, Russia, China and Japan



Dr Jolanta Airey appointed as Chief Medical Officer to drive Cynata's advanced clinical product pipeline



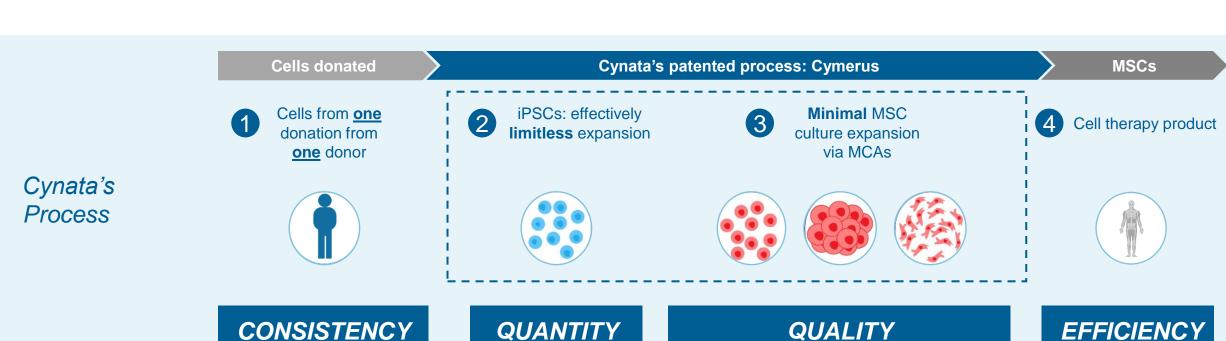
## Conventional vs. Cynata's Cymerus MSC manufacturing process

Cells from multiple donors

2 Limited quantity of MSCs isolated

3 Significant MSC expansion required

4 Cell therapy product





Conventional

**Processes** 

## Competitive strengths of the Cymerus platform

Cymerus technology elegantly addresses each of the major challenges faced by existing approaches to manufacturing MSCs, facilitating scalable and reproducible production at low cost



### **Conventional manufacture**



**Potency** 

Mandatory requirement to expand MSCs isolated from donors causes a **dramatic reduction in potency** while compromising scalability



Consistency

Reliance on multiple donors and donations compromises product consistency while posing logistical, practical and regulatory challenges



**Cost of treatment** 

Need for multiple/higher doses of product results in **high COGS** 



**Cymerus platform** 



Expansion at the iPSC stage ensures fresh, highly potent MSCs following final differentiation step



Same starting material for every batch



CYP-001 required **substantially lower number of doses** in aGvHD



### Cynata's technology addresses FDA concerns

Cynata's Cymerus process actively addresses current inefficiencies of MSC manufacturing, de-risking clinical development in the US

#### Traditional MSC manufacturing is sub-optimal

Other MSC therapy (also targeting GvHD) was not approved by the FDA due to substantial functional variability between lots.

"Substantial functional heterogeneity has been observed between MSC batches derived from different donors and expanded using different tissue culture conditions or duration, even though all of these batches meet the ISCT criteria for MSCs."

- Excerpt from **FDA ODAC Briefing** document for 13 August 2020

#### Cynata's technology is optimal



Consistency: No inter-donor variability as only one donor is required (single blood donation)



Scalability: Cynata can produce essentially limitless quantities of MSCs from initial donation



Potency: iPSC-derived manufacturing process does not require excessive culture expansion of MSCs

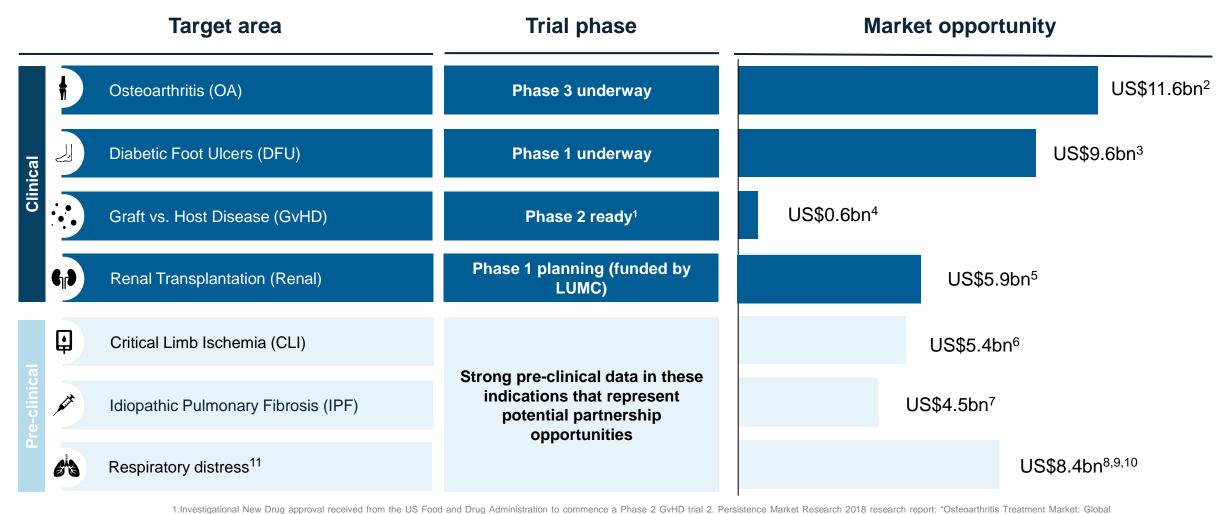


FDA advisory meeting observations to be leveraged to maximise chance of FDA approval



## Cynata has an advanced and diverse product pipeline

Cynata is targeting attractive market opportunities across a range of indications





Industry Analysis (2012-2016) and Forecast (2017-2025) (Reflect OA market by 2025); 3. Zion Market Research, 2019 (represents global treatment market in 2025); 4. Global Graft versus Host Disease Market 2019-2029 (Reflects forecast market in 2026); 5. Organ Transplant Immunosuppressant Drugs Market in 2026, Grand View Research, Inc.,2019; 6. Transparency Market Research, 2020 (Reflect global DFU treatment market by 2027). 7. HealthcareAnalyst Inc, 2019 (represents global market by 2025); 8. Vasomune Therapeutics company announcement, 2018 (Reflects ARDS global market opportunity of US\$2.5bn) 9. GlobeNewswire, 2020 (Represents CRS global market opportunity of US\$5.9bn in 2026)

11. MEND clinical trial concluded following strategic review of clinical pipeline as announced 12 August 2022

## **GvHD | Ground-breaking Phase 1 clinical trial results**

Cynata's phase 1 GvHD trial met all safety and efficacy endpoints and broke ground by being the world's first completed clinical trial of an allogeneic iPSC-derived product

Key results<sup>1</sup> demonstrate safety and efficacy of Cymerus MSCs

Published in prestigious journal<sup>2</sup>

All endpoints achieved (Day 100) Complete response



Overall response



Survival rate



Efficacy endpoints were the same required in a phase 3 trial

Response rates were higher than what we expect would be required in phase 3 (to support marketing approval)

Outstanding follow-up results (Two year)

Overall survival rate: Cynata MSCs



Compares favourably with other results

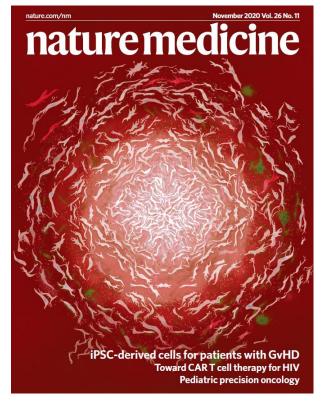


Standard of care



Other MSC products

Nature medicine is the preeminent peerreviewed medical journal worldwide





### aGvHD | Phase 2 clinical trial in aGvHD

With a cleared IND from the FDA Cynata expects to commence a clinical trial in acute GvHD by early 2023



aGvHD

Acute Graft vs Host Disease (aGvHD) remains a common complication
of allogeneic hematopoietic stem cell transplants (e.g., bone marrow
transplants) when the donor's immune cells (from the "graft") attack the
recipient of the transplant (the "host").



Unmet medical need

- The only first line treatment is corticosteroids, which is only effective in ~50% of patients
- Patients who fail current treatments face mortality rates in excess of 90%



Validated by Phase 1 results

 Cynata's phase 1 GvHD trial met all safety and efficacy endpoints and broke ground by being the world's first completed clinical trial of an allogeneic iPSC-derived product



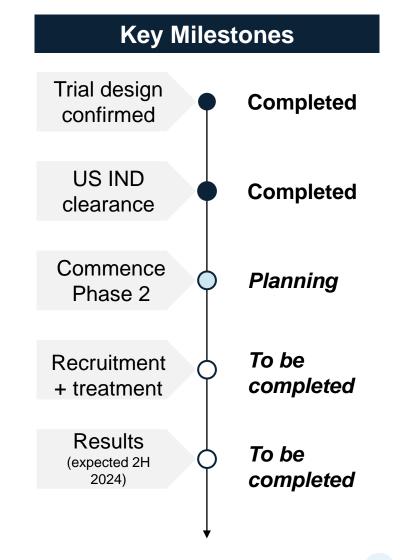
US FDA approval

 US Food and Drug Administration (FDA) has cleared Cynata's Investigational New Drug (IND) application for a phase 2 clinical trial of CYP-001 in aGvHD



Trial design

- Proposed trial will seek to recruit ~60 patients with high risk aGvHD at clinical centres in a number of countries, including US and Australia
- Final start-up activities underway in concert with CRO IQVIA





## **DFU | Phase 1 clinical trial update**

Enrolment opened in December 2021 with completion expected in 1H23



# Diabetic Foot Ulcers (DFU)

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



Huge Market Opportunity

- >400m diabetics globally, with DFU estimated to occur in ~15-25% of patients during their lifetime<sup>1</sup>
- Global market is estimated to be ~US\$10bn<sup>2</sup>



Strong preclinical data

- · Positive efficacy data of MSCs in a preclinical model
- Cymerus MSCs achieved 86% skin restoration after three days



Unique competitive positioning

- Secured a worldwide exclusive licence agreement with TekCyte to a novel polymer-coated dressing technology to deliver MSCs topically
- CYP-006TK: polymer-coated silicon dressing seeded with Cymerus MSCs



Trial design

• 30 patients with DFU will be randomly assigned to receive CYP-006TK or standard care of treatment, over 4 weeks



Timing update

 Recruitment expected to finish by mid way through 2023 with results released by the end of 2023





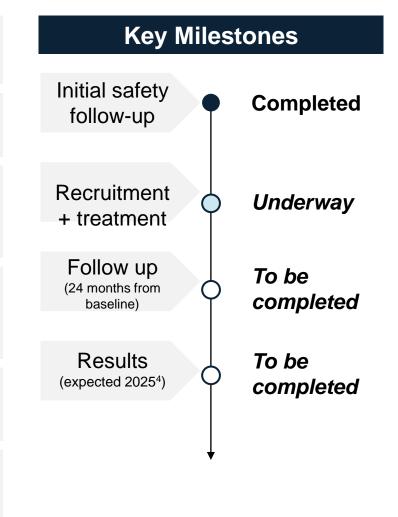
Diabetics Australia (estimated ~415m adults with diabetes in 2015); Mutluoglu M, Uzun G, Turhan V, Gorenek L, Ay H, Lipsky BA. How reliable are cultures of specimens from superficial swabs compared with those of deep tissue in patients with diabetic foot ulcers? J Diabetes Complications. 2012 May-Jun;26(3):225-9

<sup>2.</sup> Estimated DFU market (Source: Transparency Market Research, 2020 (Reflects global DFU treatment market by 2027)).

## Osteoarthritis-SCUIpTOR<sup>1</sup> | Phase 3 clinical trial update

Clinical trial underway, sponsored by the University of Sydney and funded by an NHMRC project grant







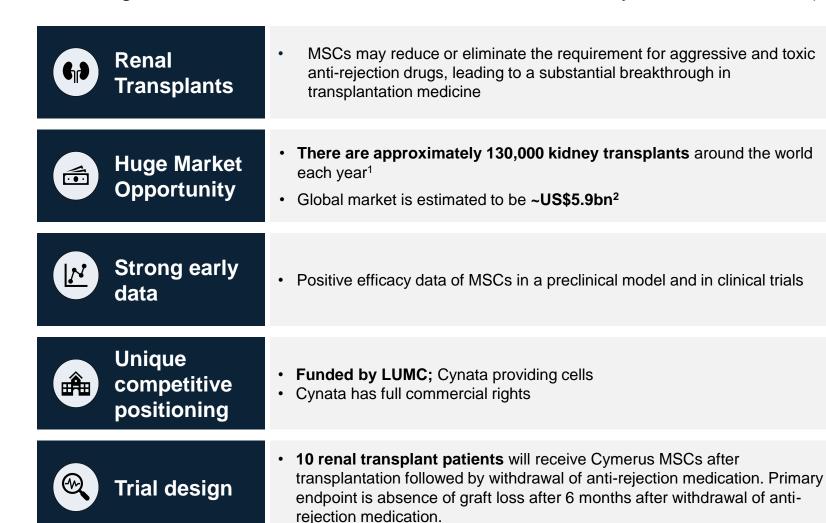
update

- . Clinical trial entitled Stem Cells as a symptom and strUcture-modifying Treatment for medial tibiofemoral OsteoaRthritis: a randomised placebo-controlled trial (SCUIpTOR)
- 2. Reflects OA market by 2025; Persistence Market Research 2018 research report: "Osteoarthritis Treatment Market: Global Industry Analysis (2012-2016) and Forecast (2017-2025).
- 3. NHMRC: National Health and Medical Research Council
- Note: Timing is dependent on a number of external factors (including COVID-19 restrictions)

of Sydney based on the current recruitment rate

## Renal | Phase 1 clinical trial update

Funding to conduct trial secured from Leiden University Medical Center (LUMC)







- . https://www.statista.com/statistics/398645/global-estimation-of-organ-transplantations/
- 2. Organ Transplant Immunosuppressant Drugs Market in 2026, Grand View Research, Inc.,2019.

## **Near term catalysts**

Cynata is in a strong position to advance its proprietary Cymerus platform technology

#### End 2022 + 1H 2023

- ✓ DSMB review in DFU trial
- ☐ Commence phase 2 trial in aGvHD
- ☐ Complete recruitment of 30 patients in DFU clinical trial

### **During 2H 2023**

- ☐ Complete recruitment of 440 patients in U Syd phase 3 osteoarthritis trial
- ☐ Announce DFU clinical trial results
- ☐ Commence renal transplant clinical trial with LUMC

#### **Ongoing**

- ☐ Further clinical trial results: expecting ongoing newsflow as our clinical pipeline matures and our broad pre-clinical pipeline enters clinical trials
- ☐ Progress commercial discussions and execute further corporate partnership(s)





### **Board & management**

Highly skilled and experienced senior leadership team with decades of experience



**Dr Geoff Brooke** Chairman

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



**Dr Ross Macdonald**Managing Director / CEO

- 30+ years experience and a track record of success in pharmaceutical and biotechnology businesses
- Previously CEO of Hatchtech



**Dr Kilian Kelly**Chief Operating Officer

- 15+ years experience in biopharma research & development
- Previously Senior Director, Drug Development at Biota Pharmaceuticals, VP, Regulatory and Clinical at Mesoblast



**Dr Jolanta Airey** Chief Medical Officer

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



Ms Janine Rolfe, GAICD Non-Exec Director

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



**Dr Paul Wotton**Non-Exec Director

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



**Dr Stewart Washer** Non-Exec Director

- 20+ years of CEO and Board experience
- Chairman of Orthocell (ASX:OCC) and Emyria (ASX:EMD), Director of Botanix Pharmaceuticals (ASX:BOT).



**Dr Darryl Maher** Non-Exec Director

- · Vice President of R&D and Medical Affairs at CSL Behring
- He was a **former President** of the Australian Pharmaceutical Physicians Association and a director of Vaccine Solutions



**Mr Peter Webse**Company Secretary

- 23+ years company secretarial experience
- MD of Platinum Corporate Secretariat Pty Ltd, providing company secretarial and other services



### **Investment 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 overcomes

overcomes suboptimalities in conventional MSC manufacturing



Positive pre-clinical and clinical data

supporting versatility and efficacy of Cynata's MSCs

**Validation** through strategic partnership with FUJIFILM



Rich clinical pipeline:

- Diabetic Foot Ulcers
- Osteoarthritis (phase 3)
- Renal transplantation to commence in 2023<sup>1</sup>
- Phase 2 aGvHD trial to commence in 2023<sup>1</sup> under cleared IND



Combined market opportunity of clinical trials underway and in planning is ~A\$38bn



Multiple pathways to commercialisation, including strategic partnering



### **Important information**

#### **Summary information**

This Presentation contains summary information about Cynata Therapeutics Limited and its subsidiaries (CYP) which is current at 21 November 2022. 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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