Neurotech Receives HREC Approval for Phase I/II PANDAS/PANS Clinical Trial

Neurotech International Limited (ASX: NTI) ("Neurotech" or "the Company"), a clinical-stage biopharmaceutical development company focused predominately on paediatric neurological disorders, today announces the receipt of written Human Research Ethics Committee (HREC) approval and Clinical Trial Notification (CTN) scheme clearance by the Therapeutic Goods Administration (TGA) to commence the 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).

Dr Thomas Duthy, Executive Director of Neurotech said *"We appreciate the timely approval of our HREC filing at the Children's Hospital at Westmead, along with CTN/TGA clearance. We look forward to commencement of patient recruitment during the current quarter, under the supervision of Co-Principal Investigator Professor Russell Dale. To our knowledge, this is the first clinical trial conducted in PANDAS/PANS patients with a novel oral full-spectrum cannabinoid drug formulation (NTI164), which seeks to provide initial evidence of clinical efficacy and safety in these patients over the twelve (12) week study period, with all patients eligible to continue to receive our treatment for up to 54 weeks."*

Dr Duthy continued *"Given the urgent unmet medical need and lack of safe and effective approved therapies, the Company intends to rapidly progress development of NTI164 in PANDAS/PANS by leveraging available regulatory mechanisms, including orphan drug designations where applicable."*

In addition to the HREC approval from the Children's Hospital at Westmead, the Company has filed site specific activation documentation to also facilitate the immediate commencement of patient recruitment at the Paediatric Neurology Unit at Monash Medical Centre, under the auspices of Co-Principal investigator Professor Michael Fahey.

Recruitment of the 15 patients is anticipated to commence during Q1 CY2023, with results of the trial anticipated in 2H CY2023.

The Phase I/II clinical trial has been registered on the Australian New Zealand Clinical Trials Registry (ANZCTR) under registration number: ACTRN12622001419752.

A synopsis of the trial design is shown in Appendix 1.

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

Media:
Lisa Blake
LBPR
lisa@lbpr.com.au
+61 (0) 429 976 718

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 and 20 weeks of treatment with NTI164. The Company will commence a Phase II/III randomised, double-blind, placebo-controlled clinical trial in ASD in Q4 CY2022. Neurotech plans to conduct 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 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.

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 PANS/PANDAS

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.

About Neurotech PANDAS/PANS Phase I/II Clinical Trial

NTIPAN1 is a single-arm, open-label, Phase I/II clinical trial that will recruit 15 paediatric patients with a clinical diagnosis of moderate to severe PANDAS/PANS to determine the efficacy and safety of orally administered NTI164 in these patients. The primary endpoints of the trial are the change from baseline at twelve (12) weeks for the Revised Children's Anxiety and Depression Scale-Parent-rated (RCADS-P) score and Clinical Global Impression (CGI) of severity (CGI-S) and improvement (CGI-I). Secondary clinical endpoints include other gold-standard, validated assessment tools: Yale Global Tic Severity Scale (YGTSS), Children's Yale-Brown Obsessive-Compulsive Scale, Conners Scale and EQ-5D-Y. Other secondary endpoints will examine the Safety and Tolerability of orally administered NTI164 (at 5,10,15 and 20 mg/kg/day). The trial intends to enrol children at two centres within Australia; the Children's Hospital at Westmead and the Paediatric Neurology Unit at Monash Medical Centre. The Phase I/II clinical trial has been registered on the Australian New Zealand Clinical Trials Registry (ANZCTR) under registration number: ACTRN12622001419752 or visit: https://www.anzctr.org.au

Appendix 1 - NTIPAN1 Clinical Trial Design

Title of Study	A Phase I/II Baseline Controlled Multi-Site Open-Label Study to Assess the Safety & Efficacy of NTI164 in Young People with Paediatric Acute-Onset Neuropsychiatric Disorder (PANS)
Co-Principal Investigators	Prof Russell Dale, Head, CHW Clinical School and Speciality of Child and Adolescent Health, The Children's Hospital at Westmead Prof Michael Fahey, Head of Paediatric Neurology, Monash Children's Hospital
Treatments	*Baseline/up-titration phase*: patients receive a baseline dose of 5mg/kg/day of NTI164 which will be increased weekly by 5mg/kg for a period of 4 weeks until the maximum tolerated dose or 20mg/kg is achieved. *Treatment phase:* patients will receive the maximum tolerated dose or 20mg/kg/day for 8 weeks, after which extension to 54 weeks will be offered if patients would like to continue (extension phase). *Down-titration phase (for patients not entering extension phase):* at the end of the 8 week treatment phase, patients will commence weaning of NTI164, gradually decreasing the maximum tolerated dose by 5mg/kg/week for a period of 4 weeks until the end of the study. *Extension phase:* Patients who choose to continue receiving the maximum tolerated dose beyond the 8 week treatment phase may do so for up to 54 weeks. Patients will undergo the down-titration phase at the end of their extension phase.
Primary Endpoints	<u>Revised Children's Anxiety and Depression Scale-Parent-rated (RCADS-P) score</u> RCADS-P is a 47 item parent-reported questionnaire that measures symptoms of depression and anxiety in children and adolescents aged 8–18. The RCADS-P consists of six subscales helpful in screening children for high prevalence disorders, including: separation anxiety disorder (SAD), social phobia (SP), generalized anxiety disorder (GAD), panic disorder (PD), obsessive compulsive disorder (OCD) and major depressive disorder (MDD). **[Timeframe: Baseline, Week 12]**

	Clinical Global Impression-Severity (CGI-S) Reflects clinician's impression of severity of illness on a 7-point scale ranging from 1=not at all to 7=among the most extremely ill. **[Timeframe: Baseline, Week 12]** Clinical Global Impression-Improvement (CGI-I) Reflects clinician's impression rates the total improvement whether or not, in the clinician's judgement, is due entirely to drug treatment on a 7-point scale ranging from 1=very much improved to 7=very much worse **[Timeframe: Baseline, Week 12]**
Secondary Endpoints	Yale Global Tic Severity Scale (YGTSS); gold-standard for clinical measurement of tics Children's Yale-Brown Obsessive-Compulsive Scale; gold-standard for clinical measurement of OCD symptoms and severity Conners Scale; gold-standard for clinical assessment of attention deficit hyperactivity disorder (ADHD) behaviours EQ-5D-Y; a globally accepted tool for measuring impairment in the domains of mobility, looking after oneself (e.g., personal hygiene habits), ability to perform usual/daily activities, having pain or discomfort, and feeling worried, sad, or unhappy Unique blood transcriptomic and/or epigenetic signature in children with PANS is improved with NTI164
Safety	Safety will be monitored and measured by full blood examinations, liver and kidney function tests. Adverse events will be assessed and evaluated by delegated study staff through discussions with the Participant at week 4 and via phone calls made to them throughout the study and by clinically significant lab results.
Multi-omic Studies	Transcriptomics – RNA Sequencing Methylomics Immune biomarker studies - Cytokines
Summary Inclusion Criteria	Participant is aged < 17 years Fulfil PANS criteria: Acute onset of OCD or severely restricted food intake

Concurrent presentation of additional neuropsychiatric symptoms from at least 2 of the following 7 categories: anxiety, emotional lability/depression, irritability, aggression or severely oppositional behaviours, behavioural regression, deterioration in school performance, sensory or motor abnormalities (e.g. tics), somatic symptoms (e.g. sleep disturbances, enuresis or increase in urinary frequency)

Symptoms not better explained by a known neurologic or medical disorder (e.g. Sydenham's chorea)

RCADS-P scores of >65 (a scale of anxiety, social phobia, panic disorder, OCD, and low mood, a score of >65 infers moderate-significant impairment)

Other patient medications (e.g. anti-psychotics) must be stable for at least 12 weeks prior to trial participation

Summary Exclusion Criteria

Infection and/or antibiotic use in the 2 weeks prior to trial participation (i.e. baseline blood tests and commencement of NTI164)

Recent changes to other patient medication (e.g. addition or escalation of anxiolytics, anti-depressants etc; medication dosage must be stable for at least 12 weeks prior to trial participation)

Intellectual disability preventing adequate assent from patient, or that would affect reporting throughout trial; patients with intellectual disability must still have the capacity to verbalise their symptoms/experiences

Ongoing immunomodulating or immunosuppressive treatment use in the previous 12 weeks, including steroids, IVIG, antibiotics, low-dose naltrexone, mycophenolate, Rituximab etc.

Currently using or has used recreational or medicinal cannabis or cannabinoid-based medications (e.g. Sativex®, Epidiolex®) in the previous 12 weeks and/or is unwilling or unable to abstain for the duration of the trial

Underlying renal impairment, cardiovascular issues (e.g. arrhythmia), current or previous thrombosis

Impaired hepatic function, defined as serum alanine aminotransferase (ALT) or aspartate aminotransferase (AST) > 2 x upper limit of normal (ULN) or total bilirubin (TBL) > 2 x ULN; this criterion can only be confirmed once baseline laboratory results are available and participants who fail this criterion will not proceed in this study

	Other diagnosed neurological condition likely to be contributing to OCD/neuropsychiatric symptoms (e.g. Huntington's disease)
Concomitant Care	Concomitant use of immune modulating or immunosuppressive therapies, including all forms of steroids (except topical), low dose naltrexone, mycophenolate, Rituximab etc. is prohibited during the trial period. Changes to the dose of existing medications (e.g. anti-anxiety or anti-psychotic treatment) is prohibited throughout the trial period. The addition of new medication, including anti-anxiety (selective serotonin reuptake inhibitors) or anti-psychotic treatments (e.g., Risperidone, Aripiprazole, Olanzapine, Quetiapine etc.) is prohibited and if a patient requires a new medication during the study period, they will be discontinued from the study