Neurotech Reports Significant Clinical Benefits and Safety in Phase I/II Rett Syndrome Clinical Trial

Key Points:

- **Further primary endpoint and secondary endpoint analysis on Neurotech's NTIRTT1 trial has highlighted significant additional benefits in Rett Syndrome girls (n=14) after 12 weeks of daily oral treatment with Neurotech's broad-spectrum cannabinoid drug therapy (NTI164)**
- **Clinical Global Impression – Improvement (CGI-I) at 12 weeks versus baseline on four core Rett-anchors highlighted 93% of patients (pts) improved with 36% "very much/much improved" (p=0.001)**
- **Key secondary endpoint, the Rett Syndrome Behavioural Questionnaire (RSBQ) showed a mean difference of -13.4 versus baseline (p<0.001) and a 205% improvement from week 4 to week 12**
- **A single serious adverse event recorded over 12 weeks of treatment (urticaria); adverse events were minimal and manageable (0% pts with diarrhoea, 14% pts vomiting, 0% pts with weight loss)**
- **All 14 girls extended to 52 weeks, with ongoing data to be collected and reported**

INVESTOR WEBINAR TODAY AT 12.00pm AEST DETAILS BELOW

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 further clinical efficacy and the 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 Company reported initial 'top-line' results on 17 April 2024, which showed a clinically significant, statistical improvement in CGI-I, the primary endpoint.

Associate Professor Carolyn Ellaway, Principal Investigator of the NTIRTT1 Clinical Trial, Senior Staff Specialist, The Children's Hospital at Westmead, Sydney Children's Hospital Network said *"The NTIRTT1 clinical trial is the first time a broad-spectrum cannabinoid drug therapy (NTI164) has demonstrated significant patient improvements in Rett Syndrome using validated clinical measures including CGI-I and RSBQ. Our data is very encouraging as we have observed clinically meaningful improvements in those symptoms repeatedly deemed as most important for treating clinicians, caregivers and patients; notably communication, hand behaviours, anxiety/mood and quality of life. These benefits have not compromised patient safety, with NTI164 displaying an excellent safety profile over the 12 weeks of the trial."*

Dr Thomas Duthy, Executive Director of Neurotech International said *"This fulsome data set reported today represents a very rapid translation of our strong conviction on the anti-neuroinflammatory and neuroprotective effects of NTI164 applied to a third paediatric neurological population, Rett Syndrome, where safe and effective therapies are urgently needed. We thank A/Prof Ellaway and her patients and families for their participation in this world first trial. The level of improvement we have observed in these girls after 12 weeks of treatment is remarkable in the context of the excellent safety profile of NTI164 where just a single serious event recorded and adverse events were minor and manageable relative to the observed standard therapy in the United States. We look forward to updating the market on these girls' progress as they progress through the 52 week extension under A/Prof Ellaway's supervision and presentation of these results at the upcoming 9th World Rett Congress, to be held in Australia later this year."*

A caregiver of a patient in the NTIRTT1 trial commented *"She seems much more in tune to what's going on around her, e.g. patting the dog (has NEVER done this before)."*

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Another caregiver of a patient in the NTIRTT1 said *"She uses eye pointing, sometimes brings food / drink to an adult - this has not happened before."*

Baseline Patient Characteristics

A total of fourteen (n=14) patients completed daily treatment of NTI164 /placebo for the full duration of the twelve (12) week trial period required for primary endpoint analysis. The average age was 8.8 years, weight of 27.5 kg, with RSBQ mean baseline measure of 44.6 and CGI- severity of illness (CGI-S) measure of 4.6.

Clinical Results – Efficacy

Neurotech is pleased to report additional statistically significant and clinically meaningful benefits of NTI164 across multiple Rett-specific assessments (including secondary endpoints). The Company is now able to provide further detailed information on the primary endpoint.

Primary Endpoint – CGI-I

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". A decrease in CGI-I score indicates improvement.

Initial top-line primary endpoint analysis reported on 17 April 2024 showed a statistically significant difference (improvement) in CGI-1 at 12 weeks versus baseline measures; mean difference of -0.3 (p=0.04). The top-line CGI-I results were based on analysis available on four (4) Rett-specific assessments (anchors) from a total of nine (9) Rett-specific measures. As this was a first in human study of NTI164 in Rett, Neurotech examined a large number of anchors (sub-domains) to further understand which important sub-domains benefits NTI164 improved that could be targeted in registration-directed trials. In late-stage clinical trials, typically 2-3 sub-domains are typically examined for CGI-I.

Rett-Specific Anchors	Top-line	Full
Communication		✓
Mental Alertness		✓
Hand Use		✓
Socialisation Eye Contact		✓
Alertiveness	✓	✓
Anxiety	✓	✓
Autonomic	✓	✓
Seizure Activity	✓	✓
Sleep		✓

With the complete data set now available for analysis, Neurotech is pleased to report **further improvement in CGI-I versus baseline with a mean difference of - 0.4 (95% Confidence Interval (CI) -0.112, -0.681; p = 0.009) across all nine Rett-specific measures.**

Of the 14 Rett Syndrome patients, as measured by CGI-I across all nine, **50% of patients showed Improvement** at 12 weeks with NTI164. **50% were minimally improved**, 43% showed no change and 1 patient (7%) was minimally worse.

	Very Much Improved	Much Improved	Minimally Improved	No Change	Minimally Worse	Much Worse	Very Much Worse
Scale	1	2	3	4	5	6	7
NTI164 (week 4)	0 (0%)	0 (0%)	6 (43%)	7 (50%)	1 (7%)	0 (0%)	0 (0%)
NTI164 (week 12)	0 (0%)	0 (0%)	7 (50%)	6 (43%)	1 (7%)	0(0%)	0 (0%)

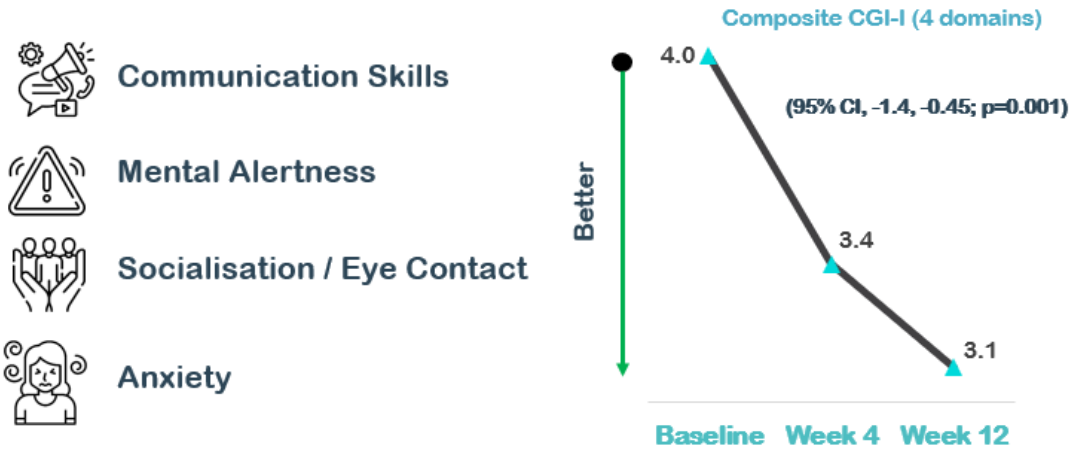
All 9 Rett-Specific Anchors

The Company has undertaken an analysis of those specific sub-domains cited by doctors, caregivers as important and where NTI164 showed strong improvements. Neurotech has shown significant improvements

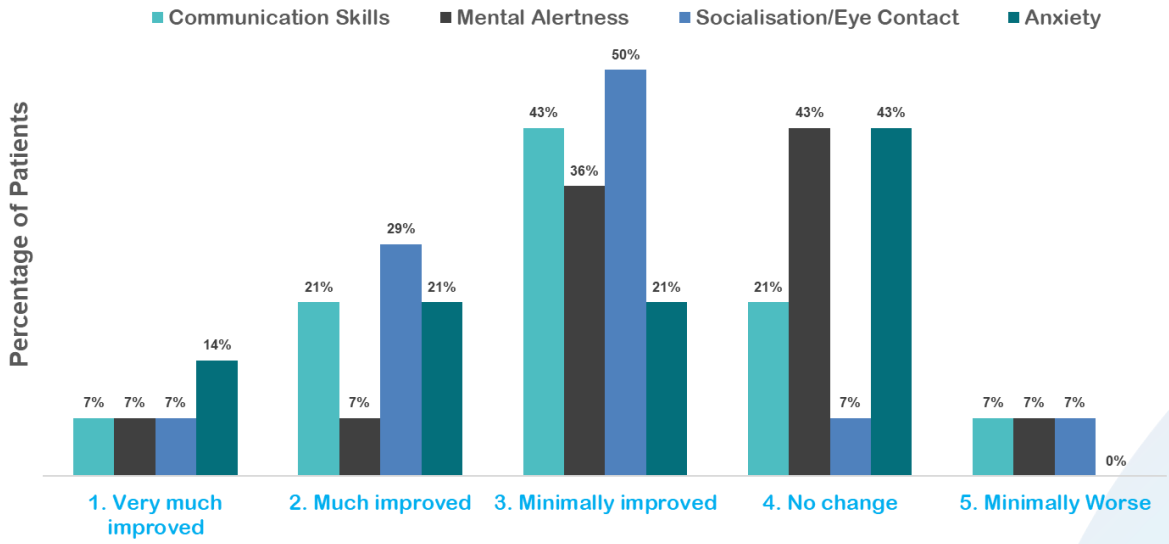
in Communication Skills, Mental Alertness, Socialisation / Eye Contact and Anxiety – which will likely form the basis of CGI-I measures for registration-directed studies.

The data showed a composite score for CGI-I (4 core domains per above) improved 23% at 12 weeks (p=0.001). **93% of patients showed Improvement at 12 weeks with NTI164; 57% were minimally improved, 29% much improved and 7% very much improved.** One patient (7%) showed no change on these four core measures.

	Very Much Improved	Much Improved	Minimally Improved	No Change	Minimally Worse	Much Worse	Very Much Worse
Scale	1	2	3	4	5	6	7
NTI164 (week 12)	1 (7%)	4 (29%)	8 (57%)	1 (7%)	0 (0%)	0 (0%)	0 (0%)



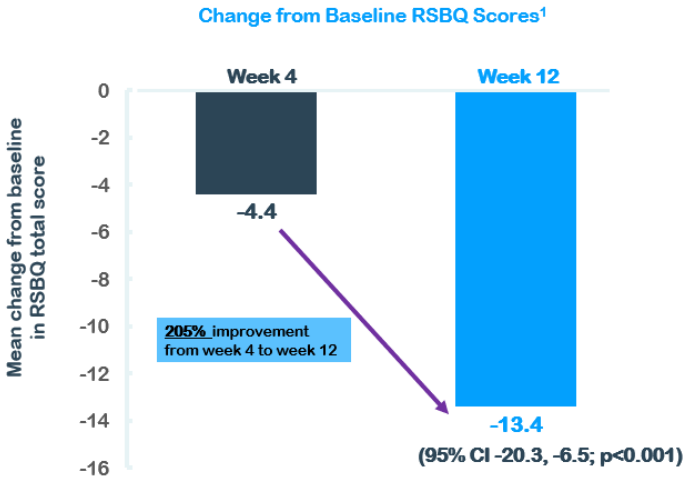
The individual measures of CGI-I in the four core composite measures at 12 weeks is shown below, all of which were statistically significant: Communication Skills (mean difference -1.0, p=0.003), Mental Alertness (mean difference -0.64, p=0.03), Socialisation/ Eye Contact (mean difference -1.2, p<0.001) and Anxiety (mean difference -1.1, p=0.004).



Secondary Endpoint - RSBQ

RSBQ consists of 45 items, rated as 0 = 'not true',1 = 'somewhat or sometimes true' or 2 = 'very true', that can be grouped into eight symptom domain subscales graded on a scale of 0–90 (maximum severity). 8 domains/subscales that reflect the core features of Rett were examined: General Mood; Breathing Problems; Hand Behaviours; Repetitive Face Movements; Body Rocking and Expressionless Face; Nighttime Behaviours; Fear/Anxiety; and Walking/Standing.

The NTIRTT1 trial showed patients receiving **NTI164 showed a 205% improvement in their mean baseline change from week 4 (-4.4) to week 12 (-13.4)**. Overall, **a clinically meaningful 30% decrease in the patients' mean RSBQ total score at 12 weeks was seen (mean difference -13.4; 95% CI -20.3, -6.5), which was strongly statistically significant (p<0.001)**. At commencement the average RSBQ total score for the patients was 44.6 compared to 31.2 at 12 weeks.



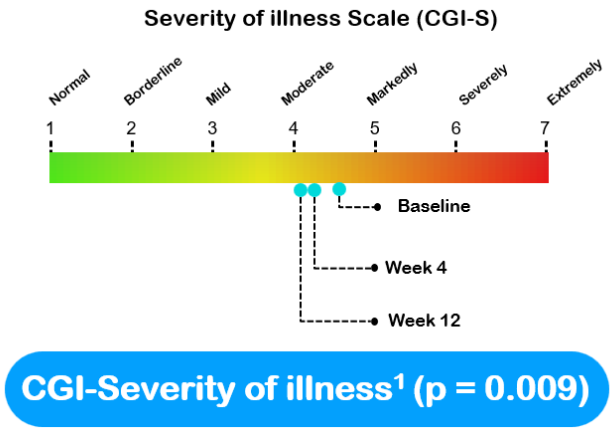
RSBQ Sub Domain Scores

Measure	12 weeks mean diff.	P value
Mood	-4.6	0.001
Breathing	-0.4	0.233
Hands	-2.0	<0.001
Face	-0.8	0.009
Body Rocking	-2.0	0.042
Nighttime	-1.0	0.161
Fear/Anxiety	-1.8	0.02
Walk/Stand	-0.8	0.104

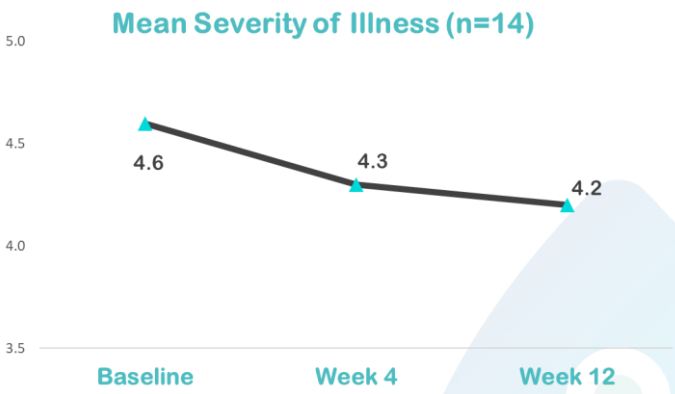
In addition NTI164 showed a significant improvement in RSBQ sub domains relating to General Mood, Hand Behaviours, Repetitive Face Movements, Body Rocking and Expressionless Face and Fear/Anxiety.

Secondary Endpoint – CGI-S

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. **There was a statistically significant improvement of -0.4 (8.7%) observed using the CGI-S scale (95% CI; -0.68, -0.12) at 12 weeks versus baseline (p=0.009).**



CGI-Severity of illness[1] (p = 0.009)



Other Secondary Endpoints

Impact of Childhood Neurologic Disability Scale (ICNDS) measures the impact that a child's condition has on the child's and the family's everyday life at the time of assessment and during the previous 3 months. It is an accurate, quick measurement tool reflecting the impact of behaviour, cognitive learning ability, physical/neurologic disability, and epilepsy on children and their families (0 = no impact, 132 = severe impact). After 12 weeks of treatment, NTI164 showed a statistically significant improvement in ICNDS versus baseline (p=0.004).

ICNDS-QoL measures the overall quality of life of the affected individual (1 – poor, 6 –excellent). After 12 weeks of treatment, patients saw a statistically significant improvement in their quality of life versus baseline (p<0.001).

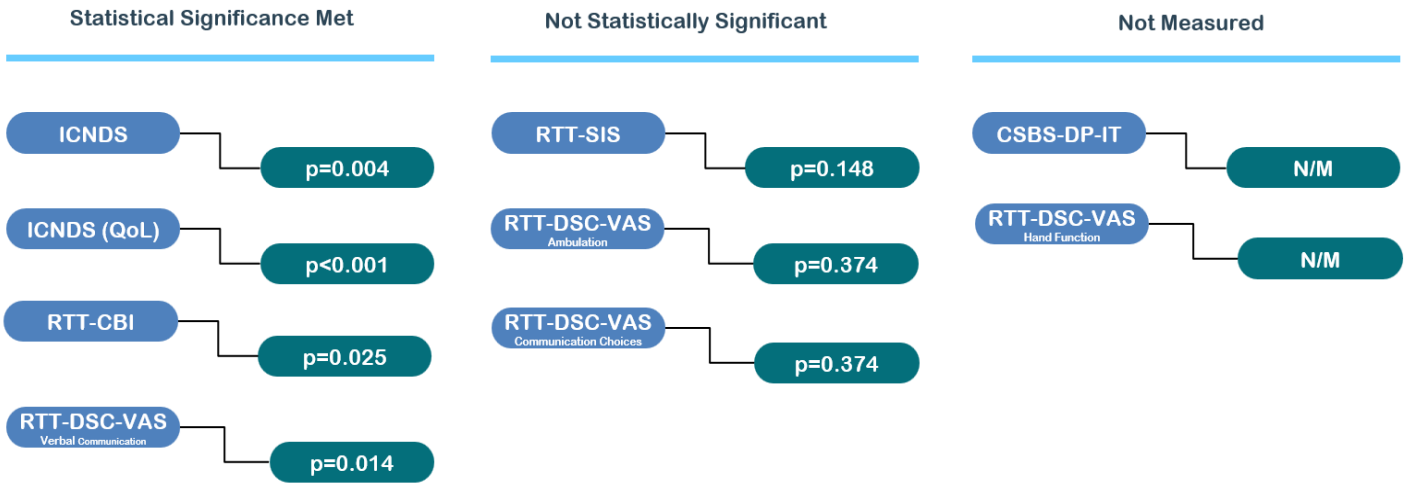
Rett Syndrome Caregiver Burden Inventory (RTT-CBI) is a syndrome-specific, caregiver-completed questionnaire that is based on the CBI designed for Alzheimer's disease (0= never, 5 = nearly always). RTT CIA represents a reliable and valid measure, providing a needed metric of caregiver burden in Rett Syndrome. After 12 weeks of treatment, NTI164 showed a statistically significant improvement in RTT-CBI versus baseline (p=0.025).

RTT-Clinician Domain Specific Concerns-Visual Analog Scale (RTT-DSC-VAS) is a clinician-completed VAS assessing the severity of concerns specific to Rett Syndrome: (1) hand function; (2) ambulation; (3) communication choices and (4) verbal communication. The four ratings are stand-alone measures and not intended to be combined for a total score.

After 12 weeks of treatment, NTI164 showed a statistically significant improvement in verbal communication versus baseline (p=0.014). The other measures were not significant or not measurable (N/M).

The Rett Syndrome Symptom Index Score (RTT-SIS) was developed by A/Professor Ellaway and examines 16 Rett-specific symptoms. There was no significant change in total score observed at 12 weeks versus baseline (p=0.148).

As patients enrolled into the trial were over 2 years of age, the Communication and Symbolic Behaviour Scales Developmental Profile™ Infant-Toddler Checklist (CSBS-DP-IT) assessment was not utilised (N/M).



Safety

One serious adverse event was reported during the 12 week treatment period, relating to the development of urticaria (hives) in one girl. Urticaria has not been previously observed in any previous and ongoing studies of NTI164.

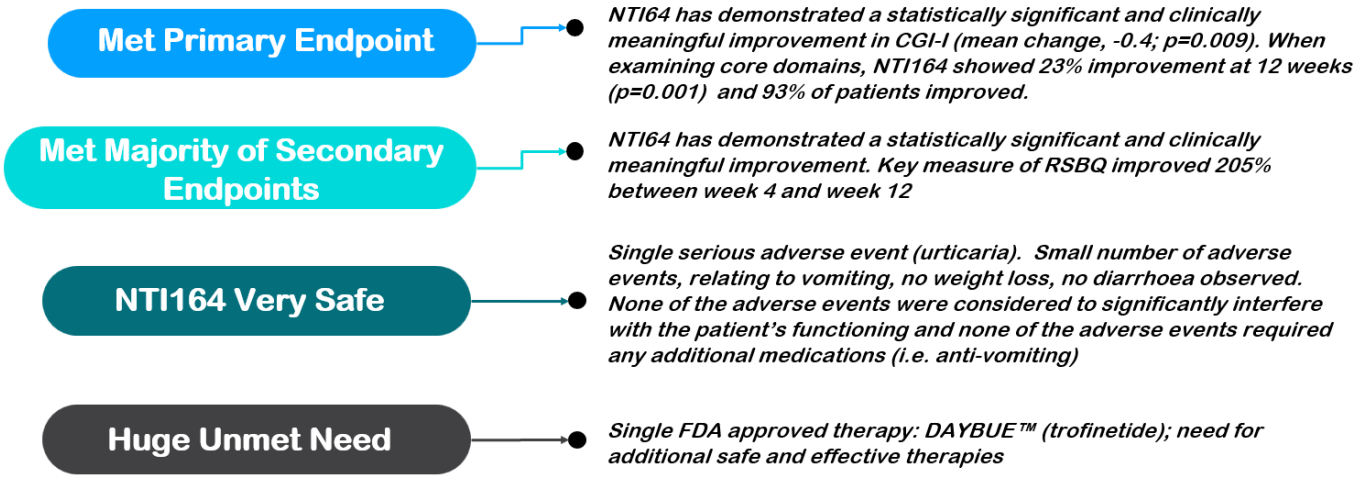
Zero patients (0%) reported diarrhoea, nausea/vomiting occurred in two patients (14%). Mean weight (kg) was largely unchanged at 12 weeks (0.3 kg gain) versus baseline, indicating overall no weight loss during the treatment period. None of the adverse events required any additional medications (i.e. anti-vomiting, medications).

Measurements pertaining to kidney and liver function along with blood chemistries and vital signs were normal over the 12 weeks. No reportable events occurred.

In conclusion, for a chronically administered (daily) oral intervention, NTI164 exhibits an excellent safety profile and minimal patient-specific side-effects in Rett Syndrome patients.

Conclusion

Neurotech thanks Associate Professor Ellaway and all participants who participated in the NTIRTT1 clinical trial and who are currently in the 52 week extension phase of the trial. The clinical benefits, coupled with the very clean safety profile means the development of NTI164 for Rett Syndrome will be accelerated wherever possible. A further registration-directed clinical trial is under consideration and further regulatory advice will be sought.



Investor Webinar

Executive Director Dr Thomas Duthy will present at **12pm AEST today**.

Shareholders, investors and interested parties are encouraged to register to attend the presentation at the following link: https://us02web.zoom.us/webinar/register/WN_rDhlblzVSaahJ6IXTspJAw

A recording will be available at the above link shortly after the conclusion of the live session, and the replay will also be available via the Company's website and social media channels. Questions can be submitted in advance to matt@nwrcommunications.com.au.

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.

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 one approved therapy in the United States. 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 examined the effects of daily oral treatment of NTI164 with 14 Rett Syndrome patients initially. The trial was 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 Behaviour Questionnaire (RSBQ), Rett Syndrome: Symptom Index Score (RTT-SIS), 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 Clinical Global Impression Scale – Severity (CGI-S).

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