



ASX ANNOUNCEMENT

7 February 2019

Study of Cynata's CYP-001 in Preclinical Model of Acute GvHD Published in Leading Peer-Reviewed Journal

Melbourne, Australia; 7 February 2019: Cynata Therapeutics Limited (ASX: CYP), a clinical-stage biotechnology company specialising in cell therapeutics, is pleased to announce that results demonstrating the efficacy and mechanism of action of CYP-001 in a preclinical model of acute graft versus host disease (GvHD) have been published in *Stem Cell Research*, a leading peer-reviewed journal. CYP-001 is Cynata's lead Cymerus™ mesenchymal stem cell (MSC) product candidate.

The paper summarises work conducted under the supervision of Associate Professor Lisa Minter at the University of Massachusetts Amherst (UMass), USA. The studies were designed to assess survival after receiving the assigned treatment, as well as potential mechanisms of action, in a humanised mouse model of severe acute GvHD.

Key Findings

- Cymerus MSCs reduce GvHD severity and significantly prolong survival in a humanised mouse model of GvHD.
- Cymerus MSCs significantly reduce levels of pro-inflammatory cytokines, which correlate with disease severity.
- The immunosuppressive effects of Cymerus MSCs result from effects on PKCθ – an enzyme expressed by donor T cells, which has been shown to play a key role in mediating GvHD.

Dr Kilian Kelly, Cynata's Vice President of Product Development, said, "The publication of this paper in a highly respected peer-reviewed journal provides further validation of the Cymerus platform. The data generated in this study were instrumental in supporting the approval of our world-first clinical trial of CYP-001 in patients with steroid-resistant acute GvHD, which has since been completed with extremely promising results. The elucidation of the mechanism of action of Cymerus MSCs in this condition is also very important with regard to further development of this product."

The paper has been published online ahead of print, and is available to download from the publisher's website (Elsevier Journals) on an open access basis. The details of the paper are:

E.I. Ozay, J. Vijayaraghavan, G. Gonzalez-Perez, et al. *Cymerus™ iPSC-MSCs significantly prolong survival in a pre-clinical, humanized mouse model of graft-vs-host disease*. *Stem Cell Research*, 2019.

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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.¹

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 and critical limb ischemia. In addition, Cynata has demonstrated utility of its Cymerus MSC technology in preclinical models of asthma, critical limb ischemia, diabetic wounds, heart attack and cytokine release syndrome, a life-threatening condition stemming from cancer immunotherapy.

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