Rett Syndrome Patients Show Further Clinical Improvement After 20 Weeks of NTI164 Treatment

Key Points:

- **Further significant clinical improvements observed in Rett Syndrome patients after 20 weeks of daily oral treatment with Neurotech's broad-spectrum cannabinoid drug therapy NTI164**
- **Continued clinical improvement at 20 weeks (versus baseline) on four core Rett-domain anchors with 100% of patients (pts) improved (p<0.001) vs. 93% at wk 12 with 57% of pts "very much/much improved" (vs. 36% at wk 12)**
- **Gold standard RSBQ measure of key Rett symptoms showed an improvement of 24% versus baseline (p<0.001), with no further improvement from week 12 to week 20 (p=0.08)**
- **No diarrhoea, vomiting/nausea reported from 12 to 20 weeks and no weight loss with all 14 pts who commenced the Phase I/II clinical trial remaining on treatment**
- **Durable clinical response, coupled with excellent safety provides strong rationale for long term administration of NTI164 for Rett Syndrome patients where new treatments are urgently required**

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 all 14 female paediatric patients who have now completed 20 weeks of daily oral treatment with NTI164 under the Company's one year extension period of the Phase I/II clinical trial investigating the use of NTI164 in Rett Syndrome.

Dr Thomas Duthy, Executive Director of Neurotech International said *"We are pleased to see these patients continue to do very well on extended treatment with NTI164, with zero safety events recorded relating to diarrhoea and nausea/vomiting from week 12 to week 20 with zero weight loss recorded. Our safety and efficacy to 20 weeks is trending favourably when compared to the current FDA approved treatment, DAYBUE™ (trofinetide). Rett Syndrome represents an attractive market opportunity for NTI164, with a potential annual market opportunity of approximately US$2.0 billion. We are currently working with our clinical advisors and Professor Ellaway (our newly appointed Chief Medical Officer) on the design of a registration directed Phase III clinical trial."*

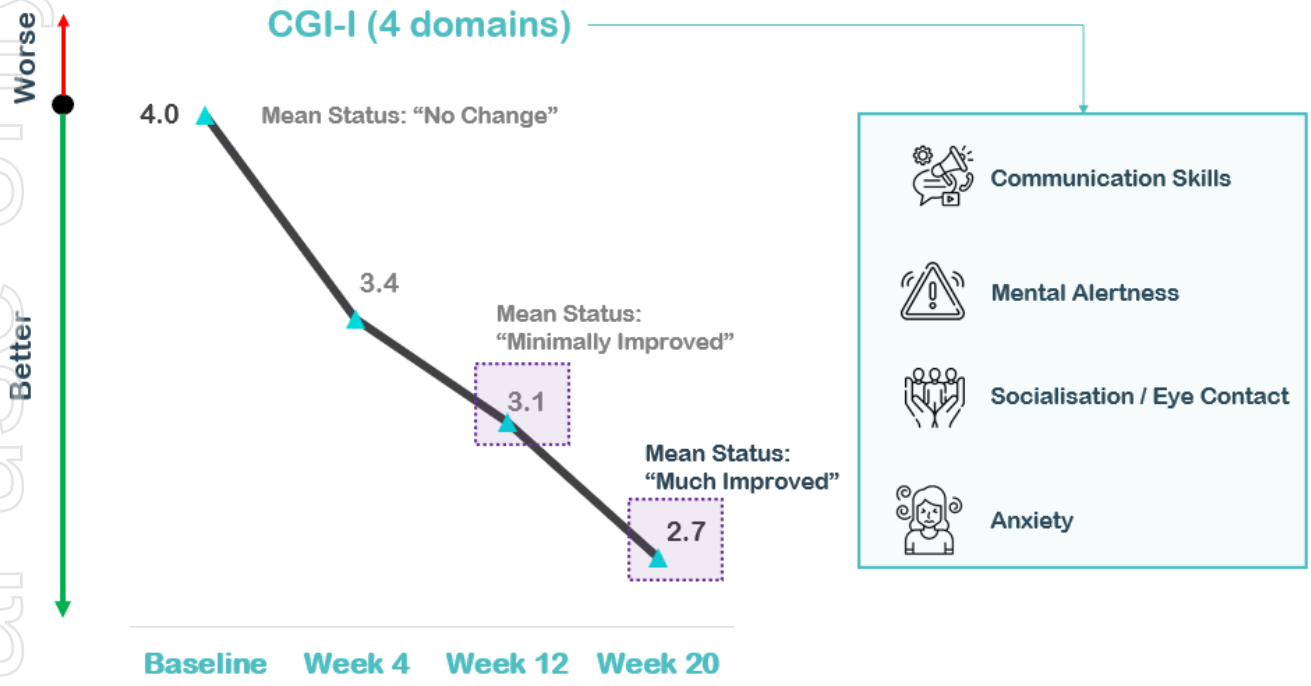
A caregiver of a patient in the NTIRTT1 trial commented after 20 weeks of treatment with NTI164 *"Increased use of eye gaze technology and increased ability to use the eye gaze accurately when making choices."*

Clinical Improvement Continues on NTI164

Clinical improvement was assessed by the clinician using the gold standard, Clinical Global Impression - Improvement (CGI-I), which measures how much the patient's illness has improved or worsened relative to a baseline state at the beginning of NTI164 treatment and ranges from 1 – "Very Much Improved" to 7 - "Very Much Worse". A decrease in CGI-I score indicates improvement. Based on the CGI-I primary endpoint at 12 weeks Neurotech has four core domains of interest – communication skills, mental alertness, socialisation/eye contact and anxiety – which will likely form the basis of the CGI-I measures required for a registration-directed Phase III clinical trial of NTI164 versus placebo.

There was a statistically significant difference (improvement) in CGI-I in these four core domains at 20 weeks versus baseline; with a mean difference of -1.3 (p=<0.001), versus mean difference of -0.9 (p=0.001)

at 12 weeks. Overall, the 20 week data showed an improvement of **33%** versus baseline (compared to 23% improvement at 12 weeks). Between 12 to 20 weeks, there was an additional CGI-I improvement of -0.4, representing a significant, additional improvement of **13% (p=0.007),** which continues the downward trajectory of clinical improvement overall.



At 20 weeks, **100% of patients** showed improvement (versus 93% of patients at 12 weeks) with; **57% very much or much improved** (versus 36% at week 12) as shown below.

	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%)
NTI164 (week 20)	**1 (7%)**	**7 (50%)**	**6 (43%)**	**0 (0%)**	**0 (0%)**	**0 (0%)**	**0 (0%)**

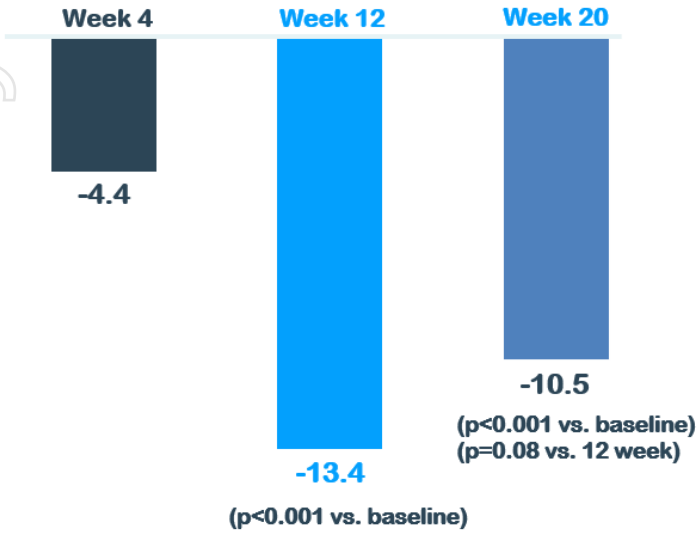
The individual measures of CGI-I in the four core composite measures at 20 weeks all showed continued improvement from 12 weeks: Communication Skills (mean difference -0.2), Mental Alertness (mean difference -0.6), Socialisation/ Eye Contact (mean difference -0.3) and Anxiety (mean difference -0.3).

Rett Syndrome symptoms via RSBQ were stable

The Rett Syndrome Behavioural Questionnaire (RSBQ) consists of 8 domains/subscales that reflect the core features of the disease: General Mood; Breathing Problems; Hand Behaviours; Repetitive Face Movements; Body Rocking and Expressionless Face; Nighttime Behaviours; Fear/Anxiety; and Walking/Standing.

At 20 weeks, patients receiving NTI164 showed a clinically meaningful 24% improvement in total RSBQ score versus baseline ($p<0.001$). There was no further improvement in RSBQ scores between week 12 and week 20 with RSBQ measures relatively stable (mean difference 2.9, $p=0.08$). At commencement the average RSBQ total score for the patients was 44.6 compared to 31.2 at 12 weeks and 34.1 at 20 weeks.

Change from Baseline RSBQ Scores



Total RSBQ Scores

Baseline	4 weeks	12 weeks	20 weeks
44.6	40.2	31.2	34.1
Improvement (v baseline) mean diff.	4.4 (10%)	13.4 (30%)	10.5 (24%)

Zero Safety Events and No Weight Loss from Week 12 to 20

There were no serious adverse events (SAEs), no adverse events (AEs) reported between 12 weeks to 20 weeks and no weight loss (mean weight was stable versus 12 weeks and weight recorded at baseline). At 12 weeks, two patients (14%) experienced nausea/vomiting effects. This safety profile compares favourably with the only FDA approved treatment for Rett Syndrome, DAYBUE™ (trofinetide). For those patients initially treated with DAYBUE™ at 40 weeks (LILAC-1 study), they recorded a CGI-I of 3.1 and a RSBQ change of -7.3 (n=44), with adverse events including diarrhoea (75%) and vomiting (29%) experienced by the entire 77 patients who completed LILAC-1.[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 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**.

[1] Source: https://acadia.com/media/news-releases/clinical-data-from-open-label-extension-lilac-1-and-lilac-2-studies-evaluating-long-term-safety-and-efficacy-of-daybue-trofinetide-in-patients-with-rett-syndrome-published/