US FDA Response to Orphan Drug Request in PANDAS/PANS

Key Points:

- **FDA believes PANDAS/PANS may not constitute the definition of a rare disease in the United States (<200,000 prevalence)**
- **FDA had no objections to Neurotech's submitted non-clinical and clinical evidence to support the application**
- **US FDA has not granted Neurotech Orphan Drug Status for NTI164 in PANDAS/PANS with the Company granted 12 months to respond to FDA comments**
- **ODD decision does not impact Neurotech's development plans for PANDAS/PANS, where new therapies are urgently needed given there are no approved treatments**
- **US FDA ODD outcome for Rett Syndrome expected prior to December 2024**

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 request for orphan drug designation (ODD) with the US Food and Drug Administration (FDA) for the use of NTI164 in children and adults diagnosed with Paediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS) and Paediatric Acute-Onset Neuropsychiatric Syndrome (PANS) has been declined. The FDA has granted Neurotech a 12-month abeyance to address the agency's objections.

Neurotech's development plans for PANDAS/PANS remain unaffected by the FDA's decision, given the strength of the clinical data to date (>52 weeks), excellent safety and new data showing NTI164 reverses immune dysregulation seen in these patients. The Company notes the FDA had no objections to Neurotech's submitted non-clinical and clinical evidence supporting the scientific rationale for the ODD, NTI164's mechanism of action, efficacy in pre-clinical and human clinical trials to date and relevance of NTI164 to PANDAS/PANS.

The FDA cited two main factors in its decision. Firstly, the agency felt it was unclear a distinction can be made for PANS as a separate disease, after consultation with the Division of Psychiatry, Office of New Drugs, Centers for Drug Evaluation and Research. Neurotech has been requested to provide the FDA with supportive data and references. In the US, the PANS/PANDAS Research Consortium, in conjunction with the National Institute of Mental Health (NIMH), has developed diagnostic criteria in 2015 and consensus treatment guidelines in 2017.

Secondly, the FDA did not agree with the prevalence data submitted by Neurotech based on a significant literature review by Neurotech and indicted PANDAS/PANS may not constitute the definition of a rare disease in the United States (<200,000 prevalence). This included the PANDAS Network in the US citing a prevalence rate of 1 in 200 children in the United States; however, this statement has no supportive peer-reviewed data.[1]

Neurotech, in consultation with its regulatory advisors, will consider providing a response to the FDA in the months ahead.

[1] https://pandasnetwork.org/get-involved/statistics/

FDA feedback has provided Neurotech with valuable regulatory insights into PANDAS/PANS as a relatively new disorder where diagnosis and prevalence data are emerging. In June 2024, the Company established a world-class clinical advisory group with significant expertise in the diagnosis and treatment of PANDAS/PANS and are considered global thought leaders. These clinicians, which includes Professor Russell Dale (Co-Principal Investigator of Neurotech's Phase I/II PANDAS/PANS clinical trial), will seek to build global consensus for this serious disorder. This includes working towards an update to the World Health Organization's International Classification of Diseases-11 (ICD-11) to provide a category for PANS alongside PANDAS, which is recognised. In addition, Professor Dale's recent proteomic data (reported on 9 September 2024) and pending genomic data analysis from PANDAS/PANS children, when published in peer-reviewed journals, will provide additional valuable insights into the underlying dysregulation in PANDAS/PANS patients.

An additional ODD request for NTI64 with the US FDA is currently under review for Rett Syndrome. The outcome is expected to be received prior to December 2024.

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

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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.