NeuroScientific
BIOPHARMACEUTICALS
ASX:NSB

ASX ANNOUNCEMENT
15 DECEMBER 2022

NEW PATENT APPLICATION FILED FOR THE COMBINATION of EMTINB® WITH COPAXONE®

HIGHLIGHTS

- **The new patent, if granted, will have a priority date of 24 November 2022 providing patent protection until at least 24 November 2042.**
- **The new patent application claims the combination of EmtinB® and Copaxone® in an *in vitro* cell culture study, conducted by a French CRO, reported that the combination of EmtinB® and Copaxone® resulted in statistically significant increase in neurite length, neuron (cell) survival as well as new myelin formation.**
- **Copaxone® (Teva) is registered for the treatment of relapsing remitting Multiple Sclerosis (MS). Teva's revenue from worldwide drug sales of Copaxone® reached US$4.2 billion, roughly 21% of the company's total revenue. Copaxone® sales have steadily declined since generic versions of Copaxone® were approved.**
- **This patent, if granted, will provide the opportunity to regain a proprietary position in the MS space as the combination of Copaxone® and EmtinB® have been shown to produce all the inflammatory related in vitro signals necessary to treat the disease of MS in a more effective way than Copaxone® alone.**
- **MS is a complex neurological disease characterized by deterioration of the myelin sheath. NSB is proud to announce its peptide therapeutic, EmtinB®, in combination with the leading treatment for relapsing remitting multiple sclerosis (Copaxone®), has, in a proof-of-concept in vitro study, been shown to produce new myelin.**

NeuroScientific Biopharmaceuticals Ltd (ASX: **NSB**) (**"NeuroScientific"** or **"the company"**) is pleased to announce it has filed a new patent, entitled "Neuroprotective compositions and methods" (The Australian provisional application number is 2022903564, establishing the priority date of 24 November 2022).

New Experimental Data Supporting the New Patent Application

An *in vitro* cell culture study using cultured rat cortical neurons was undertaken to evaluate the effect of treatments applied to the cell culture on neuron survival, neurite length and area of myelin sheath, all of which are key mechanisms involved in Multiple Sclerosis. Two dose levels of EmtinB® alone, two dose levels of Copaxone® alone and two different combinations of EmtinB® + Copaxone® were evaluated, as per the table below, to determine if a synergistic effect occurs when the two products are co-administered.

Two control groups were included in this study including a cell culture treated with β-estradiol 50nM, which is a positive control present to ensure assay validity, and untreated

control cell culture, providing a baseline measure to determine changes noted in the treatments groups as per below. 6 wells per treatment group/control group were performed.

Results are provided in the table below of the EmtinB® and Copaxone® groups, with the untreated control designated a value of 100% in all effect groups. Also noted external to the table is that β-estradiol 50nM treated groups saw significant increases ($p<0.0001$ or $p<0.001$) across al three cell effects providing confidence in the validity of the assay.

Dose Group → **Cell Effect↓**	**EmtinB® 50µg/mL**	**EmtinB® 150µg/mL**	**Copaxone® 3µg/mL**	**Copaxone® 10µg/mL**	**EmtinB® 50µg/mL + Copaxone® 3µg/mL**	**EmtinB® 150µg/mL + Copaxone® 10µg/mL**
Neuron Survival	Trending increase (+121% not significant)	**Significant increase (+155%, p<0.05)**	Trending increase (+129%, not significant)	Trending increase (+123% not significant)	**Significant increase (+165% p<0.01)**	**Significant increase (+148%, p<0.05)**
Neurite Length	**Significant increase (+154%, p<0.001)**	Trending increase (+130% not significant)	**Significant increase (+167%, p<0.0001)**	**Significant increase (+153%, p<0.001)**	**Significant increase (+154%, p<0.01)**	**Significant increase (+139%, p<0.01)**
Area of Myelin Sheath	Trending increase (+141% not significant)	**Significant increase (+172%, p<0.05)**	Trending increase (+137% not significant)	**Significant increase (+167%, p<0.05)**	**Significant increase (+171%, p<0.05)**	**Significant increase (+178%, p<0.05)**

Note: % represents % of cells in untreated control

Treatment with Copaxone® alone at 3µg/mL and 10µg/mL is not able to modulate cortical neurons survival but significantly increases, at both dose levels, the neurites length and a high dose only significantly improves myelin formation.

Treatment with EmtinB® alone promotes cortical neuron survival and myelin sheath formation with significant effect at the higher dose level. Furthermore, EmtinB® tends to increase neurites length of cortical neurons with a significant effect observed at the low dose level.

It was only the co-treatment of EmtinB® and Copaxone® that significantly promotes neurite length, cortical neuron survival and myelin sheath formation around cortical neurons in concert. This effect seems to be synergistic since the combination of EmtinB® at 50µg/mL and Copaxone® at 3µg/mL gives a statistically significant effect in all three areas. This three-pronged effect is not observed when either compound is applied alone.

These data suggests that EmtinB® may provide additional therapeutic benefit to Copaxone®, one of Teva's most successful drugs in its portfolio.

The outcome of this patent application will be communicated by NSB in due course.

About Multiple Sclerosis
Multiple sclerosis (MS) is a chronic, incurable, inflammatory disease of the central nervous system (CNS).

MS is a complex neurological disease characterized by deterioration of the myelin sheath (see Figure 1 below).

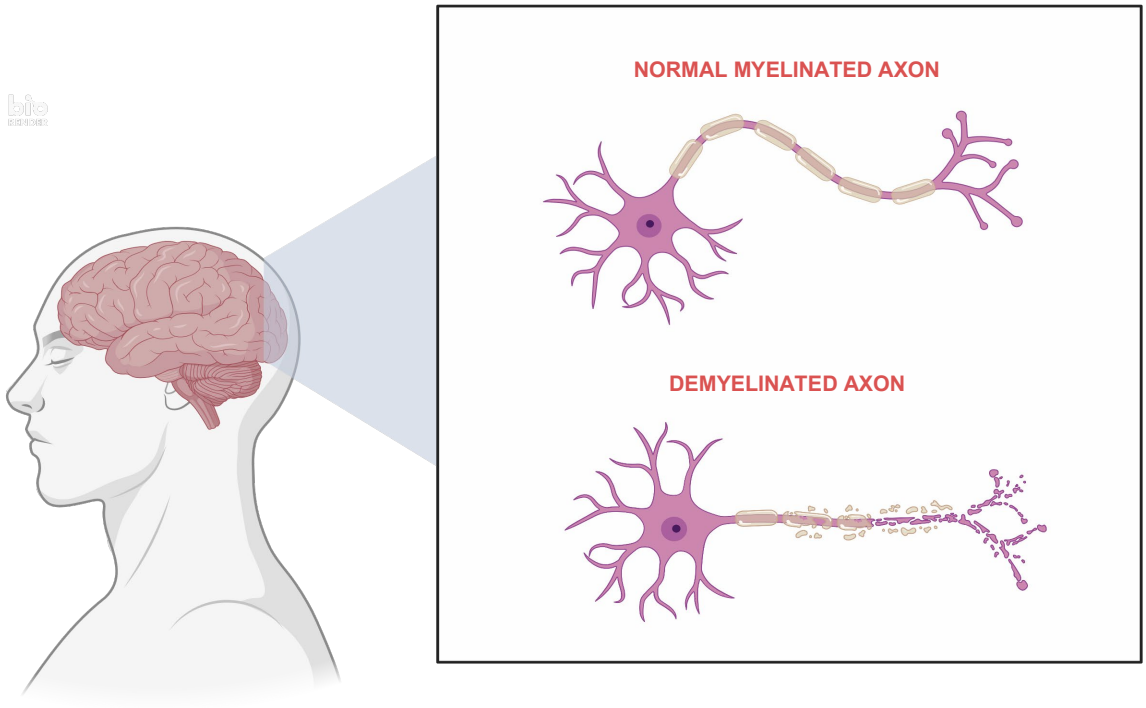

FIGURE 1. Progressive loss of myelin sheath of neurons in patients with multiple sclresosis

Prevalence of MS in the USA and Globally:
Multiple sclerosis (MS) is a chronic, inflammatory disease of the CNS that affects approximately 400,000 individuals in the United States[1]. A total of 2.8 million people are estimated to live with MS worldwide (35.9 per 100,000 population)[1].

Teva and Copaxone®
In the mid-1990s, Teva introduced a novel drug called Copaxone®, to treat multiple sclerosis. The drug was developed by a team of researchers at the Weizmann Institute of

[1] M.J. Tullman, Overview of the epidemiology, diagnosis, and disease progression associated with multiple sclerosis, Am. J. Manag. Care (2013) S15-S20.

Science in Israel and was considered the world's best treatment against the condition. COPAXONE® received the United States Food and Drug Authority (F.D.A.) approval in 1996[2]. This invention transformed Teva from a company that produced generic drugs to one that produced novel treatments. Since 2015, Copaxone® was marketed to more than 50 countries worldwide. Teva's revenue from worldwide drug sales reached $4.2 billion, roughly 21% of the company's total revenue.

Teva's Copaxone®, (glatiramer acetate) was first approved by the FDA in 1996. A 40-mg dose of Copaxone injected three-times weekly was approved by the FDA in 2014. In 2015, Glatopa (Sandoz) was approved as the first generic version of Copaxone®, given at the original 20-mg daily dose. However, sales of Copaxone® have dropped significantly since the launch of generics and keeps declining. Teva expects Copaxone® to bring in about $850 million in 2022, compared with about $1 billion in 2021 sales[3]. New IP around Copaxone® combinations with other therapies could represent significant value for the Copaxone® product line in the future.

EmtinB® is a registered trademark of Neurosceintific Biopharamaceuticals Ltd (NSB).

Copaxone® is a registered trademark of Teva Pharmaceutical Industries Limited.

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

[2] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7720355/

[3] https://www.fiercepharma.com/pharma/teva-banks-blockbuster-austedo-sales-as-covid-19-copaxone-generics-take-their-toll

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.

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