ASX ANNOUNCEMENT 14 September 2020

Results of Cynata's World-First Clinical Trial of iPSC-derived CYP-001 in GvHD Accepted for Publication in *Nature Medicine*

Melbourne, Australia; 14 September 2020: Cynata Therapeutics Limited (ASX: CYP), a clinical-stage biotechnology company specialising in cell therapeutics, is pleased to announce that a paper describing the Phase 1 clinical trial of CYP-001 in patients with graft versus host disease (GvHD) has been accepted for publication in the prestigious *Nature Medicine.*[1]

Background

The published trial results detail the world's first clinical trial of an allogeneic induced pluripotent stem cell (iPSC)-derived product. CYP-001, Cynata's lead iPSC-derived mesenchymal stem cell (MSC, also known as mesenchymal stromal cell) product candidate, broke ground by being the first MSC therapy to be produced at scale without the limitation of multiple donors through Cynata's novel Cymerus™ technology.

In the clinical trial, 15 patients with steroid-resistance acute GvHD received two infusions each of Cymerus MSCs. The trial was conducted at seven clinical centres in the UK and Australia. Publication in *Nature Medicine* is recognition of the importance of the findings from this study and the unique nature of Cynata's proprietary Cymerus technology.

Key Highlights

As previously announced, key results of the clinical trial were as follows:

- **Overall Response rate by Day 100 was 87%** (13/15 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 8/15 patients)
- **Overall survival at Day 100 was 87%**
- **No treatment-related serious adverse events** or safety concerns were identified

The co-corresponding authors of the paper are Professor John Rasko AO (Royal Prince Alfred Hospital, Sydney) and Professor Adrian Bloor (The Christie Hospital, Manchester).

Professor Rasko commented: "*iPSC-based technology facilitates the large-scale production of potential cell-based therapies in a robust and consistent manner. iPSCs have the potential to give rise to any cell in the human body. This represents the first-ever published report of safety and efficacy in a completed human clinical trial using iPSC-derived cells in any disease, worldwide. The acceptance of this manuscript by such a prestigious and high-impact journal underscores the importance of this trial to the field of cell-based medicine.*"

Professor Bloor said: "*Steroid-resistant GvHD is one of the most serious complications of bone marrow and blood stem cell transplantation. There is a major unmet need for an effective treatment and we are optimistic that CYP-001 can play an important role in the management of this life-threatening condition.*"

Dr Kilian Kelly, Cynata's Chief Operating Officer, said: *"We are delighted that this paper has been published in Nature Medicine, which is a major endorsement of our technology and the significance of this trial. We are very grateful to the many people who contributed to this trial, including the research teams, the participating patients and their families. Further development of CYP-001 for GvHD is continuing through our global licensee for this indication, Fujifilm. We also look forward to commencing*

clinical trials of Cymerus MSCs in a number of other indications, including osteoarthritis and COVID-19, in the near future."

The details of the paper, which has been published online, 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.

-ENDS-

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.

About Cynata's Partnership with Fujifilm Corporation

In 2017, Cynata entered into a Development and Commercialisation Partnership Agreement with Fujifilm Corporation of Japan, and in September 2019 Cynata granted Fujifilm an exclusive, worldwide license to develop and commercialise CYP-001 for the prevention and treatment of GvHD in humans.

[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).