ASX ANNOUNCEMENT **5 February 2025**

Comparison of Cymerus™ iPSC-derived MSCs to Conventional MSCs Published in Leading Peer-Reviewed Journal

Melbourne, Australia; 5 February 2025: Cynata Therapeutics Limited (ASX: **"CYP"**, **"Cynata"**, or the **"Company"**) is a clinical-stage biotechnology company specialising in cell therapeutics. A paper comparing Cynata's Cymerus™ iPSC[1]-derived MSCs[2] and MSCs from various other sources has been published in *npj Regenerative Medicine*, a leading peer-reviewed journal published by *Nature Portfolio*.

Background

The effects of MSCs depend largely on their "secretome", which is a term used to describe proteins and other molecules released by cells.

Conventional MSC manufacturing methods rely on isolation of cells from donated tissue. Consequently, MSCs produced in this way are known as "donor tissue-derived MSCs". Conversely, Cynata uses its novel Cymerus™ platform to manufacture MSCs from a starting material called iPSCs, avoiding the need for donor tissue.

This study, led by Dr Margeaux Hodgson-Garms and Prof Jess Frith at Monash University, Melbourne, assessed similarities and differences between the secretomes of MSCs derived from either iPSCs or a donor tissue source (bone marrow, adipose tissue or umbilical cord), under different conditions. It is important to assess MSCs under different conditions because MSCs respond to their environment, which changes their effects. Notably, MSCs are often exposed to inflammatory conditions after administration to patients.

Key Highlights

- There were substantial differences between MSCs from different sources, especially between iPSC-derived MSCs and those derived from bone marrow or adipose tissue.
- There was substantially more variability between batches of MSCs derived from donor tissue, especially bone marrow, than between batches of iPSC-derived MSCs.
- iPSC-derived MSCs released many more unique proteins than donor tissue-derived MSCs, indicating that iPSC-derived MSCs could have additional effects that are not exhibited by donor tissue-derived MSCs.
- iPSC-derived and umbilical cord-derived MSCs displayed features consistent with "younger" cells, suggesting they have sustained ability to avoid ageing (known as "senescence").
- The strong regenerative potential of iPSC-derived and umbilical cord-derived MSCs (but not bone marrow or adipose tissue-derived MSCs) was maintained under both resting and inflammatory conditions.
- *In vitro* studies of MSC secretomes found:
    - iPSC-derived and umbilical cord-derived MSCs resulted in significantly faster wound closure than bone marrow or adipose tissue-derived MSCs.
    - iPSC-derived MSCs showed a greater ability to balance the immune system (immunomodulatory effects) than MSCs derived from any donor tissue source.
    - MSCs from all sources stimulated growth of new blood vessels (known as "angiogenesis"). One measure of angiogenesis suggested that umbilical cord-derived MSCs had a greater angiogenic effect than other MSCs, but a second measure of angiogenesis suggested there was little difference between MSCs from different sources.

Prof Jess Frith, Deputy Head, Materials Science and Engineering at Monash University, said:

"*This study provides valuable insights into cell "age", the mechanisms underlying the therapeutic effects of MSCs, and the differences by source and functional state. It is clear that cell source matters a great deal, with respect to the functionality and consistency of MSC-based products. These findings may help us to design more effective MSC-based therapies and identify optimal clinical targets.*"

Dr Kilian Kelly, Cynata's Chief Executive Officer and Managing Director, said:

"*This robust and comprehensive study provides further support for our view that our iPSC-based Cymerus™ platform provides the ideal means of producing MSCs with a high level of potency and functionality, in a consistent and scalable manner. It is particularly notable that Cynata's iPSC-derived MSCs displayed very impressive immunomodulatory and wound-healing properties compared to MSCs from other sources. These findings have clear relevance to our product candidates in acute graft versus host disease and diabetic foot ulcers, both of which have already shown very promising safety and efficacy outcomes in completed clinical trials.*"

The details of the paper are as follows:

- Hodgson-Garms M, Moore MJ, Martino MM, Kelly K, Frith JE. Proteomic profiling of iPSC and tissue-derived MSC secretomes reveal a global signature of inflammatory licensing. npj Regen Med 10, 7 (2025). https://doi.org/10.1038/s41536-024-00382-y

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

CONTACTS: Dr Kilian Kelly, CEO & MD, Cynata Therapeutics, +61 (03) 7067 6940, kilian.kelly@cynata.com
Lauren Nowak, Media Contact, +61 (0)400 434 299, lauren@littlebigdeal.au

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 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 transplant; 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] iPSC = induced pluripotent stem cell
[2] MSC = mesenchymal stem (or stromal) cell