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BIOPHARMACEUTICALS
ASX:NSB

ASX ANNOUNCEMENT
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EMTINB™ SIGNIFICANTLY REDUCES MAJOR BIOMARKERS OF SEVERE COVID-19 AND POOR PROGNOSIS

HIGHLIGHTS

- **Treatment with EmtinB™ significantly reduced SAA, IP10, Eot3 biomarkers associated with severe COVID-19 in a panel of human primary cell-based systems**
- **Study results indicate EmtinB™'s therapeutic potential in preventing severe immune responses from COVID-19 infections**
- **Treatment with EmtinB™ was safe and well tolerated across all dose concentrations - suggesting it is safe to administer in future work**

NeuroScientific Biopharmaceuticals Ltd (ASX: **NSB**) (**"NeuroScientific"** or **"the company"**) is pleased to announce that EmtinB™ significantly reduced important biomarkers associated with severe COVID-19 and poor patient prognosis by more than >50% (vs. controls; $p<0.05$), indicating strong therapeutic potential for EmtinB™ in preventing severe immune responses resulting from COVID-19 infections. Additionally, EmtinB™ was shown to be safe and well-tolerated across all dose concentrations. These studies were undertaken by leading independent research organisations Eurofins, US and The Institute for Respiratory Health, Aus.

Early diagnosis and appropriate treatment are essential in reducing the morbidity and mortality of COVID-19-infected patients. Severely ill COVID-19 patients require simultaneous management of oxygenation and inflammation without compromising viral clearance. While multiple tools are available to aid oxygenation, there is unmet medical need in in immunomodulatory therapy that can adjust inflammatory immune responses and prevent fatal cytokine storms across COVID disease stages.

For the first time the team at Neuroscientific Biopharmaceuticals was able to demonstrate that EmtinB™ can dramatically reduce major immune biomarkers in human primary cell-based systems that model complex disease biology, indicating the effectiveness of EmtinB™ in preventing severe immune responses in COVID patients with poor prognosis.

NeuroScientific's Managing Director Matt Liddelow commented: *"These results demonstrate the significant therapeutic utility of EmtinB™ and its potential modulation of inflammatory processes outside of the central nervous system. For the first time, our team have demonstrated an EmtinB™-mediated effect on adaptive immune responses as evidenced by regulation of these inflammatory biomarkers".*

NeuroScientific's Non-Executive Chairman Paul Rennie said: *"These results demonstrate EmtinB™ is a true platform technology. Inflammation is now a well-recognised driver of disease progression in many diseases and Big Pharma Companies have a keen interest in this space. These data will demonstrate the wide range of potential clinical applications of EmtinB™ and therefore enhance the commercial interest in this compound".*

Among 148 clinical biomarkers tested in the human primary cell-based model, Serum Amyloid A (SAA), Interferon-gamma-inducible protein 10 (IP-10), and Eotaxin-3 (Eot3) immune markers were the most affected by EmtinB™ treatment, significantly reducing their expression (>50% vs. controls; $p<0.05$) and suggesting clinically meaningful outcomes in COVID-19 disease.

Inflammation
Inflammation is a response to a foreign organism such as viruses, bacteria, pollen, or dust particles. Ongoing studies have highlighted the role of inflammation in the progression of a variety of diseases such as cancer, atherosclerosis, asthma, and arthritis.

COVID-19 infection is accompanied by an aggressive inflammatory response with the release of a large amount of pro-inflammatory cytokines in an event known as "cytokine storm." The 'cytokine storm', is where uncontrolled levels of proinflammatory cytokines (proteins released by immune cells) which cause excessive inflammation which leads to a decrease in lung function.

Proinflammatory cytokines are produced predominantly by activated macrophages and are involved in the up-regulation of inflammatory responses. Measuring proinflammatory cytokines is a 'biomarker' of disease and its progression.

Serum Amyloid A (SAA)
SAA is a clinical biomarker for acute phase inflammation, more commonly associated with increased risk of cardiovascular events. In COVID-19 patients, high SAA concentrations are significantly associated with more severe COVID-19 disease and an increased risk of mortality in patients.[1] Therefore, regulation of SAA is important for stabilising the inflammatory processes that contribute to the severity of disease in COVID-19 patients.

Interferon-gamma-inducible protein 10 (IP-10)
Similarly to SAA, several recent publications have demonstrated IP-10 as a strong biomarker for COVID-19 disease progression and a target in preventing lung injury. Modulation of IP-10 is a suggested therapeutic strategy for treating acute respiratory distress syndrome associated with coronaviruses, including COVID-19.[2]

Eotaxin 3 (Eot3)
Eot3 modulates the migration of immune cells eosinophils and basophils to sites of tissue inflammation and is a clinical biomarker for airway eosinophilic inflammation in asthma.[3] In

[1] International Journal of Infectious Disease 2021; 105: 101016
[2] Journal of Allergy & Clinical Immunology 2020; 146: 32360286
[3] International Journal of Inflammation 2015; 2015: 630637

severe COVID-19 patients, during the second and third phases of the disease, eosinophils participate in a maladaptive immune response and directly contribute to worsening of disease symptoms. Down-regulating Eot3, and thus triggering the blockade of eosinophil activation, may aid in improving patient outcomes.[4]

This announcement is authorised by the board of NeuroScientific Biopharmaceuticals Ltd.

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About NeuroScientific Biopharmaceuticals Ltd

NeuroScientific Biopharmaceuticals Limited (ASX: NSB) is a company developing peptide-based pharmaceutical drugs that target a number of neurodegenerative conditions with high unmet medical demand. The company's product portfolio includes EmtinB™, a therapeutic peptide initially targeting Alzheimer's disease and glaucoma, as well as other Emtin peptides (EmtinAc, EmtinAn, and EmtinBn) which have demonstrated similar therapeutic potential as EmtinB™. For more information, please visit www.neuroscientific.com

About EmtinB™

EmtinB™ is a peptide-based compound that binds to surface-based cell receptors from the LDLR family, activating intracellular signalling pathways that stimulate neuroprotection, neuroregeneration and modulate neuroinflammation. EmtinB™ is modelled on a specific active domain of the complex human protein called Metallothionein-IIA, which is produced as part of the human body's innate immune response to cell injury.

Our preclinical research has established that EmtinB™ is highly specific and selective for its target receptor, safe and well tolerated at high concentrations, and is able to penetrate the blood brain barrier. A series of Phase I clinical studies will be conducted to establish the safety profile of EmtinB™ in humans.

[4] Frontiers in Pharmacology 2021; 12: 622554