A Next Generation Stem Cell Therapeutics Company

Cynata Therapeutics Limited (ASX: CYP) – AGM Presentation
15 November 2018
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1 2018 Highlights and strategy
Significant progress in 2018

**Meaningful impact on patient’s lives**

- Completed first in-human trial of Cymerus™ MSCs, treating 15 patients with acute graft-versus-host disease who had failed all other approved treatment options and had a bleak outlook

  *Improved health outcomes for patients facing extremely grim prognosis*

**Completed GvHD trial**

- Completed data collection for Phase 1 trial in GvHD
- Formal study report being finalised
- Outstanding efficacy results
- No safety concerns
- International media attention

  *Phase II trial expected to start in 2019*

**Selected next clinical trial candidate**

- Critical Limb Ischaemia (CLI): major clinical challenge and unmet need
- Severely impaired blood flow in the arteries: typically legs
- Trial design, scope, cost and schedule being developed

  *CLI Phase II trial expected to start in 2019*

**Deepened relationship with Fujifilm**

- Commenced planning for Phase II trial in GvHD with Fujifilm
- Conducted joint session with Japanese regulator (PMDA) and joint media briefings

  *Fujifilm’s actions indicate their support*

**Advanced pre-clinical programme**

- Clear supporting data for efficacy of Cymerus MSCs in multiple indications
- Broadened patent portfolio
- Enables multiple commercial discussions

  *Multiple irons in the fire*

**Secured cornerstone investment**

- Fidelity International acquired ~9.5m shares through a combination of on market buying and a share placement of $5.2m at $1.275
- Cash balance of $10.9m at 30 Sept 18

  *Strong cash runway*
**Investment Summary:** a Phase II-ready biotech with a highly scalable, proprietary platform for producing commercial quantities of allogeneic MSCs

| Scalable, globally applicable technology | ▪ Cymerus platform enables production of high quality Mesenchymal Stem Cells at scale  
 ▪ Fully patented process overcomes multiple issues with today’s on-market solutions |
|----------------------------------------|------------------------------------------------------------------------------------|
| Excellent results from Phase I trial in GvHD | ▪ All trial endpoints achieved: no adverse safety events, highly encouraging efficacy  
 ▪ GvHD programme well positioned to progress to Phase II  
 ▪ Safety data enables Cynata to move directly to Phase II in other indications |
| Clear pipeline of high-potential target areas | ▪ Cardiovascular disease identified as priority indication area for expanded trial pipeline  
 ▪ Planning for Phase II programme in Critical Limb Ischemia (CLI) underway  
 ▪ Compelling pre-clinical data in multiple other high-value target areas |
| Well-funded to progress clinical programme | ▪ Cash balance of $10.9m as at 30 September 18, reinforced by $5.2m placement of shares to leading institutional investor Fidelity International on 30-May-18;  
 ▪ Fidelity: #1 shareholder (~10%) |
| Attractive partnering business model | ▪ Fujifilm hold licence option for GvHD – will pay all costs of all further development and commercialisation plus $60m in milestone payments plus royalties if exercised  
 ▪ Licence agreements and strategic partners for other indications being explored |
| Valuable and active market | ▪ Estimated $1.7bn revenue opportunity for MSC products in GvHD and CLI alone  
 ▪ Over 850 clinical trials investigating the efficacy of MSCs across numerous indications  
 ▪ Multiple pharma companies active in stem cell M&A |
Cynata’s goal is to develop a new generation of highly potent allogeneic MSC cell therapeutics in areas of high unmet clinical need

Phase I completed, Phase II planning underway
- Fujifilm licence option

Phase II planning underway
- Licence available

A ‘hub and spoke’ business model
Intention to license Cymerus technology across a range of target areas to maximise value

Preclinical data
- Licence available

Potential future target areas
- Licence available

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

Critical Limb Ischemia

GvHD
The MSC Ecosystem

**Contract Manufacturers (CMOs)**
- Manufacture on behalf of clients – they do not have their own specific MSC manufacturing IP
- Not competitors of Cynata – companies like Cynata are potential clients

**Pharma companies**
- Typically seeking to build an MSC program
- Often seeking to in-licence innovative therapies that can be manufactured at scale
- Have resources and expertise to successfully commercialise new products
- **Ideal partners for Cynata**

**Other MSC companies**
- Typically small biotechs – limited resources
- Entirely dependent on perceived value of their existing MSC technology
- **Unlikely to be suitable partners for Cynata**
Strong clinical pipeline and program supports Cynata’s commercial objectives

New enhanced pipeline and clear pathway to commercialisation

- Direct path to market in Japan following Phase II
- Fujifilm holds a licence option for development and commercialisation of Cynata’s MSCs for GvHD

- Identified as high priority target area for Phase II trials
- Cynata engaging with potential partners: intention to license Cynata’s MSCs for CLI

Successful safety results from GvHD trial enables future indications to bypass Phase I

- Cynata will continue to develop its portfolio of target areas in pre-clinical trials with the intention of progressing selected indications directly to Phase II

- Cynata has identified a number of additional indications that it may choose to progress to pre-clinical testing or directly to Phase II in the future
- Significant volume of ongoing clinical research into MSC therapies (850+ clinical trials to date)

Potential target areas

- Other high priority indications
- 7+ indications

Pre-clinical trials

- Critical Limb Ischemia
  - US$1.4bn

Phase I

- GvHD
  - US$300m

Phase II

- Potential target areas

1. Fujifilm’s estimate of the peak annual global sales opportunity
2. ClearView’s estimate of the peak annual global sales opportunity
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)

- **Strategic exit/merger**
  (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 submission of Phase 1 trial CSR.
- On exercise Cynata receive upfront **US$3m** milestone payment
- Fujifilm responsible for all further development activities and costs

**Phase 2 and beyond (potential US$30m+ p.a.)**
- Fujifilm to pay Cynata on attaining 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 if Fujifilm forecast sales attained
Cynata is currently commercialising its Cymerus platform

- **Cynata is commercialising a platform technology** with multiple potential commercial avenues; its business model is to secure licensees to progress clinical trials and commercialise its MSC technology in a range of indications.

- The company is in **active, confidential discussions regarding licence transactions** with multiple potential partners in multiple indications; discussions ongoing with Celularity pursuant to the announced MoU.

- The company is currently negotiating non-binding, confidential **term sheets with multiple parties**; however, there can be no assurances that any of these deals will come to fruition.

- **All license discussions are confidential and inherently commercially sensitive**
  - The market will be informed via an ASX announcement as soon as any material commercial agreement has been concluded.

- The **Board and Management are pleased with commercial progress** in 2018 and are committed to this business model.
Graft vs Host Disease (GvHD)
Study update and next steps
Clinical Protocol: CYP-GvHD-P1-01

Overview of clinical trial protocol

Population: ~16 Adults with steroid-resistant acute GvHD

<table>
<thead>
<tr>
<th>Visit</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days after first dose</td>
<td>0</td>
<td>3</td>
<td>7</td>
<td>14</td>
<td>21</td>
<td>28</td>
<td>60</td>
<td>100</td>
</tr>
</tbody>
</table>

Cohort A
n = 8
1 x 10^6 cells/kg on Day 0 and Day 7 (max 1 x 10^8 cells)

Cohort B
n = 8 (7 treated)*
2 x 10^6 cells/kg on Day 0 and Day 7 (max 2 x 10^8 cells)

* The clinical investigator determined that one patient was no longer a suitable candidate for treatment, due to a medical complication that occurred shortly after enrolment (but prior to treatment with CYP-001).
Summary of Key Results

Excellent results in Phase 1 GvHD clinical trial, a clear validation of Cynata’s MSCs and the Cymerus platform

✓ All endpoints achieved

<table>
<thead>
<tr>
<th></th>
<th>Cohort A (28 days)</th>
<th>Cohort B (28 days)</th>
<th>Pooled (28 days)</th>
<th>Cohort A (100 days)</th>
<th>Cohort B (100 days)</th>
<th>Pooled (100 days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Safety</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>✓ No safety issues / treatment relate adverse events observed</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete Response</td>
<td>✓ 13%</td>
<td>✓ 57%</td>
<td>✓ 40%</td>
<td>✓ 50%</td>
<td>✓ 57%</td>
<td>✓ 53%</td>
</tr>
<tr>
<td>Overall Response</td>
<td>✓ 75%</td>
<td>✓ 86%</td>
<td>✓ 80%</td>
<td>✓ 100%</td>
<td>✓ 86%</td>
<td>✓ 93%</td>
</tr>
<tr>
<td>Overall Survival¹</td>
<td>✓ 88%</td>
<td>≥ 86%</td>
<td>≥ 87%</td>
<td>88%</td>
<td>≥ 86%</td>
<td>≥ 87%</td>
</tr>
</tbody>
</table>

1. One patient in cohort A died of pneumonia (unrelated to treatment) and one patient in cohort B withdrew from the trial on Day 22 to commence palliative care.
GvHD Response – By Subject

Substantial improvement in GvHD grades observed with the majority of patients reporting a Complete Response.
Significance of Findings

Overall response rate of 93%
A meaningful impact on patients’ lives

Key implications of clinical trial results

Endpoints
- Endpoints in this trial were the same as those required in a Phase 3 trial (in contrast to early phase trials for some other conditions)

Response rates
- Response rates were higher than what we expect would be required in Phase 3, to support marketing approval

Number of patients
- Although the Phase 1 trial involved just 15 treated subjects, even late stage trials in this condition do not necessarily involve large numbers
- For comparison, recently completed Phase 3 trials in Japan and US have involved just 25 and 55 patients, respectively

For further details of the implications of Cynata’s clinical trial, please refer to a video interview with Cynata’s VP of Product Development, Dr Kilian Kelly (available here: https://www.cynata.com/news/gvhd-trial-results-and-implications)
### Key advantages of the Cymerus™ process

#### SCALABILITY & CONSISTENCY
- Consistent product quality – single donor overcomes regulatory concerns
- Lower cost of goods on a per cell basis compared to conventional MSC products

#### FEWER CELLS PER PATIENT
- 2 infusions per patient with CYP (compared to 8-12 for bone-marrow derived products)
- Greater convenience for patients and hospitals
- Lower costs incurred by healthcare system

Results to date suggest that CYP-001 may be superior to other treatments for steroid-resistant acute GvHD

For more information on the Cymerus platform visit [Cynata's website](http://www.cynata.com)
GvHD – Next Steps

• **Preparation of a Clinical Study Report (CSR)**
  - Preparation of the CSR is a complex and time consuming process

  1. Rigorous on-site review and verification of all data
  2. Database locked and transferred to statisticians, who prepare tables, figures and listings (TFLs)
  3. Report text then written on basis of TFLs
  4. Review by key stakeholders
  5. Quality control checks and publishing

• CSR production now at an advanced stage – expect to complete ahead of industry-standard timelines

• Submission to Fujifilm per terms of the license option agreement – 90 day decision period

• **Further meeting planned with PMDA (Japanese regulatory authority) early in 2019**
  - Initial highly successful meeting took place in August 2018

• **Expect to commence Phase 2 clinical trials during 2019**
  - Trials planned to occur in Japan and rest of world (including Australia, Europe and USA)
Critical Limb Ischemia (CLI)
Overview of Cynata’s approach
Critical Limb Ischemia

Cynata has prioritised Critical Limb Ischemia as its next indication to take to clinical trials

**ABOUT CLI**

- Critical Limb Ischemia (CLI) is an **advanced stage of peripheral artery disease (PAD)** – caused by a narrowing of the arteries in the limbs
- Severely impaired blood flow causes pain, ulceration and gangrene
- **Often results in amputation** and ~25% of CLI patients who are unable to undergo vascular surgery die within a year of diagnosis

**RATIONALE FOR PURSUING CLI**

- MSCs may offer an effective treatment option for CLI, to restore blood flow and reduce inflammation
- Improvements in amputation-free survival shown in clinical trials with MSCs
- Cymerus MSCs have demonstrated **compelling efficacy in a preclinical study**
- **Development timeline is relatively rapid**, involving relatively small trials
- Peak net **commercial opportunity** in US is estimated to be $700-900m p.a.¹
Scientific support and industry enthusiasm are high for MSCs in CLI

<table>
<thead>
<tr>
<th>Scientific Rationale</th>
<th>Mechanistic Rationale / Supporting Data</th>
<th>Field Enthusiasm</th>
<th>Physician Perspective</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Small clinical MSC studies have shown amputation free survival (AFS) and ankle brachial index (ABI) endpoint benefit</td>
<td>• Experts believed localised delivery of MSCs had the potential to improve CLI</td>
<td>“If MSCs successfully dampen immune response and promote blood vessel growth, they could prevent the need for amputation.”</td>
</tr>
<tr>
<td></td>
<td>• Stempeutics, Pluristem, and Rexgenero are sponsoring ongoing MSC CLI trials</td>
<td>• Pivotal trials may last 1-2 years and require 50-100 revascularisation-ineligible patients</td>
<td>“There has been a lot of interest in the field as well as industry regarding MSCs to address CLI. It makes a lot of sense.”</td>
</tr>
<tr>
<td></td>
<td>• Endpoints include AFS and ABI, as well as ulcer healing and pain¹ (6 – 12 mo.)</td>
<td>• Pivotal trials may last 1-2 years and require 50-100 revascularisation-ineligible patients</td>
<td>“CLI trials are relatively straightforward, with easy-to-assess endpoints like ulcer healing. I think MSC’s would show benefit in a well-powered trial.”</td>
</tr>
<tr>
<td></td>
<td>• Endpoints in CLI are considered to be relatively straightforward</td>
<td>• Endpoints in CLI are considered to be relatively straightforward</td>
<td>“Recruitment is not going to be a barrier, especially if targeting patients known to be ineligible for revascularization.”</td>
</tr>
</tbody>
</table>

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.

<table>
<thead>
<tr>
<th>DAY</th>
<th>TREATED</th>
<th>CONTROL</th>
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</thead>
<tbody>
<tr>
<td>2</td>
<td><img src="image1.png" alt="Image" /></td>
<td><img src="image2.png" alt="Image" /></td>
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<tr>
<td>7</td>
<td><img src="image3.png" alt="Image" /></td>
<td><img src="image4.png" alt="Image" /></td>
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<tr>
<td>14</td>
<td><img src="image5.png" alt="Image" /></td>
<td><img src="image6.png" alt="Image" /></td>
</tr>
<tr>
<td>21</td>
<td><img src="image7.png" alt="Image" /></td>
<td><img src="image8.png" alt="Image" /></td>
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<tr>
<td>28</td>
<td><img src="image9.png" alt="Image" /></td>
<td><img src="image10.png" alt="Image" /></td>
</tr>
</tbody>
</table>

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.

Results published in a peer-reviewed journal

Cytotherapy is a peer-reviewed medical journal covering the areas of cell biology and immunology, including cytokines, cytotherapy, and molecular therapy.
Update on CLI clinical trial plans

**Cymerus MSC product for CLI** will be known as **CYP-002**

**Draft clinical trial protocol synopsis** is now in place
- Randomised, double-blind, Phase 2 study in adults with CLI

**Current working assumptions:***
- Primary endpoint will be Amputation Free Survival after 6 months
- 3 groups: (i) low dose CYP-002; (ii) high dose CYP-002; (iii) placebo
- Approximately 30 patients per group

* Subject to change based on input from external experts

**CRO selection process now ongoing**
- Once CRO is engaged, further input on protocol design will be sought from relevant key opinion leaders and decision will be taken on where trial will be conducted

**Expect trial to commence during 2019**
Pre-Clinical Pipeline
Overview of Cynata’s activities
Purpose of the pre-clinical program

Pre-clinical studies are intended to provide a rational basis for investigating the potential safety and efficacy of an experimental drug in a particular disease indication(s)

- **Demonstrate potential of MSCs**
  - MSCs have already shown promising therapeutic potential in a wide range of pre-clinical models (as well as in human patients)

- **Validate Cymerus technology**
  - Cynata has sought to collaborate with leading academic institutions and experts in various therapeutic areas to validate the potential clinical utility of the Cymerus technology

- **Cost-effective**
  - An important element has been to leverage expenditure as much as possible through grants and joint projects

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.
<table>
<thead>
<tr>
<th>Disease target area</th>
<th>Partner</th>
<th>Pre-clinical trials started</th>
<th>Proof of concept completed</th>
<th>Key highlights</th>
<th>*Global market opportunity</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARDS</td>
<td></td>
<td>✓</td>
<td></td>
<td>Study to commence to evaluate effectiveness of Cymerus MSCs in sheep with ARDS in association with the Prince Charles Hospital in Brisbane.</td>
<td>US$2.5bn by 2018</td>
</tr>
<tr>
<td>Heart attack</td>
<td></td>
<td>✓</td>
<td>✓</td>
<td>Pre-clinical trials suggest Cymerus MSCs may have the potential to restore cardiac function and reduce scar size after a heart attack</td>
<td>US$18.2bn by 2019</td>
</tr>
<tr>
<td>Brain Cancer / Glioblastoma</td>
<td></td>
<td>✓</td>
<td>✓</td>
<td>Research collaboration in genetically modified MSCs in cancer: involves modifying stem cells to target cancer</td>
<td>US$3.3bn by 2024</td>
</tr>
<tr>
<td>Diabetic Wounds</td>
<td></td>
<td>✓</td>
<td>✓</td>
<td>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</td>
<td>US$4.9bn by 2024</td>
</tr>
<tr>
<td>Coronary Artery Disease</td>
<td></td>
<td>✓</td>
<td></td>
<td>Research collaboration for the development of MSC therapies to treat coronary artery disease</td>
<td>US$22.5bn by 2021</td>
</tr>
<tr>
<td>Asthma</td>
<td></td>
<td>✓</td>
<td>✓</td>
<td>Cymerus MSCs demonstrated significant beneficial effects on three key components of asthma: airway hyper-responsiveness, inflammation and airway remodelling</td>
<td>US$25.6bn by 2024</td>
</tr>
<tr>
<td>Cytokine Release Syndrome</td>
<td></td>
<td>✓</td>
<td>✓</td>
<td>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</td>
<td>US$4.5bn by 2022 (CAR-T)</td>
</tr>
<tr>
<td>Sepsis</td>
<td></td>
<td>✓</td>
<td></td>
<td>Development partnership with RCSI (Royal College of Surgeons in Ireland), one of the foremost health sciences research institutions in Europe, to investigate the utility of Cymerus MSCs in sepsis, effective December 2019.</td>
<td>US$5.9bn by 2025</td>
</tr>
</tbody>
</table>

Successful outcomes open many other disease targets potentially benefitting from MSCs

Notes
*Reflects total global market opportunity for the relevant therapeutic category
## Pre-clinical programme—Acute Respiratory Distress Syndrome (ARDS)

<table>
<thead>
<tr>
<th>Critical Care</th>
<th>Study partner</th>
<th>Global market opportunity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Existing treatment options/products</strong></td>
<td><strong>Programme overview</strong></td>
<td>~US$2.5bn by 2018¹</td>
</tr>
<tr>
<td>▪ ARDS is an inflammatory process leading to build-up of fluid in the lungs and respiratory failure. Commonly occurs in previously healthy individuals, and it accounts for approximately 10% of all ICU admissions. There is no specific treatment; instead patients are managed with mechanical pulmonary support (ECMO)</td>
<td>▪ To investigate Cymerus MSCs as a treatment for ARDS in an animal model (sheep) with ARDS supported by ECMO, and to evaluate the effects on lung mechanics, blood flow, inflammation and lung injury, as well as safety</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Summary of progress</strong></th>
<th><strong>Current status</strong></th>
<th><strong>Next steps</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ Programme commenced mid 2017 and is proceeding well</td>
<td>▪ Project on track. Results expected Q4 2018.</td>
<td>▪ Determine most suitable commercial path following release of results</td>
</tr>
</tbody>
</table>

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1. Vasomune Therapeutics company announcement, 2018
## Pre-clinical programme—Heart attack

### Summary of progress
- The study aimed to determine the ability of Cymerus MSCs to repair the heart functionally and structurally after a heart attack in an animal model.
- Study was completed successfully in July 2018.
- Cymerus MSC treatment improved recovery of cardiac function post heart attack compared to either placebo or bone marrow-derived MSCs (BM-MSCs).
- Cymerus MSC treatment also reduced left ventricular end-systolic diameter (LVESD) compared to either placebo or BM-MSCs. LVESD reduction is associated with lower risk of further cardiac events.

### Current status
- Programme completed.

### Next steps
- Expressions of interest being sought from potential partner companies.

### Study partner
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### Global market opportunity
- ~US$18.2bn by 2019

### Existing treatment options/products
- A heart attack is a life-threatening event that occurs when a blood vessel supplying the heart itself is suddenly blocked completely, threatening to damage the heart muscle and its functions. Early treatment with clot dissolving medicines, but otherwise few medical interventions available.

### Programme overview
- The study aimed to determine the ability of Cymerus MSCs to repair the heart functionally and structurally after a heart attack in an animal model.
- Study was completed successfully in July 2018.
- Cymerus MSC treatment improved recovery of cardiac function post heart attack compared to either placebo or bone marrow-derived MSCs (BM-MSCs).
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### Next steps
- Expressions of interest being sought from potential partner companies.
### Pre-clinical programme—Brain Cancer / Glioblastoma

<table>
<thead>
<tr>
<th>Study partner</th>
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<tbody>
<tr>
<td>Existing treatment options/products</td>
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<td>Next steps</td>
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</table>

#### Existing treatment options/products
- Glioblastoma is a type of brain cancer and is the most common type of malignant brain tumor in adults. Current treatment consists of surgery, radiotherapy, and chemotherapy. Notoriously difficult to treat

#### Programme overview
- Production and testing in an animal model of Cynata MSCs genetically engineered to produce compounds that have anticancer effects: a type of “Trojan horse”.

#### Summary of progress
- Programme completed in October 2018
- Genetically engineered Cymerus MSCs were successfully produced to express diagnostic and therapeutic anti-cancer agents
- Engineered Cymerus MSCs reduced the viability of both human glioblastoma cells and human melanoma cells, and slowed tumour progression in mice

#### Current status
- Further engineered MSC pipeline developments in planning stage

#### Next steps
- Determine most suitable commercial path following further pre-clinical studies

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Global market opportunity: ~US$3.3bn by 2024

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www.cynata.com
Pre-clinical programme—Diabetic wounds

**Study partner**

**Global market opportunity**

~US$4.9bn by 2024

### Existing treatment options/products
- Diabetic wounds are prevalent among the 400m+ diabetics globally and a significant opportunity exists to improve existing treatments and meet a growing unmet medical need

### Programme overview
- Evaluation of cells from five different sources: Cymerus MSCs, bone marrow-derived MSCs, and MSCs derived from dental pulp, bone chips and gingival fibroblasts in a preclinical model of diabetic wounds (also known as diabetic ulcers), in conjunction with an active wound care dressing

### Summary of progress
- Findings announced May 2018
- Cymerus MSCs resulted in significantly faster wound healing than bone marrow-derived MSCs

### Current status
- Ongoing discussions with study partner (CRC-CTM) to commence a clinical trial

### Next steps
- Grant funding for a clinical trial being explored with CRC-CTM and their collaborators

---

1. Transparency Market Research, 2018
## Pre-clinical programme—Coronary Artery Disease

### Programme overview
- Evaluation of methods to activate Cymerus MSCs to stimulate new blood vessel formation (angiogenesis) and improve blood supply to the heart in patients with CAD.

### Summary of progress
- Programme commenced mid 2018 and is proceeding well

### Current status
- Programme on track. Results expected Q2 2019.

### Next steps
- Determine most suitable commercial path following release of results

---

### Existing treatment options/products
- CAD involves a narrowing of the coronary arteries due to a build-up of fatty deposits (plaque), also known as atherosclerosis, which reduces blood flow to the heart and the major cause of heart attack. Few medications treat CAD once it has developed

### Study partner
- UNSW Sydney

### Global market opportunity
- ~US$22.5bn by 2021

1. Smithers Apex, 2015

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**Note:**

1. Study partner: UNSW Sydney

2. Global market opportunity: ~US$22.5bn by 2021

---

**Existing treatment options/products:**
- CAD involves a narrowing of the coronary arteries due to a build-up of fatty deposits (plaque), also known as atherosclerosis, which reduces blood flow to the heart and the major cause of heart attack. Few medications treat CAD once it has developed.

**Programme overview:**
- Evaluation of methods to activate Cymerus MSCs to stimulate new blood vessel formation (angiogenesis) and improve blood supply to the heart in patients with CAD.

**Summary of progress:**
- Programme commenced mid 2018 and is proceeding well

**Current status:**
- Programme on track. Results expected Q2 2019.

**Next steps:**
- Determine most suitable commercial path following release of results
### Pre-clinical programme—Asthma

#### Study partner

**MONASH University**

#### Global market opportunity

~US$25.6bn by 2024

<table>
<thead>
<tr>
<th>Existing treatment options/products</th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ Chronic asthma is managed by steroid-type drugs (e.g. “puffers”). Severe, persistent, high-risk or difficult-to-control asthma is much more challenging to treat: this is the target patient population</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Programme overview</th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ To test the effectiveness of Cymerus MSCs in an animal model of asthma, compared with effectiveness of bone marrow derived MSCs, and corticosteroids (+/- Cymerus MSCs)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Summary of progress</th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ Treatment with Cymerus MSCs caused significantly greater reduction of airway hyperresponsiveness, airway remodelling and fibrosis compared to corticosteroid treatment</td>
</tr>
<tr>
<td>▪ Combination therapy involving Cymerus MSCs and corticosteroids resulted in a pronounced synergistic effect, producing marked anti-inflammatory effects in addition to the benefits seen with Cymerus MSC treatment alone</td>
</tr>
<tr>
<td>▪ Data published in prestigious medical journal, Federation of American Societies for Experimental Biology</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Current status</th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ Final phase of study wrapping up: histology analysis; route of administration</td>
</tr>
<tr>
<td>▪ Final results expected late 2018</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Next steps</th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ In active discussions with potential partners to support progress to a clinical trial</td>
</tr>
</tbody>
</table>

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1. Grand View Research, 2016: total asthma market. Difficult-to-treat subset is a proportion of this
# Pre-clinical programme—Cytokine Release Syndrome

<table>
<thead>
<tr>
<th>Study partner</th>
</tr>
</thead>
<tbody>
<tr>
<td>University of Massachusetts Amherst</td>
</tr>
</tbody>
</table>

| Global market opportunity |
| ~US$4.5bn by 2022 (CAR-T)¹ |

## Existing treatment options/products
- Immunotherapies e.g. CAR-T cells are very promising cancer treatments, however their use is often associated with potentially fatal adverse effects, most notably the cytokine release syndrome (CRS). The management of CRS is a challenging clinical problem and no one modality has been shown to be particularly effective.

## Programme overview
- Evaluate the effectiveness in a preclinical model of Cymerus MSCs to ameliorate the effects of CRS

## Summary of progress
- Programme completed in September 2018
- Cymerus MSC shown to be effective in protecting against CRS in mouse models

## Current status
- Programme completed

## Next steps
- Expressions of interest being sought from potential partner companies active in immunotherapy product development

*¹ Evaluate Pharma, 2017

---

Global market opportunity ~US$4.5bn by 2022 (CAR-T)¹

Existing treatment options/products

- Immunotherapies e.g. CAR-T cells are very promising cancer treatments, however their use is often associated with potentially fatal adverse effects, most notably the cytokine release syndrome (CRS). The management of CRS is a challenging clinical problem and no one modality has been shown to be particularly effective.

Programme overview

- Evaluate the effectiveness in a preclinical model of Cymerus MSCs to ameliorate the effects of CRS

Summary of progress

- Programme completed in September 2018
- Cymerus MSC shown to be effective in protecting against CRS in mouse models

Current status

- Programme completed

Next steps

- Expressions of interest being sought from potential partner companies active in immunotherapy product development

---

1. Evaluate Pharma, 2017
## Pre-clinical programme—**Sepsis**

### Programme overview
- Evaluate the effectiveness of Cymerus MSCs to treat sepsis
- Programme costs highly leveraged through RCSI Strategic Industry Partnership Seed Fund

### Summary of progress
- Programme commenced in July 2018 and is proceeding well

### Current status
- Programme on track. Results expected Q1 2020.

### Next steps
- Determine most suitable commercial path following release of results

### Existing treatment options/products
- Sepsis is the most common cause of death in Intensive Care Units despite management with antibiotics and supportive therapy. New therapies are urgently needed to address the huge unmet clinical need associated with sepsis.

### Study partner
- RCSI

### Global market opportunity
- ~US$5.9b by 2026

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1. GlobalData, 2017
Outlook and Next Steps
Key focus areas for next 12 months

- Commence Phase II GvHD trial, with or without Fujifilm (noting that, while Fujifilm has not yet exercised its license option, it has, in association with Cynata, commenced preparations for clinical trials and product manufacture)
- Commence Phase II trial in Critical Limb Ischemia
- Advance commercial discussions for multiple indications & geographies
- Continue to selectively progress the highest potential target areas from our pre-clinical programme

Cynata has had a strong 12 months, with excellent operational and commercial progress. A chart of Cynata’s share price performance appears on slide 40.

The Cynata team, management and Board are excited about the next 12 months, with significant operational and commercial milestones expected.
## Key upcoming milestones

<table>
<thead>
<tr>
<th></th>
<th>H1 CY2018</th>
<th>H2 CY2018</th>
<th>H1 CY2019</th>
<th>H2 CY2019</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GvHD</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase I clinical trials</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Completed</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fujifilm licence option expires</td>
<td></td>
<td></td>
<td>If Fujifilm do not exercise their option, Cynata intends to progress to Phase 2 independently or with an alternative partner</td>
<td></td>
</tr>
<tr>
<td><strong>Critical Limb Ischemia (CLI)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Detailed trial plan announced</td>
<td></td>
<td></td>
<td>Detailed trial plan to determine timeline</td>
<td></td>
</tr>
<tr>
<td>Recruitment commences</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>All other pre-clinical</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ongoing pre-clinical programme includes studies focused on Asthma, ARDS, Heart Attack, Coronary Artery Disease, Brain Cancer / Glioblastoma, Diabetic Wounds, Sepsis, CRS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Commercial</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cynata board and management seek and assess partnering and licensing opportunities on an ongoing basis and will announce material developments as they arise</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

- **Completed**: Fujifilm licence option expires
- **Today**: Phase I clinical trials start
Appendix
Corporate Overview
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 has commenced; trial expected to begin in 2019

- **Attractive licensing-driven business model:** Fujifilm licence option for GvHD potentially worth over US$60m, plus royalties

- **Valuable market opportunity:** Estimated US$1.7bn revenue opportunity for MSC products for GvHD and CLI alone

- **Well-funded to progress clinical programme:** Cash balance of $10.9m¹

---

¹ Cash balance at 30 September 2018
Corporate overview

Company profile

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

Financial information

<table>
<thead>
<tr>
<th>Information</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Share price (31-Oct-18)</td>
<td>A$1.06</td>
</tr>
<tr>
<td>52 week low / high</td>
<td>A$0.56  / A$1.58</td>
</tr>
<tr>
<td>Shares on issue¹</td>
<td>100.8m</td>
</tr>
<tr>
<td>Market capitalisation</td>
<td>A$107m</td>
</tr>
<tr>
<td>Cash (as at 30-Sep-18)</td>
<td>A$10.9m</td>
</tr>
<tr>
<td>Debt (as at 30-Sep-18)</td>
<td>-</td>
</tr>
<tr>
<td>Enterprise value</td>
<td>A$96m</td>
</tr>
</tbody>
</table>

Source: IRESS
Notes:
1. Excludes 6.0m unquoted options with exercise prices ranging from $0.53 to $1.50 and expiry dates between 22-Feb-2019 and 4-Aug-2020 (1m subject to vesting conditions)
2. Represents shareholding if all options held by the Board and Management (total of 2.7m) are exercised

Share price performance (last 12 months, A$)

Top shareholders

<table>
<thead>
<tr>
<th>Shareholder</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fidelity International</td>
<td>9.4%</td>
</tr>
<tr>
<td>Fujifilm Corporation</td>
<td>8.0%</td>
</tr>
<tr>
<td>Board and Management</td>
<td>6.1%</td>
</tr>
<tr>
<td>Board and Management (fully diluted)²</td>
<td>8.6%</td>
</tr>
</tbody>
</table>
Cynata has the only platform in the world to produce commercial quantities of Mesenchymal Stem Cells from a single source: iPSCs

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

<table>
<thead>
<tr>
<th>REGULATORY ISSUES</th>
<th></th>
<th>REDUCED EFFICACY</th>
</tr>
</thead>
<tbody>
<tr>
<td>✗ Sourcing cells from multiple donors leads to variability in the sourced cells, which is a major regulatory hurdle</td>
<td>✗ Massive cell expansion is required to create enough cells for therapeutic use, which may result in reduced efficacy</td>
<td></td>
</tr>
</tbody>
</table>

| 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
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**

Number of MSC clinical trials (cumulative)

- Diabetes complications
- Diabetic foot ulcers
- GvHD
- Fistula
- Asthma
- Acute respiratory distress syndrome
- Brain cancer / Glioblastoma
- Osteoarthritis
- Critical limb ischemia
- Crohn’s disease
- Heart attack

MSCs were approved for use as a therapeutic treatment in Japan in September 2015 and Europe in March 2018.
Cell therapy is an active market attracting big pharma M&A interest

- **USD 307M**: Acquired by Fujifilm in 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 Astellas in 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 Takeda in January 2018¹
  - 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

¹. Transaction pending completion following acceptance of bid by TiGenix shareholders
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 Velocix; 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 Celantis 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)
- 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
Thank you for your attention

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Victoria 3053
Australia

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