ASX ANNOUNCEMENT 28 September 2021

Preclinical Study Showing Beneficial Effects of Cymerus™ MSCs in Heart Attacks Published in Leading Peer-Reviewed Journal

Melbourne, Australia; 28 September 2021: Cynata Therapeutics Limited (ASX: **"CYP"**, **"Cynata"**, or the **"Company"**), a clinical-stage biotechnology company specialising in cell therapeutics, has today announced that a scientific paper describing the use of Cymerus™ mesenchymal stem cells (MSCs) in a model of myocardial infarction (heart attack) has been published in the peer-reviewed journal Cytotherapy, the official journal of the International Society for Cell & Gene Therapy (ISCT).

The paper, entitled "*Pluripotent stem cell derived mesenchymal stromal cells improve cardiac function and vascularity after myocardial infarction*", has been published online on the Cytotherapy website, and will appear in a print edition in the near future. This paper validates the importance of Cymerus MSCs in treating serious and debilitating diseases and provides further recognition of Cynata's advanced technology.

Background

The paper summarises the results of studies led by Associate Professor James Chong (Westmead Institute for Medical Research, Sydney).

The effects of Cymerus MSCs and bone marrow-derived MSCs were evaluated in a rat model of myocardial ischaemia-reperfusion – a well-established preclinical model of heart attack, which leads to severe dysfunction of the left ventricle of the heart. In humans, left ventricular dysfunction after myocardial infarction is associated with heart failure and sudden cardiac death.

Rats (14-15 per group) were randomly assigned to receive Cymerus MSCs, bone marrow-derived MSCs or placebo control. In cell-treated animals, a total of 5 million cells were injected into the wall of the heart. The results were positive and demonstrated the efficacy of Cymerus MSCs in this model of myocardial infarction.

A/Prof Chong said:

"*Our studies found that Cymerus MSCs achieved better therapeutic effects compared to conventional bone marrow-derived MSCs in this preclinical model. iPSC-derived MSCs offer an exciting opportunity for an "off-the-shelf" stem cell therapy for cardiac repair, due to their consistency and manufacturing scalability."*

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

"We are pleased to see this paper being published in a leading peer-reviewed journal. The studies conducted by A/Prof Chong and his team have generated important insights into the potential utility of Cymerus MSCs in the treatment of heart attacks, as well as the mechanisms of action that lie behind these beneficial effects. This further strengthens the body of data that we have built up in support of the Cymerus platform over the last few years."

Key Results

- Cymerus MSCs (p=0.01), but not bone marrow-derived MSCs (p=0.63), significantly enhanced left ventricular cardiac function.

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- Both Cymerus MSCs (p=0.001) and bone marrow-derived MSCs (p=0.003) significantly increased the number of new capillaries (very small blood vessels between arteries and veins) in the damaged area of the heart.
- Cymerus MSCs (p<0.0001), but not bone marrow-derived MSCs (p=0.09), significantly increased the number of new arterioles (the smallest branches of arteries) in the damaged area of the heart.
- The beneficial effects of Cymerus MSCs in this model appear to result from the release of molecules that stimulate new blood vessel growth, rather than engraftment of the MSCs or reduction in the size of the scar in the heart muscle. Notably, the levels of relevant molecules released by Cymerus MSCs were up to two to four times as high as those released by bone marrow-derived MSCs.
- Administration of MSCs was found to be safe, and did not cause irregular heart rhythms.

-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. Clinical trials of Cymerus MSC products in osteoarthritis (Phase 3) and in patients with respiratory failure are currently ongoing. Planning is also underway for further clinical trials of Cymerus MSC products in GvHD (through licensee Fujifilm), diabetic foot ulcers, critical limb ischemia, idiopathic pulmonary fibrosis, and renal transplantation. In addition, Cynata has demonstrated utility of its Cymerus MSC technology in preclinical models of numerous diseases, including the clinical targets mentioned above, as well as 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.