ASX ANNOUNCEMENT **16 May 2025**

Third-Party Exclusivity Does Not Impede CYP-001's FDA Approval Pathway

Melbourne, Australia; 16 May 2025: Cynata Therapeutics Limited (ASX: **"CYP"**, **"Cynata"**, or the **"Company"**), a clinical-stage biotechnology company specialising in cell therapeutics, notes recent publications regarding the orphan-drug exclusive approval recently granted by the US Food and Drug Administration ("US FDA") to Ryoncil® (remestemcel-L-rknd), for the treatment of steroid-refractory acute graft versus host disease (aGvHD) in paediatric patients 2 months of age and older.

Cynata advises that this orphan-drug exclusivity will not impede the potential approval of Cynata's product CYP-001.

CYP-001 is Cynata's Cymerus™ off-the-shelf product for intravenous infusion, which is currently under investigation in a global Phase 2 trial in adults with newly diagnosed high-risk aGvHD. The US FDA has granted Orphan Drug Designation[1] to CYP-001 for the treatment of aGvHD.

On 18 December 2024, the US FDA granted marketing approval to Ryoncil® (which also has Orphan Drug Designation) for the treatment of steroid refractory aGvHD in paediatric patients 2 months of age and older. One of the benefits of Orphan Drug Designation for a product with marketing approval is that "*effective on the date of FDA approval as stated in the approval letter of a marketing application for a sponsor of a designated orphan drug, no approval will be given to a subsequent sponsor of the **same drug** for the **same use or indication** for 7 years, except as otherwise provided by law or in this part*"[2] (emphasis added).

Cynata advises that CYP-001 does not contain "the same drug" as Ryoncil®, which consists of a certain type of bone marrow-derived mesenchymal stromal or stem cells (MSCs). For the avoidance of doubt, CYP-001 does not contain "the same drug" as any other MSC-based product that the Company is currently aware of. The active agent in CYP-001 is MSCs derived from induced pluripotent stem cells (iPSCs) using Cynata's proprietary Cymerus™ technology, which facilitates scalable production of consistent quality MSCs from a single donor source.

It is well established that MSCs derived from different sources and/or manufactured using different methods have significantly different properties and functionality. Numerous scientific papers have been published illustrating this. Notably, as announced by Cynata on 5 February 2025, this includes a paper comparing Cynata's Cymerus™ iPSC-derived MSCs with MSCs derived from bone marrow and various other sources.[3]

Furthermore, Cynata notes that the indication it is currently pursuing for CYP-001 (newly diagnosed aGvHD in adults) is not the same as the indication that the recently granted orphan-drug exclusivity relates to (steroid-refractory aGvHD in paediatric patients).

Considering the clear differences in active agent and indication, Cynata considers that the orphan-drug exclusivity recently granted by the US FDA will not impede the approval of CYP-001.

The Company also notes that CYP-001 is supported by a robust patent portfolio in the United States and other relevant jurisdictions, and as CYP-001 is not a "biosimilar", it will not be necessary for the Company to refer to any existing Biologics License Application to support approval of CYP-001.

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

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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) to achieve economic manufacture of cell therapy products, including mesenchymal stem cells (MSCs), at commercial scale without the limitation of multiple donors.

Cynata has demonstrated positive safety and efficacy data for its Cymerus™ product candidates CYP-001 and CYP-006TK, in Phase 1 clinical trials in steroid-resistant acute graft versus host disease (GvHD), and diabetic foot ulcers (DFU), respectively. Further clinical trials are now ongoing: a Phase 2 trial of CYP-001 in GvHD under a cleared US FDA IND; a Phase 1/2 trial of CYP-001 in patients undergoing kidney transplantation; and a Phase 3 trial of CYP-004 in osteoarthritis. In addition, Cynata has demonstrated utility of its Cymerus™ technology in preclinical models of numerous other 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.

[1] Orphan Drug Designation qualifies Cynata for incentives including extended marketing exclusivity, tax credits and fee waivers.
[2] US Code of Federal Regulations, Title 21 Chapter I Subchapter D Part 316.
[3] Hodgson-Garms M, et al. npj Regen Med 10, 7 (2025). https://doi.org/10.1038/s41536-024-00382-y

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