ASX ANNOUNCEMENT **21 August 2023**

Approval of Clinical Trial of CYP-001 in Kidney Transplant Recipients

Melbourne, Australia; 21 August 2023: Cynata Therapeutics Limited (ASX: "**CYP", "Cynata",** or the **"Company"**), a clinical-stage biotechnology company specialising in cell therapeutics, has been advised that the Competent (regulatory) Authority in the Netherlands (Centrale Commissie Mensgebonden Onderzoek, CCMO) has approved the Phase 1 clinical trial of CYP-001 in patients who have received a kidney transplant.

CYP-001 is Cynata's Cymerus™ iPSC[1]-derived MSC[2] product candidate for intravenous use. This trial will be funded and managed by Leiden University Medical Centre (LUMC). Cynata will supply CYP-001 and retains full commercial rights.

The trial, entitled the "*Safety and Efficacy of MCA-derived Mesenchymal Stromal Cell Therapy in Renal Transplant Recipients: The Nereid Study*", will be led by Prof Ton Rabelink, Professor of Internal Medicine and Head of the Division of Nephrology and the Department of Internal Medicine at LUMC. Prof Rabelink also acts as the Figurehead of the Regenerative Medicine route of the Dutch Science Agenda.

Prof Rabelink said:

"The side effects from anti-rejection drugs in kidney transplant recipients are a major problem. Risks include an increased incidence of serious infections and cancer, as well as potential damage to the transplanted kidney. We believe that MSC therapy could help to facilitate dose reduction or even withdrawal of these drugs, which would be a huge step forward in the management of these patients. Cynata's Cymerus MSCs are of particular interest, due to the consistency and scalability of the iPSC-based platform."

The Primary Objective of the trial is to study the safety and efficacy of CYP-001 in allowing tacrolimus reduction after kidney transplantation. Tacrolimus is a calcineurin inhibitor, which is a type of immunosuppressant drug used to prevent the rejection of transplanted organs. Prof Rabelink and colleagues have previously published encouraging data from a clinical trial in which MSCs 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 renal transplantation.[3]

The trial will seek to recruit a total of up to 16 patients who have undergone a renal 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.

Dr Kilian Kelly, Cynata's Chief Executive Officer & Managing Director, said:
"We are delighted that this trial has received regulatory approval. This expands Cynata's reach in the field of transplant medicine, adding to our existing graft versus host disease program. Prof Rabelink and his team at LUMC have a very strong track record of conducting research in the field of kidney transplantation, including very encouraging prior studies with MSCs. We look forward to continuing to work with them on this exciting project."

-ENDS-

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

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[1] iPSC = induced pluripotent stem cell
[2] MSC = mesenchymal stem (or stromal) cell
[3] Reinders et al: *Autologous bone marrow-derived mesenchymal stromal cell therapy with early tacrolimus withdrawal: The randomized prospective, single-center, open-label TRITON study*. Am J Transplant. 2021;21:3055–3065

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. A Phase 2 clinical trial in GvHD under a cleared US FDA IND, as well as trials of Cymerus products in osteoarthritis (Phase 3) and diabetic foot ulcers (DFU) are currently ongoing. In addition, Cynata has also demonstrated utility of its Cymerus technology in preclinical models of numerous 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.

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