Successful Landmark Study in Paediatric ASD Progresses to Pivotal Drug Registration Stage

- **Study demonstrates safety and tolerability across the dosing regime**
- **No Serious Adverse Events (SAEs) reported**
- **Review of data to date shows consistent positive changes in trial patients for key behavioural indicators specifically relating to irritability, social interaction, mood and communication**
- **Study scheduled to progress to Phase II/III registration trial at Monash Children's Hospital**
- **Discussions initiated with the TGA and NTI has initiated pre-IND activities in relation to US FDA**

Neurotech International Limited (ASX: NTI) ("Neurotech" or "the Company") is pleased to announce successful developments relating to safety and tolerability of NTI164 and key behavioural parameters that impact Autism Spectrum Disorder (ASD) patients. NTI164 is one of NTI's proprietary Dolce Cann Global cannabis strains in respect of neurological applications and is the world's first full-spectrum medicinal cannabis product (less than 0.3% THC) to be successfully studied in children with ASD at Monash Children's Hospital in Melbourne.

The ongoing Study is designed to vigorously assess the safety and efficacy of NTI164 in a dose escalation regime and assess the behaviour, focus and cognitive related parameters using validated neuro-psychological tools. This Study is designed to form the foundation for follow up studies in therapies relating to the treatment of a wide range of neurological disorders such as Multiple Sclerosis, Motor Neuron Disease, Rett's Disease and Cerebral Palsy.

Study Design and Outline:

- Open label study.
- The study population: children aged between eight years old through to seventeen years that have a medical diagnosis of Level II and III Autism Spectrum Disorder (ASD) as confirmed by the Autism Diagnostic Observational Schedule (ADOS-2) criteria.

Study Primary Endpoints:

- Safety and tolerability - across dose regime (5mg/kg, 10mg/kg, 15mg/kg and 20 mg/kg).
- Safety is monitored and measured by full blood examinations, liver, and renal function tests in addition to parent/carer and physician questionnaires.

Study Secondary Endpoints:

- Efficacy monitored and measured through parent/carer and physician questionnaires to assess:
  - Irritability
  - Hyperactivity
  - Mood
  - Self-stimulation

- Sleep disorders
- Behavioural crises
- Social interaction
- Communication

In total, over 2,250 assessment points will be analysed through the landmark study.

Study Outcomes to date:

- Demonstrated safety and tolerability across the dosing regimen.
- No Serious Adverse Events (SAEs) reported.
- Patients are showing positive trends and improvements compared to their baseline assessments measured at the commencement of the trial.
- Improvements were observed with trial patients in key behavioural indicators related to irritability, social interaction, mood and communication.
- The improvements were unique to each trial participant given the complexities of how ASD affects children.

The rigorous clinical study design involves assessments and feedback from the neuropsychologist monitoring trial participants, the parents/carers, and the participants themselves. Most importantly, parental/carer observations cite consistent improvement in the trial participant's 'overall functioning' when compared to baseline at the commencement of the trial.

Specific instances of markedly improved behaviours (i.e. reduction in fear, agitation and anxiety) are being further investigated to fully assess and understand the positive neuro-psychological impact of NTI164 treatment in these patients. This research along with further data assessment from the Trial will be completed in Q2. These key areas of neuro-behavioural change will be the key focus of the upcoming drug registration trials due to commence in Q3 calendar 2022.

The only drug currently approved by the FDA for children with ASD is Risperidone. Prescribed for children to assist with irritability, common side effects include headaches, drowsiness, anxiety and uncontrollable muscle movements. Given the NTI trial results showed no serious adverse side effects and high patient compliance, we believe the Company is very well placed to make significant inroads into the ASD treatment market expected to be around US$5.5bn by 2028*.

"We are very pleased with the landmark results from our world first trial. NTI has the potential to introduce to the market a treatment option for paediatric ASD which is natural, safe and based on the results to date, offers positive behavioural improvements in ASD," said Company Chairman Brian Leedman. "We will move quickly to a Phase II/III drug registration trial, initiate TGA and FDA pathways and expedite strategic partner discussions."

Newly appointed CEO, Dr Alexandra Andrews said, "The Company has accelerated its commercial discussions with several strategic pharmaceutical companies who have been following the trial's progress. What cannot be underestimated is the application of our full spectrum strain to other neurological disorders which will now be accelerated considering the current ASD results."

**https://www.globenewswire.com/news-release/2021/12/14/2351376/0/en/Autism-Spectrum-Disorder-Therapeutics-Market-Size-2021-2028-is-Expected-to-be-Worth-USD-5-15-Billion.html)*

The Company has initiated discussions with the Therapeutics Good Administration (TGA) to assess product scheduling and classification for the Australian Market. In collaboration with regulatory experts, the Company is now mapping out a full regulatory development roadmap/pathway for the registration and commercialisation of NTI164 for ASD and other neurological indications. The Company has initiated pre-IND (Investigational New Drug) discussions with the FDA and is the process of developing a clear roadmap for product registration and commercial development in the USA.

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

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About Neurotech

Neurotech International Limited is a medical device and solutions company conducting clinical studies to assess the neuro-protective, anti-inflammatory and neuro-modulatory activities of our proprietary NTI/Dolce cannabis strains. Neurotech has submitted key provisional patents relating to the composition and use of NTI164 for the treatment of a range of neurological disorders including ASD. 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 and Mente Autism please visit http://www.neurotechinternational.com

APPENDIX - Study Details

This study is conducted in accordance with this protocol, ICH GCP guidelines, federal and local governing regulatory requirements and laws and in accordance with HREC guidelines.

Title: Phase I/II Open – Label Study to Evaluate the Safety and Efficacy of Orally Administered Full-Spectrum Medicinal Cannabis Plant Extract (0.08% THC) – NTI164 in Children with Autism Spectrum Disorder.

Site: Monash Children's Hospital
Clayton, Melbourne Victoria.

Study Population: Aged between 8 to 17 years old population that have a medical diagnosis of Level 2 or 3 Autism Spectrum Disorder (ASD) as confirmed by the Autism Diagnostic Observational Schedule (ADOS-2) criteria.

Subject 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 to 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.

Subject 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 Å~ upper limit of normal (ULN) or total bilirubin (TBL) > 2 Å~ 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 ≥ 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.

Assessments of efficacy:

Efficacy will be monitored and measured through parent/carer and physician questionnaires.

The secondary outcomes measures listed below will be used to assess potential improvements of:

- Irritability
- Hyperactivity
- Mood
- Self-stimulation
- Sleep disorders
- Seizures
- Behavioural Crises
- Social Interaction
- Communication

Secondary Endpoints

1. 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).

2. 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.

3. 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.

4. 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.

5. Autism Family Experience Questionnaire (AFEQ)
Parent/Caregiver form used to measure impact of autism interventions on family experience and quality of life. Items are rated on a 5-point scale where 1=always and 5=never.

6. Anxiety Scale for Children - Autism Spectrum Disorder - Parent Versions (ASCASD-P)
Parent/Caregiver 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.

7. Anxiety Scale for Children - Autism Spectrum Disorder (ASC-ASD-C) - Child
Versions

Child 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.

8. The Child Behaviour Checklist for Ages 8 – 17 (CBCL)
A parent/carer measure to assess patterns of behaviour. The measure is a Likert scale rated over 3 or 4 points.

9. Caregiver 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. Provided as Baseline and Post- Baseline questionnaires.

10. Caregiver 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.

11. Clinical Global Impression Scale -Improvement (CGI-I)
This is a 7-point scale measuring symptom change from baseline. Provided as baseline and post-baseline Caregiver and Clinician questionnaires.

12. 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.