ASX Announcement

22 October 2021

Successful completion of preclinical Multiple Sclerosis studies using NTI164

- **Preclinical studies confirm that NTI164 can significantly suppress the expression of key MS biomarkers, IL-12 and TNF-alpha in human derived microglial cells**
- **NTI164 has shown to be more effective than CBD alone and CBD/THC by up to 2.5 times**
- **MS therapies market size is valued at over $40 Billion USD globally and estimated to grow at 6.3% per annum***
- **Results provide a unique opportunity for the development and commercialisation of potential human therapy for the management of MS**

Neurotech International Limited (ASX: NTI) ("Neurotech" or "the Company") is pleased to announce that it has successfully completed preclinical studies assessing the effects of NTI164, its proprietary medical cannabis strain, against Cytokines in Multiple Sclerosis (MS) models. The studies were performed in collaboration with RMIT University and Monash University.

Results have confirmed the potent anti-inflammatory and neuro-regulatory activity of the NTI164, specifically:

- NTI164 reduced the inflammatory cytokine IL-12 by 44%, substantially outperforming CBD alone (15% reduction) and CBD/THC in combination (19% reduction)
- NTI164 reduced the inflammatory cytokine TNF-alpha by 42%, outperforming CBD alone (29% reduction) and CBD/ THC in combination (25% reduction)

The preclinical studies demonstrated that NTI164 strain can suppress the expression of key MS markers, IL-12 and TNF-alpha, in human derived microglial cells. These studies are an expansion of the earlier findings (refer ASX Announcement 25 May 2021) in which NTI164 significantly suppressed the expression of COX-2 inhibition in human derived microglial cells.

Cytokines play an important role in the neuroinflammatory responses. Cytokines regulate the body's response to disease and infection, as well as mediate normal cellular processes in our body.**

MS is a progressive inflammatory disease characterised by the loss of myelin sheath which results in complex neuro-inflammatory symptoms such as spasticity, loss of movement and pain. Immune system dysregulation is believed to be a major underlying mechanism for MS and disease progression. IL-12 and TNF-alpha are both elevated in MS patients and are thought to play a major role in the pathology.

Multiple Sclerosis – substantial market with many unmet needs

The global MS therapies market was valued at over $40 Billion USD in 2021 and is projected to reach $48 Billion USD by 2026*. Current therapies in the treatment of MS include steroid based medicines, disease - modifying therapies and more recently antibody-based therapies.

Sativex™ is the only medicinal cannabis-based FDA approved product for the treatment of MS***. The Company has assessed similar formulations in these preclinical models, 1:1 CBD/THC mixtures. Results have shown that NTI164 is significantly more effective in suppressing key biomarkers versus CBD/THC formulation.

Recent patent filings by NTI will also allow the Company to assess combination formulation options with NTI164 and proven MS therapies to improve treatment efficacy and reduce side effects.

This strong preclinical data further supports the potent anti-inflammatory properties of NTI164 and broadens the potential applications to now include MS in addition to Autism Spectrum Disorder (ASD).

Neurotech's Chairman, Mr Brian Leedman said:

"These are very exciting developments and more importantly re-confirm the potency and the uniqueness of our low THC medicinal cannabis strains. Current therapies have many unwanted side effects, so to have the opportunity to develop naturally derived low THC strains is a great commercial opportunity for our Company. Our Company remains committed to the development of a solid portfolio for the expansion of application and use of NTI strains beyond Autism."

Authority
This announcement has been authorised for release by the Board of Neurotech International Limited.

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About Neurotech

Neurotech International Limited is a medical device and solutions company conducting clinical studies to assess the neuro-protective, anti-inflammatory and neuro-modulatory activities of our proprietary NTI/Dolce cannabis strains. Neurotech is also commercialising Mente, the world's first home therapy that is clinically proven to increase engagement and improve relaxation in autistic children with elevated Delta band brain activity. For more information about Neurotech and Mente Autism please visit http://www.neurotechinternational.com

**https://www.prnewswire.com/news-releases/multiple-sclerosis-drugs-market-size-worth--42-46-billion-globally-by-2028-at-6-3-cagr-verified-market-research-301352043.html*
***https://pubmed.ncbi.nlm.nih.gov/30447707/*
****https://mstrust.org.uk/a-z/sativex-nabiximols*
#Impaired interleukin-12 production in multiple sclerosis patients
C Rohowsky-Kochan 1 , D Molinaro, A Choudhry, M Kahn, S D Cook
https://pubmed.ncbi.nlm.nih.gov/10516776/

Results Summary

Treatment	Cytokine	Results Expressed as: Average +/- Standard Deviation (SD)	Statistical Significance Reduction Compared to Control Alone
Control: Interleukin and Interferon Activation	IL-12 TNF -alpha	99.91 +/- 12.88 N=8	
NTI164	IL-12 TNF -alpha	56.30 +/-18.24 N=8 58.28 +/- 15.08 N=8	44% reduction, P=0.0001 42% reduction, P<0.0001
CBD alone	IL-12 TNF -alpha	84.40 +/- 6.54 N=8 71.13 +/- 12.81 N=8	15% reduction, P=0.008 29% reduction, P=0.0005
CBD /THC (1:1)	IL-12 TNF -alpha	80.77 +/- 12.23 N=8 74.49 +/- 14.30 N=8	19% reduction, P=0.008 25% reduction, P=0.01

Assay details:

- Studies were carried out using Multiplex Quantitation System. The system allows for the accurate measurement of these neuro-markers levels. Measurements are done via fluorescence and expressed as F1 values.
- Positive controls: Interleukin and Interferon activity at 100%.
- Results are compared to positive control expressed as 100% activation and CB, CBD | THC where applicable

Significance between NTI164 versus CBD alone and CBD / THC combinations (1:1)

NTI164 IL-12 P=0.0011 versus CBD alone 44% versus 15% (n=8)	***Highly significant***
NTI164 TNF-alpha P=0.0575 versus CBD alone 42% versus 29% (n=8)	***Significant***
NTI164 IL-12 P= 0.0069 versus CBD/THC combination 44% versus 19% (n=8)	***Highly significant***
NTI164 TNF-alpha P= 0.0446 versus CBD/THC combination 42% versus 25% (n=8)	***Positive trend***

Key Findings

Preclinical studies focused on the key cytokines involved in MS and various inflammatory disease states:

Cytokine	Activity/Function
IL-12 (MS biomarker)	Plays an important role in immune regulation/important role in MS progression.

IL-12 is a cytokine that plays a key role in the pathogenesis of MS. #Published data and studies demonstrate that blocking this Cytokine via a neutralizing antibody causes dramatic improvements in animal models of the disease, and multiple human trials found the antibody to be safe and effective in humans.

Cytokine	Activity/Function
TNF-alpha (MS biomarker)	Plays an important role in dysregulation of acute inflammation involved in MS onset.

- NTI164 is statistically more potent in suppressing the key cytokines (biomarkers): IL-12 and TNF-alpha when compared CBD alone and CBD/ THC (1:1) mixture
- Results are very encouraging and reconfirm the potent properties of the NTI164 strains in modulating inflammatory processes in neurological disorders where inflammation induced by immune responses in dysregulated.
- These preclinical studies have successfully paved the way forward to the further expanding our knowledge base and the potential application of our unique strains in the treatment of neuro-anti-inflammatory disorders.

Background

What is MS?

It is a chronic, typically progressive disease involving damage to the sheaths of nerve cells in the brain and spinal cord, whose symptoms may include numbness, impairment of speech and of muscular coordination, blurred vision, and severe fatigue, chronic pain, blindness.

CBD has assisted many patients with their overall pain management and improved quality of life (reference: https://msra.org.au/medicinal-cannabis-ms/). According to MS Research Australia a review of up to 600 patients with MS who took medicinal cannabis felt that their spasticity was reduced and felt that their pain related to spasticity and sleep disturbance were also improved. The study participants were able to complete a walking task faster, but not all objective measurements of spasticity were improved. (reference: https://msra.org.au/medicinal-cannabis-ms/)