

Genomic Analysis on PANDAS/PANS Patients Confirms NTI164 Normalises Immune System Gene Expression with Positive Patient Benefits

Key Points:

- **Genomic analysis in PANDAS/PANS patients who participated in Neurotech Phase I/II clinical trial shows reversal of immune system dysregulation – consistent with prior protein expression results**
- **NTI164 shown to modulate the immune system, protein translation, and epigenetic factors at both a gene expression (genomic) level and protein (proteomic) level in PANDAS/PANS children**
- **Data reinforces that administration of NTI164 is safe and effective under the inflammatory conditions experienced by PANDAS/PANS children (no activation of potentially damaging cellular pathways)**
- **Additional patent application filed**

Neurotech International Limited (ASX: NTI) ('Neurotech', 'NTI' or 'the Company') a clinical-stage biopharmaceutical development company focused predominately on paediatric neurological disorders, today announces the primary results of a genomic analysis undertaken by Professor Russell Dale's group on Neurotech study patients with Paediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS) and Paediatric Acute-Onset Neuropsychiatric Syndrome (PANS) who participated in the now complete Phase I/II clinical trial.

The NTIPANS1 trial, which reported statistically significant and clinically meaningful improvements in patients related to the severity of their illness, anxiety and depression at 12, 24 and 52 weeks included an exploratory endpoint at 12 weeks, which aimed to elucidate potential biomarkers of disease based on changes to the proteomic and genomic profile of patients who received NTI164 versus baseline and a normative control group. On 9 September 2024, the Company reported the results of its proteomic (protein) analysis, which showed NTI164 positively modified immune cell function and gene translation dysregulation, improving overall health and functional outcomes of children.¹

Utilising cutting-edge single-cell RNA sequencing that characterised the gene expression profile of single immune cells (those cells involved in immune regulation: neutrophils, monocytes, dendritic cells, CD8+ T cells, and CD4+ T cells) at baseline, and following 12 weeks of daily oral treatment with NTI164, was examined.

At baseline (Day 0), there was significant down-regulation in PANDAS/PANS patients versus normal controls across pathways relating to immune function in all cell types analysed above and across several categories, including cytokine production, regulation and responses. Also at baseline there was significant up-regulation in pathways relating to protein translation and ribosomal function, particularly in dendritic cells and CD8+ T cells. Ribosomes play a critical role in brain development. After 12 weeks of NTI164 treatment, the gene signature observed as baseline was largely reversed.

The genomic results further support the proteomic results that protein formation is occurring abnormally in children with PANDAS/PANS, which is resulting in the significant neurological issues observed in these patients. Accordingly, the data today reinforces Neurotech's earlier observation that NTI164 appears to have both significant anti-inflammatory effects, as well as potential as an epigenetic modulator.

¹ See ASX announcement dated 9 September 2024

The results of the genomic analysis are expected to be compiled and submitted to a leading scientific journal in due course. A summary of the scientific findings is shown in Appendix 1.

Authority

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

Further Information

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About Neurotech

Neurotech International Limited (ASX:NTI) is a clinical-stage biopharmaceutical development company focused predominately on paediatric neurological disorders with a broad-spectrum oral cannabinoid drug therapy called NTI164. Neurotech has completed a Phase II/III randomised, double-blind, placebo-controlled clinical trial in Autism Spectrum Disorder (ASD) with clinically meaningful and statistically significant benefits reported across a number of clinically-validated measures and excellent safety. In addition, Neurotech has completed and reported statistically significant and clinically meaningful Phase I/II trials in ASD and Paediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS) and Paediatric Acute-Onset Neuropsychiatric Syndrome (PANS), collectively PANDAS/PANS along with Rett Syndrome. Neurotech has received human ethics committee clearance for a Phase I/II clinical trial in spastic cerebral palsy.

For more information about Neurotech please visit <http://www.neurotechinternational.com>.

About NTI164

NTI164 is a proprietary drug formulation derived from a unique cannabis strain with low THC ($M < 0.3\%$) and a novel combination of cannabinoids including CBDA, CBC, CBDP, CBDB and CBN. NTI164 has been exclusively licenced for neurological applications globally. Pre-clinical studies have demonstrated a potent anti-proliferative, anti-oxidative, anti-inflammatory and neuro-protective effects in human neuronal and microglial cells. NTI164 is being developed as a therapeutic drug product for a range of neurological disorders in children where neuroinflammation is involved.

About PANDAS/PANS

Paediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS) and Paediatric Acute-Onset Neuropsychiatric Syndrome (PANS), collectively PANDAS/PANS, is a clinical diagnosis given to children who have a dramatic (typically within one day) onset of neuropsychiatric symptoms including Obsessive-Compulsive Disorder (OCD) and/or restrictive eating. Children may exhibit repetitive tic movements, become moody, irritable/aggressive and anxious and have difficulty with schoolwork. The cause of PANS is unknown in the majority of cases; however, the disorder is hypothesised to be triggered by infections, metabolic disturbances, and other inflammatory reactions. PANDAS is considered a subset of PANS.

Appendix 1 – Summary Scientific Findings

The table shows the 10 most up- and down-regulated pathways in PANS patients at baseline compared to controls (column 1, "prevscon"), and after 12 weeks on NTI164 compared to baseline (column 2, "postvspre") in cell types essential for immune homeostasis including neutrophils, monocytes, dendritic cells, CD8+ T cells, and CD4+ T cells. At baseline, there was significant down-regulation in patients in pathways relating to immune function in all cell types analysed (blue circles). In dendritic cell and CD8+ T cells, there was significant up-regulation in pathways relating to translation and ribosomal function at baseline in PANS patients compared to controls (red circles).

