ASX ANNOUNCEMENT 14 June 2022

# Pre-clinical Study of Lung Disease Supports High Potency of Cynata's Cymerus™ MSCs

**Key Highlights:**

- **Pre-clinical study in an animal model of idiopathic pulmonary fibrosis (IPF), a serious lung disease, identifies molecular basis for high potency of Cynata's Cymerus mesenchymal stem cells (MSCs)**
- **Treatment with Cymerus MSCs significantly ameliorated the mediators of lung inflammation in the model at the same time as promoting anti-inflammatory effects**
- **Provides further evidence supporting the potent effects of Cymerus MSCs in bleomycin induced inflammatory lung disease**
- **Outlines the mechanisms of action by which Cymerus MSCs provide therapeutic efficacy as a potential treatment option for idiopathic pulmonary fibrosis (IPF)**

**Melbourne, Australia; 14 June 2022:** Cynata Therapeutics Limited (ASX: **"CYP"** or **"Cynata"**), a clinical-stage biotechnology company specialising in cell therapeutics, is pleased to announce the completion of a pre-clinical study that has provided further evidence in support of the highly potent anti-inflammatory effects of Cynata's proprietary Cymerus MSCs. The study, conducted by Professor Chrishan Samuel, a Monash Biomedicine Discovery Fellow and Head of the Fibrosis Laboratory, Department of Pharmacology at Monash University, was in mice subjected to bleomycin (BLM)-induced pulmonary fibrosis, which mimics features of idiopathic pulmonary fibrosis (IPF) in humans. Professor Samuel intends to submit a report of the study for publication in an appropriate scientific journal.

**Dr Kilian Kelly, Cynata's Chief Operating Officer, said:**

*"This further study by Professor Samuel, the commencement of which was announced on 2 March 2021, provides extensive detail around the molecular mechanisms associated with the observed high potency of Cynata's proprietary Cymerus mesenchymal stem cells. The results provide additional data in support of investigating the clinical utility of our MSCs in fibrotic diseases of the lungs and potentially of other organs, a pathway we are seeking to pursue with potential commercial partners."*

The key findings of the study, which involved Cymerus MSC dosing, either once or once-weekly over a 2-week treatment period and comparison with saline controls (n = 6-10 per group, p values from <0.05 to <0.001), were as follows:

- Significantly ameliorated the BLM-induced M2 macrophage, dendritic cell and T cell influx into the airways/lungs as well as pro-inflammatory TNF-α, IL-6 and IL-1β levels within the airways/lung;
- Significantly promoted anti-inflammatory IL-10 and IFN-γ levels within the airways/lung;
- Significantly reduced the BLM-induced pSmad2 levels and restored the BLM-induced loss of Smad7 levels within the airways/lung (without affecting pSmad3 levels);
- Did not affect MAP kinase levels nor CTGF, PDGF or ET-1 levels within the airway/lungs;

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- Significantly restored or promoted the BLM-induced loss of MMP-13 and MMP-2 levels as well as the MMP-13/TIMP-1 and MMP-2/TIMP-2 balance (without affecting MMP-9 levels or the MMP-9/TIMP-1 balance); and
- Significantly reduced the BLM-induced interstitial collagen area, interstitial collagen area to tissue area ratio, interstitial collagen fibre density, thickness and length (without affecting interstitial collagen fibre cross-linking).

-ENDS-

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

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**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. Planning for a Phase 2 clinical trial in GvHD under a cleared US FDA IND is presently underway. Clinical trials of Cymerus products in osteoarthritis (Phase 3), respiratory failure and diabetic foot ulcers (DFU) are currently ongoing. In addition, Cynata has demonstrated utility of its Cymerus technology in preclinical models of numerous diseases, including the clinical targets mentioned above, as well as 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.**