ASX ANNOUNCEMENT 11 November 2020

Phase 3 Osteoarthritis Clinical Trial Commences

Melbourne, Australia; 11 November 2020: Cynata Therapeutics Limited (ASX: "**CYP", "Cynata",** or the **"Company"**), a clinical-stage biotechnology company specialising in cell therapeutics, is pleased to announce that the Phase 3 SCUlpTOR ("Stem Cells as a symptom- and strUcture-modifying Treatment for medial tibiofemoral OsteoaRthritis") Trial of CYP-004, Cynata's Cymerus™ mesenchymal stem cell (MSC) product for osteoarthritis, has now commenced.

This trial is sponsored by the University of Sydney and funded by an Australian Government National Health and Medical Research Council (NHMRC) competitive Project Grant. The trial will take place at study centres in Sydney and Tasmania and subject treatment will commence with an initial four patients from the University's volunteers' database, who will be assessed for four weeks, before the study opens for enrolment more widely. As no additional volunteers are being sought at this time, patients who are interested in participating in the trial should wait until wider enrolment commences before contacting study centres, which is expected to happen early in 2021. The aim of the trial is to assess the effect of Cymerus MSCs compared to placebo on clinical outcomes and knee joint structure over a two-year period, in 440 patients with osteoarthritis of the knee.

Professor David Hunter, Principal Investigator, said:
"There is no cure for osteoarthritis and current treatment options largely focus on alleviating pain, rather than modifying the course of the underlying disease. We are delighted to commence this trial, which is designed to evaluate the disease modifying potential of Cymerus MSCs. We believe that it will be the largest randomised controlled trial of MSCs conducted in patients with osteoarthritis worldwide. Consequently, we anticipate that it will be an enormously influential trial, with the potential to inform clinical practice guidelines globally."

Dr. Kilian Kelly, Cynata's Chief Operating Officer, said*:*
"The commencement of the SCUlpTOR Trial is a very important achievement. This clinical trial aims to determine whether Cynata's proprietary Cymerus MSC technology, which has been evaluated in a wide range of disease targets, including graft-versus-host disease (GvHD), sepsis, and respiratory diseases such as acute respiratory distress syndrome (ARDS), is active in the setting of knee osteoarthritis.

Our Cymerus technology uniquely enables the scalable manufacture of robust MSCs, without the substantial functional inconsistency that has been observed between MSC batches manufactured using conventional methods. We look forward to advancing this clinical trial to investigate the potential benefits our MSCs could have to treat osteoarthritis patients with this common and debilitating disease."

A presentation is attached to this announcement and provides an overview of osteoarthritis including the opportunity, preclinical research and the clinical trial plans.

Phase 3 osteoarthritis trial sponsored by the University of Sydney

The trial is led by Professor David Hunter, who is the Florance and Cope Chair of Rheumatology and Professor of Medicine at the University of Sydney and has been Chief Investigator of numerous clinical trials in osteoarthritis. He has more than 500 publications in high-impact journals, including the *New England Journal of Medicine*, *Journal of the American Medical Association* and *British Medical Journal*.

The research team also includes Professor Changhai Ding (University of Tasmania), Professor Stefan Lohmander (Lund University, Sweden), Dr Rachel O'Connell (University of Sydney) and Dr Xia Wang (University of Sydney), as well as numerous associate investigators.

-ENDS-

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

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About the Phase 3 Clinical Trial in Osteoarthritis (The SCUlpTOR trial)

The clinical trial, entitled *Stem Cells as a symptom- and strUcture-modifying Treatment for medial tibiofemoral OsteoaRthritis: a randomised placebo-controlled trial*, is funded by an Australian Government NHMRC Project Grant, in addition to in-kind contributions from participating institutions. Cynata will supply Cymerus™ MSCs for use in the trial and will not be required to contribute any cash to fund the project.

The trial will be a randomised, double-blind placebo-controlled trial. Subject to satisfactory completion of an initial phase of the study in four subjects who will be assessed for a period of four weeks (two who will receive placebo and two who will receive Cymerus MSCs), the trial will seek to enrol 440 patients with osteoarthritis of the knee. Participants will receive intra-articular injections of Cymerus MSCs or placebo on three occasions over a period of 1 year, and will be followed up for a total of two years from enrolment. The co-primary endpoints are: (i) the proportion of participants achieving patient-acceptable symptom state (PASS) for knee pain at 24 months; and (ii) central medial femorotibial (cMFT) cartilage loss from baseline to 24 months. Secondary outcome measures will include assessments of pain, other symptoms, physical function, quality of life.

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 severe complications arising from COVID-19, GvHD and critical limb ischemia and a Phase 3 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

Overview of Cynata Therapeutics' osteoarthritis clinical program
November 2020

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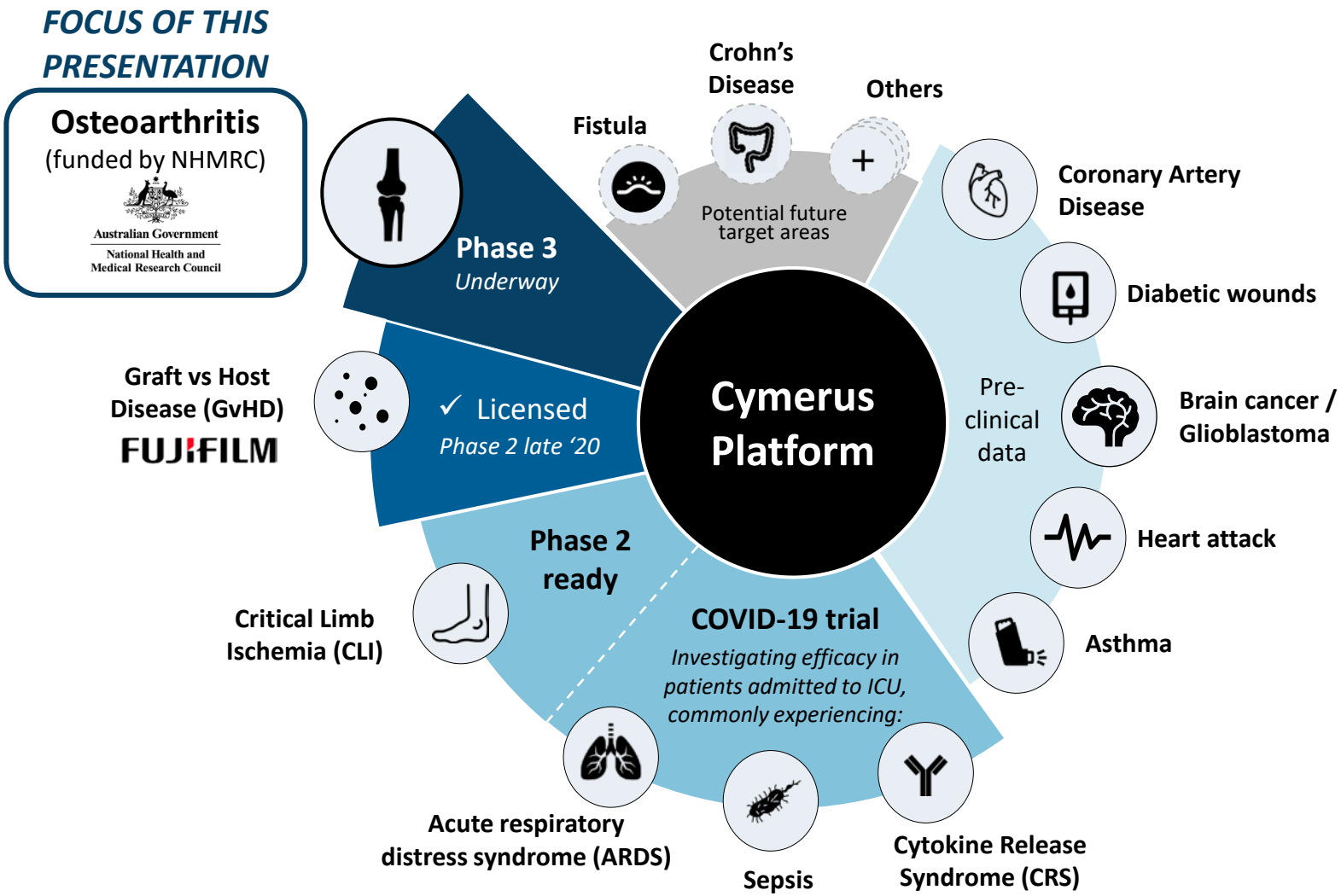
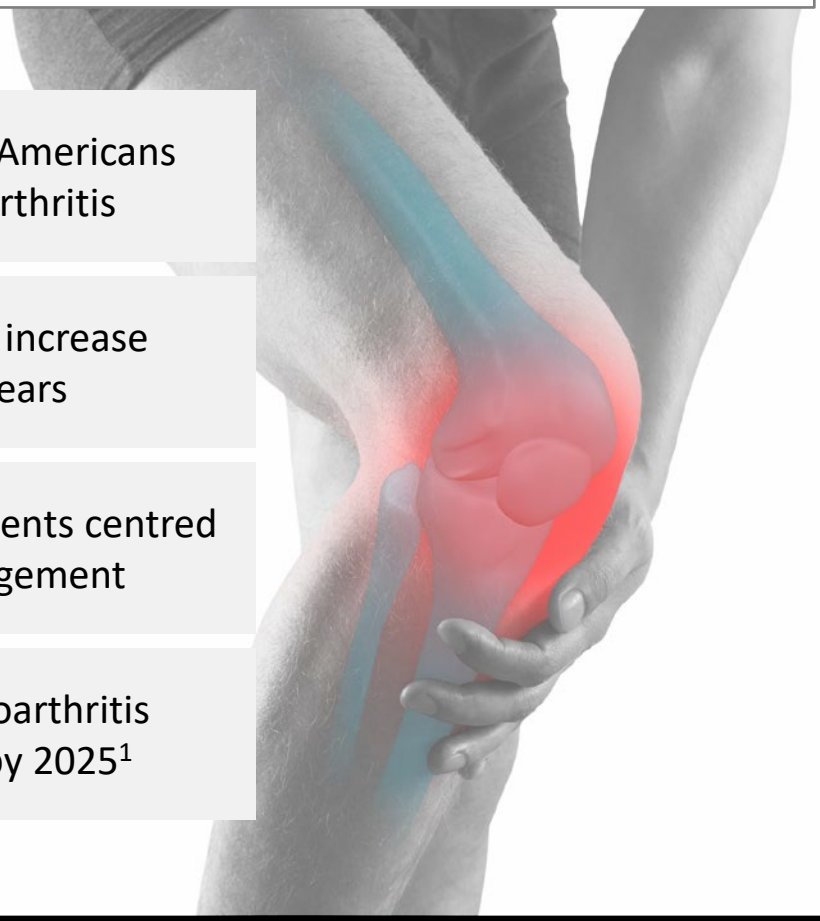
Cynata's Cymerus platform has potential applications across a wide range of diseases



Osteoarthritis presents a significant medical need and huge commercial opportunity

Osteoarthritis (OA) occurs when the protective layer between bones (cartilage) in a joint wears away, which can cause pain, swelling and difficulty with movement

~30m	Estimated number of Americans affected by osteoarthritis
>50%	Estimated incidence increase in the next 15 years
No cure	Current available treatments centred on symptom management
>US$11.6bn	Forecast global osteoarthritis treatment market by 2025[1]



1. Persistence Market Research 2018 research report: "Osteoarthritis Treatment Market: Global Industry Analysis (2012-2016) and Forecast (2017-2025).

MSCs present a potential treatment for osteoarthritis

MSCS can exert a number of important effects that may improve outcomes in patients with OA

Preclinical research has shown that MSCs:

- ✓ Reduce inflammation and promote tissue repair[1]
- ✓ Promote new blood vessel formation
- ✓ Regenerate compromised cartilage

Cynata well placed to manufacture consistently high quality MSCs at scale to address OA needs

- ✓ **Consistent product quality:** single, one-time donor overcomes regulatory concerns
- ✓ **Bypasses invasive surgeries used in conventional MSC sourcing** with a scalable and cost-effective process
- ✓ **Lower cost of goods on a per cell basis** compared to conventional MSC products[2]

1. Through the release of cytokines and growth factors
2. In GvHD

Key milestones achieved towards osteoarthritis Phase 3 clinical trial

Sponsored by the University of Sydney

Funded by a NHMRC project grant[1]

Ethics approval and TGA clearance for a Phase 3 clinical trial[2]

Patient recruitment commenced[3]

Cynata's trial will be one of the largest MSC clinical trials world-wide, showcasing Cynata's ability to manufacture MSCs at scale

 1. Funded by an Australian National Health and Medical Research (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 and will retain full commercial rights to the use of Cymerus MSCs in osteoarthritis 2. By the University of Sydney Human Research Ethics Committee. 3. Initially, 4 patients will be assessed over 4 weeks before the trial opens for recruitment more widely

SCUlpTOR | Osteoarthritis Phase 3 clinical trial[1]

Osteoarthritis

The trial will assess the effect of CYP-004 (Cymerus MSC osteoarthritis product) on clinical outcomes and knee joint structures of patients with osteoarthritis of the knee

Program design

- Randomised, double-blind placebo-controlled trial seeking to enrol 440-patients at study centres in Sydney and Tasmania
- **Co-primary endpoints are:**
  - i. the proportion of participants achieving patient-acceptable symptom state (PASS) for knee pain at 24 months and
  - ii. central medial femorotibial (cMFT) cartilage loss from baseline to 24 months
- **Secondary outcome** measure include: assessments of pain, other symptoms, physical function and quality of life

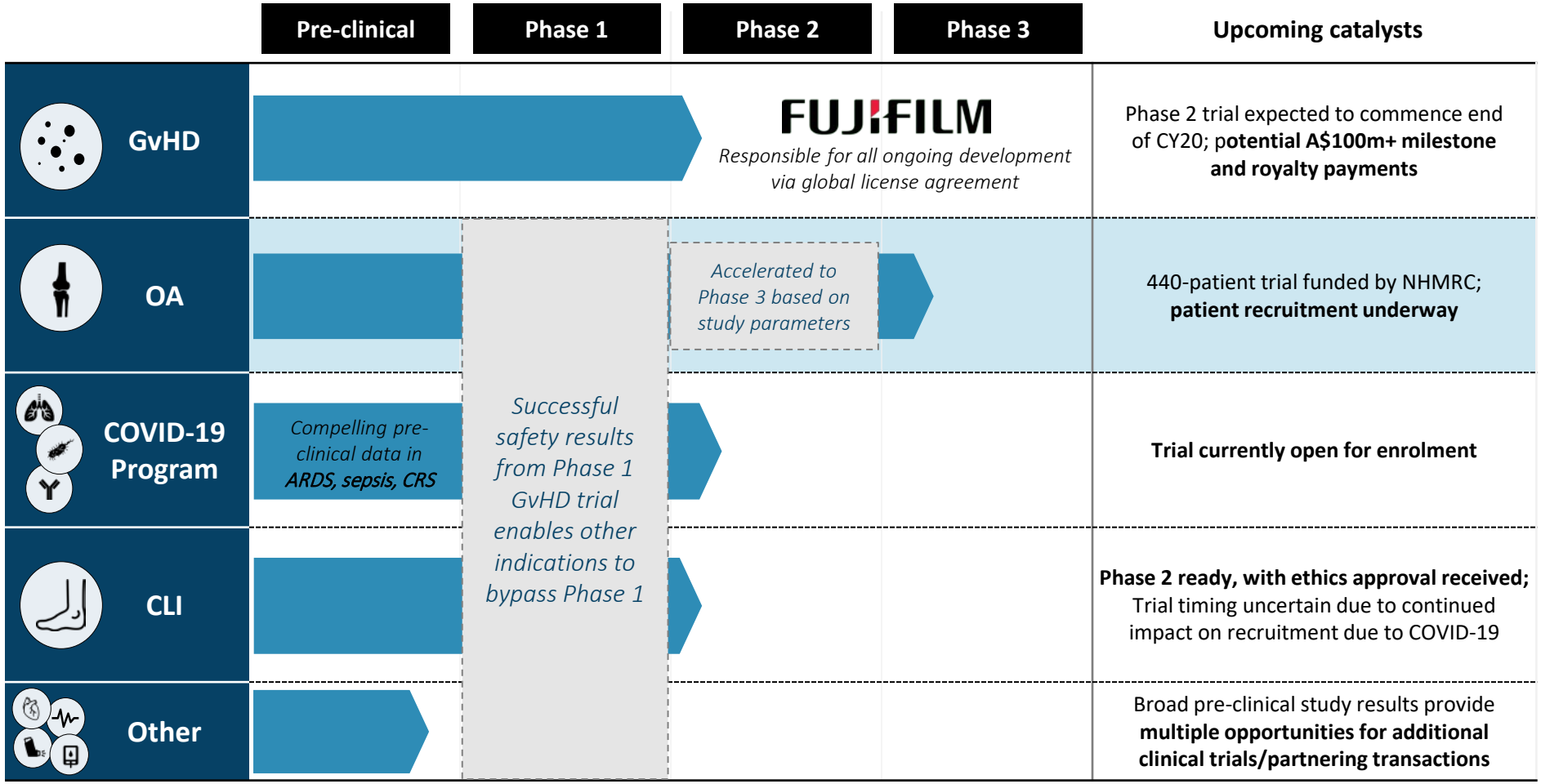
1. Clinical trial entitled Stem Cells as a symptom – and strUcture-modifying Treatment for medial tibiofemoral OsteoaRthritis: a randomised placebo-controlled trial (SCUlpTOR)

Phase 3 trial in 440 patients with osteoarthritis of the knee is underway

Preparation	Recruitment	Treatment	Results
Logistic and procedural activities to advance to patient enrolment	Enrol 440-patients at study centres in Sydney and Tasmania	Each participant receives injections of Cymerus MSCs (or placebo) on **three occasions** over 1 year	Comparison from baseline **up to 24 months** in each participant

✓ ***COMPLETE*** ***Underway***

Broad, advanced development pipeline with multiple near-term catalysts



Appendix

Investment Summary

Scalable, globally applicable technology	▪ Cymerus platform technology enables commercial-scale production of mesenchymal stem cells ▪ Fully patented process overcomes multiple issues with today's on-market solutions ▪ Value of platform to a range of diseases demonstrated across clinical and pre-clinical studies
Attractive licensing business model	▪ 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 ▪ Licence granted to FUJIFILM for GvHD on attractive terms, including A$100m+ in milestone payments, royalties on product sales, and FUJIFILM responsible for further product development
Successful clinical trial results	▪ All clinical endpoints achieved in trial of Cymerus MSCs in GvHD, with no safety concerns identified and highly encouraging efficacy ▪ FUJIFILM endorsement supports further development of Cynata's products in other indications
Clear pipeline of high potential target areas	▪ Multiple Phase 2 clinical trials with preparations underway to commence in 2020: COVID-19 (open for enrolment); GvHD (via FUJIFILM license); critical limb ischemia (CLI) ▪ Phase 3 Osteoarthritis trial (funded by NHMRC) commenced ▪ Compelling pre-clinical data in other high-value target areas supports further clinical trials
Well positioned in regenerative medicine	▪ Cell therapeutics is an area of increasing interest from major pharmaceutical companies ▪ Global market opportunity of US$1.4bn for CLI and US$11.6bn for OA ▪ Cynata's unique Cymerus technology ideally placed to solve current MSC manufacturing challenges

Globally experienced board and management team

Dr Geoff Brooke
Chairman

- 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 Chairman of Actinogen Media Limited and non-executive director of Acrux Limited

Extensive life sciences and financial expertise in US and Australia

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 Paul Wotton
Non-Exec Director

- 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 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 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

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*[1]
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*[2]
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[3]	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

Thank you for your attention

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