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Level 1, 45 Stirling Highway
Nedlands WA 6009 Australia
www.neuroscientific.com

EmtinB Demonstrates Significant Therapeutic Potential as a Novel Treatment for Multiple Sclerosis

- **EmtinB had a significant positive effect on the proliferation and differentiation of oligodendrocytes in Multiple Sclerosis (MS) model, indicating a very significant effect on remyelination**
- **EmtinB significantly increased the total number of cells by up to 5x (+438% vs control p<0.001) after 5 days and ~3.5x (+267% vs control p<0.001) after 11 days**
- **EmtinB significantly increased the number of oligodendrocyte precursor cells (OPCs) by ~7x (+607% vs control p<0.001) after 5 days and ~4.5x (+357% vs control p<0.001) after 11 days**
- **EmtinB significantly increased the number of mature oligodendrocytes by ~10x (+875% vs control p<0.001) after 5 days and ~9x (+826% vs control p<0.001) after 11 days**

Perth, Australia; 18 March 2020: Drug development company NeuroScientific Biopharmaceuticals Ltd (ASX:NSB, "NSB" or the "Company") is pleased to report significant positive results of a preclinical study of its lead drug candidate EmtinB in an in vitro model for Multiple sclerosis (MS). The study was completed by independent contract research organization Neuron Experts, France.

MS is one of the most common immune-mediated neurodegenerative conditions, with an age of onset between 20-to-50 years. The disease causes damage to the protective sheath (myelin) that covers nerve fibers, disrupting communication between the brain and the rest of the body. The damage to nerves caused by MS is permanent and there is a need for disease modifying treatments that prevent the ongoing deterioration of myelin (demyelination).

Support cells of the central nervous system called oligodendrocytes provide the myelin sheath that surround the nerve fibers. These cells develop as oligodendrocyte precursor cells (OPCs), proliferate and migrate towards demyelinating nerves where they differentiate into mature oligodendrocytes and remyelinate nerves (**Figure 1**). Unfortunately, the efficiency of this process decreases with both age of the patient and longevity of the disease. Therefore, improvement in the efficiency of remyelination of nerve cells is a major aim of MS research and a novel disease modifying treatment pathway.

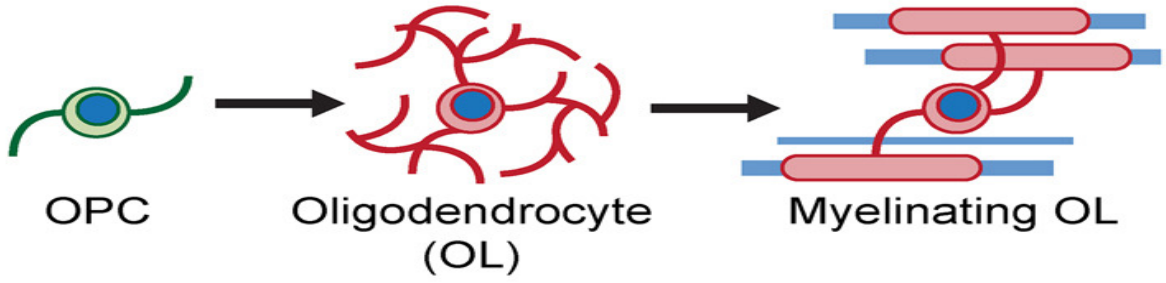

Figure 1: Oligodendrocyte maturation and remyelination process[1]

[1] Mayoral et al. 2018

Under non-diseased circumstances, oligodendrocyte precursor cells (OPCs) proliferate and differentiate into mature oligodendrocytes which provide myelin for nerve fibers. In MS, myelin is damaged and the nerve fibers deteriorate.

The aim of the study conducted by Neuron Experts was to evaluate the effect of EmtinB on the proliferation and differentiation of oligodendrocytes in their validated MS model as a means to assess the therapeutic potential of EmtinB as a treatment for MS. Cell markers for proliferating OPCs (A2B5 positive cells) and mature oligodendrocytes (MAG positive cells) were used to quantify cell types on day 5 and 11 following a single dose of EmtinB. Therefore, increases in the number of A2B5 and MAG cells post incubation with EmtinB demonstrates the compound's effect on stimulating the remyelination process.

Five concentrations of EmtinB were used: 15µg/ml, 30µg/ml, 60µg/ml, 120µg/ml, and 150µg/ml. At the 5-day incubation period, all concentrations of EmtinB increased the total number of cells (**Figure 2A**) very significantly (respectively +163%, +249%, +358%, +386%, +438%; p<0.001). The total number of A2B5 cells (OPCs) after 5-days of incubation were very significantly increased across all concentrations of EmtinB (respectively +307%, +395%, +521%, +591%, and +607%; p<0.001) (**Figure 2B**). The total number of MAG cells (oligodendrocytes) after 5-days of incubation were very significantly increased across all concentrations of EmtinB (respectively +441%, +546%, +699%, +869%, and +875%; p<0.001) (**Figure 2C**).

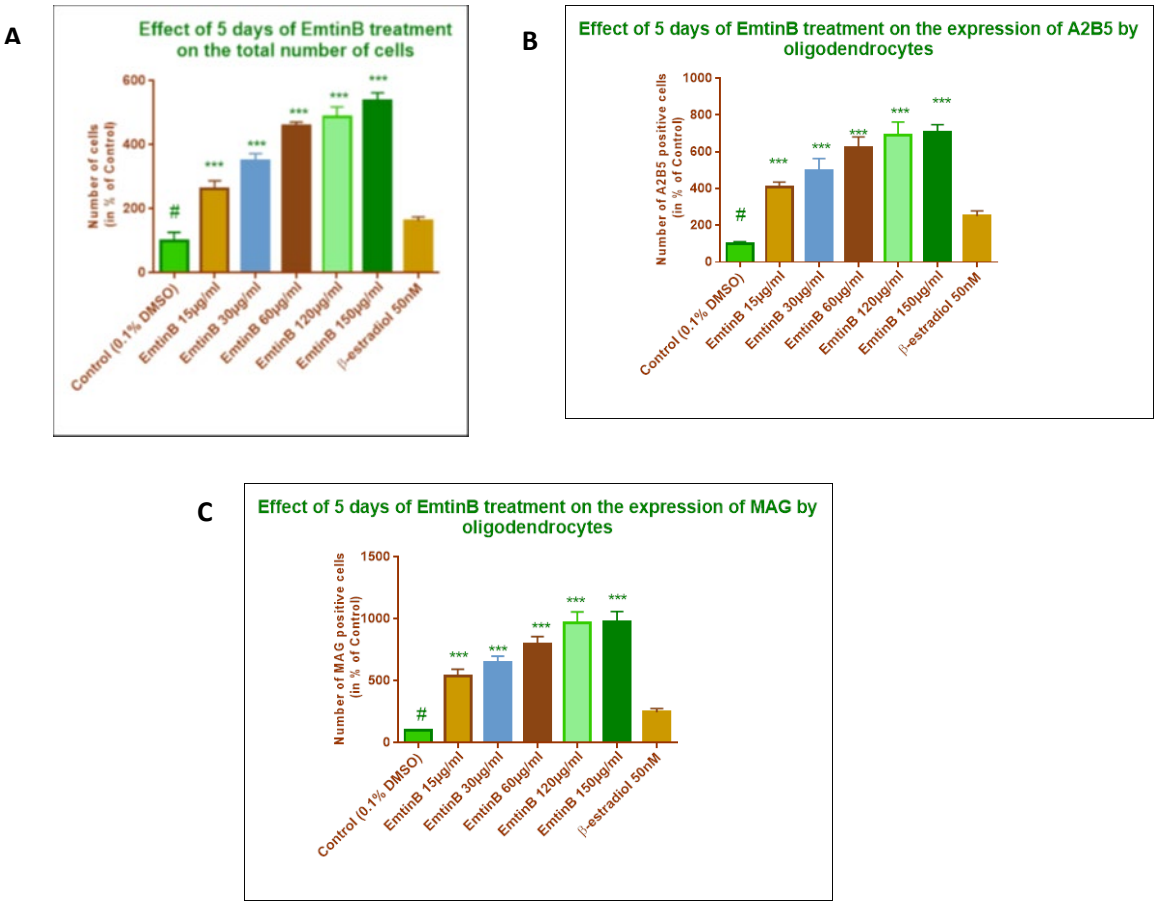

Figure 2: Effect of EmtinB after 5-days of incubation in MS cell culture model
(A) *Effect of EmtinB on total number of cells after 5 days of incubation. Results are expressed in percentage of control (mean ± s.e.m; * p < 0.05; ** p< 0.01; *** p<0.001; compounds vs control; one way Anova followed by Dunnett's test).* ***(B)*** *Effect of EmtinB on total number of A2B5 cells after 5 days of incubation. Results are expressed in percentage of control (mean ± s.e.m; * p < 0.05; ** p< 0.01; *** p<0.001; compounds vs control; one way Anova followed by Dunnett's test).* ***(C)*** *Effect of EmtinB on total number of MAG cells after 5 days of incubation. Results*

*are expressed in percentage of control (mean ± s.e.m; * p < 0.05; ** p< 0.01; *** p<0.001; compounds vs control; one way Anova followed by Dunnett's test).*

After 11-days of incubation, EmtinB significantly increased the total number of cells at concentrations of 30µg/ml (+137% p<0.05), 60µg/ml (+212% p<0.001), 120µg/ml (+248% p<0.001), and 150µg/ml (+267% p<0.001) (**Figure 3A**). After 11-days of incubation, EmtinB significantly increased the number of A2B5 cells (OPCs) across all concentrations (respectively +149%; p<0.005, +211%, +252%, +306%, +357%; p<0.001) (**Figure 3B**). After 11-days of incubation, EmtinB very significantly increased the number of MAG cells (oligodendrocytes) at concentrations 30µg/ml (+603% p<0.001), 60µg/ml (+620% p<0.001), 120µg/ml (+788% p<0.001), and 150µg/ml (+826% p<0.001) (**Figure 3C**).

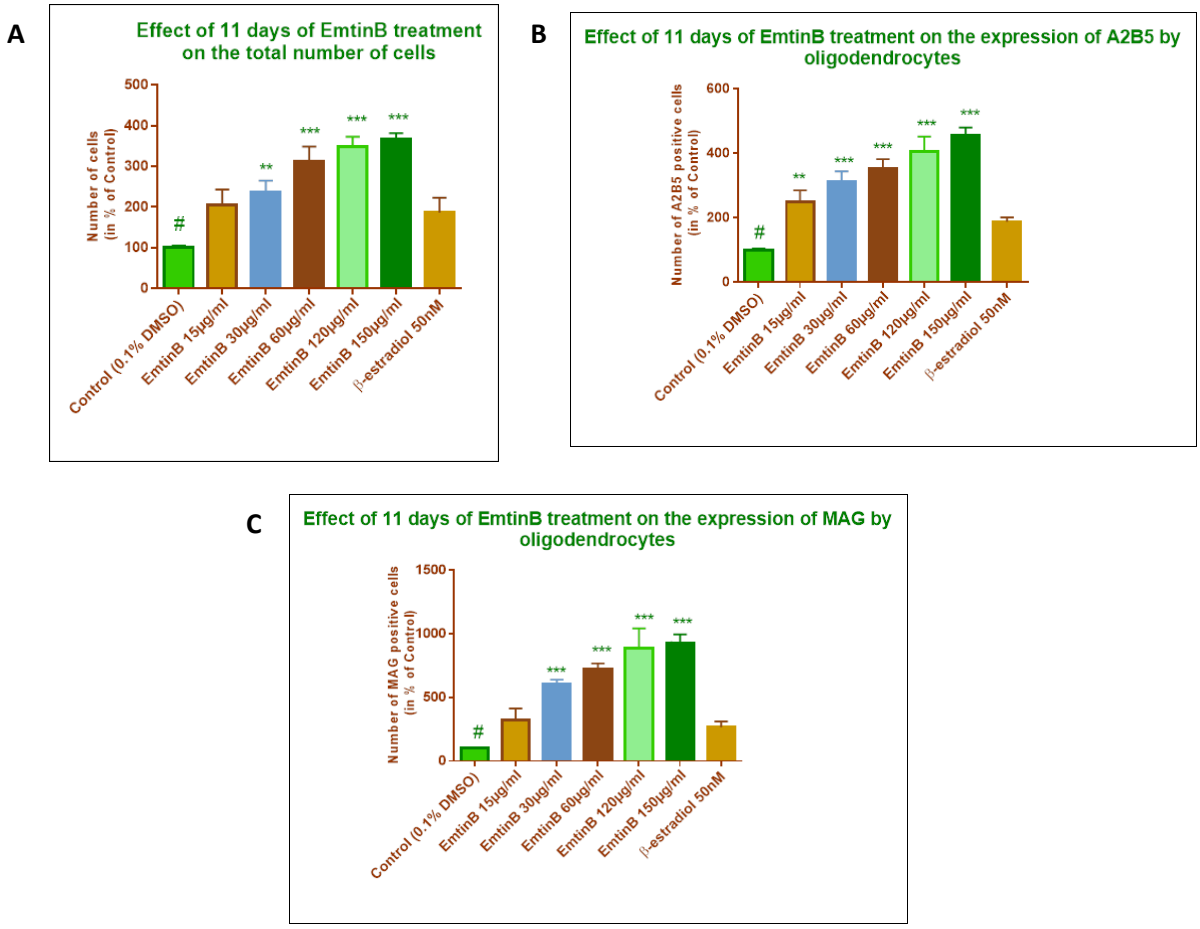

Figure 3: Effect of EmtinB after 11-days of incubation in MS cell culture model
(A) *Effect of EmtinB on total number of cells (number of nuclei) after 11 days of incubation. Results are expressed in percentage of control (mean ± s.e.m; * p < 0.05; ** p< 0.01; *** p<0.001; compounds vs control; one way Anova followed by Dunnett's test).* ***(B)*** *Effect of EmtinB on total number of A2B5 cells after 11 days of incubation. Results are expressed in percentage of control (mean ± s.e.m; * p < 0.05; ** p< 0.01; *** p<0.001; compounds vs control; one way Anova followed by Dunnett's test).* ***(C)*** *Effect of EmtinB on total number of MAG cells after 11 days of incubation. Results are expressed in percentage of control (mean ± s.e.m; * p < 0.05; ** p< 0.01; *** p<0.001; compounds vs control; one way Anova followed by Dunnett's test).*

“Coming off the back of the company-defining results reported last week in the glaucoma pig model, these results also exceeded our expectations and profoundly demonstrate the efficacy of EmtinB in MS and across a number of other neurodegenerative conditions”, commented Matthew Liddelow, CEO and Managing Director of NeuroScientific Biopharmaceuticals. “These results also indicate positive implications for EmtinB treatment of demyelinating conditions that affect the optic nerve, such as optic neuritis and the company plans to further explore this as part of our ophthalmology R&D program.”

References

Mayoral, S., Etxeberria, A., Shen, YA., and Chan, JR. 2018 “Initiation of CNS myelination in the optic nerve is dependent on axon caliber” Cell Reports, 25, 544-550

This announcement has been authorised for release by Matthew Liddelow.

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About NeuroScientific Biopharmaceuticals Ltd

NSB (ASX:NSB) is a drug development company focused on developing peptide-based pharmaceutical drugs for the treatment of neurodegenerative conditions with high unmet medical need. The Company’s product portfolio includes EmtinB, a novel therapeutic peptide most advanced as a treatment for Alzheimer’s disease; and other related peptides (EmtinAc, EmtinAn, and EmtinBn) which have demonstrated similar therapeutic potential as EmtinB. For more information, please visit www.neuroscientific.com

Contacts

Matthew Liddelow
CEO and Managing Director
ml@neuroscientific.com
+61 8 6382 1805

Brian Leedman
Chairman
bl@neuroscientific.com
+61 (0) 412 281 780