



NeuroScientific
BIOPHARMACEUTICALS

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ASX Announcement

NeuroScientific Biopharmaceuticals to investigate treatment for post-COVID Fibrosis

- **NeuroScientific Biopharmaceuticals (NSB) is partnering with The Institute of Respiratory Health and The University of Western Australia to test the effectiveness of EmtinB and other Metallothionein derived peptides (EmtinAc, EmtinAn, EmtinBn) as potential therapy for long term respiratory complications of Covid-19.**
- **With the number of COVID cases exceeding 50 million since December 2019 and rising rapidly, post-COVID fibrosis could become one of the largest future burdens on global healthcare.**
- **COVID patients who develop Acute Respiratory Distress Syndrome (ARDS) may survive the acute phase of the illness but can die as a result of progressive pulmonary fibrosis. Post-COVID fibrosis can cause lasting damage to the lungs even in young adult patients.**
- **Recently published data by an independent research organization demonstrated that Metallothionein, a natural form of EmtinB, can protect lungs from injury and fibrosis**
- **The preliminary data from this new program is expected to be available during the first half of 2021.**

Perth Australia, 20 November 2020: NeuroScientific Biopharmaceuticals Limited (ASX: NSB) (**NeuroScientific** or the **Company**) is pleased to announce that it has initiated a new preclinical program in partnership with The Institute of Respiratory Health and The University of Western Australia to study the effects of EmtinB and other compounds derived from Metallothionein-II as a potential treatment for patients suffering '**post-COVID fibrosis**'.

Post-COVID fibrosis is irreversible and can result in severe functional limitations, such as severe cough, shortness of breath, need for oxygen and in some cases lung transplants. Most recent published data indicate that pulmonary fibrosis due to COVID-19 is occurring in increasing numbers of patients in their 20s and 30s, creating serious future global healthcare burden.

The preclinical program will be carried out by the Molecular Pathology Research Unit at the Institute of Respiratory Health and UWA using NeuroScientific's peptide-based compounds, with NeuroScientific owning any intellectual property generated from the studies. NeuroScientific will provide funding of \$122,000 to the Institute of Respiratory Health for undertaking the screening phase with the initial term of the research agreement set at 4 months.

"The COVID-19 pandemic is bringing huge economic, social, and health-care challenges. Once the wave of viral infection starts to recede, other problems will emerge that will need to be addressed. Given recently emerging data indicating that metallothionein (and hence EmtinB) can be extremely helpful in preventing the long-term fibrotic consequences that might follow this pandemic, we believe it becomes our duty to investigate that aspect of our experimental product and we are happy to conduct these studies together with The Institute of Respiratory Health, Australia's only scientific and clinical research institute dedicated specifically to investigating respiratory disease," said Brian Leedman, Chairman of NeuroScientific Biopharmaceuticals.

"The University of Western Australia is delighted to be working with NeuroScientific Biopharmaceuticals on a ground-breaking research project that we hope will see positive benefits for patients who have contracted COVID-19. UWA, a leading research-intensive university will be analysing the effect EmtinB has on cells to test its effectiveness. If successful, the treatment could be commercialised providing a much-needed treatment to help minimise short-term and long-term damage to lungs from the virus," said Rolee Kumar, Industry Engagement Manager at UWA's Faculty of Health and Medical Sciences.

Pulmonary fibrosis in the aftermath of the COVID pandemic: Lifelong Lung Damage

Whilst the global society is getting used to living with and handling the COVID-19 pandemic, the medical community and healthcare agencies have identified that even young people who survive the disease can have lasting complications.

There are several reports now of COVID-19 survivors that required a lung transplant to treat a condition now being called post-COVID fibrosis.

Holes in the lung now known as post-COVID fibrosis are potentially due to the coronavirus causing the immune system to form blood clots, which then prevent blood from getting to segments of the lung, leading to local cell death. The body replaces cells damaged by the virus with scar tissue, which is thick and stiff and has no respiratory capacity.

Most recent observations in patients who died from COVID indicates marked fibrotic lung parenchymal remodelling, characterised by fibroblast proliferation, airspace obliteration, and micro-honeycombing. In addition, the fibrotic pathological findings are unlikely to regress in patients with severe COVID-19 who survive (Grillo et.al., *Lancet Infect Dis.* 2020 Jul 28).

A further complicating factor in the COVID-19 pandemic is that many patients around the world will be receiving anti-interleukin therapies for severe disease, including anakinra or anti-IL-6 therapies (profibrotic). The effects of anti-interleukin therapy in the long term, although potentially beneficial, are completely unknown and could lead to worse fibrosis (George et.al., *Lancet Respir Med.* 2020 Aug; 8(8): 807–815).

Staggering Statistics

Available data indicates that about 40 per cent of patients with COVID-19 develop ARDS, and 20 per cent of ARDS cases are severe. The prevalence of post-COVID-19 fibrosis will become apparent in time, but early analysis from patients with COVID-19 on hospital discharge indicates that more than a third of recovered patients develop fibrotic abnormalities. Additionally, 47 per cent of patients have impaired diffusing capacity of the lungs for carbon monoxide (DLCO) and 25 per cent have reduced total lung capacity (TLC) (Vazarmidi et.al., *Exp Ther Med.* 2020 Sep; 20(3): 2557–2560).

Planned studies and new evidence of Metallothionein/EmtinB as potential therapy for post-COVID fibrosis

The newly initiated study will examine the effects of peptides generated from the alpha (EmtinA) and beta (EmtinB) domains of metallothionein (MT), on lung cell function and tissue fibrosis. There is strong evidence from the literature that MT is protective against tissue injury, inflammation and fibrosis and early studies demonstrated that peptides generated from MT induced neurite outgrowth and increased neuronal survival through binding to receptors of the low-density lipoprotein receptor family (LDLR). The study will explore whether EmtinB and its derivatives can have similar effects in lung tissue.

Using the widely accepted bleomycin model of lung scarring (fibrosis pre-clinical model), as well as primary cell cultures, Company will test whether the administration and use of EmtinB induces reduction of lung fibrosis.

This year, a study by an independent group has demonstrated that Metallothionein can play a significant role in the prevention of pulmonary consequences of long-term intermittent hypoxia exposure, protecting lungs from fibrosis and ultimately improving survival in the progression of acute lung injury in mice (Lin et.al., *Inflamm Res* 2020 Jan;69(1):15-26). It was also shown that the primary target of EmtinB, the LRP-1 receptor, is highly expressed in the lung (Wujac et al., 2016). This prior independent research represents a strong starting point to further investigate the role of EmtinB in these processes and as potential therapy for long term respiratory complications of Covid-19.

The preliminary data from this new pre-clinical study is expected to be available during the first half of 2021.

About Neuroscientific Biopharmaceuticals Limited

NeuroScientific Biopharmaceuticals (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

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Announcement authorised by the Board of Directors of NeuroScientific Biopharmaceuticals

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