

Cynata's Cymerus™ MSCs Ameliorate Cytokine Release Syndrome in Preclinical Study

- *Cymerus MSCs demonstrate substantial protection against CRS symptoms, a serious adverse reaction caused by cancer immunotherapies such as CAR-T*

Melbourne, Australia; 19 September 2018: Australian stem cell and regenerative medicine company Cynata Therapeutics Limited (ASX: CYP) is pleased to announce data from a preclinical model demonstrating that its proprietary Cymerus™ mesenchymal stem cells (MSCs) significantly ameliorate the effects of cytokine release syndrome (CRS), a potentially severe and life-threatening adverse reaction to cancer immunotherapy.

Key Highlights

- Cymerus MSC treatment is effective in protecting against CRS in murine models, with statistically significant improvements in body temperature and clinical scores relative to control animals.
- Cynata intends to partner with companies developing cancer immunotherapies to evaluate the treatment approach in humans.

Dr Kilian Kelly, Cynata's Vice President, Product Development, said, "Cancer immunotherapy is one of the most exciting fields in medicine today, offering a potentially curative treatment option to patients with otherwise intractable and advanced disease. However, CRS is a common, unpredictable and potentially fatal complication that may limit treatment uptake. These results suggest that administering a single dose of Cymerus MSCs before, during or even shortly after cancer immunotherapy treatment may provide significant therapeutic benefit and a straightforward way of limiting adverse CRS reactions. We look forward to continuing to explore the benefits of our MSCs in humans through partnerships with companies commercialising cancer immunotherapies, such as CAR-T."

Study Design

The study, led by Associate Professor Lisa Minter, Ph.D., at the University of Massachusetts Amherst, evaluated Cymerus MSCs in a humanised murine model of CRS. The murine model was created by engrafting human peripheral blood mononuclear cells in NOD-SCID-gamma mice, and then administering OKT3 (anti-human CD3) antibody by intra-peritoneal (IP) injection. This resulted in consistent and significant decreases in body temperature, as well as increased clinical scores (indicating deterioration) and increased T cell expression of the immune response activation marker, CD69.

Mice were randomly assigned to a control group (no treatment) or one of eight treated groups. Animals in the treatment groups received a single dose of Cymerus MSCs by intravenous (IV) or IP injection at various timepoints, ranging from 5 hours before to 30 minutes after OKT3 administration.



Body temperature, clinical scores and biomarkers were analysed at pre-determined timepoints following CRS induction.

Study Outcomes

Cymerus MSCs administered by IV or IP injection demonstrated substantial protection against CRS symptoms, with IV administration demonstrating a generally more robust effect on cytokine reduction. Notably, by 24 hours after CRS induction, statistically significant improvements in body temperature and clinical scores were demonstrated relative to control animals.

Next Steps

Cynata intends to partner with companies developing cancer immunotherapies to evaluate this treatment approach in humans.

Ends

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About Cytokine Release Syndrome

Cancer immunotherapy seeks to harness the power of a patient's own immune system to eradicate cancer. Treatment can involve the use of monoclonal antibodies, cancer vaccines or cell-based therapies, including chimeric antigen receptor T cell (CAR-T) therapy, which has been shown to be highly effective in treating certain blood cancers.

However, the high levels of immune system activation induced by cancer immunotherapy can lead to cytokine release syndrome (CRS), a result of a surge of cytokines into the blood from immune cells. CRS causes a range of symptoms that may include decreased or increased body temperature, nausea, headache, rash, rapid heartbeat, low blood pressure and difficulty breathing. CRS can be severe and even life-threatening.

About Cynata Therapeutics (ASX: CYP)

Cynata Therapeutics Limited (ASX: CYP) is an Australian clinical-stage stem cell and regenerative medicine company that is developing a therapeutic stem cell platform technology, Cymerus™, originating from the University of Wisconsin-Madison, a world leader in stem cell research. The proprietary Cymerus technology addresses a critical shortcoming in existing methods of production of mesenchymal stem cells (MSCs) for therapeutic use, which is the ability to achieve economic manufacture at commercial scale. Cymerus utilises induced pluripotent stem cells (iPSCs) to produce a particular type of MSC precursor, called a mesenchymoangioblast (MCA). Cymerus provides a source of MSCs that is independent of donor limitations and an "off-the-shelf" stem cell platform for therapeutic product use, with a pharmaceutical product business model and economies of scale. This has the potential to create a new standard in the emergent arena of stem cell therapeutics, and provides both a unique differentiator and an important competitive position.