Q&A on Phase I/II PANDAS/PANS Clinical Trial Results

Neurotech International Limited (ASX: NTI) ("Neurotech" or "the Company"), recently announced strong clinical results for the 15 patient, open-label Phase I/II clinical trial of NTI164 in children diagnosed with Paediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS) and Paediatric Acute-Onset Neuropsychiatric Syndrome (PANS) (ASX release: 6 October 2023) ("Announcement").

Following the Announcement of these world first PANDAS/PANS results, Neurotech has had a number of stakeholders questions and enquiries on these results and the Company in general. Neurotech has put together a summary of key questions and answers set out below.

The Announcement noted "clinically significant and meaningful improvements in clinical function, with excellent safety and tolerability over 12 weeks of daily oral treatment ". *What does the Company do with the exceptional results achieved in the PANDAS/PANS trial and what does it mean in terms of a key company objective in actually having a treatment available to patients?*

This is a significant milestone for the Company. The study re-validates the effectiveness of our novel biopharmaceutical therapy NTI164 in treating complex neuro-inflammatory disorders following our successful Phase I/II trial in paediatric patients with ASD. This is also a huge step forward in the Company's human clinical program as NTI is the only company in Australia that is carrying out a rigorous pharmaceutical development program using a biopharmaceutical that is derived from low THC medicinal cannabis, NTI164.

The results of our Phase I/II PANDAS/PANS trial have demonstrated that NTI164 is effective for the treatment of PANDAS/PANS – these are paediatric disorders characterised by sudden onset neuropsychiatric symptoms, often triggered by an infection.[1] This world first study is a significant step forward in understanding and managing these complex disorders and, ultimately, improving the quality of life for those affected.

Our successful trial has effectively reduced some of the symptoms associated with PANDAS/PANS, such as obsessive-compulsive behaviours, anxiety, tics, mood disturbances, cognitive difficulties, and other neurological symptoms. The treatment was also well-tolerated by the patients involved in the trial with no serious adverse events recorded. It is important to add that all 15 participants elected to remain on the therapy at the conclusion of the trial.

PANDAS/PANS is a complex disorder with no "approved" therapy or specific drug (Refer to the Announcement). There is an urgent need to develop potential therapies for this disorder hence why NTI is pursuing its orphan drug approach with PANDAS/PANS. This presents an exciting potential commercial opportunity for the Company.

The Company has a clear path forward for the development and commercialisation of NTI164 as a treatment for PANDAS/PANS. Given the initial PANDAS/PANS results, NTI will look towards developing an orphan drug pathway with all the advantages that it offers and intends to progress with applications for an Orphan Drug Designation for NTI164 associated with the treatment of PANDAS/PANS in the US, and EU.

[1] https://pandasnetwork.org/understanding-pandas/diagnosis/

Please describe the main symptoms of PANDAS/PANS patients and what impact NTI164 had on these symptoms to considerably improve their quality of life and general well being?

PANDAS/PANS are conditions that are characterized by sudden-onset neuropsychiatric symptoms in children. The main symptoms of PANDAS/PANS can include:

1. *Obsessive-compulsive symptoms (OCD): Children may develop sudden and severe obsessions or compulsions that significantly interfere with their daily activities and routines.*

2. *Tics: Motor and/or vocal tics, such as repetitive movements or sounds, may appear suddenly or worsen in intensity.*

3. *Emotional and behavioural changes: Children may experience mood swings, irritability, anxiety, depression, or aggression that are out of character for them.*

4. *Regression: Children may experience a sudden loss of previously acquired skills, such as handwriting, toileting, or verbal communication.*

5. *Anxiety and separation anxiety: Children with PANDAS/PANS may exhibit excessive and irrational fears, as well as difficulty being separated from their caregivers.*

6. *Sleep disturbances: Insomnia, frequent awakenings, night terrors, or bedwetting may occur.*

7. *Sensory issues: Children may become hypersensitive or hyposensitive to sensory stimuli, leading to difficulties with processing sensory information.*[2]

In a world first, NTI successfully demonstrated that its lead biopharmaceutical product, NTI164 was able to reduce and alleviate some of the main symptoms of PANDAS/PANS as described above. These changes and improvements were deemed to considerably improve the quality of life of participants (Refer to Announcement). NTI164 successfully improved OCD like behaviours, significantly reduced anxiety, improved emotional changes – leading to outstanding patient outcomes when compared to where they were at the start of the trial.

Were there any major side effects experienced by patients during the trial?

We were extremely pleased with the safety data from the trial. There were some reported occurrences of nausea and vomiting from 3 of the 15 participants over 12 weeks of daily oral treatment, however none of these events were deemed to be severely adverse. It is likely that the majority of these occurrences are from the taste and volume of medication that the participants ingest.

It is important that side effects are minimal for multiple reasons. Firstly, side effects can impact the overall well-being and quality of life for individuals undergoing the treatment. Secondly, side effects can pose risks to the safety of paediatric patients. Some side effects can be serious or even life-threatening especially if they occur in vulnerable paediatric populations. Additionally, minimizing side effects also helps to improve treatment compliance and patient satisfaction. If individuals experience significant side effects, they may be more likely to discontinue or avoid treatments altogether, which can hinder the effectiveness of therapy.

[2] https://pandasnetwork.org/understanding-pandas/signs-and-symptoms/

Are you expecting any further results from the trial?

Yes. We are awaiting further data from Professor R. Dale who is undertaking a series of molecular mechanism of action studies (Refer to Announcement). He is conducting a world first study designed to provide evidence of cellular changes from baseline measures to after 12 weeks of PANDAS/PANS treatment with NTI164 to correlate and assist in identifying relevant biomarkers of the disorder. If successful, this could give great insight into the method of action of NTI164 which could significantly assist the company in its efforts to gain registration of the drug. These studies will also assist the company select the most appropriate disorders to treat.

What is Orphan Drug designation and what will securing an Orphan Drug Designation actually mean for Neurotech from a commercialisation perspective?

Orphan Drug Designation is a specific regulatory mechanism that exists in the US and EU through the FDA and EMA to encourage investment and development of new drugs for rare diseases. It was established to encourage research into rare diseases and encourage corporates to commercialise drugs for such indications. NTI believes that PANDAS/PANS meets the criteria of a rare disease under the FDA and EMA guidelines for an Orphan Drug.

Orphan Drug Designation will also allow NTI to gain significant benefits, such as market exclusivity periods, financial incentives, reduced clinical requirements and assistance in the drug development process.

There have been recent ASX examples of biotech companies successfully demonstrating the commercial significance of an Orphan Drug development strategy. The most recent is Neuren Pharmaceuticals Limited (ASX:NEU)("Neuren"). Neuren has successfully commercialised a drug called Trofinetide which secured multiple Orphan Drug Designations and subsequently achieved FDA approval in 2023. Neuren has a market capitalisation now of over $1.3Bn.

How best can you describe the Company's current strategy for commercialising NTI164?

Neurotech's short term strategy is to generate clinical evidence of safety and benefit for NTI164 across multiple paediatric neurological disorders to add substantial value to our NTI164 therapeutic platform. In parallel, NTI continues to pursue a strategy of establishing strategic partnerships aimed at progressing FDA, TGA and EMA drug registrations in the US, Australia and the EU. The clinical evidence of benefit generated from this successful PANDAS/PANS trial along with earlier long term clinical results in ASD will continue to assist with this key strategic objective.

What can we look forward to in terms of Company updates over the coming months?

There are a number of key objectives and future milestones for the Company including:

- *Results of the landmark 54 patient Phase II/III double blinded – placebo-controlled ASD trial which is nearing completion of patient recruitment at Monash Children's Hospital with results anticipated in Q1 2024*
- *Molecular mechanism of action studies conducted under the guidance of Professor Dale. A World first study designed to provide further evidence of genomic molecular changes from baseline measures to after 12 weeks of PANDAS/PANS treatment with NTI164 to correlate and assist in identifying relevant biomarkers of the disease.*
- *The Company is aiming to apply for an Orphan Drug Designation for NTI164 associated with the treatment of PANDAS/PANS in the US and EU.*

- *Results from NTI's Phase I/II clinical trial investigating the use of NTI164 in children with Rett Syndrome patients in Q1 2024.*

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

Investors:
Dr Thomas Duthy
Executive Director
td@neurotechinternational.com
+61 (0)402 493 727

About Neurotech

Neurotech International Limited (ASX:NTI) is a clinical-stage biopharmaceutical development company focused predominately on paediatric neurological disorders. Neurotech has completed a Phase I/II clinical trial in Autism Spectrum Disorder (ASD), which demonstrated excellent safety and efficacy results at 28 days, 20 weeks and 52 weeks of treatment with NTI164. The Company commenced Phase II/III randomised, double-blind, placebo-controlled clinical trial in ASD in Q4 CY2022. Neurotech is also conducting additional Phase I/II trials in Paediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS) and Paediatric Acute-Onset Neuropsychiatric Syndrome (PANS), collectively PANDAS/PANS, along with Rett Syndrome and Cerebral Palsy during CY2023. 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 please visit http://www.neurotechinternational.com.