Neurotech Reports Positive Top-Line Phase I/II Rett Syndrome Clinical Trial Results

Key Points:

- **NTIRTT1 is the first clinical trial to show a statistically significant clinical improvement in Rett Syndrome patients (n=14) with a broad-spectrum cannabinoid drug therapy (NTI164)**
- **Primary endpoint of Clinical Global Impression – Improvement (CGI-I) at 12 weeks versus baseline was met; mean improvement of -0.3, (p=0.04)**
- **CGI-I compares favourably to the only FDA approved Rett Syndrome drug DAYBUE™ (trofinetide) Phase 3 CGI-I data vs placebo in Rett -0.3, 8% improvement (p=0.003)**
- **All 14 girls completed 12 weeks of daily oral treatment with NTI164, all extended to 52 weeks**
- **Third neurological disorder in children where NTI164 has shown a statistically significant clinical benefit, alongside autism and PANDAS/PANS[1]**
- **Data collection is ongoing with additional analysis on primary endpoint, key secondary endpoints and safety to be available in the next 2-4 weeks**

Neurotech International Limited (ASX: NTI) ("Neurotech" or "the Company"), a clinical-stage biopharmaceutical development company focused predominately on paediatric neurological disorders, today is pleased to report top-line clinical efficacy and safety results for 14 female paediatric patients who completed 12 weeks of daily oral treatment with NTI164 under the Company's Phase I/II clinical trial investigating the use of NTI164 in Rett Syndrome. The NTIRTT1 clinical trial was designed to examine safety, and gold standard measures of clinical symptoms associated with Rett Syndrome at 12 weeks of daily oral NTI164 treatment compared to baseline measures. Initial primary endpoint analysis has shown a statistically significant difference (improvement) in CGI-1 at 12 weeks versus baseline measures; mean difference of -0.3 (p=0.04). A decrease in CGI-I score indicates improvement.

Dr Thomas Duthy, Executive Director of Neurotech International said *"We warmly congratulate our 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 on these world-first results and the participation of her Rett Syndrome patients and families. There remains an urgent need for more safe and effective therapies in Rett Syndrome. Data analysis and interpretation continues, and we are very much looking forward to finalising and reporting further detailed clinical findings over the next 2-4 weeks and thereafter presenting this data at a major scientific meeting."*

Clinical Global Impression (CGI) - is a physician/observer-rated scale synthesizing the clinician's impression of the global state of an individual & frequently employed in clinical trials for neuropsychiatric disorders. CGI- Improvement (CGI-I) is a 7-point scale that requires the clinician to assess how much the patient's illness has improved or worsened relative to a baseline state at the beginning of the intervention and ranges from 1 – "Very Much Improved" to 7 - "Very Much Worse". CGI-I was a co-primary endpoint in the registration Phase III clinical trial ("LAVENDAR") of DAYBUE™ (trofinetide), the first Rett Syndrome therapy approved by the FDA in March 2023; developed by Neuren Pharmaceuticals (ASX:NEU) and Acadia Pharmaceuticals (NASDAQ:ACAD) and showed a CGI-I improvement of -0.3 (8% improvement) in the trofinetide arm versus placebo (p=0.003).[2]

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.[1] The market is estimated at over US$2 billion annually.[2]

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 with a broad-spectrum oral cannabinoid drug therapy called NTI164. Neurotech has completed a Phase II/III randomised, double-blind, placebo-controlled clinical trial in Autism Spectrum Disorder (ASD) with clinically meaningful and statistically significant benefits reported across a number of clinically-validated measures and excellent safety. In addition, Neurotech has completed and reported statistically significant and clinically meaningful Phase I/II trials in ASD and Paediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS) and Paediatric Acute-Onset Neuropsychiatric Syndrome (PANS), collectively PANDAS/PANS along with Rett Syndrome. Neurotech has received human ethics committee clearance for a Phase I/II clinical trial in spastic cerebral palsy.

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

[1] https://reverserett.org/about-rett-syndrome/
[2] https://www.livewiremarkets.com/wires/a-de-risked-biotech-with-4x-upside

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 I/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.

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

[1] Paediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS) and Paediatric Acute-Onset Neuropsychiatric Syndrome (PANS)

[2] Neul, J.L. et al. Trofinetide for the treatment of Rett syndrome: a randomized phase 3 study. Nat Med 29, 1468–1475 (2023).

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