**20 December 2018**

# End of Year Newsletter

Dear Investor

As we approach the start of a new year, I'd like to take this opportunity to reflect on Cynata Therapeutics' significant achievements over the past 12 months and to highlight our key focus areas for 2019 (as outlined over the following pages).

Our clinical trial in GvHD exceeded our expectations and not only demonstrated meaningful clinical outcomes for patients but also clearly validated the safety and efficacy of Cynata's MSCs and our scalable Cymerus™ platform.

This time last year we had a single Phase 1 trial in progress. We look forward to 2019 with three Phase 2 clinical trials expected to commence in the coming year and we continue to evaluate other high-potential target areas, dramatically expanding the commercial opportunities we are actively pursuing. We will continue to demonstrate the broad applicability of our platform technology and are currently in active, confidential discussions with potential strategic partners in multiple indications and geographies. We look forward to adding to our portfolio of clinical studies and strategic partners.

On behalf of the Cynata management team and Board, I'd like to wish you a safe and festive holiday season and thank you for your continued support and interest in our company as we move closer to commercialisation.

Yours sincerely
*Dr Ross Macdonald*
*CEO & Managing Director*

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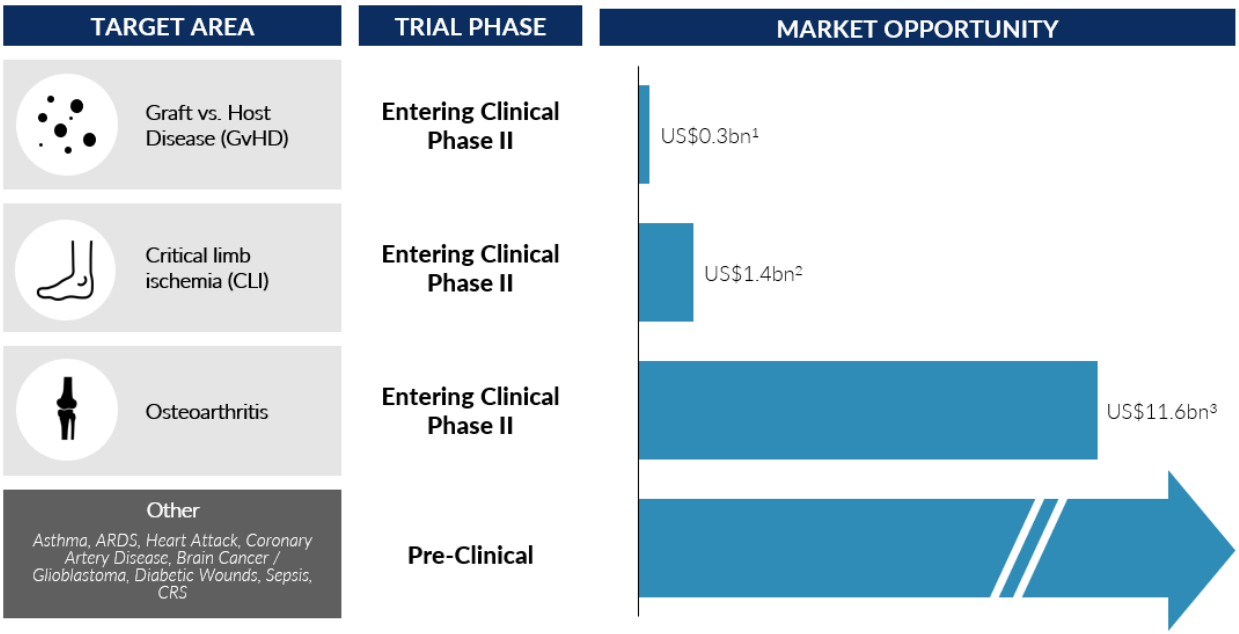
# Target indication pipeline




Notes:
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)."

# Key achievements in 2018

## Completed a world first clinical trial, generating a meaningful clinical impact for patients

- Cynata's Phase 1 clinical trial of CYP-001 in patients with graft-versus-host disease (GvHD) was the first completed clinical trial in the world using an allogeneic induced pluripotent stem cell (iPSC)-derived cell therapy product
- All the patients in our clinical trial had steroid-resistant acute GvHD, for which the prognosis is typically extremely poor (~90% mortality rate)
- CYP-001 met all safety and efficacy endpoints:
    - 13 out of 15 patients achieved a response to our treatment, improving by at least 1 grade in severity
    - 8 out of 15 showed a Complete Response, meaning the GvHD signs and symptoms had resolved completely
- We are immensely proud that treatment with Cymerus MSCs resulted in substantial improvements in critically ill patients with GvHD, for whom all other approved treatment options had failed

## Generated clinically and commercially significant outcomes from GvHD trial

- The endpoints in our Phase 1 trial were the same as those that would be required in a Phase 3 trial (in contrast to early phase trials for some other conditions)
- Response rates in our Phase 1 trial were higher than what we expect would be required to support marketing approval
- The Phase 1 trial included 15 treated subjects, which is significant because even late stage trials in GvHD do not necessarily involve large numbers.
    - For comparison, recently completed Phase 3 trials in Japan and USA have included just 25 and 55 patients, respectively
- Cynata has secured Orphan Drug Designation for CYP-001 in the USA, making CYP-001 eligible for important incentives in that market

## Identified second indication for Phase 2 clinical trials

- The results achieved in our Phase 1 GvHD clinical trial provide clear validation of Cynata's MSCs and the Cymerus platform, and support the continued evaluation of Cynata's MSCs in GvHD in a Phase 2 trial, in partnership with Fujifilm (assuming exercise of the license option)
    - The favourable safety profile observed also allows Cynata to progress directly to Phase 2 in other indications
- To continue demonstrating the broad applicability of our Cymerus platform, we engaged the services of a Boston-based healthcare consultancy, Clearview Healthcare Partners, to help prioritise our selection process for further target indications
- We selected critical limb ischemia (CLI) as our next indication and announced our intention to commence a Phase 2 trial for CLI in 2019
- The CLI trial will be a randomized, double-blind trial expected to enroll approximately 90 CLI patients
    - The primary endpoint is proposed to be amputation free survival after 6 months
    - We are presently reviewing proposals from contract research organisations (CROs) to undertake the trial
    - The trial is expected be financed by Cynata

## Announced a Phase 2 clinical trial in osteoarthritis, funded by an NHMRC project grant

- The 448-patient Phase 2 clinical trial in osteoarthritis is expected to commence in 2019
    - The trial will be substantially funded by National Health and Medical Research Council (NHMRC), with no cash contribution from Cynata

- Cynata will supply Cymerus MSCs to use in the trial

- This trial will be one of the largest MSC trials ever conducted, representing a breakthrough achievement for Cynata and showcasing our capacity to produce MSCs at scale
- Cynata retains full commercial rights to the use of Cymerus MSCs in osteoarthritis, representing a market opportunity that, based on published market research, will be approximately US$11.6 billion globally by 2025
- Osteoarthritis represents the third Phase 2 indication for Cynata, highlighting demand for our Cymerus MSCs in multiple therapeutic areas

## Continued advancements in pre-clinical studies

- Pre-clinical studies using Cymerus MSCs in heart attack, asthma and diabetic ulcers were successfully completed
- Cynata added new indications to our target portfolio, including coronary artery disease (CAD), sepsis and diabetic wounds
- We confirmed the potential use of Cymerus MSCs as an adjunct to immunotherapies such as CAR-T in cancer treatment, to ameliorate the effects of cytokine release syndrome (CRS) – a serious adverse reaction that is seen in response to current immunotherapy products

## Strengthened the intellectual property portfolio

- Cynata filed several new patent applications
- We were granted patents on core aspects of the Cymerus technology in major commercial jurisdictions

## Deepened relationships with strategic partners, institutional investors and broker community

- Cynata commenced planning for a Phase 2 trial in GvHD with Fujifilm, including conducting a joint meeting with Japanese regulator (PMDA) and joint media briefings
- We completed the clinical study report for our Phase 1 trial and provided it to Fujifilm on 18 December 2018 which sets the expiry for the licence option at 19 March 2019
    - in our view, Fujifilm's actions indicate an intention to exercise the licence option for GvHD
- We secured a $5m cornerstone investment from Fidelity International, a major global asset manager, via a placement conducted at $1.275 (a premium to the prevailing market price)
- Our engagement with the investor community continued, both in Australia and abroad

- We secured strong international analyst support with share price targets ≥ $2.00

## Key focus areas for 2019

2019 promises to be a significant year for Cynata as we commence our Phase 2 clinical trials in GvHD, CLI and osteoarthritis and progress commercial interactions with potential strategic partners in multiple indications and geographies.

### Commence three Phase 2 clinical trials in GvHD, CLI and osteoarthritis

- We expect to commence Phase 2 clinical trials in GvHD, CLI and osteoarthritis during 2019
- The GvHD trial will be led by Fujifilm, subject to exercise of the licence option
- The CLI trial will be led by Cynata: the final design, scope, cost and schedule of which is currently being developed
- The osteoarthritis trial will be led by Professor David Hunter from the University of Sydney

### Actively pursue commercial transactions in multiple indications

- Cynata is commercialising a platform technology with multiple potential commercial avenues
- Our business model is to secure business partnerships to build value through undertaking clinical trials and to commercialise our proprietary Cymerus MSC technology in a range of indications
- We are currently in active, confidential discussions regarding commercial transactions with multiple potential partners in number of indications
- We are 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 commercial 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
- Our primary commercial focus for 2019 is to progress these confidential discussions to maximise value for our shareholders

### Continue to demonstrate the broad applicability of our Cymerus platform

- MSC-based therapeutic products have the potential to make a meaningful impact on the health and quality of life for many people suffering from serious and life-threating diseases
- With our proprietary Cymerus stem cell platform technology, Cynata is well positioned in the regenerative medicine space to continue to develop cell therapy products to treat a wide variety of these diseases

- In addition to the Phase 2 trials that we plan to commence during 2019, we will be actively pursuing additional pre-clinical and clinical opportunities in partnership with research institutions and other potential strategic partners

**Ends**

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## 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 and without the limitation of multiple donors.

Cynata's lead product candidate CYP-001 met all clinical endpoints and demonstrated positive safety and efficacy data for the treatment of steroid-resistant acute graft-versus-host disease (GvHD) in a Phase 1 trial. Cynata plans to advance its Cymerus™ MSCs into Phase 2 trials for GvHD, critical limb ischemia and osteoarthritis. In addition, Cynata has demonstrated utility of its Cymerus MSC technology in preclinical models of asthma, diabetic wounds, heart attack and cytokine release syndrome, a life-threatening condition stemming from cancer immunotherapy.