



# A Next Generation Stem Cell Therapeutics Company

AGM Presentation: Cynata Therapeutics Limited  
27 November 2019

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**MD & CEO**

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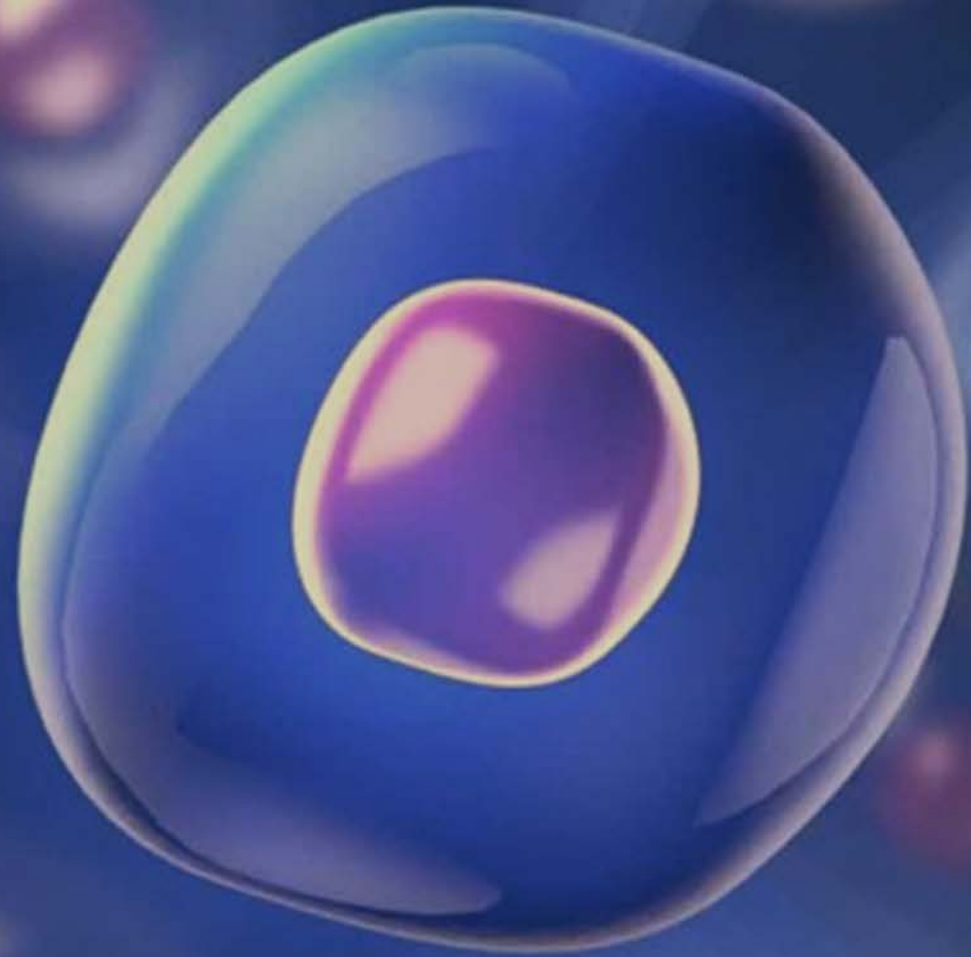
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# Our focus

Using our proprietary Cymerus™ platform technology to develop commercially scalable cellular therapeutic products to treat serious chronic disorders



# Agenda

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**2019 Highlights:** driving clinical and commercial success

2

**FUJIFILM:** license for GvHD

3

**Current strategic focus:** attractive licensing business model

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**Cymerus:** a scalable, globally applicable technology

5

**Market:** attractive regenerative medicine industry

6

**Outlook:** three upcoming Phase II trials

## 2019 Highlights: Driving Clinical and Commercial Success

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**FUJIFILM license agreement**

*FUJIFILM endorsement validates Cynata's Cymerus platform*



**Progressing to three Phase II trials**

*Expected to commence in CY20 for GvHD, CLI, and Osteoarthritis*



**Advanced pre-clinical program**

*Therapeutic potential in numerous additional target areas*

**Cynata continues to focus on early commercialisation of Cynata's Cymerus MSC products, and is in active commercial discussions for numerous therapeutic targets**

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

License / partner with big Pharma to develop specific target areas

Strategic exit/merger



## FUJIFILM case study

- ✓ Exclusive global licence in GvHD
- ✓ Multiple cash flow events:
  - US\$3m equity @ 35% premium
  - US\$3m upfront license fee received
  - US\$40m in potential milestone payments
  - Double digit royalties (worth potentially >US\$30m p.a.)
- ✓ Represents a major endorsement by Big Pharma
- ✓ Ongoing relationship with potential for further commercial agreements

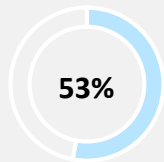
FUJIFILM transaction provides validation of the Cymerus platform and supports the licensing of additional target areas

# Value inflection point following clear data and first commercial transaction, with Cynata's focus on further license agreements

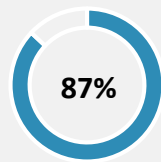
## Successful clinical study data

### Demonstrating efficacy of our technology platform

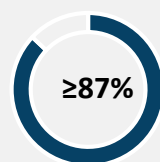
- ✓ **World-first allogeneic iPSC-derived cell therapy clinical trial** in steroid-resistant acute GvHD
- ✓ **Successful clinical trial results** with all endpoints achieved



*Complete response*



*Overall response*



*Survival rate*

- ✓ **Clinically meaningful findings** validate progress to multiple Phase II trials
- ✓ **Endorsement by FUJIFILM** supports the continued commercialisation of Cynata's cell therapeutic products in other indications

## Cynata's current focus

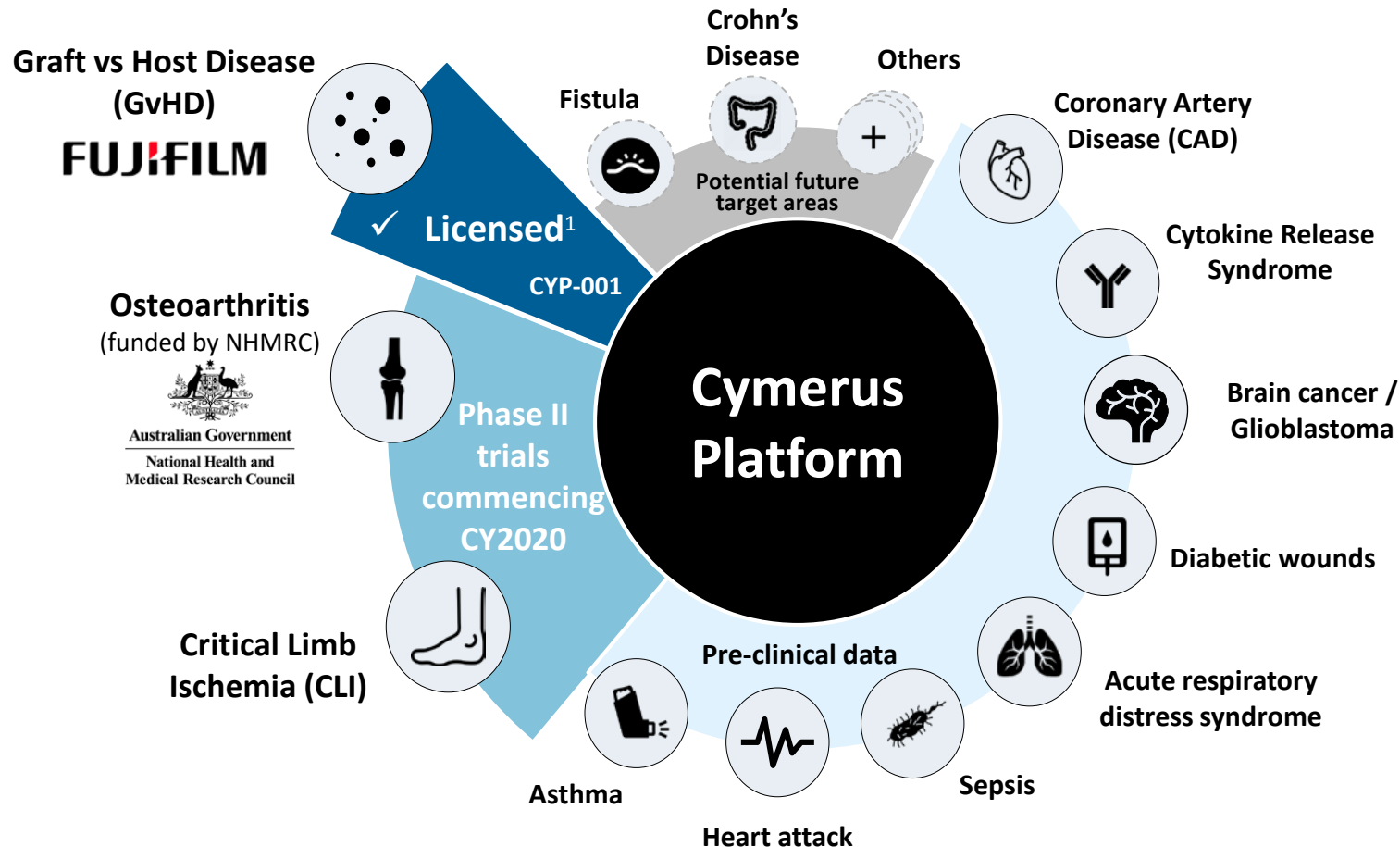
### Commercialise technology via further licence agreements

- A **'hub and spoke' business model** – the intention is to license Cymerus technology across a range of target areas to maximise value, or progress indications to Phase II independently
- Cynata is in **active ongoing commercial discussions** with multiple pharma companies



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

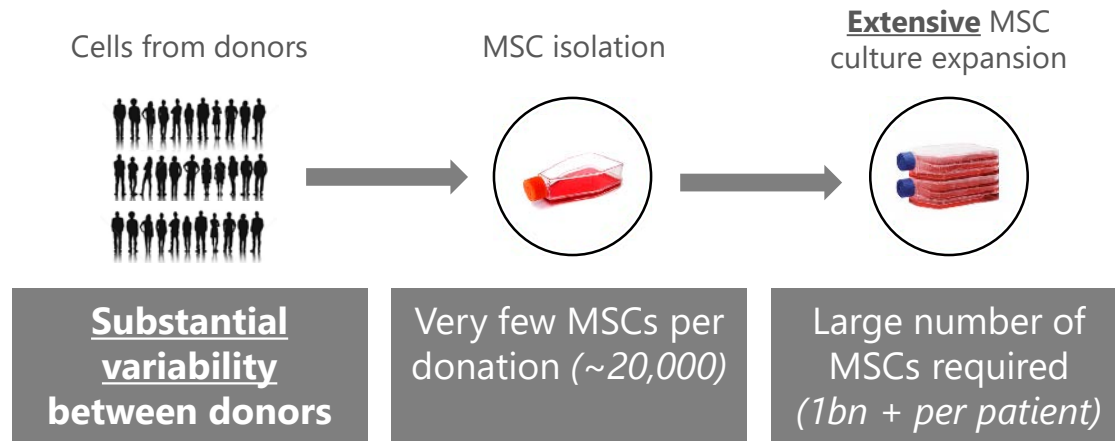
Cynata's current focus: commercialise technology via further licence agreements



**Dr Kilian Kelly**  
**COO**

# Our patented Cymerus platform enables the production of iPSC-derived cellular therapeutics from **a single adult donor**

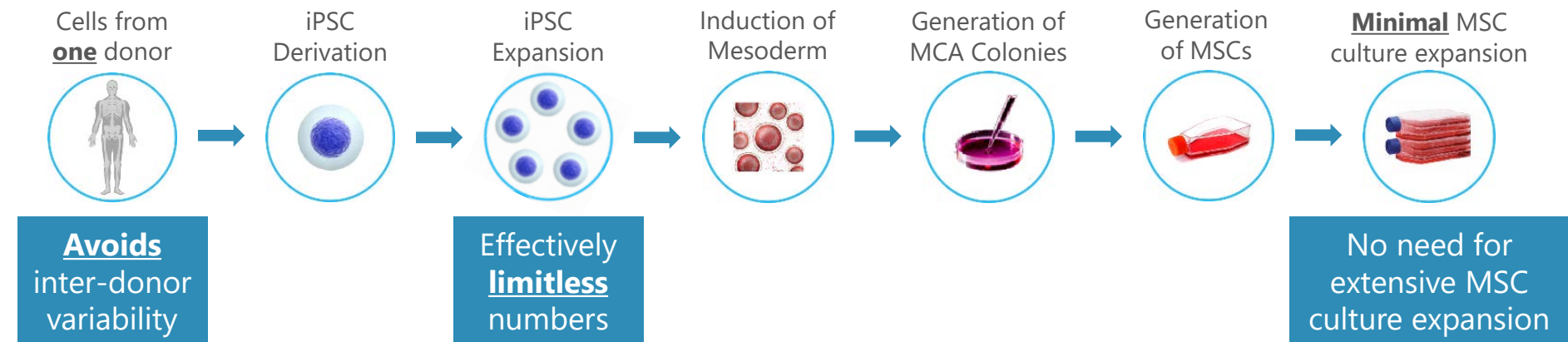
## Conventional MSC processes



**MSCs change when excessively expanded:** loss of potency, senescence, decreased efficacy

- limits number of doses that can be produced per donation
- new donors required more frequently
- more variability

## Cymerus iPSC-derived process



## Cynata's MSCs are high quality and commercially scalable

### Key advantages of the Cymerus process

#### CONSISTENCY & SCALABILITY

- ✓ **Consistent product quality** – single donor overcomes regulatory concerns
- ✓ **Bypasses complex and invasive surgeries** with a scalable and cost-effective process
- ✓ **Lower cost of goods on a per cell basis** compared to conventional MSC products

#### FEWER CELLS PER PATIENT

- 2 infusions per patient** in GvHD, compared to 8-12 for bone-marrow derived products
- ✓ **Greater convenience** for patients and hospitals
- ✓ **Lower costs** incurred by healthcare system

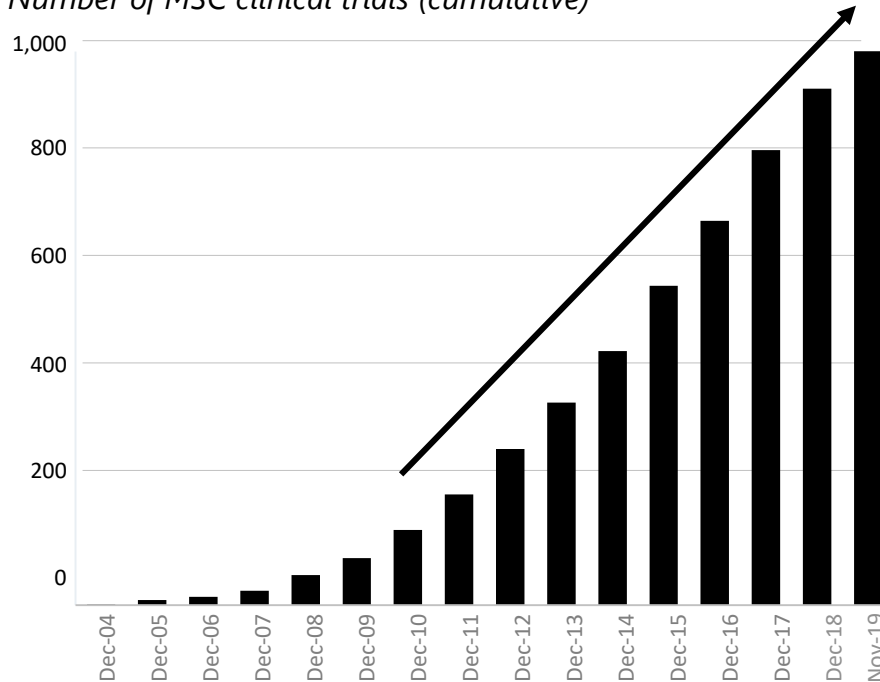
**Cynata has the only platform in the world able to produce commercial quantities of MSCs from a single source**

# Clinical use of MSCs continues to grow

## Over 1,000 clinical trials with MSCs have been initiated<sup>1</sup>

## Growing body of evidence for the role of MSCs in repair and regeneration

Number of MSC clinical trials (cumulative)



**Regenerate diseased and damaged tissue**



**Modulate the immune system and reduce inflammation**



**Accelerate recovery from the effects of disease or injury**

# Multiple MSC-based therapies are now **on the market**

## Approved treatments:



Cupistem<sup>®</sup> (Anterogen) for Crohn's fistula  
 Queencell<sup>®</sup> (Anterogen) for connective tissue disorders  
 NeuroNata-R<sup>®</sup> (Corestem) for motor neurone disease



TEMCELL<sup>®</sup> (JCR Pharma) for acute GvHD



Stempeucel<sup>®</sup> (Stempeutics) for CLI due to Buerger's Disease







Alofisel<sup>®</sup> (TiGenix) for Crohn's fistula

- Conditional approvals have also been granted in Canada and New Zealand for acute GvHD
- First US approval of an MSC-based therapy likely in the near future

## Further MSC marketing approvals expected in near future

### ~30 Phase 3 trials with MSC-based therapies currently active

#### Indications include:

- Heart failure
- Heart attack 
- Stroke
- Type II diabetes
- Degenerative disc disease
- Peripheral artery disease 
- Diabetic foot ulcer
- Non-healing fractures
- Chronic GvHD 
- Chronic obstructive pulmonary disease
- Crohn's disease 

### Cynata is well placed in the MSC-based therapy market



Many ongoing Phase 3 trials involve very common conditions, representing **multi-billion** dollar market opportunities



Approvals in any of these indications will significantly **increase Big Pharma's interest** in MSCs

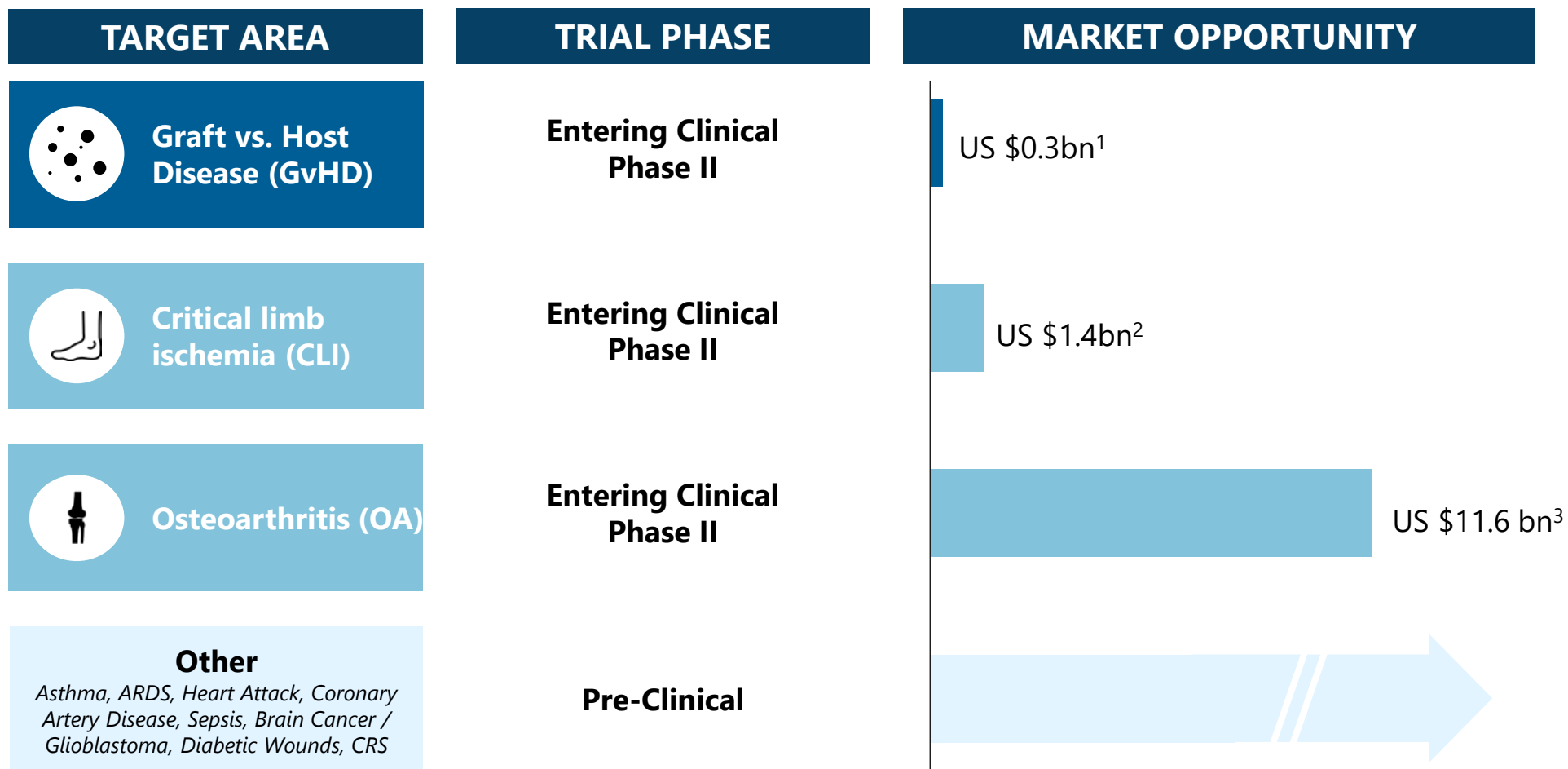


Demand for large quantities of product will focus attention on the **major manufacturing challenges** associated with conventional production methods



**Cynata's uniquely scalable and consistent process is ideally placed to solve these manufacturing challenges**

# Cynata is targeting significant market opportunities



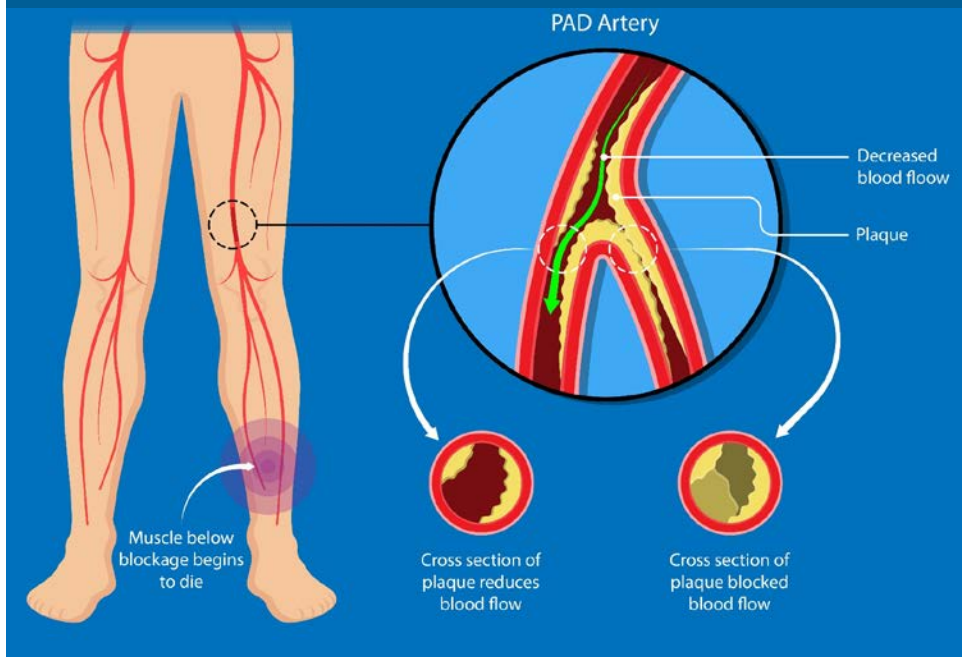
1. Fujifilm's estimate of the peak annual global sales opportunity
2. ClearView's estimate of the peak annual global sales opportunity
3. Persistence Market Research 2018 research report: "Osteoarthritis Treatment Market: Global Industry Analysis (2012-2016) and Forecast (2017-2025)"





# Critical limb ischemia (CLI)

## CLI is an advanced stage of PAD<sup>2</sup> caused by a narrowing of the arteries in the limbs<sup>1</sup>



- PAD affects 3-10% of people aged <70 and 15-20% of people >70<sup>1</sup>
- Risk factors include diabetes,, atherosclerosis, smoking, high blood pressure, high cholesterol
- Severely impaired blood flow causes pain, ulceration and gangrene
- >30% of PAD patients have a major artery completely blocked before diagnosis
- CLI often results in amputation; **~25% of CLI patients die within a year of diagnosis**

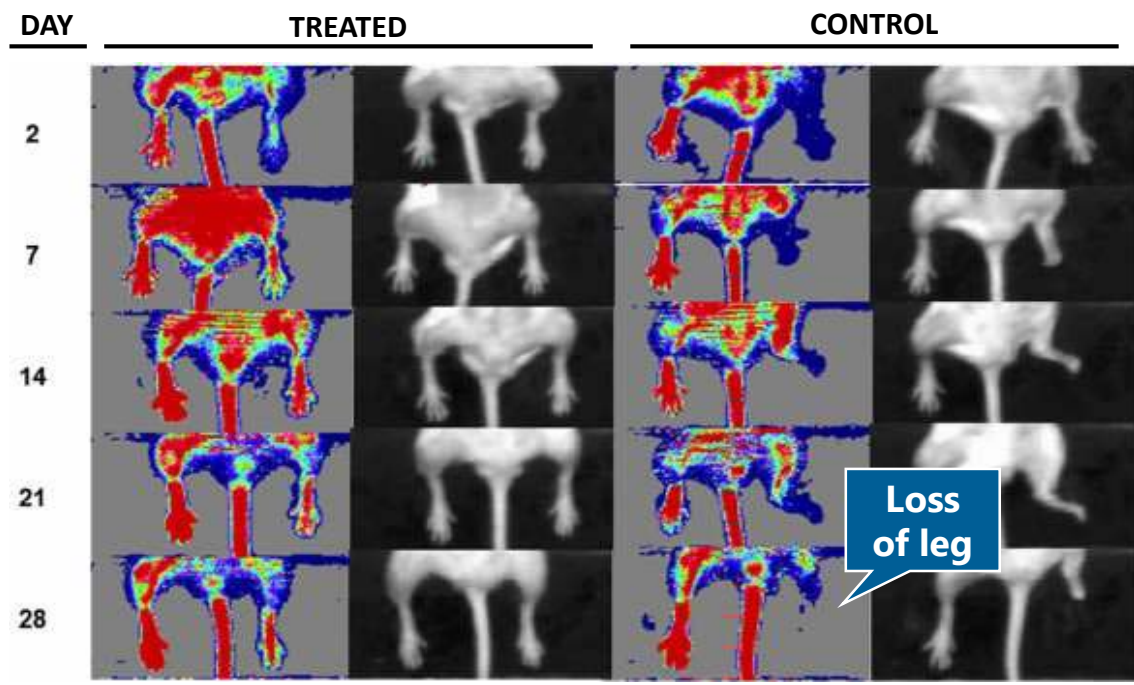
## Existing treatment options have very limited success rates

- **Lifestyle modification:** diet, exercise, smoking cessation
- **Treating related conditions:** diabetes, high blood pressure, high cholesterol
- **Revascularisation:** e.g. arterial bypass, angioplasty, stent placement



# Substantial body of evidence supporting use of MSCs to treat CLI/PAD

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

Liew and O'Brien *Stem Cell Research & Therapy* 2012, 3:28  
<http://stemcellres.com/content/3/4/28>

stem cell research therapy

REVIEW

Therapeutic potential for mesenchymal stem cell transplantation in critical limb ischemia

Aaron Liew and Timothy O'Brien\*

Stem cell and progenitor cell therapy in peripheral artery disease  
 A critical appraisal

Holger Lawall<sup>1</sup>, Peter Bramlage<sup>2</sup>, Berthold Amann<sup>3</sup>

<sup>1</sup>SRH Klinikum Karlsruhe Langensteimbach, Angiology / Diabetology, Karlsruhe, Germany; <sup>2</sup>Institute for Cardiovascular Pharmacology and Epidemiology, Muhlvi, Germany; <sup>3</sup>Department of Internal Medicine, Franziskus Krankenhaus, Berlin Vascular Center, Berlin, Germany

Diabetes Research and Clinical Practice  
 International Diabetes Federation

Comparison of bone marrow mesenchymal stem cells with bone marrow-derived mononuclear cells for treatment of diabetic critical limb ischemia and foot ulcer: A double-blind, randomized, controlled trial

Debin Lu<sup>a</sup>, Bing Chen<sup>a\*</sup>, Ziyuan Liang<sup>a</sup>, Wuquan Deng<sup>a</sup>, Youzhao Jiang<sup>a</sup>, Shufa Li<sup>a</sup>, Jing Xu<sup>b</sup>, Qinan Wu<sup>a</sup>, Zhonghui Zhang<sup>a</sup>, Bing Xie<sup>a</sup>, Sihao Chen<sup>c</sup>

Gupta et al. *Journal of Translational Medicine* 2013, 11:143  
<http://www.translational-medicine.com/content/11/1/143>

JOURNAL OF TRANSLATIONAL MEDICINE

RESEARCH Open Access

A double blind randomized placebo controlled phase I/II study assessing the safety and efficacy of allogeneic bone marrow derived mesenchymal stem cell in critical limb ischemia

Pawan K Gupta<sup>1</sup>, Anoop Chullikana<sup>1</sup>, Rajiv Parakh<sup>2</sup>, Sanjay Desai<sup>1</sup>, Arjan Das<sup>1</sup>, Sanjay Gottipamula<sup>1</sup>, Sagar Kishnamurthy<sup>1</sup>, Naveen Anthony<sup>1</sup>, Arun Pherwani<sup>1</sup> and Anish S Majumdar<sup>1</sup>

Combination Stem Cell Therapy for the Treatment of Severe Limb Ischemia: Safety and Efficacy Analysis

Gabriel P. Lasala, MD, FACC<sup>1</sup>, Jose A. Silva, MD, FACC<sup>1</sup>, Philip A. Gardner, MD<sup>2</sup>, and Jose J. Mingueli, PhD<sup>1</sup>

Angiology 41(6) 551-556  
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 DOI: 10.1177/000319710934413  
<http://ang.sagepub.com>  
 SAGE



# Critical Limb Ischemia | Overview of Cynata-led Phase II program



## 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 CLI patients who are ineligible for revascularization<sup>2</sup>, to promote angiogenesis and reduce inflammation



### Rationale for selection

- Cymerus preclinical studies were compelling
- Large body of data on use of MSCs in general in PAD/CLI
- Development timeline is relatively rapid



### Preliminary program design

- Approximately 90 patients with advanced CLI
- Clinical centres in UK and Australia
- Positive meeting with UK MHRA in Feb 2019, clinical trial application now submitted



### Key milestones

- Phase II clinical trial in Critical Limb Ischemia expected to commence in early CY2020







# Osteoarthritis | New Phase II program funded by National Health and Medical Research Council



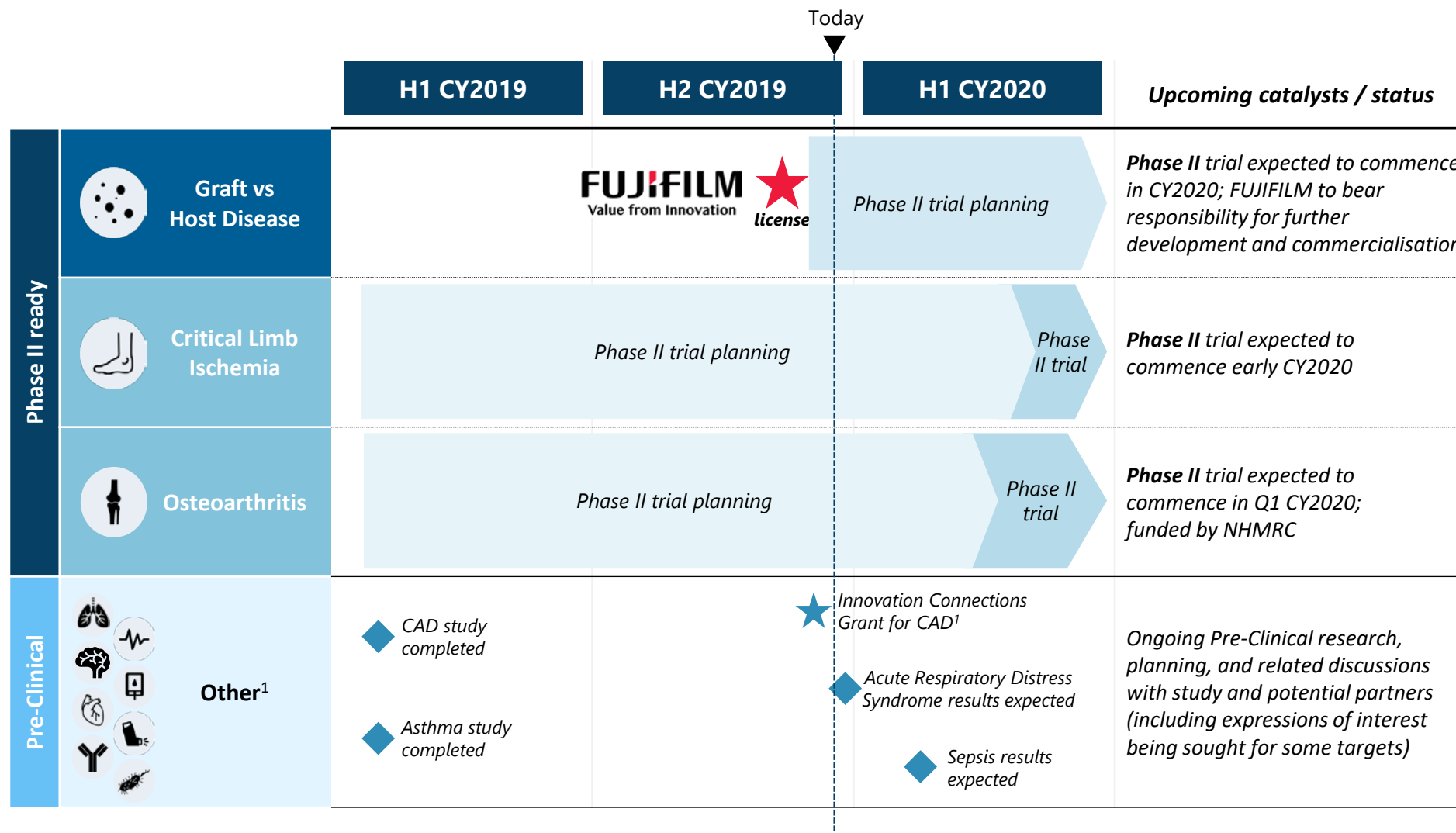
## Estimated market size

**30,000,000**  
People in the USA affected by osteoarthritis

**~US\$11.6B<sup>1</sup>**  
Forecast global market opportunity by 2025

|  |   |
|--|---|
|  <h3>Osteoarthritis</h3>              | <ul style="list-style-type: none"> <li>Assess the effect of Cymerus MSCs on clinical outcomes and knee joint structures of patients with osteoarthritis of the knee (compared to a placebo)</li> </ul>  |
|  <h3>Rationale for selection</h3>     | <ul style="list-style-type: none"> <li>Preclinical research showed MSCs can exert a number of important effects, including:             <ul style="list-style-type: none"> <li>Release of cytokines/growth factors that reduce inflammation and promote tissue repair</li> <li>New blood vessel formation</li> <li>Regeneration of compromised cartilage</li> </ul> </li> </ul> |
|  <h3>Preliminary program design</h3> | <ul style="list-style-type: none"> <li>448-patient trial funded by an NHMRC project grant and in-kind contributions from participating institutions (no cash contribution from Cynata)</li> <li>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</li> </ul>                   |
|  <h3>Key milestones</h3>            | <ul style="list-style-type: none"> <li>Phase II clinical trial expected to commence in 1Q CY2020</li> </ul>   |

# Cynata has a large pipeline of indications with upcoming catalysts





Thank you for your attention

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