ASX ANNOUNCEMENT 8 May 2020

Cynata Receives Ethics Approval to Commence Clinical Trial in COVID-19 and Clinical Development Update

Melbourne, Australia; 8 May 2020: Cynata Therapeutics Limited (ASX: "**CYP", "Cynata",** or the **"Company"**), a clinical-stage biotechnology company specialising in cell therapeutics, is pleased to announce that it has received ethics committee approval to commence a clinical trial to investigate early efficacy of Cynata's proprietary Cymerus™ mesenchymal stem cells (MSCs) in adults admitted to intensive care with COVID-19. In addition, the Company also provides updated guidance on its wider clinical development pipeline.

Key highlights

- **Ethics approval received for clinical trial in patients in intensive care with COVID-19 in Australia: the MEND (MEseNchymal coviD-19) Trial**
- **Compromised lung function, which can ultimately progress to acute respiratory distress syndrome (ARDS), is a major complication in COVID-19 patients**
- **This trial will build on Cynata's strong pre-clinical study results in ARDS, sepsis and cytokine release syndrome, all of which are common hallmarks of severe COVID-19 cases**
- **The MEND trial is an open-label, randomised controlled clinical trial to investigate early efficacy of Cymerus MSCs**
- **Given restrictions in place for other clinical programs, Cynata is accelerating the COVID-19 / respiratory clinical development strategy**

Dr. Ross Macdonald, Cynata's CEO and MD, said:
"The ethics approval of this proposed clinical trial is a major milestone for Cynata and our proprietary Cymerus MSC technology. Our substantial pre-clinical database in relevant disease models, together with the urgent need for more effective treatments for critically ill patients with COVID-19, allowed us to accelerate planning and rapidly achieve ethics committee approval. We are pleased to be able to move so quickly to further investigate the potential benefits our MSCs could have to treat patients in dire need during this global pandemic."

"This trial forms part of a broader clinical development strategy for our Cymerus MSC product to be trialled in COVID-19 patients in other countries. Our decision to focus on this new clinical development area is a logical and prudent step based on the current global environment and Cynata's solid pre-clinical foundations in respiratory and related diseases."

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The MEND Trial is to be conducted at centres in New South Wales in collaboration with the Cerebral Palsy Alliance Research Institute and investigators from the COVID-19 Stem Cell Treatment (CSCT) Group. The study will be an open-label, randomised controlled clinical trial to investigate early efficacy of Cymerus MSCs in 24 adult patients admitted to intensive care with COVID-19 and respiratory distress.

Twelve patients will be randomised to receive Cymerus MSC infusions, in addition to standard of care, while 12 patients will be randomised to the control group and will receive current standard of care.

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The primary efficacy endpoint will be improvement in PaO_2/FiO_2 ratio (a measure of hypoxemia, a low level of oxygen in the blood caused by compromised lung function) by Day 7. Safety and tolerability up to Day 28 will also be a primary endpoint. Recruitment is expected to commence subject to finalisation of relevant agreements with study centres.

In addition, Cynata is currently assessing clinical development opportunities to expand this COVID-19 trial to other jurisdictions. Cynata's Cymerus MSCs have demonstrated promising pre-clinical trial results in several conditions that can arise from a severe COVID-19 infection, significantly in ARDS, as well as in other inflammatory conditions including sepsis and cytokine release syndrome.

ARDS is an inflammatory process leading to build-up of fluid in the lungs and respiratory failure. It can occur due to infection, trauma and inhalation of noxious substances, and is one of the most common life-threatening complications of COVID-19. There are currently no therapeutic options for the treatment of ARDS.

Update on clinical development pipeline

Cynata's license partner, FUJIFILM, continues to progress further development of CYP-001, the Cymerus™ product for the treatment of graft-versus-host disease (GvHD). Cynata continues to work collaboratively on the trial planning and start-up activities.

While the clinical trial recruitment restrictions implemented in response to the COVID-19 pandemic remain in place (as announced on 1 April 2020), the study start-up activities for the osteoarthritis (OA) and critical limb ischaemia (CLI) Phase 2 trials are continuing.

The Phase 2 OA trial has been reviewed by The University of Sydney Human Research Ethics Committee, which granted approval in principle, subject to the review of certain additional information, with the final approval expected in the near future. Cynata has been advised that the trial sponsor, the University of Sydney, intends to utilise the Therapeutic Good Administration's Clinical Trial Exemption (CTX) clinical trial approval route for this trial; Cynata does not expect this to have a material impact on the timing of trial commencement given the COVID-19 delays to trial recruitment.

The Phase 2 CLI trial, which was approved by the UK Medicines and healthcare Products Regulatory Agency (MHRA) in January this year, has now also received approval in Australia from the Melbourne Health HREC. Cynata and its clinical advisors expect that the COVID-19 pandemic is likely to have continued impact on potential recruitment in this trial for a lengthy period because patients with CLI are at high risk of developing serious complications of COVID-19, due to their age and underlying medical conditions. As such, Cynata considers that it would be imprudent to commence recruitment in this trial under these circumstances, even after more general restrictions are relaxed. In light of these challenges and the new opportunities that have arisen through the COVID-19 program, Cynata has decided to re-direct its financial and operational resources to focus on its COVID-19 and ARDS development strategy to accelerate clinical development and the attainment of potential value catalysts.

Cynata continues to monitor the current COVID-19 situation and will continue discussions relating to partnership opportunities for OA, CLI and other indications.

-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. Cynata plans to advance its Cymerus™ MSCs into Phase 2 trials for severe complications arising from COVID-19, GvHD, critical limb ischemia and 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.

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