ASX ANNOUNCEMENT **25 February 2019**

Further Study of Cynata's Cymerus™ MSCs in Preclinical Model of Asthma Published in Leading Peer-Reviewed Journal

Melbourne, Australia; 25 February 2019: Cynata Therapeutics Limited (ASX: CYP), a clinical-stage biotechnology company specialising in cell therapeutics, is pleased to announce that results demonstrating the efficacy of Cymerus MSCs in combination with, or in comparison to, the corticosteroid dexamethasone in a preclinical asthma study have been published in The FASEB Journal, one of the top ranked biology journals globally.[1]

The paper summarises work conducted under the supervision of Associate Professor Chrishan Samuel and Dr Simon Royce of the *Monash Lung Biology Network*,[2] using a well-established mouse model of chronic allergic airways disease, which closely resembles asthma in humans. Corticosteroids, such as dexamethasone, are considered to be the most effective medications for controlling asthma (when taken regularly).

Key Highlights

- **Clear efficacy data for Cynata's proprietary Cymerus MSCs in final phase of preclinical asthma study**
- **Cymerus MSCs alone demonstrated striking anti-fibrotic effects, and reduced airway hyperresponsiveness by up to 75%**
- **When Cymerus MSC were administered with the corticosteroid dexamethasone, the positive effects of both treatments alone were retained**
- **Results suggest that the combination of Cymerus MSCs with corticosteroids may be a viable treatment option offering the potential of superior asthma control**

Dr Kilian Kelly, Cynata's Vice President of Product Development, said, "This is the latest in a series of important studies describing the efficacy of Cymerus MSCs in preclinical models of various diseases, and its publication in a leading peer-reviewed journal provides further independent validation of the promise that the Cymerus platform holds. It broadens the solid evidence supporting the therapeutic utility of Cynata's Cymerus technology in lung disease and adds to the clinical data from our recently completed Phase 1 trial in graft-versus-host disease (GvHD)."

The paper has been published online ahead of print on the FASEB Journal website. The details of the paper are:

Royce SG, Mao WY, Lim R, Kelly K and Samuel CS. *iPSC- and mesenchymoangioblast-derived mesenchymal stem cells provide greater protection against experimental chronic allergic airways disease compared with a clinically used corticosteroid*. FASEB J, 2019.

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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.[3] 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 8 weeks (from days 21 to 77). The study involved a total of 40 mice, which were randomly assigned to one of the following five groups (eight animals per group):

1. Untreated controls (no asthma)
2. Untreated sensitised animals (asthma)
3. Sensitised animals (asthma), treated with IN infusion of MSCs
4. Sensitised animals (asthma), treated with IN infusion of dexamethasone (DEX)
5. Sensitised animals (asthma), treated with IN infusion of MSCs + DEX

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). DEX (0.5mg/ml) was administered once daily from weeks 9-11. The following endpoints were then measured at week 11 (after two weeks of MSC ± DEX 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 airway remodelling (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).

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.

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[1] The FASEB Journal is the official journal of the Federation of American Societies for Experimental Biology

[2] The Monash Lung Biology Network is a consortium, which includes researchers from the Biomedicine Discovery Institute and Department of Pharmacology at Monash University, Melbourne.

[3] 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;53(10):849-56.