ASX ANNOUNCEMENT 7 September 2020

Cymerus MSCs Demonstrate Efficacy in Preclinical Lung Disease Study

Melbourne, Australia; 7 September 2020: Cynata Therapeutics Limited (ASX: "**CYP", "Cynata",** or the **"Company"**), a clinical-stage biotechnology company specialising in cell therapeutics, has today announced positive efficacy data from a study of its induced pluripotent stem cell (iPSC)-derived Cymerus™ mesenchymal stem cells (MSCs) in a preclinical rodent model of idiopathic pulmonary fibrosis (IPF).

Key highlights:

- **Efficacy demonstrated in preclinical rodent model of IPF, a disease which causes severe lung damage and leads to respiratory failure**
- **Existing treatments for IPF have limited efficacy**
- **Treatment with Cynata's Cymerus MSCs led to statistically significant improvements in multiple harmful effects of IPF, including interstitial fibrosis, dynamic lung compliance and airway resistance**

Dr. Kilian Kelly, Cynata's Chief Operating Officer, said*:*
"These latest results with Cymerus MSCs add to the large body of evidence on the potency of these cells and their potential utility in treating a wide range of devastating diseases. IPF represents an enormous unmet medical need, as existing treatment options have only modest effects on disease progression and survival rates. We will continue to work with Professor Samuel and our other advisors to determine the next steps for this important program."

IPF is a currently incurable disease of unknown cause, which results in extensive scarring or fibrosis of the lungs. Lung damage is often advanced by the time the condition is initially diagnosed, and existing treatment options have very limited efficacy. It invariably progresses to respiratory failure, with only 20-30% of patients surviving 5 years from the time of diagnosis.[1] The value of the global IPF market is expected to reach around US$5.9b by 2025 with an annual growth of 13%.[2]

It is notable that fibrosis is observed in the lungs of COVID-19 patients with severe disease and may become an important factor in the longer-term effects in such surviving patients. It also occurs in surviving patients of acute respiratory distress syndrome (ARDS) from other causes. As previously announced, Cynata are conducting a Phase 2 clinical trial in patients with respiratory distress associated with COVID-19.

The effect of Cymerus MSCs is being studied in the widely used and clinically relevant bleomycin-induced IPF model, which is the gold-standard preclinical model of this condition. Compared to placebo, Cymerus MSC treatment led to statistically significant improvements in:

- **Dynamic lung compliance** (the lung's ability to stretch and expand)
- **Airway resistance** (a measure of the airway's opposition to airflow into the lungs)
- **Interstitial lung inflammation** (swelling in the tissue surrounding the airways)
- **Interstitial lung fibrosis** (fibrosis in the tissue surrounding the airways)
- **Epithelial and subepithelial thickness** (additional signs of fibrosis)

The initial phase of the IPF preclinical study found that control animals suffered a 40% loss of dynamic lung compliance after bleomycin administration, as expected in this model. However, when Cymerus MSC treatment was administered in a single dose 3 weeks later, or as a double dose at 3 and 4 weeks later, the loss of dynamic lung compliance was just 15%. Similarly, while bleomycin administration led to profound interstitial inflammation and fibrosis, as well as increases in airway resistance, epithelial thickness and subepithelial thickness, Cymerus MSC treatment dramatically reduced each of these harmful effects.

The study is led by Professor Chrishan Samuel, Department of Pharmacology at Monash University, Melbourne, and follows on from his previous studies which demonstrated that Cymerus MSCs significantly reduce fibrosis and inflammation in a model of asthma.[3,4]

Professor Samuel commented:
"*These results are extremely encouraging. While they are very consistent with our previous studies of these cells in a model of asthma, it was important to confirm that the potent anti-inflammatory and anti-fibrotic effects of Cymerus MSCs would be replicated in IPF, which is a disease with very different underlying pathophysiology. We look forward to publishing our results in a peer-reviewed journal in due course.*"

-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 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) and cytokine release syndrome.

---

[1] Ley B, et al. Clinical course and prediction of survival in idiopathic pulmonary fibrosis. Am J Respir Crit Care Med. 2011;183(4):431-40.
[2] https://www.ihealthcareanalyst.com/report/idiopathic-pulmonary-fibrosis-treatment-market/
[3] Royce SG, et al. iPSC- and mesenchymoangioblast-derived mesenchymal stem cells provide greater protection against experimental chronic allergic airways disease compared with a clinically used corticosteroid. FASEB J. 2019;33(5):6402-11
[4] Royce SG, et al. Intranasal administration of mesenchymoangioblast-derived mesenchymal stem cells abrogates airway fibrosis and airway hyperresponsiveness associated with chronic allergic airways disease. FASEB J. 2017;31(9):4168-78