ASX ANNOUNCEMENT 26 May 2022

US FDA Clears IND for Cynata's Phase 2 Clinical Trial of CYP-001 in GvHD

Key Highlights:

- **US FDA has cleared Cynata's IND application for a Phase 2 clinical trial of CYP-001 in patients with aGvHD – a major milestone and value catalyst for the Company**
- **Phase 2 clinical study in aGvHD expected to commence subsequent to customary and satisfactory completion of negotiations with study centres and receipt of relevant ethics/administrative approvals**
- **Transformative event for Cynata as it provides a gateway in the USA to potential further clinical targets and is a critical validation step for Cynata's ongoing commercial partnering activities**

Melbourne, Australia; 26 May 2022: Cynata Therapeutics Limited (ASX: **"CYP"** or **"Cynata"**), a clinical-stage biotechnology company specialising in cell therapeutics, is delighted to announce that the United States (US) Food and Drug Administration (FDA) has cleared the Investigational New Drug (IND) application for Cynata's Phase 2 clinical trial of CYP-001[1], Cynata's lead product, in patients with acute graft versus host disease (aGvHD).

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

"Clearance of our IND application confirms that the FDA is satisfied with both the clinical and preclinical data as well as the manufacturing and quality control data on our product that we submitted in support of this application. This achievement represents a hugely important milestone in the development of CYP-001 and our Cymerus platform. We had previously completed several positive interactions with the FDA, as well as securing Orphan Drug Designation for CYP-001 in 2018. However, the planned Phase 2 aGvHD trial will be our first clinical trial conducted in the US, which is the largest healthcare market worldwide. We look forward to commencing this Phase 2 study, which aims to build on the very encouraging Phase 1 clinical trial results.[2]"

Dr Ross Macdonald, Cynata's Chief Executive Officer, said:

"A cleared IND represents a very significant achievement for any pharmaceutical or biotech company and underpins a major valuation catalyst; I would like to thank our shareholders for their patience during this process. We are delighted to have crossed this threshold and will continue to leverage the momentum in our negotiations with study centres with an expectation to commence a US trial in aGvHD by the end of the year."

The proposed Phase 2 clinical trial will seek to recruit approximately 60 patients with high risk aGvHD, at clinical centres in a number of countries, including the US and Australia. Participants will be randomised to receive either CYP-001 or placebo, in addition to corticosteroids. The primary objective of the trial is to assess efficacy of CYP-001 in subjects with high risk aGvHD by Overall Response Rate

[1] Cymerus™ induced pluripotent stem cell (iPSC)-derived mesenchymal stem cells (MSCs).

[2] Bloor AJC, et al. Production, safety and efficacy of iPSC-derived mesenchymal stromal cells in acute steroid-resistant graft versus host disease: a phase I, multicenter, open-label, dose-escalation study. *Nat Med.* 2020;26(11):1720-1725.

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(ORR) at Day 28. The trial is expected to commence enrolment by later this year, with results of the primary evaluation expected in early 2024.

-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 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.

About Graft versus host disease

GvHD is a complication that can occur after a bone marrow transplant or similar procedure, when the donor's immune cells (from the "graft") attack the recipient of the transplant (the "host"). First line treatment for acute GvHD is corticosteroid therapy, which is typically only effective in about 50 percent of patients. When GvHD fails to improve or worsens despite steroid treatment, patients are described as having steroid-resistant acute GvHD. The prognosis for these patients is poor, with mortality rates in excess of 90 percent[3]. High risk acute GvHD refers to patients with newly diagnosed acute GvHD who have been identified as being likely to progress to steroid-resistant acute GvHD, based on pre-defined clinical features of the disease.

About the Proposed Phase 2 clinical trial (Protocol Number: CYP-GvHD-P2-01)

The trial is entitled "*A Multicenter, Randomized, Double-blind, Placebo-Controlled Phase II Study to Investigate the Efficacy and Safety of CYP-001 in Combination with Corticosteroids vs Corticosteroids Alone for the Treatment of High-Risk Acute Graft Versus Host Disease*". Participants must be adults who have undergone an allogeneic haematopoietic stem cell transplant (HSCT) and subsequently been diagnosed with high risk Grade II-IV acute GvHD. After enrolment upon meeting eligibility criteria, participants will be randomised to receive either corticosteroids plus CYP-001, or corticosteroids plus placebo. On D1 and D4, each participant will receive an IV infusion of 2 x 10^6 Cymerus MSCs/kg of body weight (up to a maximum of 200 million cells), or placebo. The primary objective of the trial is to assess efficacy of CYP-001 in subjects with HR-aGvHD by Overall Response Rate (ORR) at Day 28. The primary evaluation period will conclude 100 days after the first dose in each patient. After the completion of the primary evaluation period, participants will enter a longer term non-interventional follow-up period, which will continue for up to two years after the initial dose.

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

[3] Westin JR, Saliba RM, De Lima M, et al. Steroid-Refractory Acute GVHD: Predictors and Outcomes. Adv Hematol. 2011; 2011:601953.