NeuroScientific
BIOPHARMACEUTICALS
ASX:NSB

ASX ANNOUNCEMENT
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NEW DATA DEMONSTRATES EMTINB™ REGULATES KEY DRIVERS OF CHRONIC INFLAMMATION AND AUTOIMMUNE DISEASES

HIGHLIGHTS

- **Lead drug candidate EmtinB™ reduces key drivers of chronic inflammation and autoimmune diseases, interleukins (IL)-17A, IL-17F. and IL-6**
- **These inflammatory cytokines significantly contribute to the progressive loss of neurons in Multiple Sclerosis and Alzheimer's disease and their down regulation further validates the disease modifying potential of EmtinB™ in these conditions**
- **IL-17A and IL-6 are therapeutic targets for approved drugs in psoriasis (global market of size of US$14.5B[1]) and rheumatoid arthritis (global market size of US$26.0B[2])**
- **This data is the first to directly demonstrate the effect of EmtinB™ on inflammatory responses of the adaptive immune system**
- **The Company is in the final stages of preparations for submission of its safety data package for approval to commence a first-in-human Phase I study**

NeuroScientific Biopharmaceuticals Ltd (ASX: **NSB**) (**"NeuroScientific"** or **"the company"**) is pleased to announce results from a recently completed assessment of lead drug candidate EmtinB™ in human primary cell-based systems modelling autoimmune disease in which EmtinB™ significantly reduced inflammatory cytokines **Interleukin (IL)-17A**, **IL-17F**, and **IL-6**. These cytokines are strongly associated with multiple autoimmune diseases such as psoriasis, rheumatoid arthritis, and ankylosing spondylitis and play a prominent role in the damaging inflammatory responses seen in Multiple sclerosis (MS) and Alzheimer's disease (AD).[3] Down regulation of the production of **IL-17A**, **IL-17F**, and **IL-6** significantly supports the disease-modifying effect of EmtinB™ as a treatment for these neurodegenerative conditions. The study was undertaken by leading independent contract research organisation Eurofins, Missouri USA.

NeuroScientific's Managing Director and Chief Executive Officer Matt Liddelow commented: *"These impressive results reinforce the multi-faceted therapeutic potential of EmtinB™ as a disease-modifying treatment for both Multiple sclerosis and Alzheimer's disease. While chronic inflammation is central to disease pathology of Multiple sclerosis, inflammatory responses are thought to be a secondary cause of neurodegeneration in Alzheimer's disease. Therefore, EmtinB™ has the potential to positively influence neuroprotection, neuroregeneration, and the inflammatory environment that acts to exacerbate tissue damage in these neurodegenerative conditions. Please also note that the Company is in the final stages of preparations for the submission of its safety data for ethics approval for commencement of a first-in-human Phase I study of EmtinB™ and further updates will be provided in the coming weeks."*

THE ROLE OF INTERLEUKIN (IL)-17A, IL-17F, AND IL-6 IN AUTOIMMUNITY IS WELL KNOWN

IL-17A, IL-17F, and IL-6 are chemical signalling compounds called cytokines that induce inflammation and play a key role in protecting the body from invading pathogens. IL-17A and IL-17F are produced by activated T cells

[1] Psoriasis drugs market research report 2021: www.researchandmarkets.com
[2] Rheumatoid arthritis drugs market research report 2022: www.researchandmarkets.com
[3] Milovanovic et al. 2020 Interleukin 17 in chronic inflammatory neurological disease.

(Th17) of the adaptive immune system and stimulate the production of other cytokines (IL-1β, TNF, and IL-6) by various cell types.[4] IL-6 helps regulate the inflammatory response by acting on Th17 cells.[5]

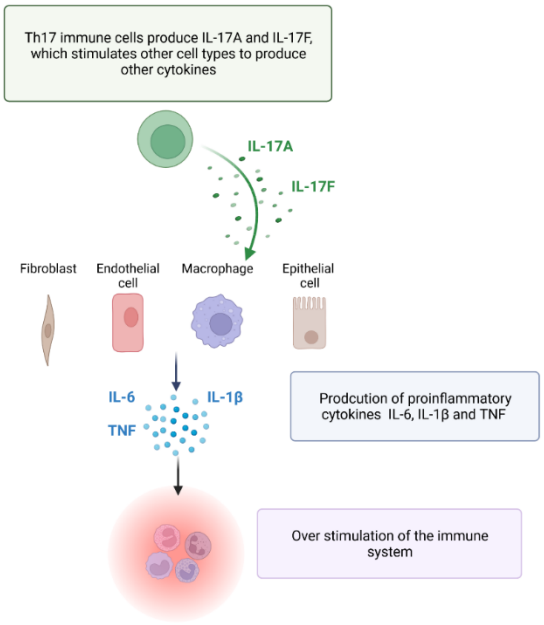
In chronic inflammation, dysfunctional production of IL-17A and IL-17F by Th17 immune cells upregulates production of IL-1β, TNF, and IL-6 leading to overstimulation of the immune system and the destruction of tissue (**Figure 1**). IL-17A and IL-17F have been recognised as key drivers of chronic inflammatory and autoimmune diseases. Targeting IL-17A has been a successful strategy in the development of approved drugs for the treatment of psoriasis and compounds that block IL-6 activity have been successfully approved for the treatment of rheumatoid arthritis.[6]

EMTINB™ A NEW REGULATOR OF INFLAMMATION

EmtinB™ binds to a receptor called the low-density lipoprotein receptor-related protein (LRP)-1 that is present in nerve cells and activates pathways within these cells that enhance survival and regeneration after injury.[7] LRP-1 is also expressed by a number of cell types involved in inflammatory processes and has been shown to modulate inflammation in neurodegenerative diseases including in AD and MS.[8]

In addition to its expression in nerve cells, LRP-1 is present in cells of other tissues of the body and is positively associated with reducing the inflammatory environment in diseases of the kidney, lung, and heart.[9] The results from this current study are further evidence of the role LRP-1 plays in regulating inflammation in tissues found outside the central nervous system (CNS) and are fundamentally important in linking EmtinB™ activation of LRP-1 to a downstream reduction in key cytokines (IL-17A, IL-17F, and IL-6) that are known to drive inflammatory processes of chronic inflammation and autoimmune diseases.

FIGURE 1: The role of IL-17A, IL-17F, and IL-6 in chronic inflammation and autoimmune disease



[4] Zwicky et al. 2019 Targeting interleukin-17 in chronic inflammatory disease: a clinical perspective.
[5] Milovanovic et al. 2020.
[6] Zwicky et al. 2019.
[7] Ambjorn et al. 2008 Metallothionein and a peptide modelled after metallothionein, EmtinB, induce neuronal differentiation and survival through binding to recpetors of the low-density lipoprotein receptor family.
[8] Milovanovic et al. 2020.
[9] Garcia-Fernandez et al. 2021 From the low-density lipoprotein receptor-related protein 1 to neuropathic pain: a potentially novel target.

UPDATE ON THE COMMENCEMENT OF FIRST-IN-HUMAN PHASE I STUDY

The team at NeuroScientific is continuing to finalise all necessary activities for submission of the safety data package for EmtinB™ for review by the Human Research Ethics Committee and expects to report the safety outcomes before the end of Q1 CY22. The Company will provide more detail on the initiation of the first-in-human Phase I trial in a separate announcement in the coming weeks.

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.