ASX ANNOUNCEMENT 18 November 2020

Cynata's Ground-Breaking MSC Technology Featured on Cover of *Nature Medicine*

Melbourne, Australia; 18 November 2020: Cynata Therapeutics Limited (ASX: CYP), a clinical-stage biotechnology company specialising in cell therapeutics, is pleased to announce that its proprietary Cymerus™ MSC technology has been featured on the front cover of the latest issue of the prestigious journal, *Nature Medicine.*[1]

The cover is also displayed on the journal's website.[2] The illustration (by Patton'd Studios, Melbourne) represents an induced pluripotent stem cell (iPSC)-derived mesenchymoangioblast colony, which is a crucial intermediate step in the Cymerus process.

This issue of *Nature Medicine* also includes the paper describing the Phase 1 clinical trial of CYP-001 in patients with steroid-resistant graft versus host disease (GvHD), which was recently published online in the first instance (as announced on 15 September 2020).

Dr Kilian Kelly, Cynata's Chief Operating Officer, said: *"We are honoured by the decision of the Nature Medicine editorial team to feature our ground-breaking research on the cover of the latest issue. This is further recognition of the importance of this study to the wider field of regenerative medicine. The publication of our paper online has already generated a great deal of interest in our technology, and we expect that to increase further as this issue is distributed to its many subscribers worldwide."*

The details of the paper describing the Phase 1 clinical trial of CYP-001 are as follows:
Bloor AJC, Patel A, Griffin JE, Gilleece MH, Radia R, Yeung DT, Drier D, Larson LS, Uenishi GI, Hei D, Kelly K, Slukvin I and Rasko JEJ. Production, safety and efficacy of iPSC-derived mesenchymal stromal cells in acute steroid-resistant graft versus host disease: a Phase I, multi-centre, open label, dose-escalation study. *Nat Med* **26**, 1720–1725 (2020).

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Authorised for release by Dr Ross Macdonald, Managing Director & CEO

CONTACTS: Dr Ross Macdonald, CEO, Cynata Therapeutics, +61 (0)412 119343, ross.macdonald@cynata.com
Claire LaCagnina, U.S. Media Contact, +1 315.765.1462, clacagnina@6degreespr.com

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 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.

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 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 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 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 severe complications arising from COVID-19, GvHD and critical limb ischemia and a Phase 3 trial in osteoarthritis. In addition, Cynata has demonstrated utility of its Cymerus MSC technology in preclinical models of asthma, diabetic wounds, heart attack, sepsis, acute respiratory distress syndrome (ARDS) cytokine release syndrome and pulmonary fibrosis.

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[1] Nature Medicine is one of the most cited and prestigious medical journals worldwide, with a five-year impact factor of 34.85 (a measure of the importance of a journal based on the number of times that articles published in a journal are cited in other articles).

[2] https://www.nature.com/nm/

Cynata Therapeutics Limited

Level 3, 62 Lygon Street, Carlton, Victoria 3053, Australia | PO Box 7165, Hawthorn North, Victoria 3122, Australia

T: + 613 9824 5254 **F:** + 613 9822 7735 **E:** info@cynata.com **ABN:** 98 104 037 372