

Cynata Completes Clinical Study Report for Phase 1 Trial of CYP-001 in GvHD

Melbourne, Australia; 18 December 2018: Cynata Therapeutics Limited (ASX: CYP), a clinical-stage biotechnology company specializing in cell therapeutics, is pleased to announce that the clinical study report (CSR) describing full details of the results from the Phase 1 clinical trial of CYP-001 for the treatment of steroid-resistant acute graft versus host disease (GvHD) has been completed.

A copy of the CSR has now been provided to Fujifilm in accordance with the terms of the license option between Cynata and Fujifilm. Fujifilm now has 90 days in which to exercise the license option. Fujifilm, in collaboration with Cynata, continues product development activities for CYP-001 with the intent to commence a Phase 2 clinical program in 2019.

CYP-001 is Cynata's lead Cymerus™ mesenchymal stem cell (MSC) product candidate. The Phase 1 trial of CYP-001 represents the first time a clinical trial using an induced pluripotent stem cell (iPSC)-derived therapy has been completed. Key highlights of the final results from the primary evaluation period are:

- **Overall Response rate by Day 100 was 87%**
13 out of 15 patients showed an improvement in GvHD severity by at least one grade compared to baseline
- **Complete Response rate by Day 100 was 53%**
GvHD signs and symptoms completely resolved in 8 out of 15 patients
- **Overall survival at Day 100 was at least 87%**
- **No treatment-related serious adverse events** or safety concerns were identified

During Cynata's final review and verification of trial data, the response in one patient was revised from Partial Response to Stable Disease. This patient had skin GvHD at baseline, and the skin symptoms improved by Day 28, consistent with response to treatment. On source data verification, they were however noted to have developed minor (stage 1) gastrointestinal symptoms after baseline, which persisted beyond Day 100, before resolving completely. In light of this, the final review concluded that the improvement prior to Day 100 was insufficient to meet the rigid criteria for a Partial Response, as predefined in the study protocol.

Dr Adrian Bloor (The Christie Hospital, Manchester), the UK Chief Investigator for the trial, said, "We are very pleased with the results of this important trial. Importantly, no safety concerns have been identified, and the Overall Response and Complete Response rates are very encouraging. We look forward to further evaluating CYP-001 in later phase clinical trials in the near future."

Dr Ross Macdonald, Cynata's Chief Executive Officer, said, "Completing the clinical study report is a major milestone for Cynata, as it marks the formal and successful completion of our Phase 1 clinical trial of CYP-001 with the attainment of all safety and efficacy endpoints. We now look forward to accelerating Phase 2 development of CYP-001 and to receiving Fujifilm's decision on exercising the license option."

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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 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 were required to be adults who had 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 1 million cells per kilogram of body weight (cells/kg), up to a maximum dose of 100 million cells. Seven participants in Cohort B received two infusions of CYP-001 at a dose of 2 million cells/kg, up to a maximum dose of 200 million cells. There was one week between the two CYP-001 infusions in each participant.

The trial's primary objective was to assess the safety and tolerability of CYP-001, while the secondary objective was to evaluate the efficacy of two infusions of CYP-001 in adults with steroid-resistant GvHD. The primary evaluation period concluded 100 days after the first dose in each participant. Efficacy was 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 entered 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 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.

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