



# A Next Generation Stem Cell Company

Investor Presentation: Cynata Therapeutics Limited

June 2018

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# Investment Summary: a Phase II-ready biotech with a highly scalable, proprietary platform for producing commercial quantities of MSCs

<b>Scalable, globally applicable technology</b>	<ul style="list-style-type: none"><li>▪ Cymerus™ platform enables production of high quality Mesenchymal Stem Cells at scale</li><li>▪ Fully patented process overcomes multiple issues with today's on-market solutions</li></ul>
<b>Excellent results from Phase I trial in GvHD</b>	<ul style="list-style-type: none"><li>▪ All trial endpoints achieved to date: no adverse safety events, highly encouraging efficacy</li><li>▪ GvHD programme well positioned to progress to Phase II</li><li>▪ Safety data enables Cynata to move directly to Phase II in other indications</li></ul>
<b>Clear pipeline of high-potential target areas</b>	<ul style="list-style-type: none"><li>▪ Cardiovascular disease identified as priority indication area for expanded trial pipeline</li><li>▪ Planning for Phase II programme in Critical Limb Ischemia (CLI) to commence in H2 2018</li><li>▪ Compelling pre-clinical data in multiple other high-value target areas</li></ul>
<b>Well-funded to progress clinical programme</b>	<ul style="list-style-type: none"><li>▪ Pro-forma cash balance of \$13.5m based on cash balance of \$8.3m as at 31-Mar-18, reinforced by \$5.2m placement of shares to leading institutional investor Fidelity International on 30-May-18</li></ul>
<b>Attractive licensing-driven business model</b>	<ul style="list-style-type: none"><li>▪ Fujifilm hold licence option for GvHD – will pay all costs of all further development and commercialisation <u>plus</u> \$60m in milestone payments <u>plus</u> royalties if exercised</li><li>▪ Licence agreements and strategic partners for other indications being explored</li></ul>
<b>Valuable and active market</b>	<ul style="list-style-type: none"><li>▪ Estimated \$1.7bn revenue opportunity for MSC supplier for GvHD and CLI products alone</li><li>▪ Over 850 clinical trials investigating the efficacy of MSCs across numerous indications</li><li>▪ Multiple pharma companies active in stem-cell M&amp;A</li></ul>

# Cynata has the only platform in the world to produce commercial quantities of Mesenchymal Stem Cells from a single source

## Today's on-market MSC manufacturing solution has a number of shortcomings

### REGULATORY ISSUES

- × Sourcing cells from multiple donors leads to **variability in the sourced cells**, which is a **major regulatory hurdle**

### REDUCED EFFICACY

- × **Massive cell expansion** is required to create enough cells for therapeutic use, which may **result in reduced efficacy**



Surgery required to source MSCs from bone marrow



Multiple donors



Complex surgery



Cell expansion

## Patented Cymerus Platform overcomes shortcomings

### ✓ CONSISTENT PRODUCT QUALITY

*Single donor overcomes regulatory concerns*

### ✓ MAINTAINED PRODUCT EFFICACY

*Cymerus overcomes need for excessive expansion*



For more information on the Cymerus platform visit [Cynata's website](https://www.cynata.com)



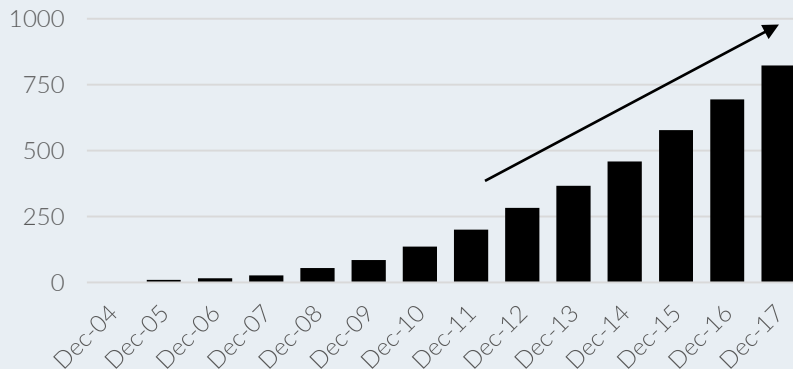
# MSCs are a highly potent form of stem cell attracting significant clinical interest – and in need of a scalable commercial solution

**Mesenchymal Stem Cells (MSCs) are believed to play a vital role in repair and regeneration**

- ✓ Modulator of the immune system
- ✓ Secrete bioactive molecules and have immunosuppressive and immunoregulatory properties

**Over 850 clinical trials investigating the efficacy of MSCs in treating diseases have been initiated<sup>1</sup>**

Number of MSC clinical trials (cumulative)



- ✓ MSCs were approved for use as a therapeutic treatment in Japan in September 2015 and Europe in March 2018

**Global commercial potential, with multiple target areas potentially benefiting from MSC treatment**



Diabetes complications



Diabetic foot ulcers



GvHD



Fistula



Asthma



Acute respiratory distress syndrome



Brain cancer / Glioblastoma



Osteoarthritis



Critical limb ischemia



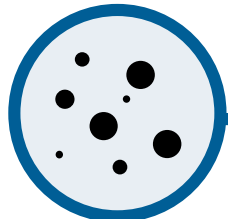
Crohn's disease



Heart attack

# Cynata's goal is for its patented Cymerus platform to become the preferred solution for Big Pharma to commercially produce MSCs

Phase I near completion, Phase II planned



**GvHD**

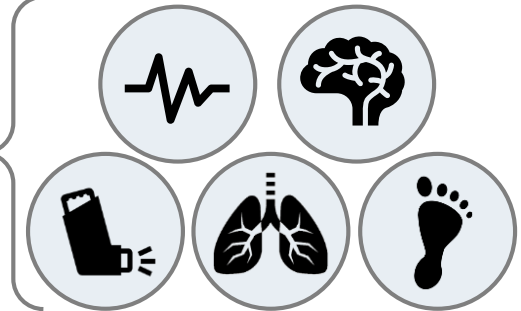
✓ Fujifilm licence option

✓ Licence available

**A 'hub and spoke' business model**

**Intention to license Cymerus  
across a range of target areas  
to maximise value**

Preclinical data



Phase II planned



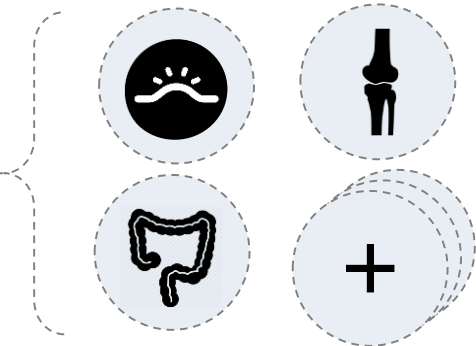
**Critical Limb  
Ischemia**

✓ Licence available

✓ Licence available

Following successful GvHD  
trial, a new indication will  
progress direct to Phase II

Potential future target areas



# Trial update | Excellent results in Phase 1 GvHD clinical trial, a clear validation of Cynata's MSCs and the Cymerus platform

Cynata is nearing completion of a successful Phase 1 clinical trial, demonstrating **safety** and **meaningful impact** on the patients' quality of life

## ✓ All endpoints achieved to date

(as at Cohort B 28-day trial update, announced on 21-Jun-18)

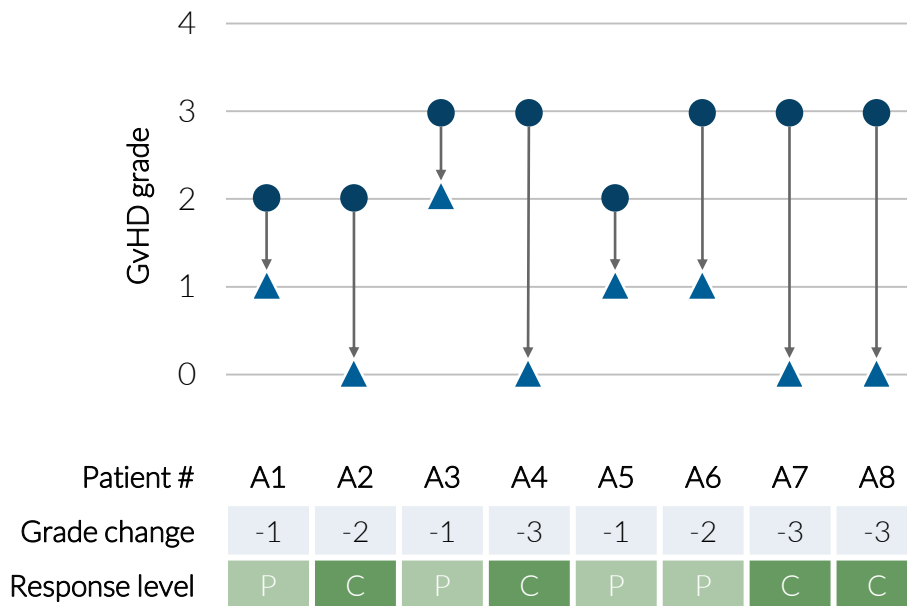
	Cohort A (at 28 days)	Cohort A (at 100 days)	Cohort B (at 28 days)
Safety	✓ No safety issues / adverse reactions observed		
Complete response <i>Absence of GvHD</i>	✓ 12.5%	✓ 50%	✓ 57%
Partial response <i>Improvement by at least 1 GvHD grade</i>	✓ 75%	✓ 100%	✓ 86%
Overall survival <sup>1</sup>	✓ 87.5%	✓ 87.5%	✓ 100%

Excellent safety data allows multiple future indications  
to progress directly to Phase II

# Trial update | Substantial improvement in GvHD grades observed with the majority of patients reporting a Complete Response

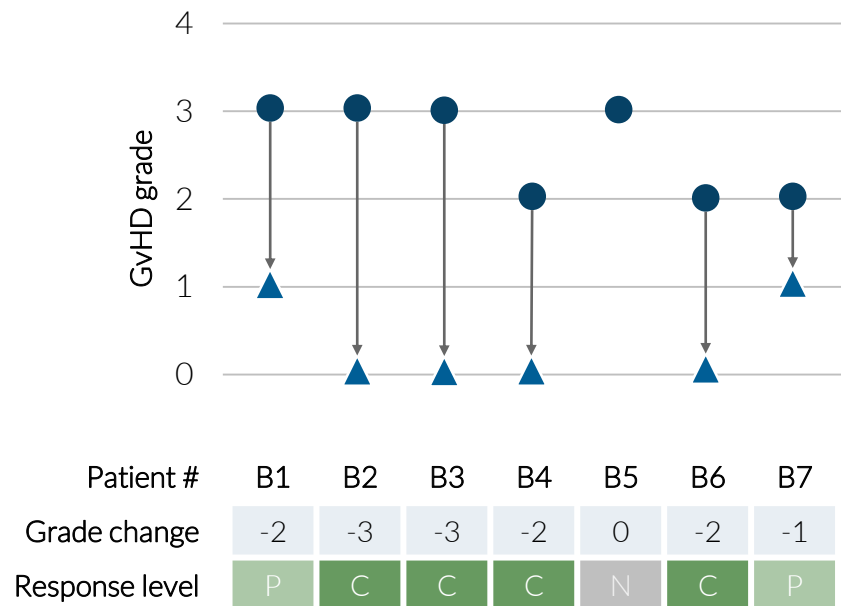
Cohort A, lower dose (as at 100-day readout)

Complete Response rate of 50%



Cohort B, higher dose (as at 28-day readout)

Complete Response of 57%



## Legend

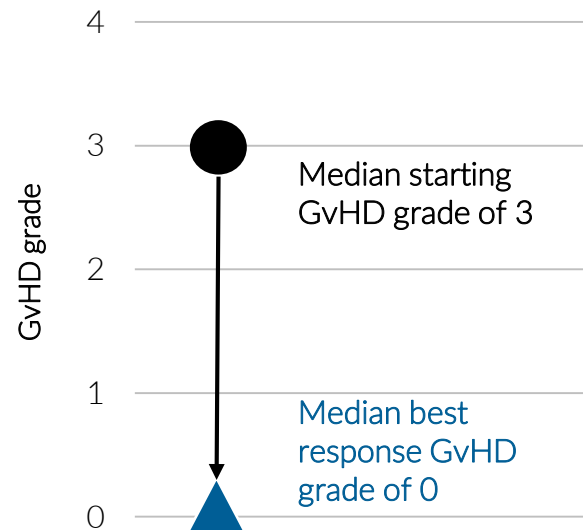
● GvHD grade: As at day 0    ▲ GvHD grade: Best response    C Complete response    P Partial response    N No response



# Trial update | Response rate represents a meaningful improvement for a life-threatening, severe disease, in a \$300m market opportunity<sup>1</sup>

## Trial results to date<sup>2</sup>

### Substantial improvement in GvHD grade



## GvHD grade scale<sup>3</sup>

### Overall GvHD grade based on a combination of skin, liver and gut stages

Stage	Skin stage % of body surface area affected	Liver stage Bilirubin (mg/dl)	Gut stage Stool volume (ml/day)
4	>50% with skin peeling or blistering	≥ 15.0	> 1,500 mL and severe abdominal pain (with or without ileus)
3	>50%	6.0 – 14.9	> 1,500 mL
2	25-50%	3.0 – 5.9	1,000 mL – 1,500 mL
1	<25%	2.0 – 2.9	500 mL – 1,000 mL (or persistent anorexia, nausea and vomiting)
0	0%	< 2.0	≤ 500ml

*GvHD is a devastating disease that impacts patients who are already suffering and in need of transplants  
A change in GvHD grade of only 1 has a meaningful impact on these patients' quality of life*

# Trial update | Phase 1 GvHD trial was designed to demonstrate safety of Cynata's MSCs and support evaluation of efficacy

## What is GvHD?

Graft versus host disease (GVHD) is a condition where following a transplant the donor's immune cells in the transplant (graft) make antibodies against the patient's tissues (host) and attack vital organs. Organs most often affected include the skin, gastrointestinal (GI) tract and the liver.

## Overview of GvHD clinical trial

### World's first allogeneic iPSC-derived cell therapy clinical trial

Clinical trial protocol CYP-GvHD-P1-01

Population ~15 adults with steroid-resistant acute GvHD

Clinical sites 7 (UK and Australia)

Endpoints

- Safety and tolerability (primary)
- Complete/Partial Response by Day 28/Day 100
  - Complete response = absence of GvHD
  - Partial response = improvement by at least 1 grade
- Overall survival at Day 28/Day 100

Current status

- Cohort A – dosing completed Nov 2017, final 100 day readouts completed Feb 2018
- Cohort B – dosing completed May 2018, final 100 day readouts expected in September 2018

## Clinical trial design

### Screening criteria

- Adults with steroid resistant acute GvHD
- Life expectancy of at least 1 month
- Other conditions screened out that may impact results

### Cohort A

May-17 – Dec-17  
n=8

1x10<sup>6</sup> cells/kg on Day 0 and Day 7<sup>1</sup>

28 day read-out ✓

100 day read-out ✓

Data and Safety Monitoring Board (DSMB) assessed Cohort A 28-day data and **approved commencement of Cohort B**

### Cohort B

Jan-18 – May-18  
n=7<sup>3</sup>

2x10<sup>6</sup> cells/kg on Day 0 and Day 7<sup>2</sup>

28 day read-out ✓

100 day read-out

# Cell therapy is an active market attracting big pharma M&A interest

USD  
307M



Acquired by



March 2015

- Enables Fujifilm to combine technologies with Cellular Dynamics to develop new iPSC based cell therapies
- Founder of Cellular Dynamics also founded Cynata

USD  
379M



Acquired by



February 2016

- Enables Astellas to establish a leading position in cell therapy
- Ocata CEO prior to acquisition was Paul Wotton, current Chairman of Cynata

USD  
628M



Acquired by



January 2018<sup>1</sup>

- Extends existing partnership between Takeda and TiGenix to develop and commercialize Cx601 (darvadstrocel)
- TiGenix was the first company to receive approval for an MSC therapy in Europe

# Cynata is executing on a clear scientific and commercial vision and continually assesses pathways to maximise 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's existing option for GvHD)*

Asset sale  
*(e.g. Strategic acquirer)*

Fujifilm holds a licence option for development and commercialisation of Cynata's MSCs for GvHD

### Exercise of Fujifilm option (US\$3m)

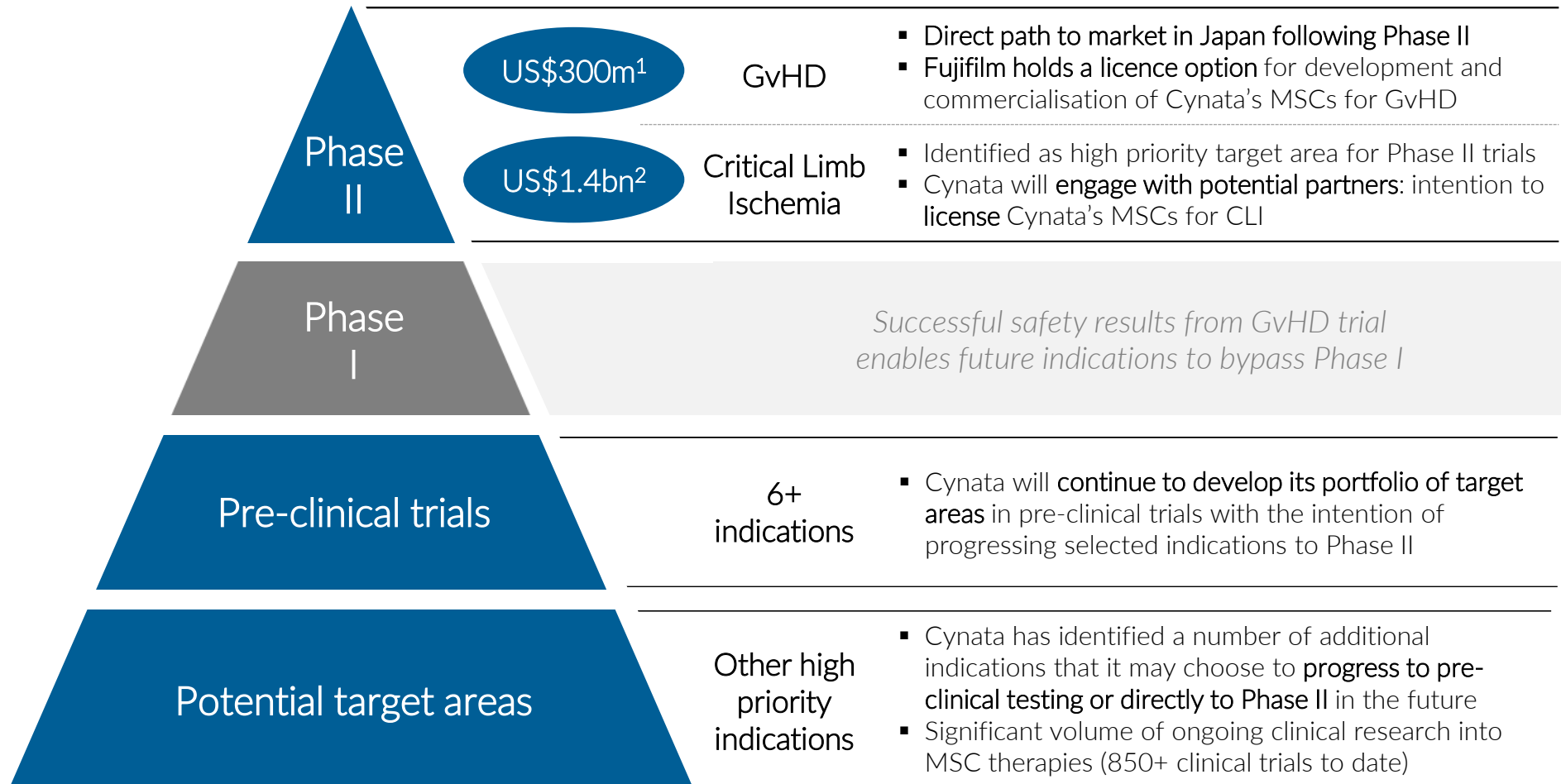
- Fujifilm can exercise up to 90 days after completion of Phase 1 trial.
- On exercise Cynata receive upfront **US\$3m** milestone payment
- Fujifilm responsible for all further development activities and costs

### Phase 2 and beyond (US\$30m+ p.a.)

- Fujifilm to pay Cynata agreed milestones (**\$60m+**) and double-digit royalties on product sales
- Fujifilm's projections for the GvHD market suggest **>US\$30m** per year in royalties for Cynata

# Cynata intends to demonstrate broad global applicability of its Cymerus platform

## New enhanced pipeline and clear pathway to commercialisation



# ClearView were commissioned to evaluate the full landscape of MSC opportunities to identify high priority indications

## Indication prioritisation process

**CLEARVIEW**  
Healthcare Partners  
*Study commissioned*

ClearView identified  
~20 high potential target areas  
with clear scientific and  
commercial attractiveness

Cardiovascular disease selected by Cynata  
as highest priority indication area

- ✓ Primary indication: **Critical Limb Ischemia**
- ✓ Progress to clinical trials (direct to Phase II)

## Key metrics used to evaluate potential MSC indications



### Mechanical / Scientific Attractiveness

- Expert perspectives and scientific evidence supporting rationale for use of an MSC approach



### Clinical Development Attractiveness

- Overall burden (i.e., trial duration, trial size, recruiting hurdles)
- Likelihood of success (endpoint feasibility) of clinical development



### Commercial Attractiveness

- Estimated sales based on interviews with key opinion leaders on MSC therapy concepts and accounting for the future competitive landscape

# New Phase II programme in Critical Limb Ischemia | Opportunity Overview



Estimated market size

230,000

Addressable events per year

~US\$1.4B<sup>1</sup>

Forecast annual global market sales



## Critical Limb Ischemia (CLI)

- MSC therapy for effective treatment of critical limb ischemia patients who are ineligible for revascularization, to promote angiogenesis and reduce inflammation



## Rationale for selection

- Cymerus preclinical studies were compelling, animals treated with Cymerus MSCs experienced improved blood flow ( $p < 0.006$ ) and faster blood flow recovery ( $p < 0.001$ ) when compared to the control group treated with saline
- Development timeline is relatively rapid



## Preliminary programme design

- Pivotal trials may last 1–2 years and require 50–100 revascularisation-ineligible patients (patients not eligible for surgery intended to restore blood flow)
- Endpoints likely to include amputation-free survival and ankle-brachial index, ulcer healing, and pain (reviewed over 6–12 months)

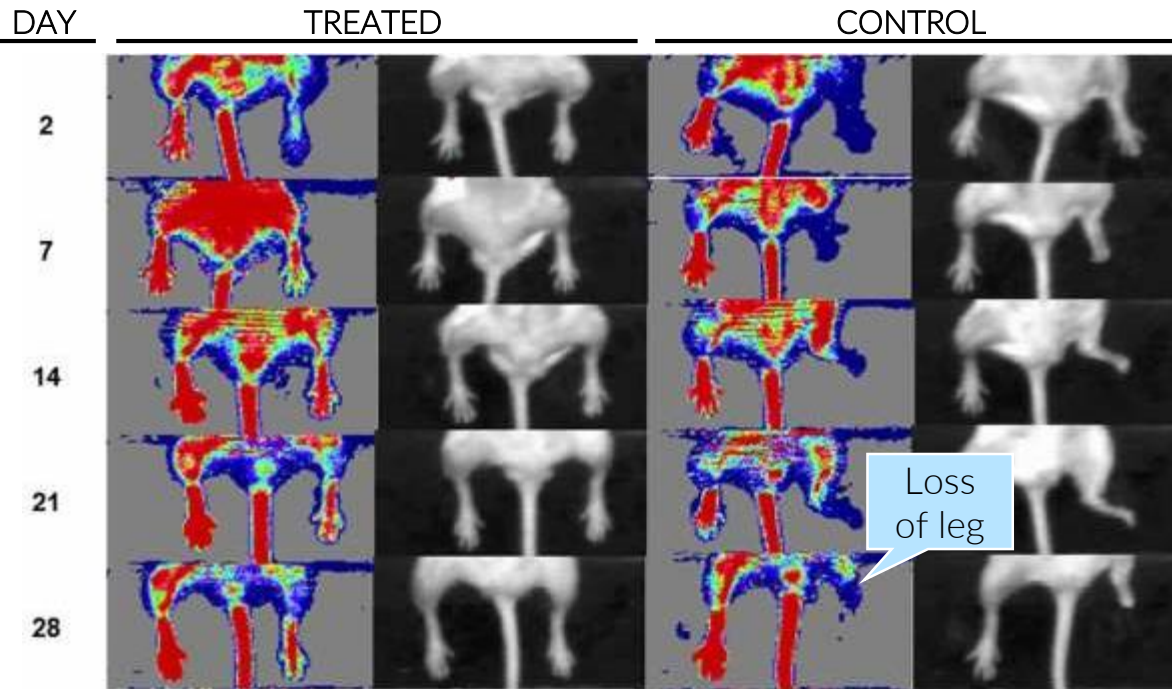


## Key milestones

- Planning for Phase II programme in Critical Limb Ischemia to commence in H2 2018

# Critical Limb Ischemia clinical study follows excellent results from an earlier pre-clinical study

Mice dosed with Cymerus MSCs experienced significantly improved outcomes when compared with control group



Animals treated with Cymerus MSCs experienced improved blood flow ( $p < 0.006$ ) and faster blood flow recovery ( $p < 0.001$ ) when compared to the control group treated with saline

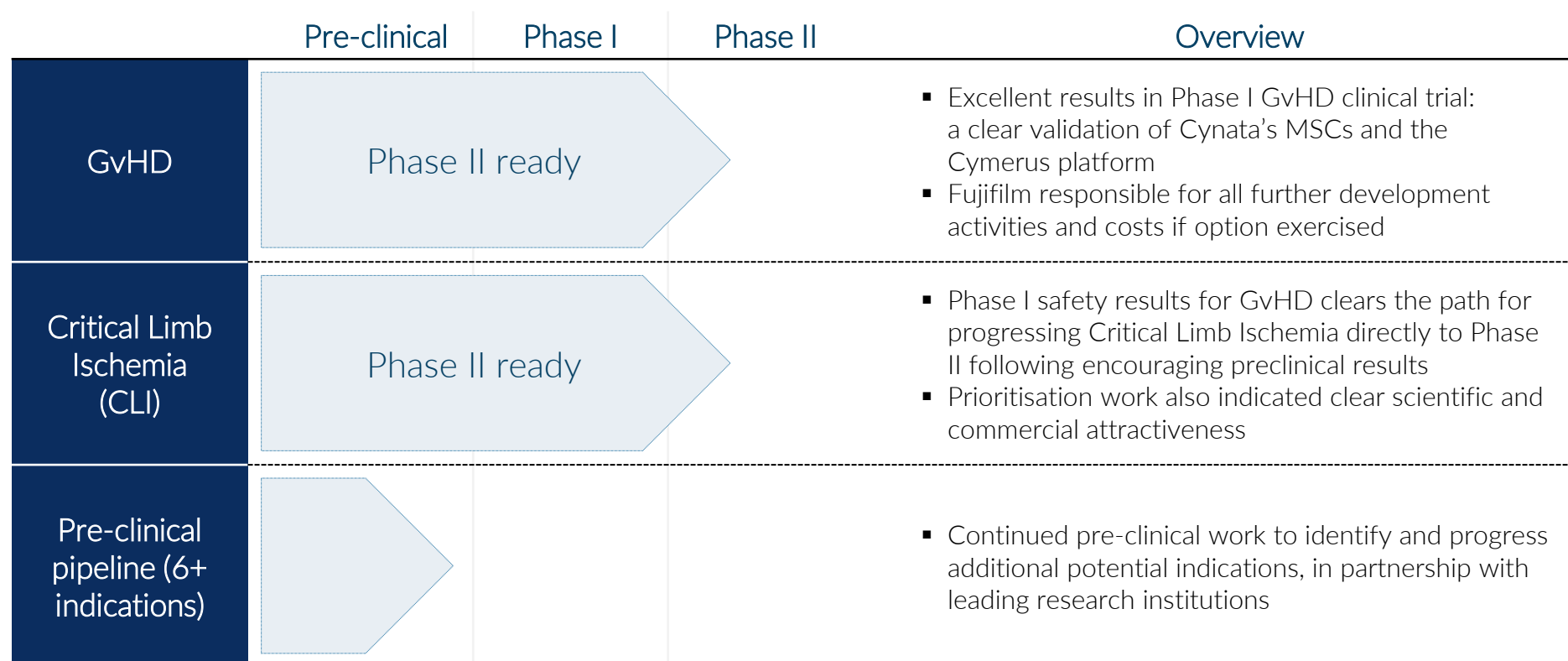
All results published in a peer reviewed journal



Cytherapy is a peer-reviewed medical journal covering the areas of cell biology and immunology, including cytokines, cytotherapy, and molecular therapy



# Cynata is well funded to progress its enhanced clinical pipeline



**Cynata is well funded:**

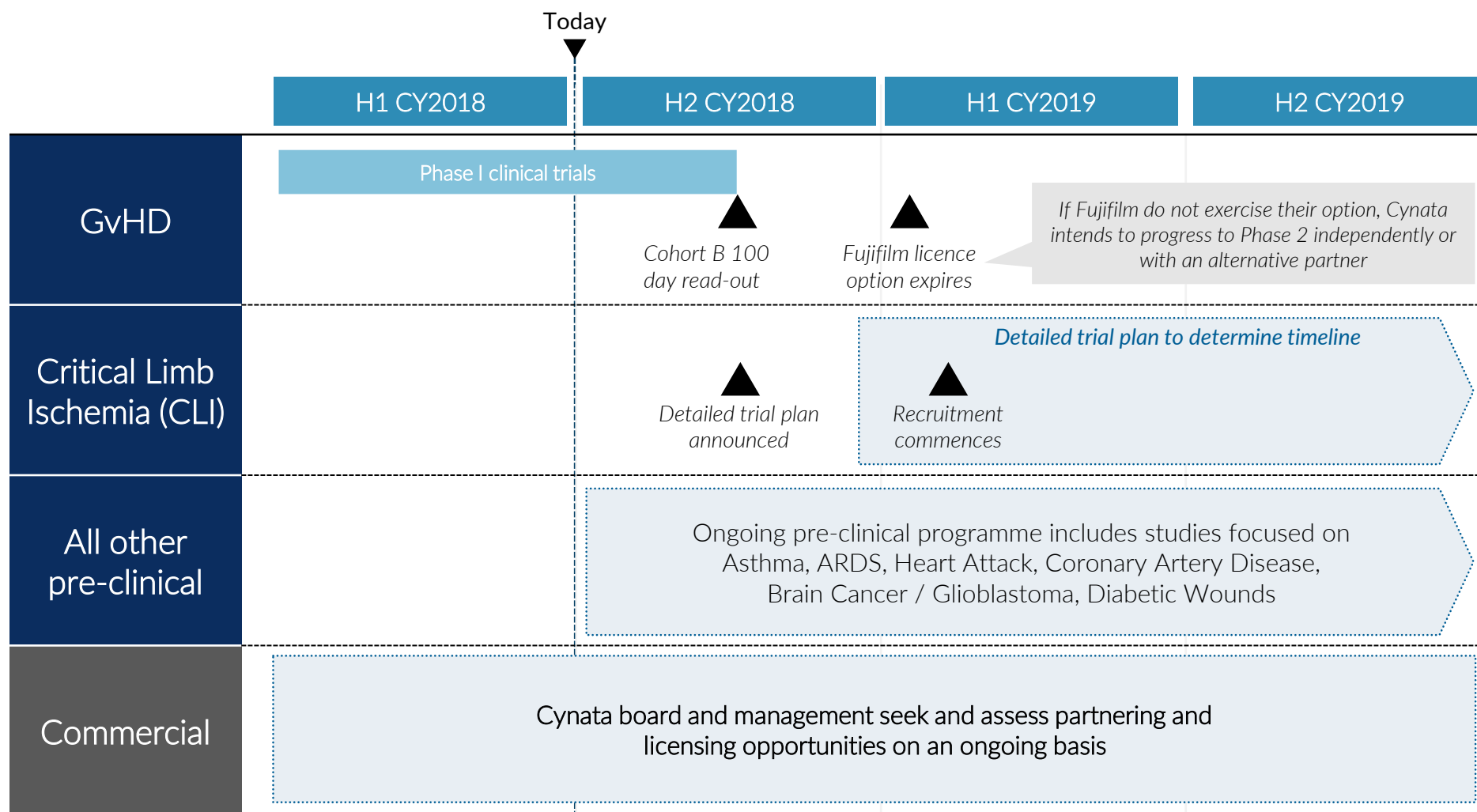
\$13.5m pro-forma cash balance<sup>1</sup>

\$6.5m in-the-money stock options<sup>2</sup>







Cost sharing with licence partners

R&D expenditure eligible for rebates

# Key upcoming milestones



# Cynata will continue to progress pre-clinical studies with leading academic and commercial partners

Disease target area			Pre-clinical trials started	Proof of concept completed	Key highlights
Asthma		Monash University	✓	✓	Cymerus MSCs demonstrated significant beneficial effects on three key components of asthma: airway hyper-responsiveness, inflammation and airway remodelling
ARDS		Critical care research group	✓		Study to commence to evaluate effectiveness of Cymerus MSCs in sheep with ARDS in association with the Prince Charles Hospital in Brisbane.
Heart attack		University of Sydney	✓		Pre-clinical trials suggest Cymerus MSCs may have the potential to restore cardiac function and reduce scar size after a heart attack (US\$18.2 billion market by 2019 <sup>1</sup> )
Brain Cancer / Glioblastoma		Harvard/BWH	✓		Research collaboration in genetically modified MSCs in cancer: involves modifying stem cells to target cancer
Diabetic Wounds		CRC for Cell Therapy Manufacturing	✓	✓	Independent study by CRC for Cell Therapy Manufacturing received positive data which demonstrates the efficacy of Cymerus MSCs in a preclinical model of diabetic wounds
Coronary Artery Disease		University of New South Wales	✓		Research collaboration for the development of MSC therapies to treat coronary artery disease

Successful outcomes open many other disease targets potentially benefiting from MSCs

# Globally experienced board and management team



**Dr Paul Wotton**  
Chairman

Former CEO of Ocata Therapeutics (NASDAQ: OCAT) managing it through a take-over 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; member of the boards of Vericel Corporation 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 Chief Executive Officer

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-Executive Director

20+ years of CEO and Board experience in medical technology, biotech and agrifood companies

Chairman of Orthocell Ltd and Minomic International

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 John Chiplin**  
Non-Executive Director

Significant international experience in the life science and technology industries

Recent transactions include US stem cell company Medistem (acquired by Intrexon), Arana (acquired by Cephalon), and Domantis (acquired by GSK)

Was head of the \$300M ITI Life Sciences investment fund in the UK and his own investment vehicle, Newstar Ventures

Overseen and managed a broad range of life sciences transactions



**Mr Peter Webse**  
Non-Executive Director  
Company Secretary

+25 years' company secretarial experience

Managing Director of Platinum Corporate Secretariat Pty Ltd, a company specialising in providing company secretarial, corporate governance and corporate advisory services

25+ years company secretarial and management experience



**Dr Kilian Kelly**  
Vice President, Product Development

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)

Academic and commercial excellence, extensive relevant management experience

# Investment Highlights

- **Scalable, world-first technology:** Cymerus platform overcomes inherent challenges of other production methods and enables mass-production of therapeutic MSCs
- **Phase II ready:** Excellent Phase I results provide validation of Cynata's Cymerus platform; Cynata well positioned to progress to Phase II in GvHD and other indications
- **Cardiovascular disease identified as priority indication area for clinical programme:** Planning for Phase II in Critical Limb Ischemia to commence in H2 2018
- **Attractive licensing-driven business model:** Fujifilm licence option for GvHD worth over US\$60m plus royalties
- **Valuable market opportunity:** Estimated US\$1.7bn revenue opportunity for MSC supplier for GvHD and CLI products alone
- **Well-funded to progress clinical programme:** Pro forma cash balance of \$13.5m



# Appendix | Key recent newsflow: last 6 months

Release date	Announcement
<b>GvHD</b>	
21-Jun-18	Positive 28-day data from Cohort B
12-Jun-18	Positive 6-month data from Cohort A
24-May-18	Enrolment completed in Cynata's Phase 1 Clinical Trial
28-Mar-18	FDA Grants Orphan Drug Designation to Cynata for CYP-001
27-Feb-18	Excellent 100-day data from Cohort A
24-Jan-18	Cynata treats first patient in Cohort B
22-Jan-18	Encouraging early data – DSMB recommendation to progress to Cohort B
<b>Pre-clinical / other</b>	
18-Jun-18	Research Collaboration with UNSW for Coronary Artery Disease
31-May-18	Cynata's MSCs Effective in Model of Diabetic Wounds
7-May-18	Notice of Allowance from EPO for Cymerus Technology Patent Application
20-Apr-18	CYP completes patent application related to CAR-T Therapy
11-Apr-18	Further US patent granted for Cynata's Cymerus Technology
5-Feb-18	Cynata engineered MSC study interim data review reveals promising results
<b>Commercial</b>	
30-May-18	\$5.2m placement of shares to Fidelity International
23-Jan-18	Cynata & Cellularity Inc Execute MOU

# Appendix | Corporate overview

## Company profile

Cynata Therapeutics is an Australian stock exchange listed clinical-stage biotechnology company developing disruptive regenerative medicines.

## Financial information

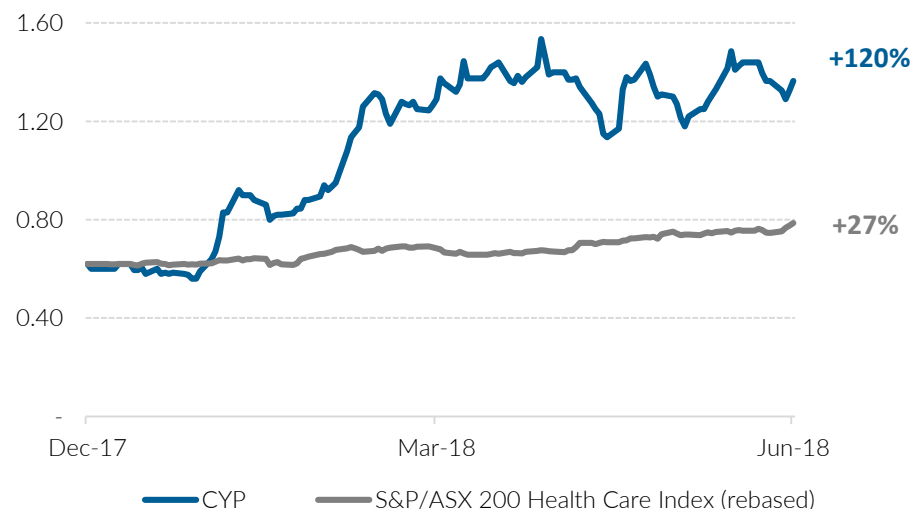
Share price (21-June-18)	A\$1.37
52 week low / high	A\$0.54 / A\$1.54
Shares on issue <sup>1</sup>	95.1m
Market capitalisation	A\$129.8m
Pro-forma Cash (as at 31-March-18) <sup>2</sup>	A\$13.5m
Debt (as at 31-March-18)	-
Enterprise value	A\$116.3m

Source: IRESS

Notes:

1. Excludes 11.2m unquoted options with exercise prices ranging from \$0.40 to \$1.50 and expiry dates between 27-Sep-2018 and 4-Aug-2020 (1m subject to vesting conditions), and 750k unlisted incentive options with exercise price \$0.49 and expiring 16 December 2018
2. Pro-forma cash calculated as cash balance at 31-Mar-2018 (\$8.3m), adjusted for \$5.2m cash from 30-May-2018 placement
3. Represents shareholding if all options held by the Board and Management (total of 8.55m) are exercised

## Share price performance (last 6 months, A\$)



## Top shareholders

Shareholder	
Fidelity International	10.0%
Fujifilm Corporation	8.5%
Board and Management	0.6%
Board and Management (fully diluted) <sup>3</sup>	8.8%

Thank you for your attention

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