CLARIFICATION ANNOUNCEMENT

NeuroScientific Biopharmaceuticals Ltd (ASX: **NSB**) notes that the following announcement serves as a clarification to the previously released announcement on the 15 June 2022, to provide further information regarding the specifics of the study mentioned within the announcement.

OVERVIEW OF STUDY DESIGN

The objective of the study was to assess the effect of EmtinB™ in the myelin oligodendrocyte glycoprotein-induced experimental autoimmune encephalomyelitis (MOG-EAE) mouse model of Multiple sclerosis across a dose range (5mg/kg, 10mg/kg, 20mg/kg and 40mg/kg) during a treatment period of 30-days (**Table 1**). The results from this study will be used to inform the selection of the two most effective doses for a larger study to be undertaken during the 2H 2022.

The control group involved MOG-EAE mice that were not treated with EmtinB™. These mice received a solution (vehicle) that was identical to formulated EmtinB™ except that it did not contain any EmtinB™ active pharmaceutical ingredient.

Table 1: Experimental groups for assessing EmtinB™ treatment effect in the MOG-EAE mouse model of Multiple sclerosis across a dose range.

Group	Treatment	N	Terminal CSF and Plasma Collection (N)	Terminal Spinal cord Analysis (N)
A	EAE + Vehicle	4	4	4
B	EAE + EmtinB 5mg/kg	4	4	4
C	EAE + EmtinB 10mg/kg	4	4	4
D	EAE + EmtinB 20mg/kg	4	4	4
E	EAE + EmtinB 40mg/kg	4	4	4

The endpoints of the study included the following –

(a) The daily assessment of clinical symptoms for the duration of the study (30 days) using a standardised scoring system (**Table 2**). Higher scores mean more severe symptoms.

Table 2: Standardised scoring system for assessing clinical symptoms in the MOG-EAE mouse model of Multiple sclerosis.

Clinical Score	Description
0	No clinical symptoms
0.5	Loss of tone in the tip of tail
1	Complete loss of tail tone (floppy tail)
1.5	Floppy tail and weak hind limbs
2	Floppy tail, clasping of hind limbs when lifted, and weakness of hind limbs when walking
2.5	Floppy tail, clasping of hind limbs when lifted, and partial paralysis of hind limbs when walking
3	Floppy tail and complete hind limb paralysis
3.5	Floppy tail, complete hind limb paralysis, and unable to right when overturned
4	Limp tail, complete hind limbs paralysis, unable to right, and partial front leg weakness/paralysis
4.5	Complete hind and partial front leg paralysis, no movement around the cage. >20% weight loss
5	Moribund (euthanatized)

(b) Analysis of concentrations of neurofilament light polypeptide (NfL) in cerebral spinal fluid (CSF) and plasma at the terminal time point following the 30-day treatment period.

(c) Quantitative assessment of the expression of myelin basic protein (detected using the antibody MBP) in tissue sections from spinal cords at the terminal time point following the 30-day treatment period.

(d) Quantitative assessment of activated T cells (detected using the antibody CD3) in tissue sections from spinal cords at the terminal time point following the 30-day treatment period.

(e) Quantitative assessment of microglia and macrophages (detected using the antibody Iba-1) in tissue sections from spinal cords at the terminal time point following the 30-day treatment period.

(f) Quantitative assessment of astrocytes (detected using the antibody GFAP) in tissue sections from spinal cords at the terminal time point following the 30-day treatment period.

EMTINB™ TREATMENT CONSISTENTLY IMPROVED CLINICAL SCORES IN 10MG/KG AND 20MG/KG DOSE GROUPS

Mice treated with 10mg/kg and 20mg/kg EmtinB™ consistently achieved lower clinical scores, indicating reduced disease severity, from the onset of symptoms and through to the peak of the disease in comparison to the untreated controls. The clinical scores for mice treated with 5mg/kg and 40mg/kg EmtinB™ exhibited more variability and were considered less reliable in comparison to 10mg/kg and 20mg/kg EmtinB™ dose groups.

EMTINB™ TREATMENT REDUCED BIOMARKER INDICATIVE OF NEURONAL DAMAGE
Neurofilament light polypeptide (NfL) is a biomarker associated with damaged neurons that can be detected in CSF and blood plasma samples.

Mice treated with 5mg/kg, 10mg/kg, 20mg, and 40mg/kg EmtinB™ had lower concentrations of NfL in cerebral spinal fluid (CSF) and plasma samples in comparison to the untreated control group at the conclusion of the 30-day treatment period.

EMTINB™ TREAMENT INCREASED MYELIN IN 10MG/KG AND 20MG/KG DOSE GROUPS
Myelin is important for the efficient function of nerve cells. The destruction of myelin contributes to the onset of neurological dysfunction associated with MS.

Mice treated with 10mg/kg and 20mg/kg EmtinB™ consistently exhibited higher levels of myelin in comparison to the untreated control group. Results were more variable for mice treated with 5mg/kg and 40mg/kg of EmtinB™ and considered less reliable.

EMTINB™ TREATMENT REDUCED CHRONIC INFLAMMATORY IMMUNE RESPONSES ACROSS ALL DOSE GROUPS
The study assessed a number of markers associated with chronic inflammatory responses of MS. Fundamental to the dysfunctional immune responses of MS in humans, activated T cells (CD3) penetrate the blood brain barrier and stimulate inflammatory responses of the CNS, activating resident immune defence cells such as microglia and macrophages (Iba-1), and astrocytes (GFAP).[1]

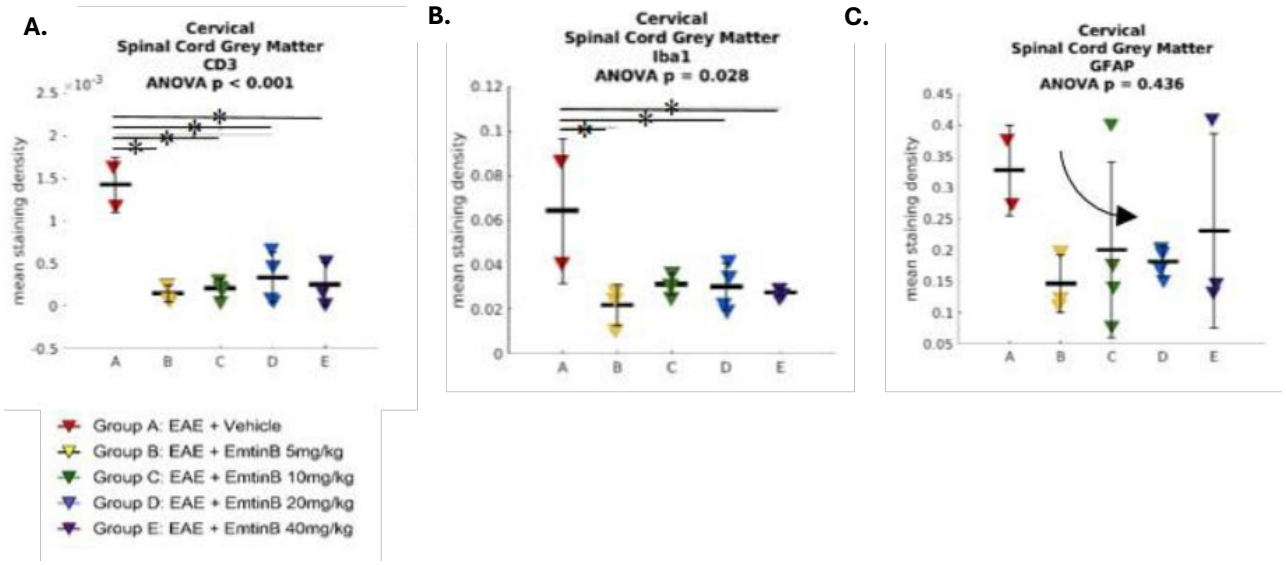
Mice treated with 5mg/kg, 10mg/kg, 20mg/kg and 40mg/kg EmtinB™ exhibited lower levels of CD3 expressing T cells in comparison to the untreated control group following the 30-day treatment period (**Figure 1A**).

Mice treated with 5mg/kg, 10mg/kg, 20mg/kg and 40mg/kg EmtinB™ exhibited lower Iba-1 expression in tissue samples, indicating less microglia and macrophages, in comparison to the untreated control group following the 30-day treatment period (**Figure 1B**).

Mice treated with 5mg/kg, 10mg/kg, 20mg/kg and 40mg/kg EmtinB™ exhibited lower GFAP expression in tissue samples, indicating less activated astrocytes, in comparison to the untreated control group following the 30-day treatment period (**Figure 1C**).

[1] Balasa, R. et al. 2020 Then action of TH17.1 cells on blood brain barrier in multiple sclerosis and experimental autoimmune encephalomyelitis. 81(5): 237-43.

Figure 1: Assessment of (A) activated T cells (CD3), (B) microglia and macrophage cells (Iba-1), and (C) activated astrocytes (GFAP) in spinal tissue samples from MOG-EAE mice treated with EmtinB™ (5mg/kg, 10mg/kg, 20mg/kg, or 40mg/kg).



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.