

Neurotech Receives HREC Approval for Phase I/II Clinical Trial in Rett Syndrome

Neurotech International Limited (ASX: NTI) ("Neurotech" or "the Company"), a clinical-stage biopharmaceutical development company focused predominately on paediatric neurological disorders, today announces 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 investigating the use of NTI164 in female Rett Syndrome patients.

The trial will be conducted across three centres in Australia with Principal Investigator Associate Professor Carolyn Ellaway, Senior Staff Specialist NSW Genetic Metabolic Disorders Service, the Sydney Children's Hospital Network and Metabolic Genetics at The Children's Hospital at Westmead and Associate Principal Investigators Professor Michael Fahey, Head of the Paediatric Neurology Unit at Monash Medical Centre, Director of Neurogenetics and Dr Giuliana Antolovich, Department of Neurodevelopment & Disability, Royal Children's Hospital Melbourne.

Dr Thomas Duthy, Executive Director of Neurotech International said "We are pleased to have received HREC approval following our submission in early April. Rett Syndrome is the second leading cause of intellectual disability in girls, with an urgent medical need to develop safe and effective therapies to treat this progressive neurological disease. With its positive effects on neuroinflammation, we believe NTI164 could represent an effective intervention in Rett Syndrome, where mutations in the MECP2 gene are known to exacerbate neuroinflammation.¹"

Associate Professor Carolyn Ellaway commented "Girls who suffer from Rett Syndrome require continued supportive care, with the disease negatively impacting their quality of life and activities of daily living. Despite recent advances in the field, as a clinician who has witnessed first hand the impact of this progressive disorder on my patients, I am very excited to be involved with this clinical trial which will assess safety, tolerability and effectiveness of daily oral NTI164 in these girls. We certainly look forward to the results of the study following 12 weeks of initial treatment."

The Phase II clinical trial will examine the effects of daily oral treatment of NTI164 and is targeting the recruitment of 14 Rett Syndrome patients initially. The proposed primary endpoint at 12 weeks of treatment is an improvement from baseline in the Clinical Global Impression Scale - Improvement (CGI-I). Key secondary endpoints include safety, adverse events and measures associated with hand function, motor skills, communication, and quality of life.

If successful, the Company will follow with a 14-week double-blind, randomised, placebo-controlled Phase II in 34 participants to determine further efficacy and safety, which will require a separate HREC submission and approval.

Patient recruitment is expected to commence in early Q3 CY2023. The preliminary (top-line) results of the trial are anticipated in Q1 CY2024.

The Phase II clinical trial has been registered on the Australian New Zealand Clinical Trials Registry (ANZCTR) under registration number: ACTRN 12623000563662.

¹ <https://www.nature.com/articles/s41598-021-90517-8>

A summary of the Trial is attached as Appendix 1.

Rett Syndrome is a rare genetic neurological and developmental disorder and is almost exclusively the result of a mutation(s) in the methyl CpG binding protein 2 (MECP2) gene located on the X chromosome, which is required for normal brain development and function. Rett Syndrome occurs almost exclusively in girls, with incidence of one in 10,000 female live births. The prevalence is approximately 15,000 girls and women in the US and 350,000 globally.²

Authority

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

Further Information

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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, 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>.

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 Rett Syndrome

Rett Syndrome is a rare genetic neurological and developmental disorder and is almost exclusively the result of a mutation(s) in the methyl CpG binding protein 2 (MECP2) gene located on the X chromosome, which is required for normal brain development and function. Rett Syndrome occurs almost exclusively in girls compared to boys (mostly fatal within one year of birth), with incidence of approximately 1 in 10,000 female live births across all racial and ethnic groups worldwide. According

² <https://reverserett.org/about-rett-syndrome/>

to the Rett Syndrome Research Trust, the prevalence is approximately 15,000 girls and women in the US and 350,000 globally.

Rett syndrome is characterized by typical early normal development between 7-18 months after birth, followed by a slowing of development, loss of functional use of the hands, distinctive hand movements along with difficulty walking, communicating, irritability and seizures. There is currently no cure for Rett Syndrome and no approved therapies. Current treatments only address symptoms and provide support that may improve movement, communication and social participation into adulthood.

About NTIRTT1

The NTIRTT1 Phase II clinical trial will examine the effects of daily oral treatment of NTI164 and is targeting the recruitment of 14 Rett Syndrome patients initially. The trial will be an open-label, exploratory study, over 16 weeks of treatment with NTI164 at the maximum tolerated dose or 20mg/kg/day. The primary endpoint at 12 weeks of treatment is the change in Clinical Global Impression Scale-Improvement (CGI-I). Key secondary endpoints include the Rett Syndrome: Symptom Index Score (RTT-SIS), Rett Syndrome Behaviour Questionnaire (RSBQ), RTT- Clinician Domain Specific Concerns – Visual Analog Scale (RTT-DSC-VAS), Communication and Symbolic Behaviour Scales Developmental Profile™ Infant-Toddler Checklist (CSBS-DP-IT Social), Impact of Childhood Neurological Disability Scale (ICND), RTT Caregiver Burden Inventory (RTT-CBI), Overall Quality of Life Rating of the Impact of Childhood Neurological Disability Scale (ICND-QoL) and improvement in the three domains of the Clinical Global Impression Scale – Severity (CGI-S), Severity of Illness, Global Improvement and Therapeutic Effect.

If successful, the Company will follow with a 14-week double-blind, randomised, placebo-controlled Phase II in 34 participants to determine further efficacy and safety, which will be subject to a second HREC filing and approval.

Appendix 1 – NTIRT1 Clinical Trial Summary

Title of Study

A Phase I/II study to assess the safety and efficacy of full-spectrum medicinal cannabis plant extract 0.08% THC (NTI164) in the treatment of Rett syndrome (RTT)

Investigators

Associate Professor Carolyn Ellaway, Senior Staff Specialist NSW Genetic Metabolic Disorders Service, the Sydney Children's Hospital Network and Metabolic Genetics at The Children's Hospital at Westmead (Principal)

Professor Michael Fahey, Head of the Paediatric Neurology Unit at Monash Medical Centre, Director of Neurogenetics (Associate)

Dr Giuliana Antolovich, Department of Neurodevelopment & Disability, Royal Children's Hospital Melbourne (Associate)

Treatments

The study involves the following phases:

- Baseline/Up-titration phase: Children will receive a baseline dose of 5mg/kg/day of NTI164 that 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: Children will receive the maximum tolerated dose daily or 20mg/kg/day for an 8-week period.
- Down-titration phase: At the end of the Treatment Phase, children will receive a dosage that will be gradually decreased by 5mg/kg/week for a period of 4 weeks until the end of the study.

Adherence to intervention will be monitored by drug product return accountability, completion of online drug administration forms and study-specific questionnaires.

Primary Endpoints

Change in Clinical Global Impression

Baseline (pre-dose), 4, 12 & 16 weeks post-commencement of treatment.

Secondary Endpoints

Rett Syndrome: Symptom Index Score (RTT-SIS)

Rett Syndrome Behaviour Questionnaire (RSBQ)

RTT- Clinician Domain Specific Concerns – Visual Analog Scale (RTT-DSC-VAS)

Communication and Symbolic Behaviour Scales Developmental Profile™ Infant-Toddler Checklist (CSBS-DP-IT Social)

Impact of Childhood Neurological Disability Scale (ICND)

RTT Caregiver Burden Inventory (RTT-CBI)

Overall Quality of Life Rating of the Impact of Childhood Neurological Disability Scale (ICND-QoL)

Improvement in the three domains of the Clinical Global Impression Scale – Severity (CGI-S), Severity of Illness, Global Improvement and Therapeutic Effect

Safety

Safety will be monitored and measured by full blood examination, liver and renal function to monitor safety.

Summary Inclusion Criteria

Girls and women, aged 5-20 years

Weight greater than or equal to 12kg

Classical/typical RTT

Documented disease-causing mutation in MECP2 gene

At least 6 months post regression at screening (ie. no loss or degradation in ambulation, hand function, speech, nonverbal communicative or social skills within 6 months of screening)

Rett Syndrome Clinical Severity Scale rating of 10-36

CGI score of 4 or higher.

Stable pattern of seizures, or has had no seizures, within 8 weeks of screening.

Summary Exclusion Criteria

Current clinically significant cardiovascular, endocrine (such as hypo- or hyperthyroidism, type 1 diabetes, or uncontrolled type 2 diabetes), renal, hepatic, respiratory, or gastrointestinal disease (such as celiac disease or inflammatory bowel disease), or major surgery planned during the study.

Known history or symptoms of long QT syndrome.

QTcF interval greater than 450 ms, history of risk factor for torsades de pointes or clinically significant QT prolongation deemed to increase risk.

Treatment with insulin, IGF-1, or growth hormone within 12 weeks of baseline.

Currently receiving treatment with DAYBUE (trofinetide)

Currently using other unregistered drugs for Rett, such as Anavex.

Currently using or has used recreational or medicinal cannabis, cannabinoid-based medications (including Sativex® and Epidiolex®) within the 12 weeks prior to screening and is unwilling to abstain for duration of the trial.

Patient has known or suspected hypersensitivity to cannabinoids or any of the excipients.