

ASX ANNOUNCEMENT

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Cynata's MSC Technology Demonstrates Significant Efficacy in Preclinical Asthma Study

- Data suggests Cynata's unique Cymerus™ iPSC-generated MSCs may have potential clinical use as a treatment for asthma
- Intranasal administration of Cymerus™ MSCs completely normalised airway hyper-responsiveness in a mouse model of asthma

Melbourne, Australia; 17 October 2016: Australian stem cell and regenerative medicine company, Cynata Therapeutics Limited (ASX: CYP), announced today that it has received compelling data from a proof of concept study of its Cymerus™ mesenchymal stem cells (MSCs) in an experimental model of asthma.

Asthma is a chronic, long term lung condition that impacts over 330 million people globally.¹ Cynata, through its partnership with Monash University has been investigating the use of its Cymerus™ technology as a potential alternate treatment for asthma sufferers.

In this study, conducted under the supervision of Associate Professor Chrisan Samuel and Dr Simon Royce at Monash University, in the Department of Pharmacology and the Monash Biomedicine Discovery Institute, Melbourne, the well-established chronic allergic airways disease model was induced by sensitising and challenging mice with a protein called ovalbumin. The features of this model closely resemble the clinical manifestations of asthma in humans.

As expected, subjecting mice to the ovalbumin sensitisation regime caused them to exhibit significantly increased airway hyper-responsiveness (AHR; $p < 0.001$ vs saline-treated control group), which is the key characteristic of asthma. Intravenous administration of Cynata's MSCs in these animals caused a statistically significant (60-70%) decrease in AHR ($p < 0.01$) relative to untreated sensitised animals. Moreover, intranasal administration of Cynata's MSCs completely normalised AHR, to a level that was no longer different to healthy animals, in which the asthma model had not been induced. No adverse safety findings were observed during the study.

"We are very excited by these results, which indicate that Cymerus™ MSCs could have a profound effect in the treatment of asthma. This is a debilitating condition, which affects about 10% of the population, resulting in close to 40,000 hospitalisations and several hundred deaths each year, in Australia alone",² said Cynata Vice President of Product Development, Dr Kilian Kelly. "Although a number of drugs are approved for the treatment of asthma, studies have shown that conventional treatments result in as few as 5% of asthma patients achieving full control of their condition.³ Consequently, there is a widely recognised need for novel treatments that address – and potentially eliminate – the underlying disease", added Dr Kelly.

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“This study has clearly demonstrated that Cynata’s MSCs have a dramatic effect on AHR in our model, particularly when directly administered into the allergic lung. We look forward to continuing our analysis of the effects of these unique cells on markers of inflammation and airway remodelling, and we are optimistic of building on the very positive data we have generated so far”, said Associate Professor Samuel.

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About Cynata Therapeutics (ASX: CYP)

Cynata Therapeutics Limited (ASX: CYP) is an Australian 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). The Cymerus™ platform provides a source of MSCs that is independent of donor limitations and provides 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.

About the Preclinical Study in the Ovalbumin-Induced Allergic Airways Disease Model

Female wild-type BALB/c mice at 7–8 weeks of age were maintained under specific pathogen-free conditions, under a fixed lighting schedule with access to food and water *ad libitum*. A well-established ovalbumin-induced chronic allergic airways disease model was used as previously described.⁴ Briefly, mice were sensitised with intraperitoneal injections of ovalbumin and alum on days 1 and 14, and then challenged with a nebulised aerosol solution of ovalbumin for 30 minutes, three times a week for 6 weeks (from days 21 to 63).

The study involved a total of 48 mice, which were randomly assigned to one of the following six groups (eight animals per group):

1. Untreated controls (no asthma)
2. Controls (no asthma), treated with intravenous (IV) MSC injections
3. Controls (no asthma), treated with intranasal (IN) infusion of MSCs
4. Untreated sensitised animals (asthma)
5. Sensitised animals (asthma), treated with IV MSC injections
6. Sensitised animals (asthma), treated with IN infusion of MSCs

All MSC-treated animals received a dose of 1 million cells by the specified route of administration on three occasions (once weekly from weeks 9-11). AHR in response to the bronchoconstrictor methacholine was measured by invasive plethysmography.

¹ Global Asthma Network – <http://www.globalasthmareport.org/about/about.php>

² Asthma Australia – <http://www.asthmaaustralia.org.au/national/about-asthma/what-is-asthma/statistics>

³ Braido F. Failure in Asthma Control: Reasons and Consequences. *Scientifica*. 2013; 2013: 549252.

⁴ Temelkovski J et al. An improved murine model of asthma: selective airway inflammation, epithelial lesions and increased methacholine responsiveness following chronic exposure to aerosolised allergen. *Thorax*. 1998 Oct;53(10):849-56.

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