

## Cynata Investor Presentation

**Melbourne, Australia; 14 August 2020:** Cynata Therapeutics Limited (ASX: CYP), a clinical-stage biotechnology company specialising in cell therapeutics, has today released a new investor presentation. This will be used to update existing shareholders, potential investors, and other parties.

The presentation highlights the key competitive advantages of Cynata's proprietary Cymerus™ technology, which leverages an induced pluripotent stem cell (iPSC)-derived process to optimise product quality and consistency. Cynata has produced a clinical-grade iPSC bank from a single blood donation and this iPSC bank has the capacity to give rise to an effectively limitless number of mesenchymal stem cell (MSC) doses, thus avoiding inter-donor variability. This enables large quantities of a highly consistent MSC product to be manufactured with minimal MSC culture expansion while maintaining potency. Cynata's Cymerus MSC products have shown encouraging human clinical efficacy results in GvHD, as well as compelling potential in pre-clinical studies for a broad range of indications. Cynata is the most advanced company worldwide in the development of iPSC-derived cell therapy products.

Some of these key advantages have been brought into stark focus by recent FDA commentary on MSC manufacturing processes that require multiple tissue donations from multiple donors.

-ENDS-

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

**CONTACTS:** Dr Ross Macdonald, CEO, Cynata Therapeutics, +61 (0)412 119343, [ross.macdonald@cynata.com](mailto:ross.macdonald@cynata.com)  
Claire LaCagnina, U.S. Media Contact, +1 315.765.1462, [clacagnina@6degreespr.com](mailto:clacagnina@6degreespr.com)

### 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. Cynata plans to advance its Cymerus MSCs into Phase 2 trials for GvHD (with licensee Fujifilm), severe complications arising from COVID-19 and critical limb ischemia, and into a Phase 3 clinical trial in osteoarthritis. In addition, Cynata has demonstrated utility of its Cymerus™ MSC technology in preclinical models of asthma, diabetic wounds, heart attack, sepsis, acute respiratory distress syndrome (ARDS) and cytokine release syndrome.



# A Next Generation Stem Cell Therapeutics Company

Investor Presentation: Cynata Therapeutics Limited  
August 2020

# Important Information

---

This presentation has been prepared by Cynata Therapeutics Limited. (“Cynata” or the “Company”) based on information available to it as at the date of this presentation. The information in this presentation is provided in summary form and does not contain all information necessary to make an investment decision.

This presentation does not constitute an offer, invitation, solicitation or recommendation with respect to the purchase or sale of any security in Cynata, nor does it constitute financial product advice or take into account any individual’s investment objectives, taxation situation, financial situation or needs. An investor must not act on the basis of any matter contained in this presentation but must make its own assessment of Cynata Therapeutics and conduct its own investigations. Before making an investment decision, investors should consider the appropriateness of the information having regard to their own objectives, financial situation and needs, and seek legal, taxation and financial advice appropriate to their jurisdiction and circumstances. Cynata Therapeutics is not licensed to provide financial product advice in respect of its securities or any other financial products. Cooling off rights do not apply to the acquisition of Cynata Therapeutics securities.

Although reasonable care has been taken to ensure that the facts stated in this presentation are accurate and that the opinions expressed are fair and reasonable, no representation or warranty, express or implied, is made as to the fairness, accuracy, completeness or correctness of the information, opinions and conclusions contained in this presentation. To the maximum extent permitted by law, none of Cynata Therapeutics, its officers, directors, employees and agents, nor any other person, accepts any responsibility and liability for the content of this presentation including, without limitation, any liability arising from fault or negligence, for any loss arising from the use of or reliance on any of the information contained in this presentation or otherwise arising in connection with it.

The information presented in this presentation is subject to change without notice and Cynata Therapeutics does not have any responsibility or obligation to inform you of any matter arising or coming to their notice, after the date of this presentation, which may affect any matter referred to in this presentation.

The distribution of this presentation may be restricted by law and you should observe any such restrictions.

## Forward looking statements

This presentation contains certain forward looking statements that are based on the Company’s management’s beliefs, assumptions and expectations and on information currently available to management. Such forward looking statements involve known and unknown risks, uncertainties, and other factors which may cause the actual results or performance of Cynata to be materially different from the results or performance expressed or implied by such forward looking statements. Such forward looking statements are based on numerous assumptions regarding the Company’s present and future business strategies and the political and economic environment in which Cynata will operate in the future, which are subject to change without notice. Past performance is not necessarily a guide to future performance and no representation or warranty is made as to the likelihood of achievement or reasonableness of any forward looking statements or other forecast. To the full extent permitted by law, Cynata and its directors, officers, employees, advisers, agents and intermediaries disclaim any obligation or undertaking to release any updates or revisions to information to reflect any change in any of the information contained in this presentation (including, but not limited to, any assumptions or expectations set out in the presentation).

# Cynata Therapeutics is a clinical stage biotech with a highly scalable, proprietary platform for developing stem cell therapeutics

## Our focus

---

Utilise our proprietary Cymerus™ platform technology to develop commercially scalable mesenchymal stem cell (MSC) therapeutic products to treat serious chronic disorders

## About Cynata Therapeutics

---

- Stem cell and regenerative medicine company developing technology from the University of Wisconsin-Madison, USA
- First product, CYP-001, licensed to Fujifilm for graft-versus-host-disease (GvHD),
- Multiple further possible license transactions
- Cymerus technology addresses a critical shortcoming in existing methods of production of mesenchymal stem cells (MSCs) for therapeutic use, which is the ability to achieve economic manufacture at commercial scale

## Financial information

---

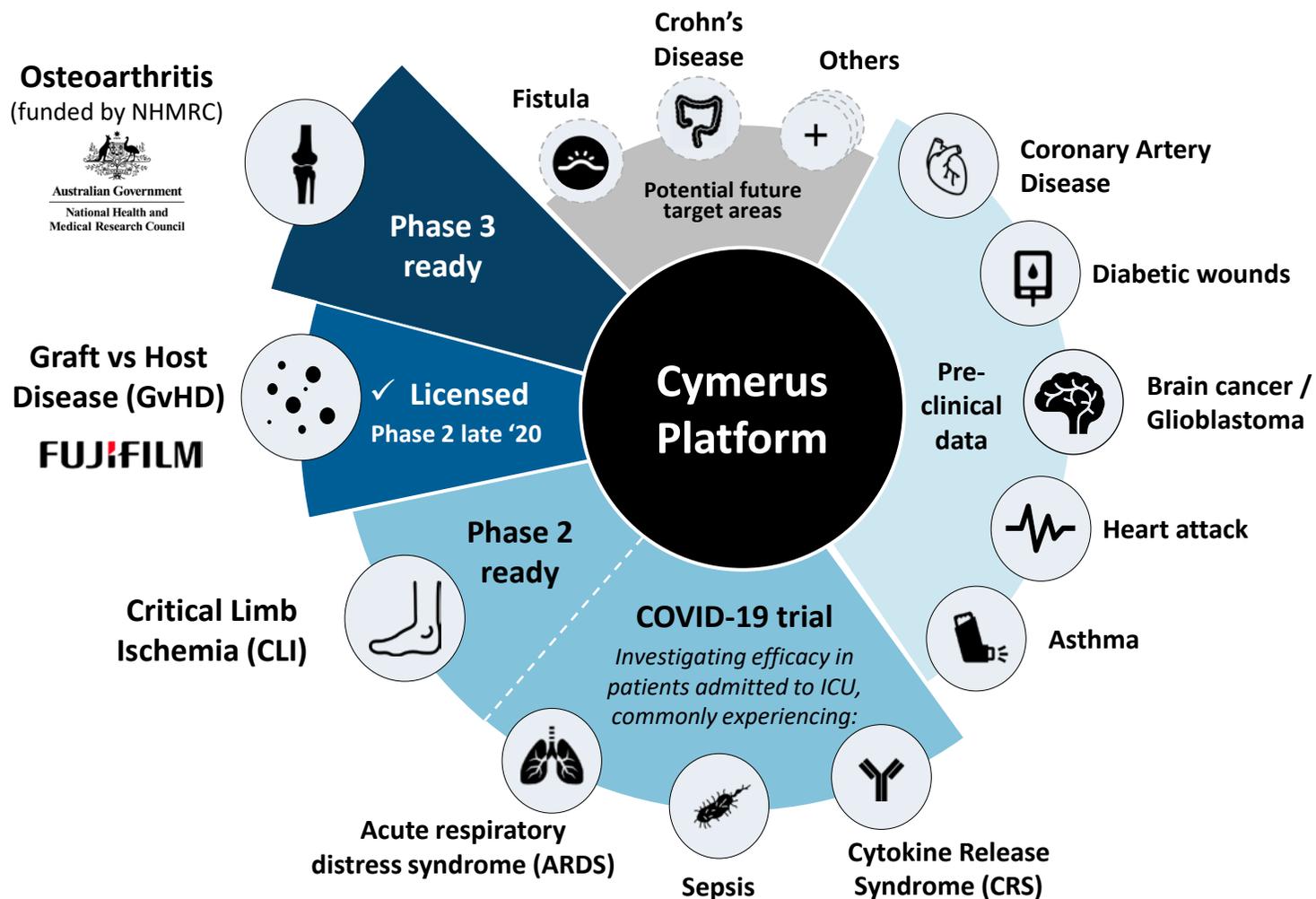
Share price (5-Aug-20)	A\$0.63
Shares on issue	117m
Market capitalisation <sup>1</sup>	A\$73.7m ~(US\$50m)
Cash <sup>2</sup>	A\$13.6m
Debt	-
Enterprise value	A\$60.1m

## Top shareholders

---

 Fidelity INTERNATIONAL	9.9%
 FUJIFILM	6.9%
Board and management	5.8%

# Cynata's Cymerus platform has potential applications across a wide range of diseases



## Cynata's MSCs in COVID-19 infection

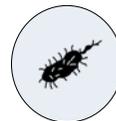
- **Increased global interest** in the potential of MSCs to treat complications of COVID-19, **with early studies demonstrating potential utility**<sup>1</sup>
- COVID-19 is a respiratory virus that in some patients causes severe complications, **particularly involving the lungs**
- **ARDS, sepsis, and CRS are the leading causes of death in COVID-19 patients**
- Cynata has compelling data from pre-clinical studies investigating the potential of its MSCs in these indications, as they each represent significant unmet needs with **broader applications to Cynata's clinical development beyond COVID-19**

ARDS



Cymerus MSCs effective in model of acute respiratory distress syndrome (ARDS)

Sepsis



Cymerus MSCs effective in model of pneumonia induced sepsis

CRS



Cymerus MSCs significantly ameliorate the effects of cytokine release syndrome (CRS)

Cynata plans to leverage recent increased interest to accelerate its development program and validate its technology for multiple indications and in multiple regions

## MEND trial | Overview of clinical trial COVID-19 patients



### Target population

- 24 adult patients with COVID-19 admitted to intensive care with compromised lung function, which can ultimately progress to ARDS



### Rationale for selection

- Respiratory distress (+ CRS and sepsis) represent significant unmet needs as consequence of a severe COVID-19 infection, as well as other causes beyond COVID-19
- Strong pre-clinical results in indications that can arise from a severe case of COVID-19
- Increased market interest, allowing accelerated program planning and approval



### Preliminary program design

- In collaboration with CPA Research Institute<sup>1</sup> and COVID-19 Stem Cell Treatment Group
- Open-label, randomised controlled clinical trial based in NSW, Australia
- Twelve patients randomised to receive Cymerus MSC infusions with standard care; twelve patients randomised as the control group, to receive current standard of care
- Primary endpoints: an improvement in PaO<sub>2</sub>/FiO<sub>2</sub> ratio, and safety & tolerability



### Key milestones

- Ethics approval obtained
- Recruitment expected to commence subject to finalisation of relevant agreements with study centres
- Cynata assessing opportunities to expand this program to other jurisdictions

# Osteoarthritis | New Phase 3 program

Funded by National Health and Medical Research Council



## Estimated market size

30,000,000

People in the USA affected by osteoarthritis

~US\$11.6B<sup>1</sup>

Forecast global market opportunity by 2025



## Osteoarthritis

- Assess the effect of Cymerus MSCs on clinical outcomes and knee joint structures of patients with osteoarthritis of the knee (compared to a placebo)



## Rationale for selection

- Preclinical research showed MSCs can exert a number of important effects, including release of cytokines and growth factors that reduce inflammation and promote tissue repair, new blood vessel formation, and regeneration of compromised cartilage which may result in improved outcomes for patients



## Preliminary program design

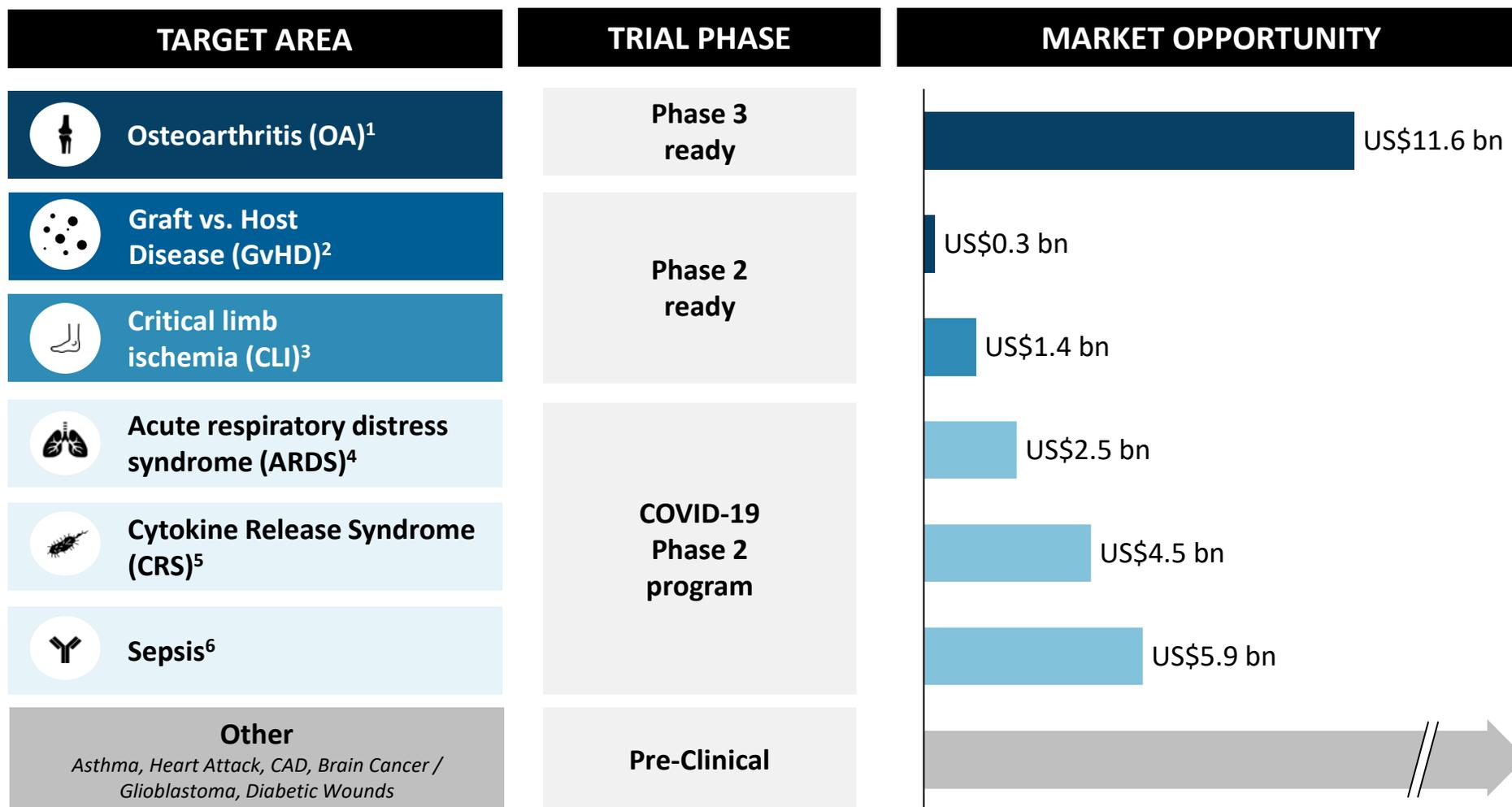
- 440-patient trial funded by an NHMRC project grant and in-kind contributions from participating institutions (no cash contribution from Cynata)
- Cynata to supply Cymerus MSCs for use in the trial<sup>2</sup> and will retain full commercial rights to the use of Cymerus MSCs in osteoarthritis



## Key milestones

- Phase 3 clinical trial in Osteoarthritis expected to commence in 2H2020

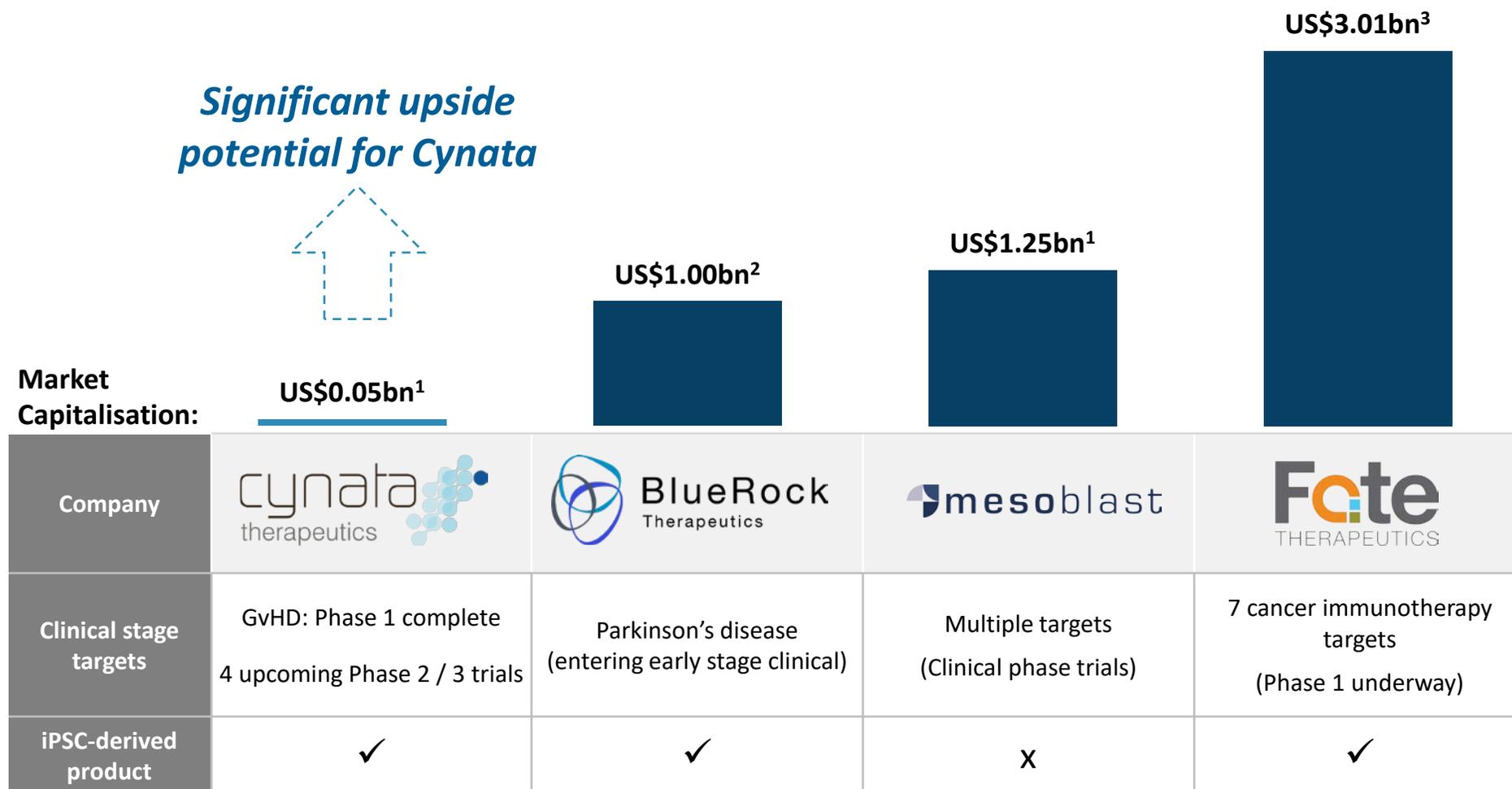
# Cynata is targeting significant market opportunities



1. Persistence Market Research 2018 research report: "Osteoarthritis Treatment Market: Global Industry Analysis (2012-2016) and Forecast (2017-2025). 2. Fujifilm's estimate of the peak annual global sales opportunity. 3. ClearView's estimate of the peak annual global sales opportunity. 4. Vasomune Therapeutics company announcement, 2018 (Reflects total global market opportunity in 2018) 5. Evaluate Pharma, 2017 (Reflects total global market opportunity in 2022); 6. GlobalData 2017 (Reflects total global market opportunity in 2026)

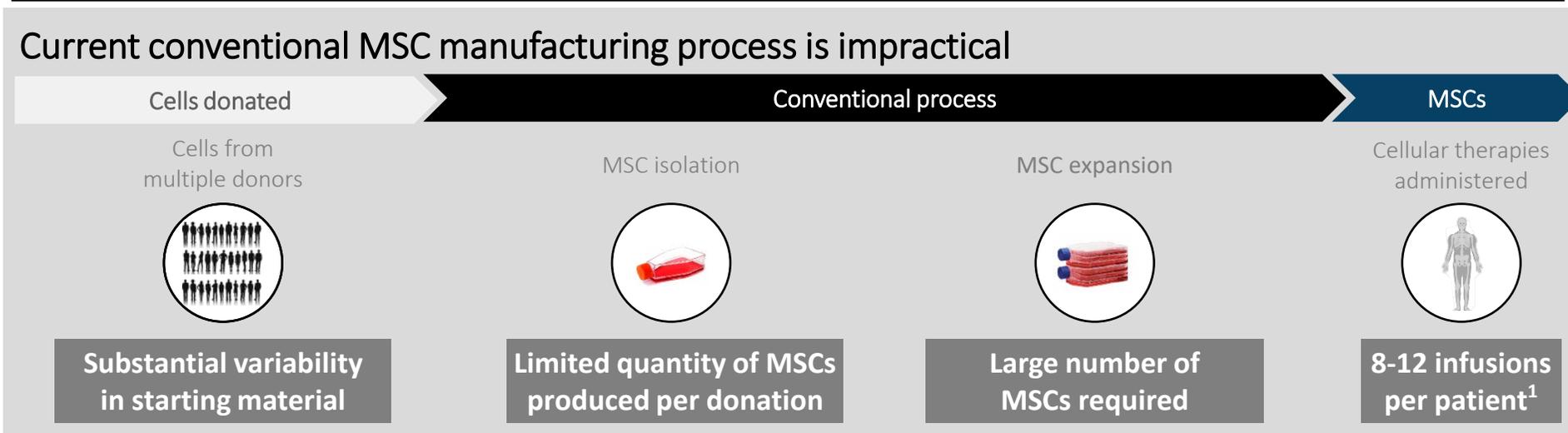
# Valuation comparison to other stem cell-therapy product companies

*Significant upside potential for Cynata*

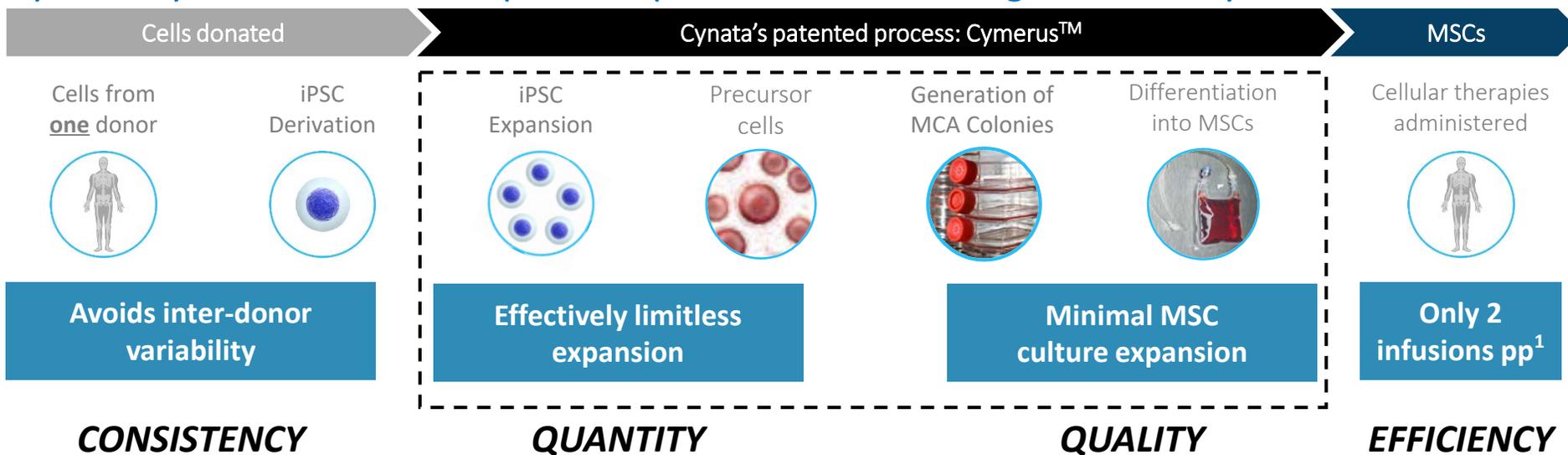


Company	cynata therapeutics	BlueRock Therapeutics	mesoblast	Fcete THERAPEUTICS
Clinical stage targets	GvHD: Phase 1 complete 4 upcoming Phase 2 / 3 trials	Parkinson's disease (entering early stage clinical)	Multiple targets (Clinical phase trials)	7 cancer immunotherapy targets (Phase 1 underway)
iPSC-derived product	✓	✓	X	✓

# Conventional vs. Cynata's Cymerus MSC manufacturing process



## Cynata's Cymerus iPSC-derived process optimises manufacturing for scalability



# Cynata has the only platform in the world able to produce commercial quantities of MSCs from a single source

	Conventional process	Cymerus™	Significance for Cynata
Donors	Continuous supply of new donors required	One donor, one time (completed)	✓ Lower cost; simplified logistics; highly consistent product
Comparability testing	Required every time a new donation is used	N/A	✓ Lower cost, minimised risk <sup>1</sup>
Number of clinical doses per donation	Significantly limited	Effectively limitless	✓ Lower cost; simplified logistics; comparative ease of scalability
Extent of MSC expansion	High (>25 population doublings)	Low (10 population doublings)	✓ Minimised expansion and low “age” ensures Cynata’s product is consistently highly potent, with potency maintained <sup>2</sup>
Cellular “age”	Variable	Low: iPSC-derived MSCs are more primitive	
Infusions per patient	8-12	~2	✓ Greater convenience for patients and hospitals; lower costs incurred by healthcare system
Risk of contamination <sup>3</sup>	Medium to high, depending on process	Negligible	✓ Lower risk of adverse reaction in patients; significant regulatory benefit

**Cymerus produces a consistent and scalable product, with lower cost of goods on a per cell basis and fewer cells required per patient compared to conventional methods**

1. MSC product from different donors must be proven to be the same: highly risky given every donor is different  
 2. Conventional manufacturing process requires extensive MSC culture expansion. MSCs change when excessively when expanded, causing a loss of potency and decreased efficacy  
 3. Contamination with off-target cell types – isolation of MSCs in original sample is associated with risk of carry-over of other cell types

# Cynata's Cymerus process actively addresses some of the key areas that the FDA is likely to focus on

## Potential issues raised

*“The issue of reliable prediction of biological activity is particularly challenging for MSCs.*

***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

## Key advantages underpinning Cymerus™:

✓ Product derived from a **single donor** provides a **highly consistent product** and addresses regulatory concerns

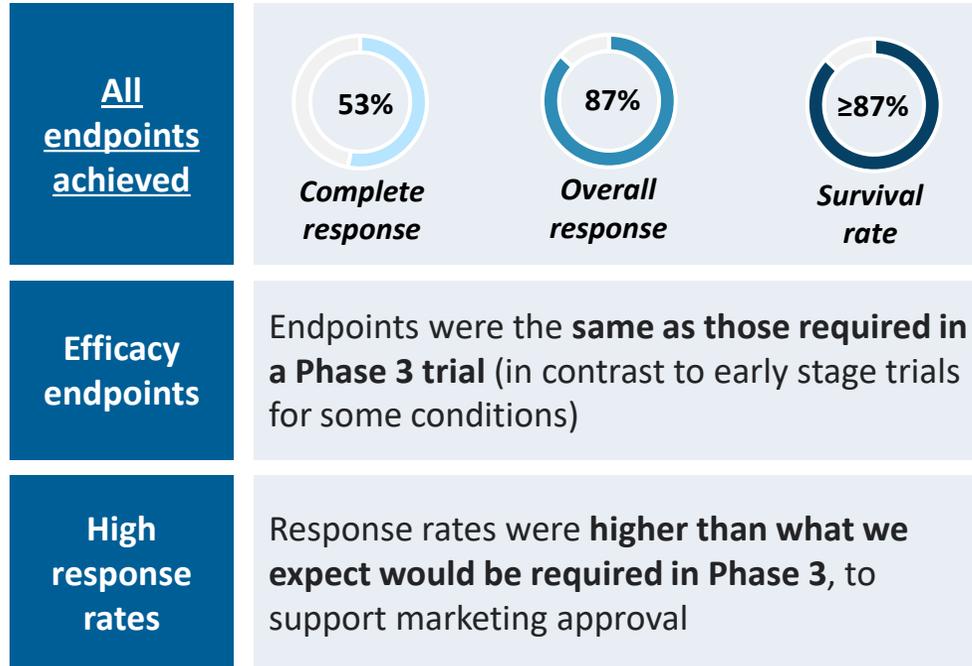
✓ Effectively **limit** iPSC expansion *before* differentiating into MSCs, maintaining potency

✓ MSCs represent a potential efficacious treatment in GvHD, **supporting Cynata's GvHD product CYP-001**

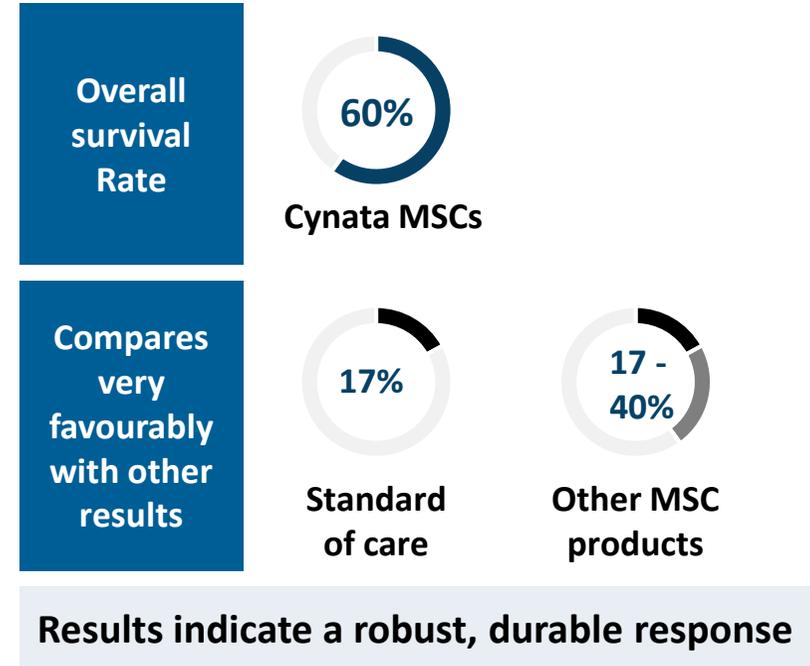
✓ FDA advisory meeting observations to be leveraged to **optimise future CYP clinical trial design for FDA approval**

# World-first allogeneic iPSC-derived cell therapy Phase 1 clinical trial in steroid-resistant acute GvHD completed, with compelling results

## Key clinical trial results (1<sup>o</sup> evaluation at Day 100)



## Two year follow-up



No treatment-related serious adverse events or safety concerns were identified

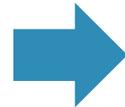
Cynata is executing on a clear scientific and commercial vision and continually assesses pathways to optimise shareholder value

## Multiple options to create shareholder value

Build value in platform independently  
*(e.g. continue running clinical trials)*

License / partner with big Pharma to develop specific target areas  
*(e.g. Fujifilm license for GvHD)*

Strategic exit/merger  
*(e.g. Strategic acquirer)*

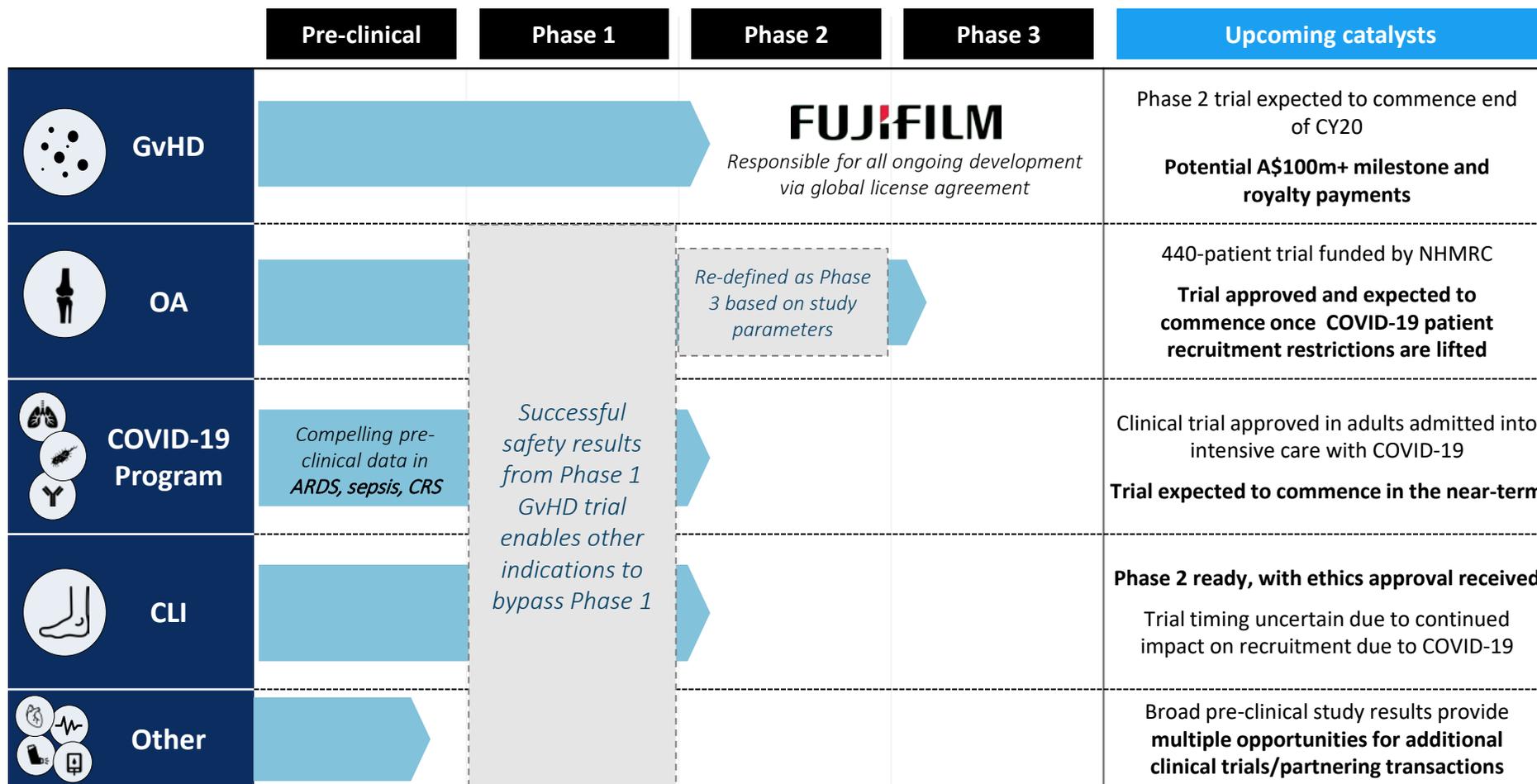


## FUJIFILM case study

- ✓ Exclusive global licence in GvHD
- ✓ All development costs met by FUJIFILM
- ✓ Multiple cash flow events:
  - ✓ A\$4m equity @ 35% premium
  - ☐ A\$100m+ in upfront license fee & potential milestone payments and royalties<sup>1</sup>
  - ☐ A\$2.86m on completion of planned Phase 2
- ✓ Represents a major endorsement by Big Pharma
- ✓ Ongoing relationship with potential for further commercial agreements

FUJIFILM transaction provides validation of the Cymerus platform and supports the licensing of additional target areas

# Broad, advanced development pipeline with multiple near-term catalysts



## Investment Summary

 <p><b>Scalable, globally applicable technology</b></p>	<ul style="list-style-type: none"> <li>▪ Cymerus platform technology enables commercial-scale production of mesenchymal stem cells</li> <li>▪ Fully patented process overcomes multiple issues with today's on-market solutions</li> <li>▪ Value of platform to a range of diseases demonstrated across clinical and pre-clinical studies</li> </ul>
 <p><b>Attractive licensing business model</b></p>	<ul style="list-style-type: none"> <li>▪ A 'hub and spoke' model: intention to license Cymerus technology across a range of target areas with Cynata in active commercial discussions with multiple parties</li> <li>▪ Licence granted to FUJIFILM for GvHD on attractive terms, including A\$100m+ in milestone payments and royalties on product sales; FUJIFILM responsible for further product development</li> </ul>
 <p><b>Successful clinical trial results</b></p>	<ul style="list-style-type: none"> <li>▪ All clinical endpoints achieved in Phase 1 trial of Cymerus MSCs in acute GvHD, with no safety concerns identified and highly encouraging efficacy</li> <li>▪ FUJIFILM endorsement supports further development of Cynata's products in other indications</li> </ul>
 <p><b>Clear pipeline of high potential target areas</b></p>	<ul style="list-style-type: none"> <li>▪ Multiple Phase 2 clinical trials with preparations underway to commence in 2020: COVID-19; GvHD (via FUJIFILM license); critical limb ischemia (CLI)</li> <li>▪ Phase 3 Osteoarthritis trial (funded by NHMRC) preparations underway to commence in 2H20</li> <li>▪ Compelling pre-clinical data in other high-value target areas supports further clinical trials</li> </ul>
 <p><b>Well positioned in regenerative medicine</b></p>	<ul style="list-style-type: none"> <li>▪ Cell therapeutics is an area of increasing interest from major pharmaceutical companies</li> <li>▪ Global market opportunity of US\$1.4bn for CLI and US\$11.6bn for OA</li> <li>▪ Cynata's unique Cymerus technology ideally placed to solve current MSC manufacturing challenges</li> </ul>

Thank you for your attention

**Cynata Therapeutics Limited**

Level 3  
62 Lygon Street  
Carlton  
Victoria 3053  
Australia

**Contact details:**



[ross.macdonald@cynata.com](mailto:ross.macdonald@cynata.com)



[www.cynata.com](http://www.cynata.com)



# Appendix

## Globally experienced board and management team



**Dr Paul Wotton**  
Chairman

- CEO, Obsidian Therapeutics
- Former CEO of Ocata Therapeutics (NASDAQ: OCAT) acquired by Astellas Pharma, in a US\$379m transaction
- Previous executive roles with Antares Pharma Inc. (NASDAQ: ATRS), Topigen Pharmaceuticals and SkyePharma
- Founding CEO, Sigilon Therapeutics; board member of Vericel Corp and Veloxis; past Chairman of the Emerging Companies Advisory Board of BIOTEC Canada

**Expertise running and monetising Ocata Therapeutics, acquired by Astellas**



**Dr Ross Macdonald**  
Managing Director / CEO

- 30 years' experience and a track record of success in pharmaceutical and biotechnology businesses
- Previous senior management positions with Hatchtech, Sinclair Pharmaceuticals, Connetics Corporation (Palo Alto, CA), and Stiefel Laboratories, the largest independent dermatology company in the world and acquired by GSK in 2009 for £2.25b

**Track record of success in pharmaceutical and biotechnology businesses**



**Dr Stewart Washer**  
Non-Exec Director

- 20+ years of CEO and Board experience in medical technology, biotech and agri-food companies
- Exec Chairman of Emerald Clinics, Chairman of Orthocell Ltd, Director of Botanix Ltd and Zelda Therapeutics Ltd
- Previously CEO roles with Calzada (ASX:CZD), Phylogica (ASX:PYC) and Celentis and managed the commercialisation of intellectual property from AgResearch in New Zealand with 650 Scientists and \$130m revenues

**Deep experience growing companies as CEO and on the Board**



**Dr Geoff Brooke**  
Non-Exec Director

- 30+ years venture capital experience
- Co-founded GBS Venture Partners
- Formerly President of Medvest, a US-based early-stage venture capital group he founded with Johnson & Johnson
- Other Board experience include non-executive director of Acrux Limited and Chairman of Actinogen Media Limited

**Extensive life sciences and financial expertise in US and Australia**



**Dr Darryl Maher**  
Non-Exec Director

- 23+ years experience at CSL Limited, one of the world's most successful developers of biologic Pharmaceutical products
- Previously Vice President of R&D and Medical Affairs at CSL Behring Australia, where he was responsible for the development of multiple successful drug products from initiation through clinical development and ultimately to commercialisation

**Former R&D Executive at CSL, with global development expertise**



**Dr Kilian Kelly**  
Chief Operating Officer

- 15 years' experience in pharmaceutical / biotechnology research and development, in both commercial and academic settings
- Previous appointments include Senior Director, Drug Development at Biota Pharmaceuticals (NASDAQ: BOTA), Vice President, Regulatory and Clinical at Mesoblast Limited (ASX:MSB)

**Extensive academic, commercial and management experience**

## Pre-clinical studies | Existing target areas

Disease target area	Partner	Pre-clinical trials started	Proof of concept completed	Key highlights	Global market opportunity*
ARDS		✓	✓	Study demonstrated effectiveness of Cymerus MSCs in sheep with ARDS in association with the Prince Charles Hospital in Brisbane.	US\$2.5bn by 2018 <sup>2</sup>
Heart attack		✓	✓	Data indicates that Cymerus MSCs may have the potential to restore cardiac function and reduce scar size after a heart attack	US\$18.2bn by 2019 <sup>3</sup>
Brain Cancer / Glioblastoma		✓	✓	Research collaboration in genetically modified MSCs in cancer: involves modifying stem cells to target cancer	US\$3.3bn by 2024 <sup>4</sup>
Diabetic Wounds		✓	✓	Independent study by CRC for Cell Therapy Manufacturing generated positive data which demonstrates the efficacy of Cymerus MSCs in a preclinical model of diabetic wounds	US\$4.9bn by 2024 <sup>5</sup>
Coronary Artery Disease		✓	✓	Research collaboration for the development of MSC therapies to treat coronary artery disease	US\$22.5bn by 2021 <sup>6</sup>
Asthma		✓	✓	Cymerus MSCs demonstrated significant beneficial effects on three key components of asthma: airway hyper-responsiveness, inflammation and airway remodelling	US\$25.6bn by 2024 <sup>1</sup>
Cytokine Release Syndrome		✓	✓	Pre-clinical model demonstrating Cymerus MSCs significantly ameliorate the effects of Cytokine Release Syndrome, a potentially severe and life-threatening adverse reaction to cancer immunotherapy	US\$4.5bn by 2022 (CAR-T) <sup>7</sup>
Sepsis		✓	✓	Development partnership with RCSI (Royal College of Surgeons in Ireland), demonstrated utility of Cymerus MSCs in sepsis, the leading cause of death in ICU's	US\$5.9bn by 2026 <sup>8</sup>

**The successful outcomes from these studies, combined with the clinical data in GvHD have facilitated a number of ongoing commercial discussions in these and other clinical indications**

Notes

\*Reflects total global market opportunity for the relevant therapeutic category

1. Grand View Research, 2016; 2. Vasomune Therapeutics company announcement, 2018 3. GBI Research, 2013; 4. Global Data, 2016; 5. Transparency Market Research, 2018; 6. Smithers Apex, 2015; 7. Evaluate Pharma, 2017; 8. GlobalData 2017