

ASX ANNOUNCEMENT 16 November 2021

#### Chairman's 2021 AGM Address

Good morning everyone and welcome to the 2021 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, as well as our Non-Executive Directors including Drs Paul Wotton, Stewart Washer and Darryl Maher. 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.

I am delighted to address you all and provide an update on Cynata's exciting achievements over the last twelve months. Following my address, Ross and Kilian will present a more detailed overview of Cynata's clinical program and upcoming catalysts.

While the impact of COVID-19 continued to dominate headlines globally, it was encouraging to see Cynata flourish and achieve multiple clinical development milestones this year, demonstrating meaningful progress and cementing our position in the regenerative medicine sector. In what has been an exciting FY21, Cynata has achieved many significant highlights:

- 1. the company has commenced and advanced recruitment in the Phase 3 osteoarthritis trial in association with the University of Sydney;
- 2. similarly commenced and expanded recruitment in its MEND trial in respiratory distress;
- 3. received ethics approval to begin a clinical trial in patients with diabetic foot ulcers (DFU);
- 4. signed a worldwide exclusive licence agreement with TekCyte Pty Ltd to utilise its advanced wound dressing technology for the planned DFU trial;
- 5. and raised approximately \$18.3m in capital via an institutional placement and non-renounceable entitlement offer, led by a \$10m cornerstone investment from renowned healthcare investor, BioScience Managers. The funds raised place the company in a strong position going forward, with a robust pipeline across multiple therapeutic targets.

The market for mesenchymal stem cell (MSC) products continues to be highly attractive, with a growing body of evidence supporting the role of MSCs in modulating the immune system and in tissue repair and regeneration in a range of devastating diseases. We are focused on generating pre-clinical and clinical data to drive value and inform our target indications, and this year our further studies demonstrated that Cynata's proprietary Cymerus™ MSCs to be efficacious in preclinical rodent models of idiopathic pulmonary fibrosis and myocardial infarction (otherwise known as heart attack). Currently, Cynata's ongoing, planned and potential future clinical trials amount to a ~\$46bn market opportunity, due to the broad applicability of MSCs. MSC products are now on the market in Japan and in Europe and as more MSC-based therapies approach commercialisation, concern continues to turn towards the production challenges associated with manufacturing commercially viable quantities of MSCs. This concern was amply demonstrated in recent commentary from the US FDA.

Pleasingly, Cynata's technology addresses these manufacturing challenges with the most advanced technology in the therapeutic MSC space. Through the considered strategic investment in the Cymerus™ technology, the Company is well placed to advance its clinical studies with a unique manufacturing platform that can produce essentially unlimited quantities of consistent, potent MSCs from a single donor from a single blood donation. Our distinctive technology leverages Nobel Prize winning iPSCs as a starting material which can then be developed



into virtually any cell in the human body. The Cymerus<sup>™</sup> MSC manufacturing process actively addresses current challenges associated with conventional methods of producing MSC-based therapies that have been identified by the US FDA, including cell heterogeneity arising from a reliance on multiple donors and manufacturing quantity limits. Accordingly, Cynata's consistent and scalable MSC manufacturing process provides a unique competitive advantage, facilitating a pathway to robust commercial scale MSC production.

Further deepening our commercial relationships, we recently entered into a new strategic partnership agreement with our long-standing partner Fujifilm. Under the agreement, Cynata will be able to leverage Fujifilm's world-leading cell therapy production capabilities to provide clinical and commercial manufacturing services for the production of our Cymerus™ MSCs at scale. Fujifilm's credibility as a proven cell therapy manufacturer will bring significant long-term benefits to Cynata and our shareholders, and they've demonstrated a strong commitment to the Company by agreeing to a further voluntary escrow over their shares. We have also regained the commercial rights to CYP-001 in GvHD, which presents a compelling opportunity to pursue a US development strategy and conduct a Phase 2 GvHD trial in the US, which will be an exciting and very valuable late-stage addition to our growing and diverse portfolio.

Cynata is well placed to progress development across existing clinical programs and drive shareholder value, with approximately \$24m in cash at the close of the most recent quarter, in addition to \$5m received from Fujifilm as part of the new strategic partnership agreement subsequent to the September quarter.

As a final note, on behalf of the Board, I would like to thank all our shareholders and partners for your continued support as we advance our Cymerus™ technology to develop breakthrough cell therapy products to treat serious and debilitating diseases. I would like to extend my gratitude to our staff for their commitment to the Company and I acknowledge that the achievements this year are a testament to our exceptional team that has managed to prudently navigate through such unforeseeable circumstances. I would finally like to thank Ross, for his leadership, which allowed us to progress our pipeline and commercial initiatives through such tumultuous times. I am confident that the team will continue to execute on our strategic priorities and kick goals for the year ahead. I would now like to pass on to Ross and Kilian to provide a comprehensive update on Cynata's clinical development and outlook.

**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 is presently underway. Clinical trials of Cymerus products in osteoarthritis (Phase 3) and in patients with respiratory failure are currently ongoing. In addition, Cynata has demonstrated utility of its Cymerus technology in preclinical



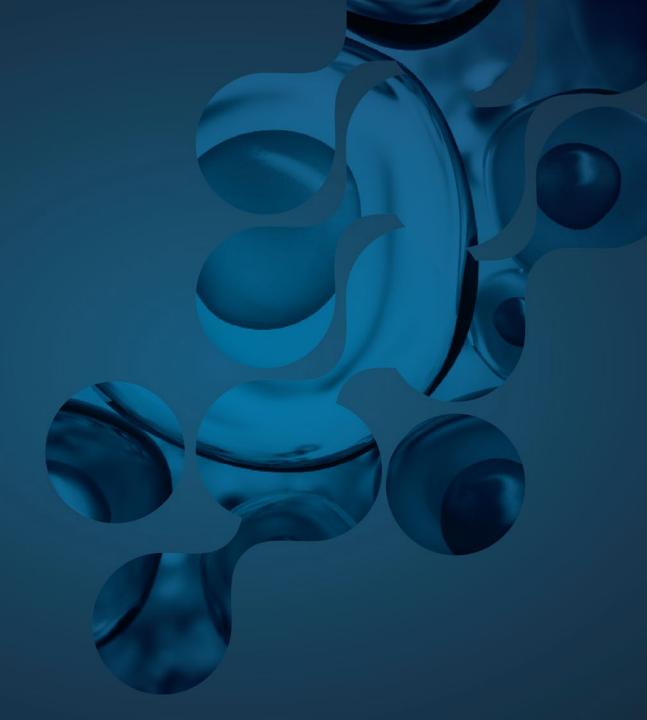
models of numerous diseases, including the clinical targets mentioned above, as well as asthma, heart attack, sepsis, acute respiratory distress syndrome (ARDS) and cytokine release syndrome.

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** 16 November 2021



#### Important information

#### **Summary information**

This Presentation contains summary information about Cynata Therapeutics Limited and its subsidiaries (CYP) which is current at 16 November 2021. 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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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 to September 2021. This information is disclosed in the 4C report lodged with ASX on 28 October 2021. Any discrepancies between totals and sums of components in tables and figures in this Presentation are due to rounding.

#### Forward-looking statements

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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## **Key Highlights: FY 2021**

#### Clinical & Pre-clinical



Commenced and advanced enrolment in Phase 3 osteoarthritis trial



Commenced
enrolment and
expanded recruitment
criteria in MEND
clinical trial



Ethics approval received to commence a clinical trial in diabetic foot ulcers



Completed Phase 1 GvHD trial two-year follow up with positive efficacy results



Progress toward expanding the pipeline in IPF and renal transplantation



Continued successful results from preclinical efficacy studies across multiple indications



Cymerus<sup>™</sup> MSC technology featured in a publication of prestigious Nature Medicine Journal



Planning underway for Phase 2 GvHD trial in the US



IPF: idiopathic pulmonary fibrosis

## **Key Highlights: FY 2021**

#### **Commercial & Corporate**



Signed a new strategic partnership agreement with Fujifilm<sup>1</sup>



Signed a licence agreement with TekCyte for their wound dressing technology



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



Raised \$18.3m in capital led by \$10m cornerstone investment from BioScience Managers



Strengthened the
Board with the
appointment of Dr.
Geoff Brooke as
Independent Chairman



## Strategic partnership with Fujifilm provides commercial benefits

Fujifilm remains very supportive of Cynata through new SPA

#### Key SPA terms<sup>1</sup>

- US\$5m fee payable by Fujifilm to Cynata
- Cynata regained all development and commercialisation rights to CYP-001
- Fujifilm agreed to further voluntary escrow over their shares in Cynata
- First rights to manufacture Cymerus therapeutic MSC products

#### Strategic benefits for Cynata

- ✓ Accelerate US development strategy: With rights to CYP-001 in GvHD regained, Cynata plans to conduct a Phase 2 GvHD trial in the US
- ✓ Network: Fujifilm is one of the largest conglomerates in the world with a significant network in the biotechnology space
- Experienced cell therapy manufacturer: Fujifilm Cellular Dynamics Inc (subsidiary of Fujifilm) developed the original iPSC line used in Cynata's Cymerus manufacturing process

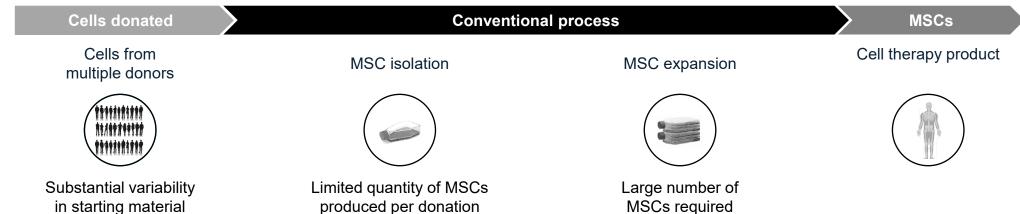


Fujifilm to provide clinical and commercial manufacturing services for Cymerus MSCs

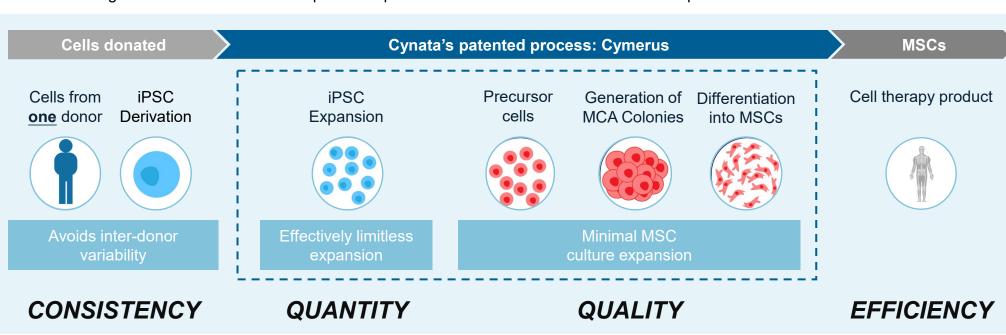


## Conventional vs. Cynata's Cymerus MSC manufacturing process

The current conventional manufacturing process is sub optimal



Cynata's
Cymerus iPSCderived process
optimises
manufacturing
for scalability





### 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, resulting in 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

Compelling safety results from Phase 1 GvHD trials<sup>1</sup> and positive preclinical data in each target indication have accelerated the pipeline





Primary evaluation at Day 100

<sup>2.</sup> Trial timing uncertain due to continued impact on recruitment due to COVID-19, and being assessed as part of broader clinical development strategy

## **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 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

53%

Overall response

87%

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



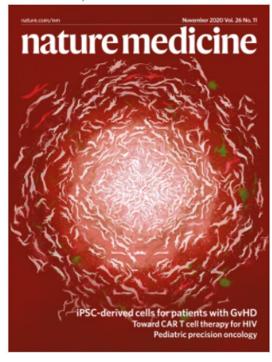
Standard of care



Other MSC products

Nature medicine is the preeminent peerreviewed medical journal worldwide

Current Issue | November 2020





## Accelerate US development strategy for GvHD

Cynata is aiming to progress a Phase 2 GvHD clinical trial in the US, after regaining clinical and commercial rights to CYP-001 in GvHD













Orphan Drug Designation awarded by FDA for CYP-001



Phase 1 trial results demonstrate strong safety and efficacy



SPA with Fujifilm, Cynata regains rights to CYP-001



Phase 2 trial design confirmed



Engage with the FDA for a Phase 2 trial in the US



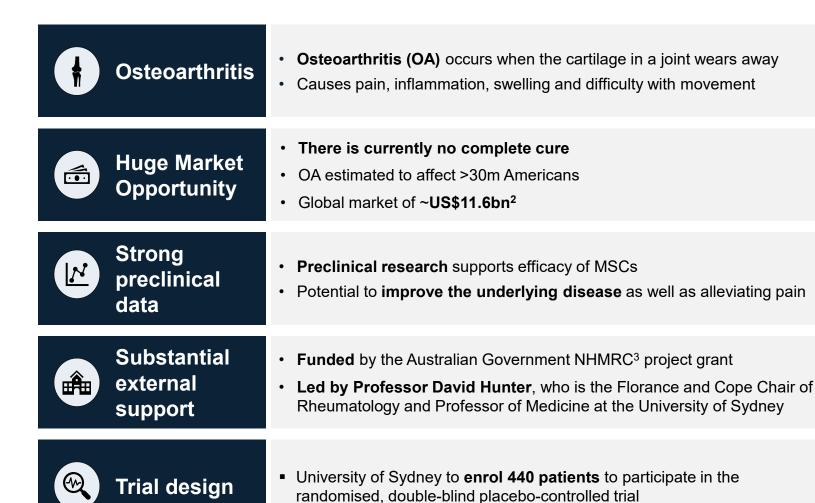
Commence Phase 2 trial

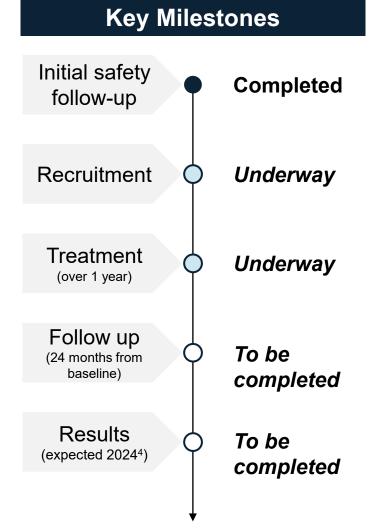




# SCUIpTOR<sup>1</sup> | Osteoarthritis Phase 3 clinical trial

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



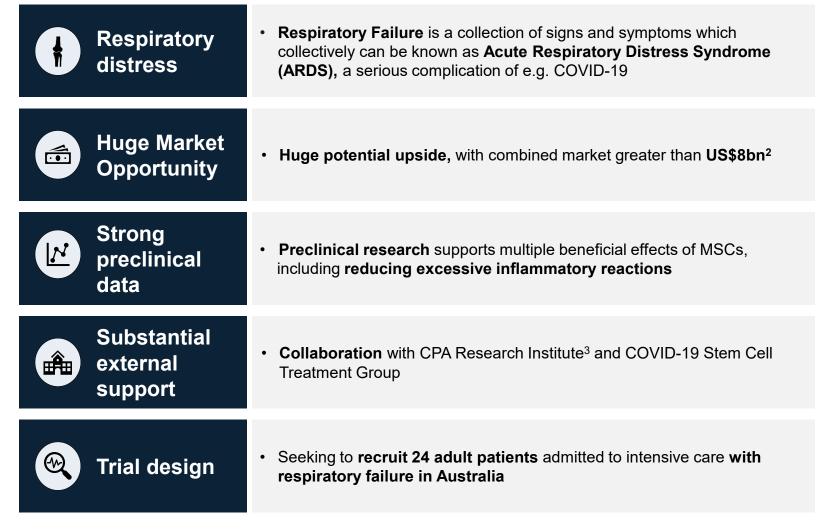


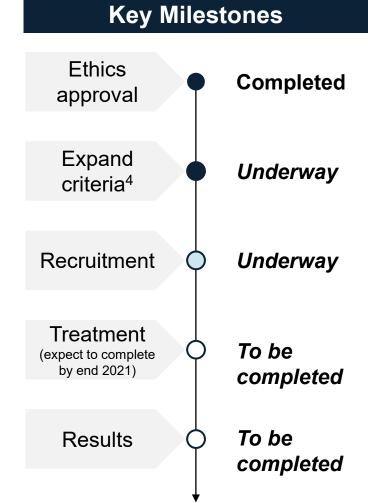


- 1. Clinical trial entitled Stem Cells as a symptom and strUcture-modifying Treatment for medial tibiofemoral OsteoaRthritis: a randomised placebo-controlled trial (SCUIpTOR)
- 2. Reflects OA market by 2025; Persistence Market Research 2018 research report: "Osteoarthritis Treatment Market: Global Industry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

## MEND<sup>1</sup> | Phase 1/2 clinical trial in respiratory distress

Patient recruitment underway, following expansion of patient population to increase pool of potential subjects







- 1 MEseNchymal coviD-19 Trial (MEND)
- 2. Source: Vasomune Therapeutics company announcement, 2018 (Reflects ARDS global market opportunity of US\$2.5bn); GlobeNewswire, 2020 (Represents Cytokine Release Syndrome (CRS) global market opportunity of US\$0.16m in 2017); GlobalData 2017 (Reflects Sepsis global market opportunity of US\$5.9bn in 2026).
  - CPA = Cerebral Palsy Alliance
  - Ethics committee approval received to expand recruitment criteria (beyond COVID-19)

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

Recruitment is expected to commence in 2H CY21, following ethics committee<sup>1</sup> approval



• 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>2</sup>
- Global market is estimated to be ~US\$10bn3



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
- Enables use of polymer-coated dressings that deliver MSCs to DFUs



Trial design

- 30 patients with DFU will be randomly assigned to receive CYP-006TK (polymer-coated silicon dressing seeded with Cymerus MSCs) or standard care of treatment, over 4 weeks
- Sign licence Completed with TekCyte **Fthics** Completed approval Trial start **Underway** up activities Recruitment To be (expected to commence 4Q21) completed To be Treatment completed

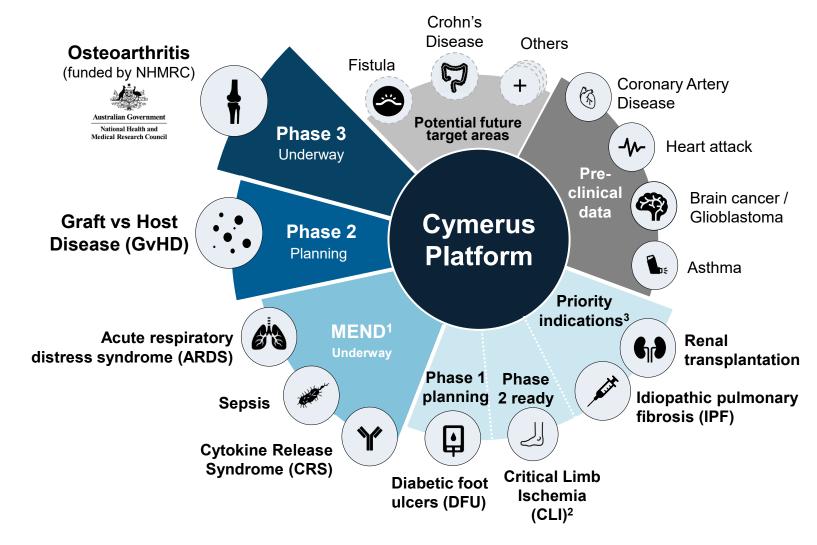
**Key Milestones** 



- 1. Central Adelaide Local Health Network Human Research Ethics Committee approval
- 2. 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
- 3. Estimated DFU market (Source: Transparency Market Research, 2020 (Reflects global DFU treatment market by 2027)).
- Trial conducted independently by the Cooperative Research Centre for Cell Therapy Manufacturing (CTM-CRC). Results of preclinical model of Diabetic Wounds announced in May 2018.
- 5. With the option to purchase the relevant technology outright; Refer to announcement on 3 June 2021 "Cynata signs License Agreement with TekCyte"

### Multiple targets to expand the clinical development pipeline

A Phase 2 trial in GvHD will be an important late-stage addition to Cynata's robust clinical pipeline



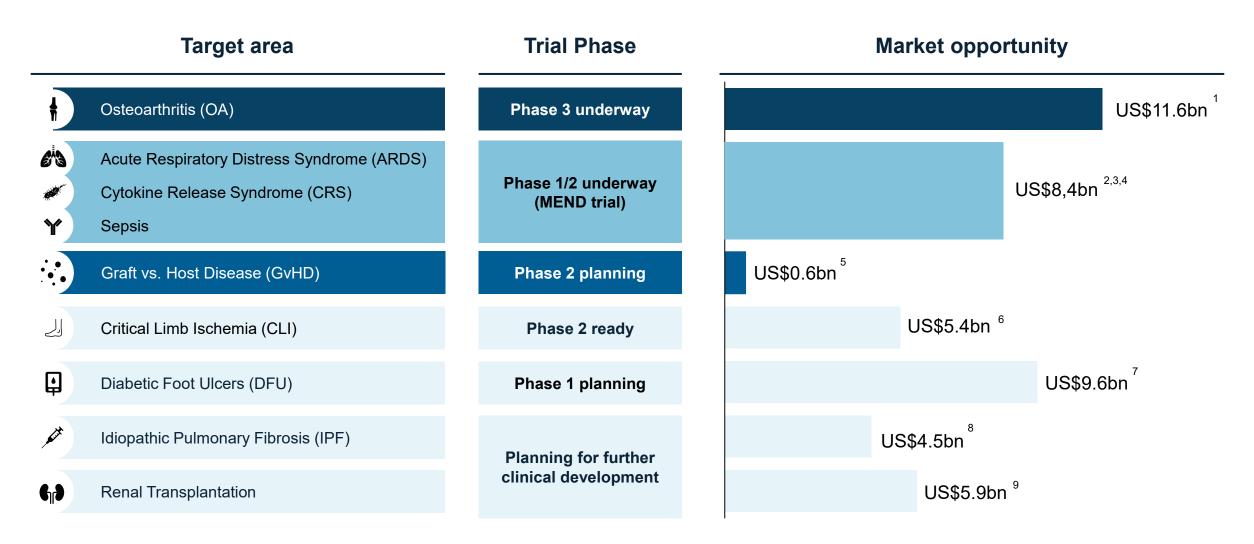


Investigating efficacy in patients admitted to ICU, commonly experiencing ARDS, sepsis and CRS

<sup>2.</sup> Currently on hold due to the COVID-19 pandemic, current planned activities for CLI will be diverted towards partnership opportunities for the trial.

## Significant market opportunities

Cynata's rich pipeline targets a range of indications with attractive market dynamics





<sup>1.</sup> Persistence Market Research 2018 research report: "Osteoarthritis Treatment Market: Global Industry Analysis (2012-2016) and Forecast (2017-2025) (Reflect OA market by 2025); 2. Vasomune Therapeutics company announcement, 2018 (Reflects ARDS global market opportunity of US\$2.5bn) 3. GlobeNewswire, 2020 (Represents CRS global market opportunity of US\$0.16m in 2017) 4. GlobalData 2017 (Reflects Sepsis global market opportunity of US\$5.9bn in 2026). 5. Global Graft versus Host Disease Market 2019-2029 (Reflects forecast market in 2026). 6. Zion Market Research, 2019 (represents global treatment market in 2025); 7. Transparency Market Research, 2020 (Reflect global DFU treatment market by 2027). 8. iHealthcareAnalyst Inc, 2019 (represents global market by 2025); 9. Organ Transplant Immunosuppressant Drugs Market in 2026, Grand View Research, Inc., 2019:

## **Near term catalysts**

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

- ☐ Complete start up activities for Phase 1 DFU trial, and...
- ☐ Commence recruitment in Phase 1 DFU trial
- ☐ Complete recruitment of 24 patients in Phase 2 MEND trial
- □ Advance US Regulatory strategy, and...
- ☐ Commence Phase 2 trial in GvHD
- ☐ Finalise clinical trial plans for IPF and renal transplantation
- ☐ Complete recruitment of 440 patients in Phase 3 osteoarthritis trial
- □ Progress commercial discussions and execute further corporate partnership(s)





### **Board & management**

Highly skilled and experienced senior leadership team with decades of experience in biotechnology



**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 Pty Ltd



**Dr Kilian Kelly**Chief Operating Officer

- 15+ years experience in biopharmaceutical research & development
- Previously Senior Director, Drug Development at Biota Pharmaceuticals, Vice President, Regulatory and Clinical at Mesoblast Limited



**Dr Jolanta Airey**Chief Medical Officer

- 25+ years experience in respiratory, rheumatology, dermatology, biologicals, international markets and listed companies
- Previously Director, Translational Development at CSL Limited and a highly experienced clinician



**Dr Paul Wotton**Non-Exec Director

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



**Dr Stewart Washer** Non-Exec Director

- 20+ years of CEO and Board experience in medical technology, biotech and agrifood companies
- Current Chairman of Orthocell Ltd, and Chairman of Minomic International Ltd



**Dr Darryl Maher** Non-Exec Director

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



**Peter Webse**Company Secretary

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



### **Summary**

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 suboptimalities in conventional MSC manufacturing



Positive pre-clinical and clinical data supporting versatility and efficacy of Cynata's MSCs

Validation through corporate partnering



Respiratory distress (ARDS) and Phase 3 osteoarthritis clinical trials underway

Phase 1 DFU trial to commence 4Q 21

Phase 2 GvHD trial to commence in 2022



Combined market opportunity of clinical pipeline is ~A\$46bn



Multiple pathways to commercialisation, including strategic partnering

Well placed to fund to major catalysts with ~A\$24m¹ in cash





### **Thank You & Questions**

### **Cynata Therapeutics Limited**

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Authorised for release by the Board