ASX ANNOUNCEMENT **12 December 2024**

First Patient Treated With CYP-001 in Kidney Transplant Trial

Melbourne, Australia; 12 December 2024: Cynata Therapeutics Limited (ASX: "**CYP**", **"Cynata"**, or the **"Company"**), a clinical-stage biotechnology company specialising in cell therapeutics, has received confirmation from its partner Leiden University Medical Centre (LUMC) that the first patient has been treated with CYP-001 in the Phase 1/2 *Nereid* kidney transplant clinical trial.

CYP-001 is Cynata's Cymerus™ iPSC[1]-derived MSC[2] product candidate for intravenous use. The trial is being funded and managed by LUMC, under the supervision of Prof Ton Rabelink[3] and Dr Siebe Spijker,[4] while Cynata will supply CYP-001 for use in the trial. Importantly, Cynata will retain full commercial rights for this indication.

The primary objective of the trial is to study the safety and efficacy of CYP-001 – to determine if administering MSCs after kidney transplantation allows patients to take a reduced amount of the immunosuppressant drug tacrolimus, which is used to prevent the rejection of transplanted organs. Although tacrolimus is effective at preventing rejection of transplanted kidneys, it is associated with significant toxicity, including increased risk of serious infections, cancer, diabetes, and kidney damage.[5,6] Consequently, there is an urgent need to identify and evaluate safer methods of preventing organ transplant rejection. If it can be demonstrated that Cymerus™ MSC-based therapy allows patients to stop taking tacrolimus, or reduce tacrolimus dosage, this would be expected to reduce the level of toxicity that they experience. Close to one hundred thousand kidney transplants are performed worldwide every year.[7]

The trial will seek to recruit a total of up to 16 patients who have undergone a kidney transplant. The first six patients will receive either one (n=3) or two (n=3) infusions of CYP-001, in addition to standard treatment. Subject to favourable safety review of the initial cohorts, a further ten patients will receive two infusions of CYP-001, followed by tacrolimus dose reduction.

Prof Rabelink and colleagues have previously published encouraging data from a clinical trial in which MSCs derived from bone marrow were used in a similar way. They found that early tacrolimus withdrawal with MSC therapy was safe, without increased rejection, and concluded that this is a potentially useful approach after kidney transplantation.[8]

Dr Spijker said:

"*One of the most useful properties of MSCs is that they can instruct the immune system to slow down, and tell it not to attack the new kidney as aggressively. This could allow patients to take less rejection medication to preserve the kidney, or potentially even stop taking rejection medication completely. Our previous studies involved MSCs derived from bone marrow, which is quite a tedious procedure, and one that produces just a limited amount of MSCs. In contrast, Cynata's iPSC-based platform allows production of an effectively limitless supply of MSCs from one cell bank. We look forward to evaluating these cells in this exciting study.*"

Dr Kilian Kelly, Cynata's Chief Executive Officer and Managing Director, said:

"*This trial will help build the growing body of data on the use of Cymerus™ iPSC-derived MSCs in a wide range of clinical indications. There are clear parallels between use of CYP-001 in kidney transplant recipients, and use of CYP-001 in graft versus host disease, which led to very promising safety and efficacy outcomes in a completed Phase 1 clinical trial.*[9,10] *We look forward to continuing to work with Prof Rabelink, Dr Spijker and the wider team at LUMC on this important project.*"

-ENDS-

Authorised for release by Dr Kilian Kelly, CEO & Managing Director

CONTACTS: Dr Kilian Kelly, CEO & MD, Cynata Therapeutics, +61 (03) 7067 6940, kilian.kelly@cynata.com
Lauren Nowak, Media Contact, +61 (0)400 434 299, lauren@littlebigdeal.au

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 has demonstrated positive safety and efficacy data for its Cymerus™ product candidates CYP-001 and CYP-006TK, in Phase 1 clinical trials in steroid-resistant acute graft versus host disease (GvHD), and diabetic foot ulcers (DFU), respectively. Further clinical trials are now ongoing: a Phase 2 trial of CYP-001 in GvHD under a cleared US FDA IND; a Phase 1/2 trial of CYP-001 in patients undergoing kidney transplant; and a Phase 3 trial of CYP-004 in osteoarthritis. In addition, Cynata has demonstrated utility of its Cymerus™ technology in preclinical models of numerous other diseases, including critical limb ischaemia, idiopathic pulmonary fibrosis, asthma, heart attack, sepsis, acute respiratory distress syndrome (ARDS) and cytokine release syndrome.

Cynata Therapeutics encourages all current investors to go paperless by registering their details with the designated registry service provider, Automic Group.

---

[1] iPSC = induced pluripotent stem cell.
[2] MSC = mesenchymal stem (or stromal) cell.
[3] Professor of Internal Medicine and Head of the Division of Nephrology and the Department of Internal Medicine at LUMC.
[4] Internist-nephrologist at LUMC.
[5] Schagen MR, et al. Expert Opinion on Drug Metabolism & Toxicology. 2023;19(7), 429-445.
[6] Rodríguez-Perálvarez M, et al. Am J Transplant. 2022 Mar 31;22(6):1671-1682.
[7] Word Health Organization Global Database on Donation and Transplantation.
[8] Reinders MEJ, et al. Am J Transplant. 2021;21:3055-3065.
[9] Bloor AJC, et al. Nat Med. 2020;26:1720-1725.
[10] Kelly K, et al. Nat Med. 2024;30(6):1556-1558.