ASX ANNOUNCEMENT **22 June 2017**

Study of Cynata MSCs in Asthma Model Published in Leading Peer Reviewed Journal

- Monash University led study of Cynata's MSCs published in the FASEB Journal, one of the world's most cited peer-reviewed biology journals
- Study demonstrated that Cymerus™ MSCs have significant beneficial effects on all three key components of asthma
- Data supports second ongoing study with the Monash Lung Biology Network that may enable progression to a clinical study

Melbourne, Australia; 22 June 2017: Australian stem cell and regenerative medicine company, Cynata Therapeutics Limited (ASX: CYP), is pleased to announce that data supporting the efficacy of its proprietary mesenchymal stem cells (MSCs) in an experimental asthma model have been published in The FASEB Journal, one of the world's most cited peer-reviewed journals.[1]

"We are pleased with the publication of these data as they suggest that Cymerus™ MSCs may provide an efficacious but safe treatment option for people suffering from asthma," said Associate Professor Chrishan Samuel, Department of Pharmacology at Monash University, Melbourne, and a lead author on the publication. "Previous studies by our team found that the intranasal (IN) administration of other types of stem cells given alone to the experimental model studied, did not produce similar effects."

The study, conducted at Monash under the supervision of Associate Professor Samuel and Dr Simon Royce, examined Cymerus' MSCs in a well-established mouse model of chronic allergic airways disease, which closely resembles the clinical manifestations of asthma in humans. Monash University is one of Australia's leading research institutions.

The study's key findings include:

- Both intravenous (IV) and IN administration of Cymerus™ MSCs caused statistically significant improvements in the three main features of asthma: airway inflammation, airway remodelling and airway hyperresponsiveness (AHR).
- IV administration of Cymerus™ MSCs partially but significantly reversed the experimentally-induced increase in AHR ($p<0.05$ relative to untreated sensitised animals), while IN administration of Cymerus™ MSCs completely normalised AHR ($p<0.001$ relative to untreated animals with chronic allergic airways disease).
- IN delivery of Cymerus™ MSCs completely reversed pathologic collagen deposition in the lungs to levels seen in animals in which the asthma model was not induced. Pathologic collagen deposition is a sign of airway remodelling/fibrosis. Previous studies by the same group found that IN administration of other types of stem cells did not have similar effects, unless used in combination with other drugs.
- No adverse safety findings were observed.

[1] FASEB J. 2017 Jun 16. pii: fj.201700178R. doi: 10.1096/fj.201700178R. [Epub ahead of print] The FASEB Journal is the official journal of the Federation of American Societies for Experimental Biology

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A further study in collaboration with the *Monash Lung Biology Network,* a consortium which includes researchers from the Biomedicine Discovery Institute and Department of Pharmacology, Monash University, is currently in progress. This additional study is focusing on the effects of Cymerus produced MSCs in combination with or in comparison to a clinically-used corticosteroid, which is the common therapeutic used to treat asthma. This further study, together with the positive result from the initial study, is paving the way towards a clinical study.

"The publication in such a highly regarded journal further validates the work of Associate Professor Samuel and his team at Monash and underscores the ability of the Cymerus technology to generate consistent and reliable MSCs with compelling therapeutic potential not seen in first-generation MSC therapies," said Dr Kilian Kelly, Cynata's VP, Product Development. "We look forward to learning the outcome of the further study in collaboration with this group, which we anticipate will support progression to the clinical stage."

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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 developing therapies based on its proprietary Cymerus™ stem cell technology platform. Cymerus overcomes critical issues in the production of therapeutic mesenchymal stem cells (MSCs) by enabling the economical manufacture of commercial-scale MSCs, independent of multi-donor limitations. Cymerus' novel approach utilises induced pluripotent stem cells (iPSCs) derived from a single blood donation to generate mesenchymoangioblasts (MCAs), a precursor that is used to manufacture an unlimited number of therapeutic MSCs. Cynata's unique "off-the-shelf" Cymerus platform has the potential to create a new standard in the development and manufacture of stem cell therapeutics.

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.[1] 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 IV MSC injections
3. Controls (no asthma), treated with 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 two occasions (once weekly from weeks 9-11). The following endpoints were then measured at week 11 (after 2 weeks of MSC treatment):

i) Inflammation score – as a measure of airway inflammation (AI)
ii) Goblet cell metaplasia – as a measure of AI-induced airway remodelling (AWR)
iii) Epithelial thickness – as a measure of AWR

iv) Sub-epithelial collagen thickness – as a measure of AWR/fibrosis

v) Total lung collagen concentration – as a measure of AWR/fibrosis

vi) Epithelial TGF-β1 staining – as a measure of AWR

vii) Subepithelial myofibroblast density – as a measure of AWR

viii) Gelatinase (MMP-2 and MMP-9) expression/activity – as a measure of AWR

ix) AHR/reactivity in response to the bronchoconstrictor methacholine, measured by invasive plethysmography (a measure of lung function).

[1] 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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