

ASX ANNOUNCEMENT

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Excellent Cohort A Data from Final Primary Evaluation Period in Cynata GvHD Phase 1 Clinical Trial

Melbourne, Australia; 27 February 2018: Australian stem cell and regenerative medicine company, Cynata Therapeutics Limited (ASX: CYP) is pleased to announce that the Primary Evaluation Period has been completed for the first cohort of patients in the clinical trial of its lead Cymerus™ mesenchymal stem cell (MSC) product CYP-001, for the treatment of steroid-resistant graft versus host disease (GvHD).

Key Highlights:

- Efficacy data following completion of the Primary Evaluation Period (100 days) **represents an improvement above the initial results announced in January**
- **Overall survival at Day 100 was 87.5%**
- **Overall Response rate by Day 100 was 100%** (all eight participants showed an improvement in the severity of GvHD by at least one grade compared to baseline)
- **Complete Response rate by Day 100 was 50%** (GvHD signs/symptoms completely resolved in four out of eight patients)
- **No treatment-related serious adverse events** or safety concerns were identified during the Primary Evaluation Period

Summary of Trial Results:

All participants in Cohort A demonstrated at least a Partial Response (defined as an improvement in the severity of GvHD by at least one grade compared to baseline), with four participants demonstrating a Complete Response (defined as the absence of any GvHD signs/symptoms). The Overall Response rate is the proportion of patients showing either a Partial or Complete Response.

GvHD is a life threatening and, in many cases, fatal disease. As such, it is encouraging that at this time, seven of the eight participants in Cohort A remain alive. As previously reported, one patient in Cohort A died after developing pneumonia, which is a common finding in recipients of bone marrow transplants and similar procedures. This death was not considered to be treatment-related.

The Primary Evaluation Period for this trial covers the first 100 days after the initiation of CYP-001 treatment. Participants in Cohort A received a dose level of CYP-001 that was anticipated to be at the lower end of the effective dose range (one million cells per kilogram of bodyweight, up to a maximum of 100 million cells per infusion). Each participant received two infusions each (one on Day 0, and one on Day 7).

Overview of acute steroid-resistant graft-versus-host disease

The clinical results from the 8 patients in Cohort A, following the Primary Evaluation Period, are particularly pleasing considering that all of these patients had failed to respond to corticosteroid therapy, which is the only approved treatment for GvHD. When GvHD fails to improve or worsens despite steroid treatment, patients are described as having **steroid-resistant GvHD**. The prognosis for these patients is extremely poor, with very high **mortality rates**¹.

The global market opportunity for GvHD has been estimated to reach approximately US\$500 million p.a. by 2021².

Next steps

In Cohort B, a total of eight participants will receive two infusions of CYP-001 at a dose of two million cells per kilogram of bodyweight, up to a maximum of 200 million cells per infusion. Enrolment of participants into Cohort B is progressing well, with seven clinical sites in the UK and Australia open for enrolment.

Dr Kilian Kelly, Cynata's Vice President, Product Development, said, "We are pleased and excited about the data generated at this point. It demonstrates the potential of our Cymerus platform, which in this case is being used to treat GvHD. Steroid-resistant GvHD is a horrific disease, which causes debilitating symptoms and a very high rate of mortality, so we are delighted to see such positive outcomes among participants in Cohort A of this ground-breaking trial. We now look forward to completing enrolment of Cohort B and evaluating the initial safety and efficacy of a higher dose level of CYP-001."

Outlook

The results provide an indication of the efficacy of the MSCs produced by Cynata's unique scalable Cymerus platform. No other company in the world has the capability to produce MSCs at an equivalent commercial scale without requiring multiple donors.

Cynata is focused on proving the broad applicability of its Cymerus-produced MSCs. Successful pre-clinical and clinical results pave the way for Cynata to leverage its technology platform across multiple disease target areas and provide significant opportunities for monetisation and commercial partnerships.

Cynata continues to assess its strategic options going forward. Pre-clinical studies already undertaken in other high need target areas include:

- Heart attack
- Asthma
- ARDS (Acute Respiratory Distress Syndrome)
- Glioblastoma (Brain cancer)
- Critical Limb Ischemia

Dr Ross Macdonald, Cynata's CEO, said, "These results, when combined with our data across other target areas, demonstrate the potential of our Cymerus platform. We will continue to work hard for

¹Westin JR, Saliba RM, De Lima M, et al. Steroid-Refractory Acute GVHD: Predictors and Outcomes. *Adv Hematol.* 2011; 2011:601953.

²[https://www.visiongain.com/Report/1794/Global-Graft-versus-Host-Disease-\(GVHD\)-Market-2017-2027](https://www.visiongain.com/Report/1794/Global-Graft-versus-Host-Disease-(GVHD)-Market-2017-2027)



our shareholders in assessing the most effective and efficient means to demonstrate and realise the value of our unique technology.”

Ends

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About Graft-versus-host-disease

Graft-versus-host-disease (GvHD) is a complication that can occur after a bone marrow transplant or similar procedure, when the donor’s immune cells (from the “graft”) attack the recipient of the transplant (the “host”). The only approved treatment for GvHD is corticosteroid therapy, which is typically only effective in about 50 percent of patients. When GvHD fails to improve or worsens despite steroid treatment, patients are described as having steroid-resistant GvHD. The prognosis for these patients is poor, with mortality rates in excess of 90 percent.³

About the Phase 1 Clinical Trial (Protocol Number: CYP-GvHD-P1-01)

The trial is entitled “An Open-Label Phase 1 Study to Investigate the Safety and Efficacy of CYP-001 for the Treatment of Adults With Steroid-Resistant Acute Graft Versus Host Disease”. Participants must be adults who have undergone an allogeneic haematopoietic stem cell transplant (HSCT) to treat a haematological (blood) disorder and subsequently been diagnosed with steroid-resistant Grade II-IV GvHD.

The first eight participants were enrolled in Cohort A and received two infusions of CYP-001 at a dose of one million cells per kilogram of body weight (cells/kg), up to a maximum dose of 100 million cells. There was one week between the two CYP-001 infusions in each participant. The next eight participants will be enrolled into Cohort B and receive two infusions of CYP-001 at a dose of two million cells/kg, up to a maximum dose of 200 million cells.

The trial’s primary objective is to assess the safety and tolerability of CYP-001, while the secondary objective is to evaluate the efficacy of two infusions of CYP-001 in adults with steroid-resistant GvHD. The primary evaluation period concludes 100 days after the first dose in each participant. Efficacy is assessed on the basis of response to treatment (as determined by change in GvHD grade) and overall survival at 28 and 100 days after the administration of the first dose. After the completion of the primary evaluation period, participants enter a longer-term, non-interventional follow-up period, which will continue for up to two years after the initial dose.

About Cynata Therapeutics (ASX: CYP)

Cynata Therapeutics Limited (ASX: CYP) is an Australian clinical-stage stem cell and regenerative medicine company that is developing a therapeutic stem cell platform technology, Cymerus™, originating from the University of Wisconsin-Madison, a world leader in stem cell research. The proprietary Cymerus™ technology addresses a critical shortcoming in existing methods of production of mesenchymal stem cells (MSCs) for therapeutic use, which is the ability to achieve economic manufacture at commercial scale. Cymerus™ utilises induced pluripotent stem cells (iPSCs) to produce a particular type of MSC precursor, called a mesenchymoangioblast (MCA). Cymerus™ provides a source of MSCs that is independent of donor limitations and an “off-the-shelf” stem cell platform for therapeutic product use, with a pharmaceutical product business model and economies of scale. This has the potential to create a new standard in the emergent arena of stem cell therapeutics and provides both a unique differentiator and an important competitive position.

³ Westin JR, Saliba RM, De Lima M, et al. Steroid-Refractory Acute GVHD: Predictors and Outcomes. *Adv Hematol.* 2011; 2011:601953.