

Engineered Cymerus™ MSCs Demonstrate Anti-Cancer Effects in Preclinical Studies

Positive results in pre-clinical models support the use of the Cymerus platform to target various cancers

Melbourne, Australia; 18 October 2018: Cynata Therapeutics Limited (ASX: CYP), a clinical stage Biotechnology company specialising in cell therapeutics is pleased to announce results from its preclinical program using the proprietary Cymerus platform technology to develop genetically engineered cells, derived from mesenchymal stem cells (MSCs), to treat cancer.

Key Highlights

- Genetically engineered cells were successfully produced using the Cymerus platform to express diagnostic and therapeutic anti-cancer agents.
- Engineered Cymerus cells can be effectively tracked by real time imaging *in vivo* in mouse tumour models
- Engineered Cymerus cells showed highly promising therapeutic benefits in different mouse tumour models.

The studies were conducted under the direction of Professor Khalid Shah, Vice Chair of Research at Brigham and Women's Hospital in Boston, Massachusetts, and Director of the Center for Stem Cell Therapeutics and Imaging at Harvard Medical School. Professor Shah commented, "Our results validate the use of this cell-based approach, as it provides a continuous pool of therapeutic protein around the tumour cells, circumventing the protein short half-lives. Overall, the study outcomes support the use of engineered Cymerus MSCs for cell therapy to target various malignancies."

Dr Kilian Kelly, Cynata's Vice President, Product Development, said, "These highly encouraging results suggest that the Cymerus platform can be exploited to produce targeted anti-cancer therapies, which may have significant advantages over conventional cancer treatments, from both a safety and efficacy perspective. Importantly, this engineering technique could also facilitate the creation of novel engineered therapies for areas of high unmet need in other therapeutic areas".

Study Design

The first stage of the program aimed to evaluate the feasibility of using a lentiviral engineering process to cause Cymerus MSCs to express transgenes (genes from other cells), and to investigate the persistence of engineered cells in mouse models.

Cymerus MSCs were also engineered to express a protein that is known to exert anti-cancer effects. The effects of these engineered Cymerus MSCs on the viability of both human melanoma (skin cancer) and human glioblastoma (brain cancer) cells were evaluated in *in vitro* test systems and the therapeutic efficacy of the engineered Cymerus MSCs was also tested in a well-defined mouse model of glioblastoma.



Study Outcomes

The preliminary studies confirmed that:

- The Cymerus platform can be successfully engineered to express transgenes in a stable manner.
- Engineered Cymerus MSCs persist *in vivo* for a sufficient length of time to facilitate a statistically significant therapeutic effect in a preclinical model of Glioblastoma.

In the second stage of the program, engineered Cymerus MSCs were shown to cause a significant reduction in the viability of human glioblastoma cells when compared to either the control ($p < 0.005$) or to direct administration of the therapeutic protein ($p < 0.05$), and a significant reduction in the viability of human melanoma cells compared to the control ($p < 0.005$). Furthermore, in an *in vivo* mouse model of glioblastoma, tumour progression was slower in mice that received the engineered Cymerus MSCs compared to those receiving the control.

Following this positive outcome Cynata intends to continue to pursue this promising new approach to cancer treatment as part of its pipeline strategy.

Ends

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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 and 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 GvHD and critical limb ischemia. In addition, Cynata has demonstrated utility of its Cymerus MSC technology in preclinical models of asthma, critical limb ischemia, diabetic wounds, heart attack and cytokine release syndrome, a life-threatening condition stemming from cancer immunotherapy.