# Neurotech Receives HREC/TGA Approval for Phase II/III ASD 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 Human Research Ethics Committee (HREC) approval and Clinical Trial Notification (CTN) scheme clearance by the Therapeutic Goods Administration (TGA) to commence the Phase II/III NTIASD2 clinical trial for children with Autism Spectrum Disorder (ASD).

***Dr Thomas Duthy, Executive Director of Neurotech*** *said "The significant improvement we showed in ASD children in our open-label Phase I/II trial across multiple, important clinical assessment tools relating to severity of illness, adaptive behaviours, social responsiveness and anxiety/depression/ mood, provide Neurotech with great confidence to progress NTI164 into a Phase II/III randomised, double-blind, placebo-controlled clinical trial and we thank the HREC for their rapid approval of our rationally designed trial protocol. Combined with standard non-drug behavioural therapies, NTI164 can be considered a patient enabling drug, by improving daily living and allowing children to integrate into society via significant improvements in socialisation and anxiety."*

NTIASD2 is a randomised, double-blind, placebo-controlled, Phase II/III clinical trial that will recruit up to 54 patients with ASD to determine the efficacy and safety of NTI164 versus placebo. The study comprises an 8-week treatment period followed by an 8-week open-label maintenance period followed by a 2-week wash-out period. Participants who choose to continue receiving NTI164 beyond the duration of the study may do so for an additional 38 weeks. They will undergo the 2-week down-titration phase at the end of their extension phase.

The primary endpoint of the trial is Clinical Global Impression-Severity (CGI-S), which reflects a 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. Key Secondary Endpoints include Change in Vineland Adaptive Behaviour Scales, Third Edition (Vineland™-3), Change in Social Responsiveness Scale, 2nd Edition (SRS-2), Change in Clinical Global Impression Scale -Improvement (CGI-I), Change in Anxiety, Depression and Mood Scale (ADAMS) and safety as measured by full blood, liver and kidney analyses at defined time points.

Recruitment is anticipated to commence in Q4 CY22 with completion of recruitment in 2H CY23. The trial will be enrolling children at the Paediatric Neurology Unit at Monash Medical Centre.

The clinical trial has been registered on the Australian New Zealand Clinical Trials Registry (ANZCTR) under registration number: **ACTRN12622001398796**.

A synopsis of the Phase II/III Clinical Trial is shown in **Appendix 1**.

**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. 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

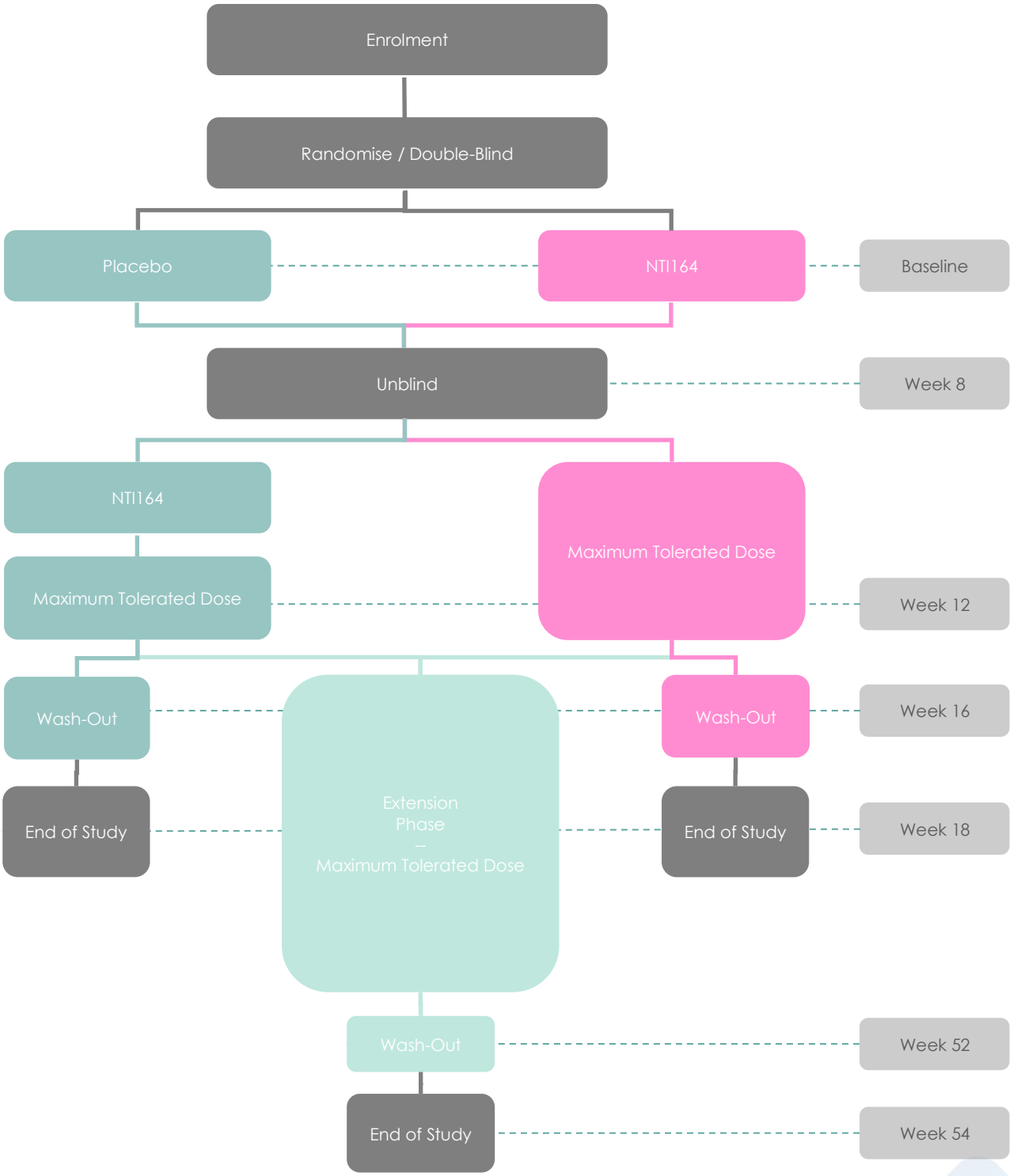
NTI164 is a proprietary drug formulation derived from a unique cannabis strain with low THC (M<0.3%) and a novel combination of cannabinoids including CBDA, CBC, CBDP, CBDB and CBN. NTI164 has been exclusively licenced for neurological applications globally. Pre-clinical studies have demonstrated a potent 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 the ASD Phase II/III Clinical Trial

NTIADS2 is a Phase II/III Double-Blind, Randomised and Controlled-to-Open-Label Study to assess the efficacy of NTI164 up to 20mg/kg/day on the severity of spectrum disorder (ASD) in up to 54 patients aged 2-17 years (inclusive). The primary endpoint of the trial is Clinical Global Impression-Severity (CGI-S), which 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].

For more information on the trial, please visit the Australian New Zealand Clinical Trials Registry (ANZCTR) under Registration Number **ACTRN12622001398796** at: https://www.anzctr.org.au

## Appendix 1 - NTIASD2 Clinical Trial Design



**Public title**

Evaluating the Efficacy of Full-Spectrum Medicinal Cannabis Plant Extract 0.08% THC (NTI164) in Young People with Autism Spectrum Disorder, a Double-Blind, Randomised and Controlled-to-Open-Label Study.

**Scientific title**

A Phase II/III Double-Blind, Randomised and Controlled-to-Open-Label Study Assessing the Efficacy of Full-Spectrum Medicinal Cannabis Plant Extract 0.08% THC (NTI164) on the Severity of Autism Spectrum Disorder in Young People

**Secondary ID [1]**

NTIASD2

**Secondary ID [2]**

**Universal Trial Number (UTN)**

**Trial acronym**

**Linked study record**

Follow-up study to registration record ACTRN12621000760875

## Health condition

**Health condition(s) or problem(s) studied:**

Autism Spectrum Disorder

**Condition category**

**Condition code**

Mental Health

Autistic spectrum disorders

## Intervention/exposure

**Study type**

Interventional

**Description of intervention(s) / exposure**

Full-spectrum medicinal cannabis plant extract with 0.08% THC (NTI164).

NTI164 is an oil that will be administered orally over the course of the study.

The study involves the following phases:

• Randomised Controlled Phase (duration = 8 weeks)
At the beginning of the study, participants will be randomised into either the active group or placebo group. Both groups will commence a double-blinded baseline dose of either 5mg/kg/day of NTI164 or Placebo that will be increased weekly by 5mg/kg for a period of 4 weeks until the maximum tolerated dose or 20/mg/kg/day is achieved.

**At the end of the 8-week period, both study groups will be unblinded and the primary endpoint of the study will be assessed.**

• Open-Label Phase (duration = 8 weeks)
Participants who received Placebo will commence NTI164. This involves a 4-week weekly up-titration of 5mg/kg until the maximum tolerated dose or 20/mg/kg/day is achieved. These participants will then continue to receive their maximum tolerated dose for an additional 4-weeks.

Participants who received NTI164 during the Randomised Controlled phase will continue receiving their maximum tolerated dose during the Open-label phase for 8-weeks.

• Wash-out phase (duration = 2 weeks)
At the end of the 16 weeks, participants have the option of ending their participation and undergoing a 2-week down-titration of NTI164. The dosage down-titration will be dependent on the maximum tolerated dose of each participant and at the discretion of the Principal Investigator.

• Extension phase (duration = 36 weeks)
Participants who choose to continue receiving NTI164 beyond the duration of the study may do so for an additional 38 weeks. They will undergo the 2-week Down-titration phase at the end of their Extension phase.

The minimum duration of this study is 18 weeks and the maximum duration is 54 weeks.

Monitoring of completion of daily online drug administration forms plus accountability of returned study product and packaging at each visit, will be conducted to ensure protocol adherence.

**Intervention code [1]**

Treatment: Drugs

**Comparator / control treatment**

The control treatment will be a virgin olive oil placebo that has a similar appearance to the active treatment.

**Control group**

Placebo

## Outcomes

**Primary outcome [1]**

Change in 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.

***Timepoint [1]***

Primary endpoint: Baseline (pre-dose), 4 & 8 weeks post-commencement of treatment.

**Secondary outcome [1]**

Change in Vineland Adaptive Behaviour Scales, Third Edition (Vineland-3) Parent/Caregiver Form. Used to measure adaptive functioning across three core domains (Communication, Daily Living Skills, and Socialization), and two optional domains (Motor Skills and Maladaptive Behaviour); items are rated on a 3-point scale (0=never; 1=sometimes; 2=usually or often). The core domains sum to a total Adaptive Behaviour Composite.

***Timepoint [1]***

Baseline (pre-dose) and 16 weeks post-commencement of treatment. Additional timepoints for Extension phase: Weeks 28, 40 & 52 post-commencement of treatment.

**Secondary outcome [2]**

Change in Social Responsiveness Scale, 2nd Edition (SRS-2), School-Age Form Five domains are assessed including: Social Awareness, Social Cognition, Social Communication, Social Motivation, and Restricted Interests and Repetitive Behaviour. Items are scored on a 4-point scale (ranging from 1=not true to 4=almost always true).

***Timepoint [2]***

Baseline (pre-dose) and 16 weeks post-commencement of treatment. Additional timepoints for Extension phase: Weeks 28, 40 & 52 post-commencement of treatment.

**Secondary outcome [3]**

Change in Clinical Global Impression Scale -Improvement (CGI-I) This is a 7-point scale measuring symptom change from baseline.

***Timepoint [3]***

Baseline (pre-dose), 4, 8, 12 & 16 weeks post-commencement of treatment. Additional timepoints for Extension phase: Weeks 28, 40 & 52 post-commencement of treatment.

**Secondary outcome [4]**

Change in Anxiety, Depression and Mood Scale (ADAMS) 28 symptom items that resolve into five subscales labelled: Manic/Hyperactive Behaviour, Depressed Mood, Social Avoidance, General Anxiety, and Compulsive Behaviour. Items are rated on 4-point scale ranging from 0=not a problem to 3=severe problem.

***Timepoint [4]***

Baseline (pre-dose) and 16 weeks post-commencement of treatment. Additional timepoints for Extension phase: Weeks 28, 40 & 52 post-commencement of treatment.

**Secondary outcome [5]**

Change in Sleep Disturbance Scale for Children (SDSC) Six subscales including Disorders of Initiating and Maintaining Sleep, Sleep Breathing Disorders, Disorders of Arousal, Sleep Wake Transition Disorders, Disorders of Excessive Somnolence, and Sleep Hyperhydrosis. Items are rated on 5-point scale where 1=never and 5=always (daily). Subscale scores sum to equal a total score

***Timepoint [5]***

Baseline (pre-dose), 4, 8, 12 & 16 weeks post-commencement of treatment. Additional timepoints for Extension phase: Weeks 28, 40 & 52 post-commencement of treatment.

**Secondary outcome [6]**

Change in Anxiety Scale for Children - Autism Spectrum Disorder - A form developed to detect symptoms of anxiety in youth with ASD. Composed of four subscales (Performance Anxiety, Uncertainty, Anxious Arousal, and Separation Anxiety), items are rated on a 4-point scale (0=never and 3=always). Subscales sum to equal a total score.

***Timepoint [6]***

Baseline (pre-dose), 4, 8, 12 & 16 weeks post-commencement of treatment. Additional timepoints for Extension phase: Weeks 28, 40 & 52 post-commencement of treatment.

**Secondary outcome [7]**

Change in Clinical Global Impression of Change (CGI-C) Target Behaviour - Reflects clinician's impression of change of behaviour on a 7-point scale ranging from 1=not at all to 7=very severe problem. Provided as Baseline and Post-Baseline questionnaires.

***Timepoint [7]***

Baseline (pre-dose), 4, 8, 12 & 16 weeks post-commencement of treatment. Additional timepoints for Extension phase: Weeks 28, 40 & 52 post-commencement of treatment.

**Secondary outcome [8]**

Change in Clinical Global Impression of Change in Attention (CGI-CA) - Reflects clinician's impression of change in attention on a 7-point scale ranging from 1=not at all to 7=very severe problem.

***Timepoint [8]***

Baseline (pre-dose), 4, 8, 12 & 16 weeks post-commencement of treatment. Additional timepoints for Extension phase: Weeks 28, 40 & 52 post-commencement of treatment.

**Secondary outcome [9]**

Safety as assessed by Full Blood Examination

***Timepoint [9]***

Baseline (pre-dose), 8 & 16 weeks post-commencement of intervention. Additional timepoints for Extension phase: Weeks 28, 40 & 52 post-commencement of treatment.

**Secondary outcome [10]**

Safety as assessed by Liver Function Tests

***Timepoint [10]***

Baseline (pre-dose), 8 & 16 weeks post-commencement of intervention. Additional timepoints for Extension phase: Weeks 28, 40 & 52 post-commencement of treatment.

**Secondary outcome [11]**

Safety as assessed by Kidney Function Tests

***Timepoint [11]***

Baseline (pre-dose), 8 & 16 weeks post-commencement of intervention. Additional timepoints for Extension phase: Weeks 28, 40 & 52 post-commencement of treatment.

## Eligibility

**Key inclusion criteria**

• Participant is aged 8 years to 17 years (inclusive)
• Participant is at a healthy weight at the discretion of the Principal Investigator.
• Parents or caregivers can give informed consent for participation in the trial with assent from individuals with autism.
• Participants can comply with trial requirements.
• According the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) criteria the participant has a diagnosis of Level 2 or 3 Autism Spectrum Disorder (ASD) confirmed by Autism Diagnostic Observational Schedule (ADOS-2) criteria
• All treatments including medications and therapies for ASD related symptoms must have been stable for 4 weeks before enrolment and for the duration of the trial wherever possible.
• Participants must be able to swallow liquid.
• Consent giver must be able to understand the requirements of the study.

**Minimum age**

8 Years

**Maximum age**

17 Years

**Gender**

Both males and females

**Can healthy volunteers participate?**

No

**Key exclusion criteria**

• Current diagnosis of bipolar disorder, psychosis, schizophrenia, schizoaffective disorder, or active major depression
• Has a diagnosis other than ASD that dominates the clinical presentation (e.g., Attention Deficit Hyperactivity Disorder [ADHD])
• Has a degenerative condition
• Changes in anticonvulsive therapy within the last 12 weeks
• Taking omeprazole, lansoprazole, tolbutamide, warfarin, sirolimus, everolimus, temsirolimus, tacrolimus, clobazam, repaglinide, pioglitazone, rosiglitazone, montelukast, bupropion, or efavirenz
• Currently using or has used recreational or medicinal cannabis, cannabinoid-based medications (including Sativex®, or Epidiolex®) within the 12 weeks prior to screening and is

unwilling to abstain for the duration of the trial
• Participant has any known or suspected hypersensitivity to cannabinoids or any of the excipients
• Participant has moderately impaired hepatic function at screening, defined as serum alanine aminotransferase (ALT) or aspartate aminotransferase (AST) > 2 × upper limit of normal (ULN) or total bilirubin (TBL) > 2 × ULN. This criterion can only be confirmed once the laboratory results are available; participants enrolled into the trial who are later found to meet this criterion must be screen-failed.
• Participant is male and fertile (i.e., after puberty unless permanently sterile by bilateral orchidectomy) unless willing to ensure that they use male contraception (condom) or remain sexually abstinent during the trial and for 12 weeks thereafter.
• Participant is female and with childbearing potential (i.e., following menarche and until becoming postmenopausal for greater than or equal to 12 consecutive months unless permanently sterile by hysterectomy, bilateral salpingectomy, or bilateral oophorectomy) unless willing to ensure that they use a highly effective method of birth control (e.g., hormonal contraception, intrauterine device/hormone-releasing system, bilateral tubal occlusion, vasectomized partner, sexual abstinence) during the trial and for 12 weeks thereafter.
• Female participant who is pregnant (positive pregnancy test), lactating or planning pregnancy during the course of the trial or within 12 weeks thereafter.
• Participant had brain surgery or traumatic brain injury within 1 year of screening.
• Participant has any other significant disease or disorder which, in the opinion of the investigator, may either put the participant, other participants, or site staff at risk because of participation in the trial, may influence the result of the trial, or may affect the participant's ability to take part in the trial.
• Any abnormalities identified following a physical examination of the participant that, in the opinion of the investigator, would jeopardize the safety of the participant if they took part in the trial
• Any history of suicidal behaviour (lifelong) or any suicidal ideation of type 4 or 5 on the Columbia-Suicide Severity Rating Scale (C-SSRS) in the last 4 weeks or at screening or randomization
• Participant has donated blood during the past 12 weeks and is unwilling to abstain from donation of blood during the trial.
• Participant has any known or suspected history of alcohol or substance abuse or positive drugs of abuse test at screening (not justified by a known concurrent medication).
• Participant has previously been enrolled into this trial.
• Participant has plans to travel outside their country of residence during the trial, unless the participant has confirmation that the product is permitted in the destination country/state