Neurotech

21 December 2020

Successful Completion of In Vitro Studies

Results Confirm Potent Anti-Inflammatory, Neuro-Modulatory & Protective Activity of DOLCE/NTI Strains

Neurotech International Limited (ASX: NTI) ("Neurotech" or "the Company") is pleased to announce the successful completion of its in-vitro studies using human brain cells to assess and validate the anti-inflammatory and neuro-modulatory properties of its proprietary DOLCE/NTI cannabis leads.

Neurotech has been undertaking a series of in-vitro studies to assess the neuroprotective, anti-inflammatory and neuro-modulatory activities of the proprietary DOLCE/NTI cannabis leads CBDA, CBDP, CBDB all with less than 0.3% THC. These studies have been conducted at three leading independent laboratories – Monash University, University of Wollongong and RMIT University.

HIGHLIGHTS

- **Final results indicate that the DOLCE/NTI strains exhibit potent anti-inflammatory activity. The DOLCE/NTI full spectrum strains work via normalising the expression of Arginase 1. The normalisation of Arginase 1 allows neuronal cells to remain in a "healthy" state.**
- **DOLCE/NTI strains were 80% more potent in controlling Arginase 1 when compared to CBD alone. Controlling Arginase 1 is an important step in the prevention and management of inflammation. *Appendix 1. Graph 1.***
- **The final results showed that DOLCE/NTI strains significantly reduce the expression of iNOS – towards "healthy" control levels. iNOS (inducible nitric oxide synthase) is a damaging agent responsible for the toxic effects of microglia cells (which are found within the brain). Oxidative damage from these cells increases in disease states – including; Autism, Epilepsy, ADHD, Alzheimer disease, Multiple Sclerosis and after injuries such as stroke or head trauma. DOLCE/NTI strains were 80% more potent than CBD alone. *Appendix 1, Graph 2.***
- **Results indicate that DOLCE/NTI strains do not increase cell death in healthy cells or in damaged cells. In contrast, CBD alone was shown to be toxic in these paradigms. Not only do DOLCE/NTI strains not kill cells, they increase neuronal cell number. *Appendix 1, Graph 3***
- **This finding is important as it indicates that the DOLCE/NTI strains *"full plant entourage" effect may work differently to CBD alone. This is also valuable safety data, as it indicates that DOLCE/NTI strains can be delivered to modulate inflammation and oxidative stress without harming healthy brain tissue.**

Summary

DOLCE/NTI strains comprise of CBDA, CBDP, CBDB all less than 0.3% THC. Neurotech previously reported the mode of action and powerful neuro-protective and modulatory properties of these unique strains versus CBD alone. These in vitro findings (released in announcements dated 2nd November 2020 and 30th November 2020) have been further validated in these final trials.

Neurotech International Ltd
ABN 73 610 205 402
Suite 5 CPC, 145 Stirling Highway
Nedlands, Western Australia 6009
www.neurotechinternational.com

DOLCE/NTI strains have shown to significantly improve neuronal cell health, cell viability and have the potent ability to reduce inflammation compared with CBD alone. All these physiological processes are vital in managing disorders with unmet need for therapies including; Autism, Epilepsy, ADHD, Alzheimer's disease and related neurological disorders.

These in vitro studies have shown the superiority of the DOLCE/NTI strains over CBD alone and now pave the way for future studies, including phase 1 clinical trials. Phase 1 clinical study preparations are currently underway to develop the optimum delivery and dosage forms. Commencement of stage 1 is expected in Q1/ 2021. Clinical trials will be conducted under the guidance and supervision of A/Professor Michael Fahey (Head of Paediatric Neurology, Monash Children's Hospital).

A/Professor Fahey recently completed his prestigious Fulbright scholarship in the USA and has extensive experience in the clinical use of medicinal cannabis in children with autism and related neurological disorders.

A/Prof Fahey and his team are experts in neurodevelopment and neuroprotection studies across various patient groups. "Preclinical studies suggest that these strains exhibit potent and unique properties when compared to CBD alone and warrant the further assessment of these strains in phase 1 clinical trials," said A/Prof Fahey.

"These final trial results are very encouraging, in particular, the powerful anti-inflammatory mode of action of our strains compared to CBD alone," said Brian Leedman, Chairman of Neurotech. These results demonstrate that the DOLCE/NTI leads may have a broader application in relation to the management and treatment of a number of neurological disorders".

This release has been authorised by the Board of Directors.

Further Information

Brian Leedman
Chairman
bleedman@neurotechinternational.com
+61 (0)41 228 1780

Winton Willesee
Non-Executive Director
winton@azc.com.au
+61 (0)41 066 7844

About Neurotech

Neurotech International Limited is a medicinal cannabis company conducting clinical studies to assess the neuroprotective, anti-inflammatory and neuro-modulatory activities of our proprietary DOLCE/NTI cannabis strains which include CBDA, CBDP and CBDB. The licensed strains contain < 0.3% THC potentially providing a clearer pathway to regulatory approval than all other cannabis companies that contain far higher THC levels. Neurotech is also commercialising Mente, the world's first home therapy 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

- The **entourage effect*** refers to the cannabinoids in the full plant to interact with each other synergistically to modulate activity and overall effects of the plant. There is growing evidence to suggest that the entourage effect is much more powerful than single isolate or extract and that synergy matters.

- The term "entourage effect" was first coined in 1998 by Dr. Ben-Shabat in his paper, **An Entourage Effect: Inactive Endogenous Fatty Acid Glycerol Esters Enhance 2-Arachidonoyl-Glycerol Cannabinoid Activity.** The concept has most notably been explained and expanded upon by Dr. Etahan Russo in his 2011 peer-reviewed article entitled, Taming THC: Potential Cannabis Synergy and Phytocannabinoid-Terpenoid Entourage Effects.

APPENDIX 1.

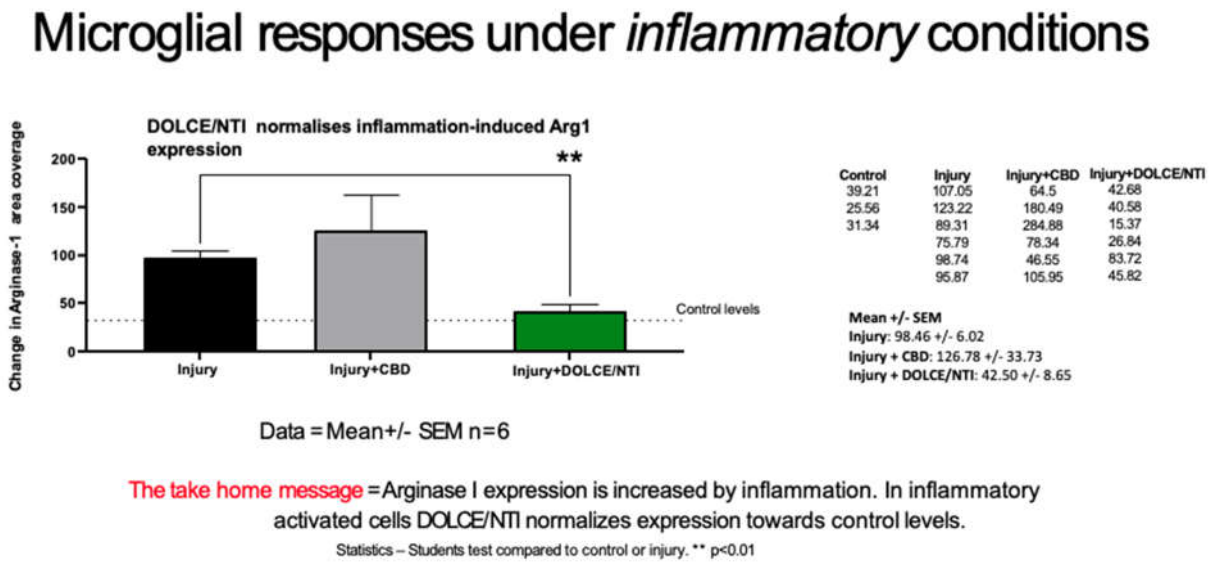
Studies conducted throughout this in vitro program include: MTT assays, por-and pre-inflammatory stimulation studies, Anti-inflammatory biomarkers assessments, Microglia activation state assessments, Bv2 assays, Excitotoxicity assays, Beta – Tubulin assays, Hoescht and Arginase expression assays. These studies were all conducted in accordance with international standards.

Experimental outline:

Microglial responses
Assessment of primary outcomes: Mitochondrial respiration (MTT reduction)
Controls: LPS and Melatonin treatments
Duration: Day 1: Preparation of cells, Day 2: Pro-inflammatory stimulation, Day 3: MTT assessments
Dosage: 2ug/ml

Neuronal responses – basal and excitotoxicity
Neurons (SHSY-5Y, Human)
Assessment of primary outcomes – mitochondrial respiration (MTT reduction), excitotoxicity via glutamate activation (3mM)
Duration: Day 1, Preparation of cells, Day 2 – pre-exposure & post -exposure, Day 3, MTT Hoechst assays
Dosage: 2ug/ml

Graph 1.



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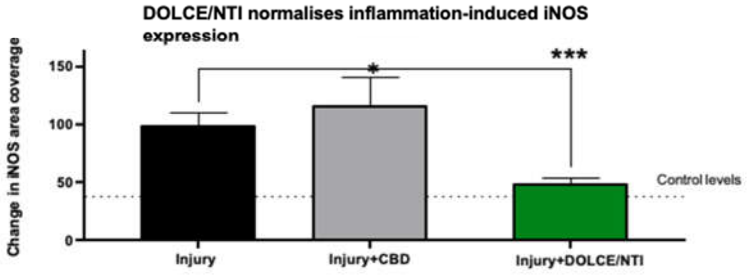
Graph 2.

Microglial responses under *inflammatory* conditions



Control	Injury	Injury+CBD	Injury+DOLCE/NTI
47.63	64.6	76.39	50.67
28.59	101.83	119.68	41.75
30.34	139.57	44.64	26.87
	80.01	102.78	44.25
	107.86	216.25	85.62
	106.14	143.66	80.98

Mean +/- SEM
Injury: 100 +/- 9.60
Injury + CBD: 127.23 +/- 22.14
Injury + DOLCE/NTI: 55.05 +/- 8.68

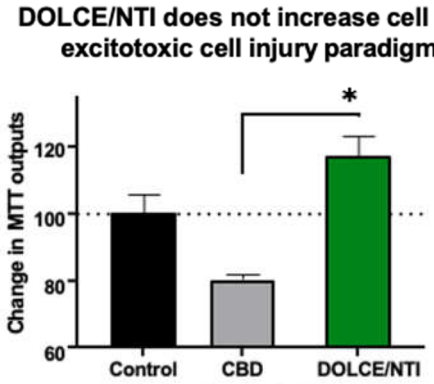
Data = Mean+/- SEM n=6

The take home message = iNOS expression is increased by inflammation. In inflammatory activated cells DOLCE/NTI normalizes expression towards control levels.

Statistics – Students test compared to control or injury. * p<0.05; p<0.001; ***

Graph 3.

Effects of DOLCE/NTI on neurons exposed to excitotoxicity



Control	CBD	DOLCE/NTI
100	85	99
101	78	96
102	85	117
99	82	139
110	84	162
90	82	111
120	78	99
80	74	128
70	78	123
130	89	132

Mean +/- SEM
Control: 81.5 +/- 5.3
Injury + CBD: 81.5 +/- 1.34
Injury + DOLCE/NTI: 118.6 +/- 6.62

Data = Mean+/- SEM n=10

Take home message – CBD is toxic in this paradigm; DOLCE/NTI are non- toxic and have positive effects on cell number

Statistics – Students test compared to control or injury. * p<0.05

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