ASX Announcement

26 October 2022

Neurotech Reports Further Significant Clinical Improvement at 20 Weeks for Paediatric Autism Patients Treated with NTI164

Highlights:

- **Significant changes for all gold-standard ASD measures at 20 weeks vs. baseline for clinical improvement; severity of illness (p=0.005), anxiety (p=0.001), social responsiveness (p=0.012) and adaptive behaviour (p=0.0005): all considered clinically important and primary goals in the treatment of children with Autism Spectrum Disorder (ASD)**
- **Significant, positive effects on severity of illness, with children re-classified from moderately ill (CGI-S: 4.3) at baseline to mildly ill (CGI-S: 3.2) at 20 weeks, representing a 26% improvement (p=0.005) with 40% of patients markedly/severely ill at baseline to 0% from week 4 onwards**
- **NTI164 potentially a patient 'enabling' drug when coupled with (non-drug) behavioural therapies, by improving daily living skills and allowing children to more fully integrate into society**
- **NTI164 continued to be well tolerated at the maximum dose for each patient, with no serious adverse events recorded and no changes to blood analysis or liver function tests over the 20 week period**
- **Strong efficacy and safety results at 20 weeks warrant progression to a Phase II/III randomised, double-blind, placebo-controlled clinical trial – HREC submission completed**

Neurotech International Limited (ASX: NTI) ("Neurotech" or "the Company"), a clinical-stage biopharmaceutical development company focused predominately on paediatric neurological disorders, today announces strong clinical results from twelve (12) paediatric Autism Spectrum Disorder (ASD) patients, following daily treatment of NTI164 over a 20 week period. In July 2022, Neurotech presented the results of the 28 day safety and efficacy data on a total of 14 patients. On the strength of the 28 day data, caregivers and clinicians recommended all patients continue to receive NTI164 treatment for an additional 54 weeks, with additional safety and efficacy results collected over that period. The 20 week results were part of the Human Research Ethics Committee (HREC) approval to extend the trial, with approximately 6,300 assessment points collected to date. The Company will continue to collect safety and efficacy data over the additional period of treatment.

Professor Michael Fahey, Head of the Paediatric Neurology Unit at Monash Medical Centre, Director of Neurogenetics and Chief Investigator of the NTI164 Trial commented *"I am extremely encouraged by the 20-week results and the clinical improvements in troubling symptoms we have seen to date. These benefits, as measured by standardised scales, relate to global improvement, severity of illness, socialisation, adaptive behaviour, communication and reduction in anxiety. These results provide positive momentum as we move to the commencement of the next phase of clinical development. This is a strong indication that NTI164 has the potential to be an enabling treatment for some of the symptoms that cause people with Autism Spectrum Disorder distress."*

Dr Thomas Duthy, Executive Director of Neurotech said *"On behalf of Neurotech, we once again extend our thanks to the patients and their families as well as the team of staff and clinicians at Monash Children's Hospital for their continued participation in this important clinical trial. Based on the significance of the efficacy outcomes shown at 20 weeks, and attractive safety profile of NTI164, we*

have now filed a clinical trial protocol with the HREC at Monash to commence a Phase II/III trial of NTI164 in approximately 55 children with ASD. Subject to the receipt of HREC approval, the Company is targeting commencement of patient recruitment in Q4 CY2022. We look forward to providing further details on our final trial protocol following HREC approval and including this important longer-term safety and efficacy data reported today into our pre-IND submission for the US Food and Drug Administration."

Clinical Results

Efficacy

Twelve (n=12) paediatric patients remained on daily treatment of NTI164 for the full duration of the 20 week period and were therefore evaluable for the analysis. Their data at this time point (20 weeks) was compared to these same patients' data at baseline and 28 days. The two patients who discontinued treatment were censored (excluded) from the analysis undertaken (not related to drug effects of NTI164). All 12 patients will be followed-up for additional safety and efficacy analysis up-to 54 weeks, as per protocol revisions, and per HREC approval received in July 2022.

Overall, the significant results achieved across a large number of well-validated clinical assessment tools in children with ASD was very encouraging. For clinicians treating children with ASD, this repetitive and sustained effect is an important and meaningful clinical finding, when coupled with NTI164's strong safety profile. This supports the observation that the results are unlikely to be the result of durable placebo effects. However, this will be confirmed via Neurotech's planned Phase II/III trial.

At 20 weeks of treatment (n=12), the mean severity of illness rating of the CGI-S was 3.2, representing an improvement of 26% from baseline (CGI-S: 4.2). The mean difference between 20 weeks of treatment and baseline was -1.1, 95% Confidence Interval (CI) = -1.772, -0.3948, p value=0.005. The mean difference of the severity of illness between 28 days of treatment and baseline was -0.714, 95% CI = -1.332, -0.097, p value=0.027.

The results demonstrate that of the ~40% of subjects markedly or severely ill at baseline – 0% of patients from week 4 onwards were classified as markedly to severely ill. In addition, these results show a significant improvement in average severity of illness scores over time. It is therefore plausible that patients may see further improvements in the severity of illness over the extended 54 weeks of treatment under the HREC approval to continue daily treatments with NTI164 in these patients.

At 20 weeks, the patients' adaptive behaviour as measured by the Vineland™-3 adaptive behaviour scores, was significantly improved overall (mean difference of 3.8; 95% CI = 2.06, 5.61, p value=0.0005), and individual domains of communication (mean difference of 3.9; 95% CI = 1.76, 6.08, p value=0.002), daily living skills (mean difference of 4.7; 95% CI = 0.93, 8.40, p value=0.019), and socialisation (mean difference of 4.6; 95% CI = 1.12, 8.05, p value=0.014). Adaptive behaviour is an important factor in predicting long-term outcomes for people with ASD and improving this behaviour is a goal of any treatment intervention in ASD.

The Social Responsive Scale, 2nd Edition (SRS-2) is an internationally recognised tool used to identify social impairment associated with ASD and quantifies its severity using a Total score plus six sub-scales (Social Awareness, Social Cognition, Social Communication, Social Motivation, Restricted Interest and Repetitive Behaviour and Social Communication and Interaction).

Of the 12 active patients, 11 completed the SRS-2. The mean total T-score for the 11 patients after 20 weeks of daily NTI164 treatment was 75.3 which is a significant improvement from baseline where it was 80.7 (mean difference of -5.45, 95% CI = -9.42, -1.49, p value=0.012).

Within the SRS-2 treatment subscales, the greatest improvements were observed in Restricted Interest and Repetitive Behaviour (mean difference of -9, 95% CI = -15.15, -2.85, p value=0.009), Social Cognition

(mean difference of -4.3, 95% CI = -7.99, -0.56, p value=0.03) and Social Communication and Interaction (mean difference of -4.1, 95% CI = -7.66, -0.52, p value=0.03).

Safety

At 20 weeks of daily therapy of NTI164 at the maximum tolerated dose for each patient, up to 20 mg/kg/day the side effects reported were not serious or severe and did not significantly interfere with patients' functioning. 58% of evaluable patients achieved approx. 20 mg/kg/day or higher dosing. No changes were observed in any patients' full blood examination, liver function or kidney function tests. There were no changes observed in the patients' vital signs or weight. Excessive weight gain is a hallmark of Risperidone treatment in ASD, with Risperidone a regulatory approved treatment to manage irritability in children with ASD.

Conclusions

NTI164 has shown to be safe and well tolerated up to doses of 20/mg/kg/day. NTI164 has shown statistically significant efficacy in improving the symptoms associated with ASD after 20 weeks of daily therapy. The side effects reported were not serious or severe and did not significantly interfere with patients' functioning. No clinically significant abnormal laboratory values were reported.

These results, combined with the extension of this study to accommodate parents/caregivers request to continue therapy, warrant for further clinical studies on NTI164 to assess long-term efficacy and safety.

Appendix 1 *provides further information on the 20 week safety and efficacy results.*
Appendix 2 *provides the important background information on the trial.*

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. Neurotech is currently conducting a world-first clinical trial to assess the potential application of NTI164 for the treatment of Autism Spectrum Disorder (ASD). Results of the Phase I/II clinical trial indicated that 93% of participants had notable improvements relating to the severity of illness with no serious side effects. The next step will be initiation of a Phase II/III clinical trial to further assess the long-term safety and efficacy of NTI164, with the potential to lead to drug registration. 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 (<0.3%) and a novel combination of cannabinoids including CBDA, CBC, CBDP, CBDB and CBN. NTI164 has been exclusively licenced from Dolce Cann Global (Ltd), 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 the Phase I/II ASD Clinical Trial

The clinical trial was a 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 (ASD).

For more information on the trial, please visit www.clinicaltrials.gov Identifier **NCT05516407** or the Australian New Zealand Clinical Trials Registry (ANZCTR) under Registration Number: **ACTRN12621000760875P**.

Appendix 1 – 20 Week Results

Summary of Efficacy Measures -

The tabulated results of all measures (statistically significant measures shaded green)

Sub-Domain	Scale	Wilcoxon Signed-Rank Test	Paired T-Test
Severity of illness	**CGI-S**	**0.010**	**0.005**
Adaptive behaviour composite (Total)	**Vineland-3**	**0.003**	**0.0005**
Communication	Vineland-3	0.004	0.002
Daily living skills	Vineland-3	0.025	0.019
Socialisation	Vineland-3	0.012	0.014
Social responsive scale – Total *T*-score	**SRS-2**	**0.013**	**0.012**
Social awareness – *T*-score	SRS-2	0.439	0.596
Social cognition – *T*-score	SRS-2	0.036	0.028
Social communication – *T*-score	SRS-2	0.018	0.019
Social motivation – *T*-score	SRS-2	0.138	0.118
Restricted interest and repetitive behaviour – *T*-score	SRS-2	0.014	0.009
Social communication and interaction – *T*-score	SRS-2	0.021	0.029
Anxiety, depression and mood scale - Total	**ADAMS**	**0.009**	**0.001**
Anxiety scale for children - Child's total	**ASC-ASD-C**	**0.012**	**0.025**
Performance anxiety	ASC-ASD-C	0.474	0.364
Anxious arousal	ASC-ASD-C	0.089	0.120
Separation anxiety	ASC-ASD-C	0.035	0.025
Uncertainty	ASC-ASD-C	0.035	0.033
Anxiety scale for children - Parent's total	**ASC-ASD-P**	**0.053**	**0.034**
Performance anxiety	ASC-ASD-P	0.096	0.070
Anxious arousal	ASC-ASD-P	0.229	0.333
Separation anxiety	ASC-ASD-P	0.033	0.025
Uncertainty	ASC-ASD-P	0.084	0.066
Sleep disturbances scale for children - Total	SDSC	0.018	0.016
Disorders of initiating and maintaining sleep	SDSC	0.026	0.010
Sleep breathing disorders	SDSC	0.042	0.047
Sleep-wake transition disorders	SDSC	0.072	0.094

Clinical Global Impression (CGI)

The CGI-S 3-item clinician-rated scale was used to analyse the therapeutic effects of NTI164 and its changes to severity of illness.

- **Global Improvement**: rates the total improvement whether or not, in the clinician's judgement, is due entirely to drug treatment.
- **Severity of Illness:** a comparison of baseline and post-baseline (28 days, up to 20 weeks)
- **Efficacy Index (Therapeutic Effect):** rated based on drug effect only. This is a calculated score based on the degrees of therapeutic effect and side effects.

Global Improvement

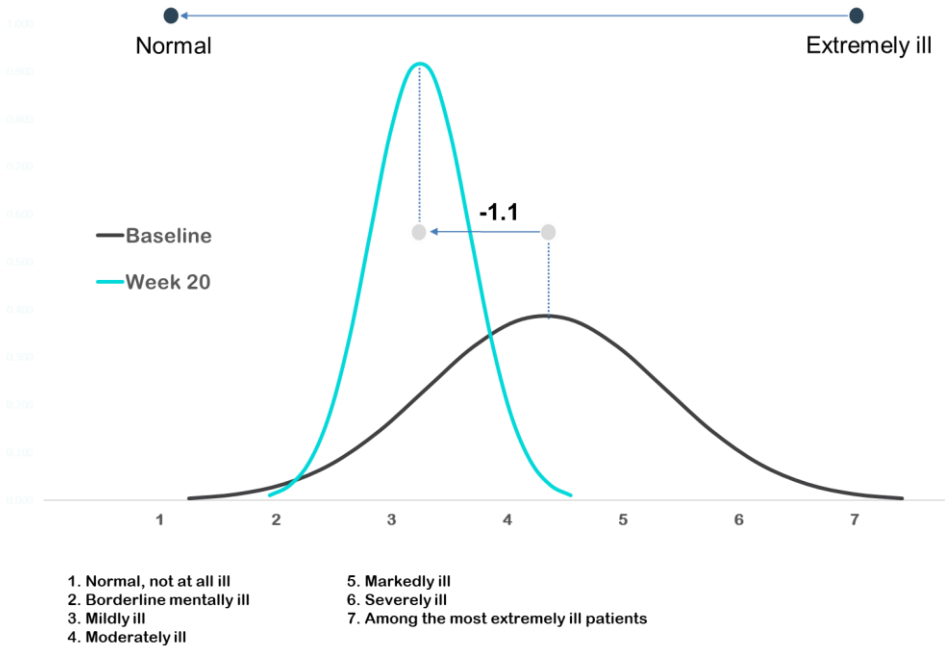
Of the 12 assessable patients at 20 weeks of daily treatment with NTI164, 100% of active patients showed improvement. All of these patients had a global improvement of 'Much improved', relative to baseline. Normalising this data for the two patients who did not complete 20 weeks of treatment, at 28 days, 100%

of the 12 patients showed improvement. 75% of these patients had a global improvement of 'Much improved' and 25% had a global improvement of 'Minimally improved', at 20 weeks relative to baseline.

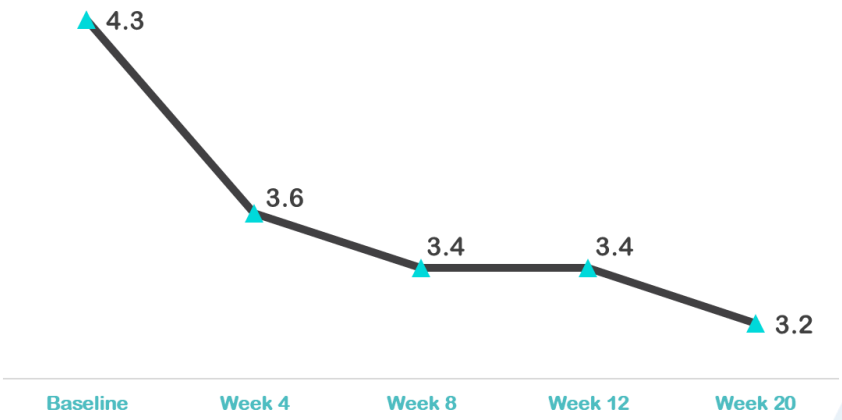
As initially reported to ASX, of the 14 assessable patients at 28 days of daily treatment with NTI164, 93% of active patients showed improvement after 28 days. 64% of these patients had a global improvement of 'Much improved', 29% had a global improvement of 'Minimally improved' and only one patient (7%) had 'No change'.

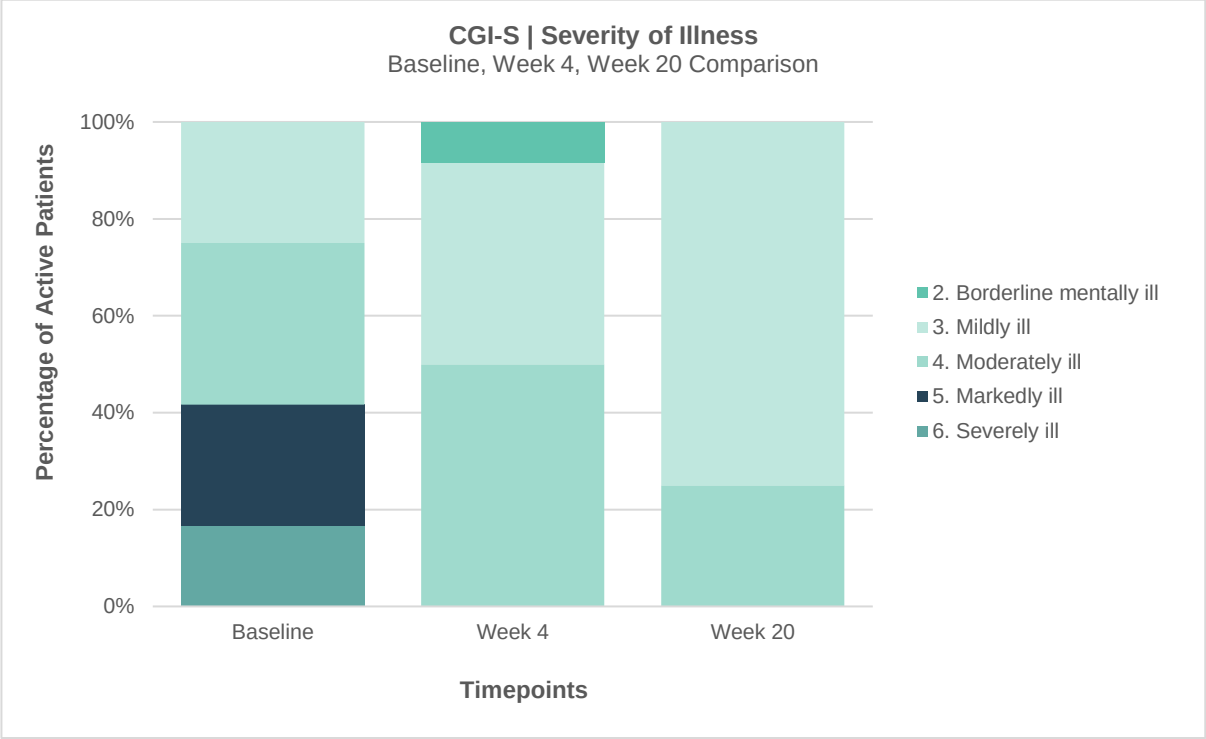
Severity of Illness

At 20 weeks of treatment (n=12), the mean severity of illness rating of the CGI-S was 3.2, representing an improvement of 26% from baseline. The mean difference between 20 weeks of treatment and baseline was -1.08, 95% Confidence Interval (CI) = -1.772, -0.3948, p value=0.005. The mean difference of the severity of illness between 28 days of treatment and baseline was -0.714, 95% CI = -1.332, -0.097, p value=0.027. The results for severity of illness at 20 weeks versus 28 days and baseline for the 12 patients assessed is shown below:



Mean Severity of Illness (n=12)





As previously reported, the average rating for the severity of illness at baseline (n=14) was 4.4. At 28 days this reduced to an average rating of 3.6 after 28 days of NTI164 treatment, representing an improvement of approximately 19% (mean difference of -0.714, 95% CI = -1.332, -0.097, p value=0.027).

The results demonstrate that of the ~40% of subjects markedly or severely ill at baseline – 0% of patients from week 4 onwards were classified as markedly to severely ill. In addition, these results show a significant improvement in average severity of illness scores over time.

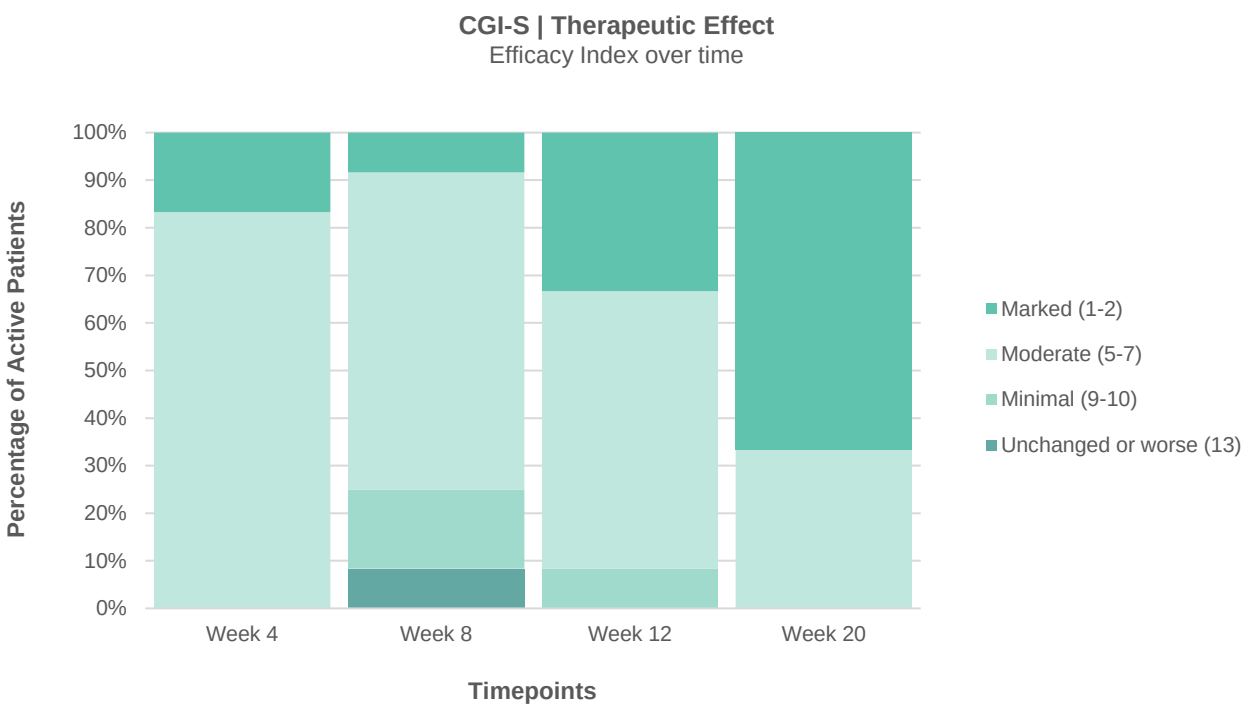
It is therefore plausible that patients may see further improvements in the severity of illness over the extended 54 weeks of treatment under the HREC approval to continue daily treatments with NTI164 in these patients.

Therapeutic Effect

After 20 weeks of daily treatment with NTI164, relative to baseline, of the 12 patients evaluable, 67% of patients demonstrated the highest and second highest possible efficacy index scores of 1 and 2: Marked therapeutic effect – Vast improvement.

Complete or nearly complete remission of all symptoms, with 50% having no side effects and 17% having side effects that do not significantly interfere with patient's functioning. The other 33% of active patients had an efficacy index of either 5, 6 or 7: Moderate therapeutic effect – Decided improvement.

Partial remission of symptoms with 17% of these patients having no side effects, 8% having side effects that do not significantly interfere with patient's functioning and 8% having side effects that significantly interfere with patient's functioning as shown below.



EFFICACY INDEX
1 = Marked - Vast improvement. Complete or nearly complete remission of all symptoms. No side effects.
2 = Marked - Vast improvement. Complete or nearly complete remission of all symptoms. Side effects do not significantly interfere with patient's functioning.
5 = Moderate - Decided improvement. Partial remission of symptoms. No side effects.
6 = Moderate - Decided improvement. Partial remission of symptoms. Side effects do not significantly interfere with patient's functioning.
7 = Moderate - Decided improvement. Partial remission of symptoms. Side effects significantly interfere with patient's functioning.
9 = Minimal - Slight improvement. Doesn't alter status of care of patient. No side effects.
10 = Minimal - Slight Improvement. Doesn't alter status of care for patient. Side effects do not significantly interfere with patient's functioning.
13 = Unchanged or Worse. No side effects.

The results at 20 weeks showed an increase in improvement of the therapeutic effect of NTI164 in those 12 patients evaluable at this time point, relative to their therapeutic scores at 28-days of daily treatment with NTI164. At 28 days, 17% of active patients demonstrated the second highest possible efficacy index of 2: *Marked therapeutic effect – Vast improvement. Complete or nearly complete remission of all symptoms with side effects that do not significantly interfere with patient's functioning*. 83% of active patients had an efficacy index of either *5 or 6*: *Moderate therapeutic effect – Decided improvement. Partial remission of symptoms* with half of these patients having *no side effects* and the other half having side effects that *do not significantly interfere with patient's functioning* as shown in the chart above.

Adaptive Behaviour – Vineland™-3

Vineland™-3 is internationally recognised as a leading instrument for supporting the diagnosis of intellectual and developmental disabilities in ASD; specifically adaptive behaviour. Adaptive functioning, which are skills people need to function independently at home, at school and in the community is an important factor in predicting long-term outcomes for people with ASD. Improving adaptive abilities in patients is therefore a desirable treatment goal. The adaptive behaviour composite consists of (a) communication, (b) daily living skills & (c) socialisation.

Vineland™-3 measures are typically assessed every 3 months. Vineland™-3 is a norm-based instrument, where adaptive function is compared to others of the same age (the normative mean of 100 and the normative standard deviation is 15).

The tabulated results for 20 weeks versus baseline for the twelve patients assessed, relative to baseline is shown below:

Vineland-3 Scale *n=12*	Mean Standard Score		Highest Score Achieved		Maximum decrease	Maximum increase	Mean Difference
	Baseline	Week 20	Baseline	Week 20			
Adaptive Behaviour Composite	66.9	70.8	82	91	-1	+9	**3.8**
Communication	70.0	73.9	88	100	-1	+12	**3.9**
Daily Living Skills	64.1	68.8	86	88	-8	+15	**4.7**
Socialisation	67.3	71.9	81	95	-3	+15	**4.6**

The results showed a statistically significant change in the adaptive behaviour composite endpoint at 20 weeks versus baseline (mean difference of 3.8; 95% CI = 2.06, 5.61, p value=0.0005), and individual domains of communication (mean difference of 3.9; 95% CI = 1.76, 6.08, p value=0.002), daily living skills (mean difference of 4.7; 95% CI = 0.93, 8.40, p value=0.019), and socialisation (mean difference of 4.6; 95% CI = 1.12, 8.05, p value=0.014).

Of the 12 active patients, one patient at the 20-week timepoint had a communication standard score of 100 which corresponds to a percentile rank of 50 (percentile rank at baseline was 21); an adaptive behaviour composite score of 91 which is close to normative mean of 100 and has a percentile rank of 27 (percentile rank at baseline was 12); and a socialisation standard score of 95 which corresponds to a percentile rank of 37 (percentile rank at baseline was 10).

Social Responsive Scale, 2nd Edition (SRS-2)

The SRS-2 is an internationally recognised tool used to identify social impairment associated with autism spectrum disorders (ASDs) and quantifies its severity using a Total score plus six sub-scales (Social Awareness, Social Cognition, Social Communication, Social Motivation, Restricted Interest and Repetitive Behaviour and Social Communication and Interaction). Total *T*-score's that range 76 or higher are classified as the *severe range* and indicate deficiencies in reciprocal social behaviour that are clinically significant and lead to severe interference with everyday social interactions.

Of the 12 active patients, 11 completed the SRS-2. The mean of the total *T*-score for the 11 patients after 20 weeks of daily NTI164 treatment was 75.3 which is a significant improvement from baseline where it was 80.7 (mean difference of -5.45, 95% CI = -9.42, -1.49, p value=0.012).

Within the SRS-2 treatment subscales, the greatest improvements were observed in Restricted Interest and Repetitive Behaviour (mean difference of -9, 95% CI = -15.15, -2.85, p value=0.009), Social Cognition (mean difference of -4.3, 95% CI = -7.99, -0.56, p value=0.03) and Social Communication and Interaction (mean difference of -4.1, 95% CI = -7.66, -0.52, p value=0.03) as shown below.

Social Responsive Scale, 2nd Edition (SRS-2) *n=11*	Mean of *T*-score		Maximum decrease	Maximum increase	Mean Difference
	Baseline	Week 20			
Total Score	80.7	75.3	-17	+3	**-5.5**
Social Awareness	68.0	66.5	-12	+16	**-1.5**
Social Cognition	78.0	73.7	-14	+6	**-4.3**

Social Responsive Scale, 2nd Edition (SRS-2) *n=11*	Mean of *T*-score		Maximum decrease	Maximum increase	Mean Difference
	Baseline	Week 20			
Social Communication	77.9	73.5	-16	+4	**-4.5**
Social Motivation	75.6	72.1	-16	+5	**-3.5**
Restricted Interest and Repetitive Behaviour	82.3	73.3	-28	+7	**-9.0**
Social Communication and Interaction	79.0	74.9	-16	+2	**-4.1**

Anxiety, Depression and Mood Scale (ADAMS)

The ADAMS scale is a 28-item tool used to assess improvements in Manic/Hyperactive Behaviour, Depressed Mood, Social Avoidance, General Anxiety, and Compulsive Behaviour. Items are rated on a 4-point scale ranging from 0=not a problem to 3=severe problem. The ADAMS scores were assessed at baseline and at week 20 and demonstrated an overall score mean difference of -16.2; 95% CI = -23.59, -8.01, p value=0.0013. This demonstrates a significant overall improvement to patients' anxiety, depression, and overall mood after 20 weeks of daily NTI164 treatment.

The total number of patients who completed the questionnaire was 11. 92% of these patients demonstrated improvement in their overall ADAMS score after 20 weeks (max change of -29) and only 1 patient (8%) displaying an increase in their overall score (max change of +2).

Safety Measures

At 20 weeks (representing the 12 assessable patients), a total of 39 adverse events were reported by 10 participants. 31% of these reports were digestive related (n=12) i.e., stomach pain, diarrhoea, vomiting. Stomach pain was the most reported adverse events and accounted for 13% of reports (n=5). No serious adverse events were reported.

This compared to the 28-day data (representing the same 12 patients) where a total of 18 adverse events were reported by nine participants. 25% of these reports were digestive related (n=5) i.e., stomach pain, diarrhoea, vomiting. Stomach pain and lack/loss of appetite were the most reported adverse events and each accounted for 14% of reports (n=3). No serious adverse events were reported.

APPENDIX 2 - Study Details

The full study details described below represent the original trial design to assess the safety and efficacy of NTI164 after 28 days of daily treatment, as reported to ASX on 8 July 2022. For more information on the trial, please visit www.clinicaltrials.gov Identifier NCT05516407 or the Australian New Zealand Clinical Trials Registry (ANZCTR) under Registration Number: ACTRN12621000760875P.

Neurotech was subsequently granted HREC approval to continue dosing patients for a further 54 weeks due to the positive therapeutic effects of NTI164 combined with feedback from parents and clinicians at 28 days. Neurotech continues to collect data on safety and efficacy measures in patients who continue to receive daily treatments of NTI164. The Company today has announced the results of continued treatment with NTI164 at 20 weeks.

This study was 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 hepatic function at screening, defined as serum alanine aminotransferase (ALT) or aspartate aminotransferase (AST) > 2 × upper limit of normal (ULN) or total bilirubin (TBL) > 2 × 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.

Safety Evaluation:

Full blood examination, liver function test, renal function test, vital signs & adverse events.

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 6–18 (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, ranging from 1. Very much improved to 7. Very much worse

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.