ASX Announcement
8 July 2022

BREAKTHROUGH RESULTS WITH NTI164 IN PAEDIATRIC ASD

- **93% of patients showed symptom improvement relating to the severity of illness after 28 days of daily treatment with NTI164.**
- **GLOBAL IMPROVEMENT**
  64% of patients had a global improvement of "much improved'"
  29% of patients had a global improvement of "minimally improved"
  7% of patients had "no change"
- **THERAPEUTIC EFFECT (EFFICACY INDEX)**
  - Two patients recorded a Marked Therapeutic Index Score of 2 = vast improvement meaning: complete or near remission of all symptoms.
  - Ten patients recorded a Moderate Therapeutic Index Score of 5 & 6 = representing "Decided improvement" – Partial remission of symptoms.
- **SEVERITY OF ILLNESS**
  The average rating for the severity of illness at baseline was 4.4. This was reduced to 3.6 after 28 days of NTI164 treatment.
- **NTI164 was well-tolerated – No serious adverse events were recorded across all doses (5, 10, 15 and 20 mg/kg). No changes were noted in blood analysis or liver function tests.**
- **The study has been granted HREC approval to continue for a further 54 weeks due to the positive therapeutic effects of NTI164 combined with feedback from parents and clinicians and their recent request for no "washout" period. Safety and efficacy assessments will continue.**
- **The Company is in discussions with the US FDA regarding a pre-IND ("Investigational New Drug") application scheduled for 2022.**
- **Existing prescribed medications for the treatment of symptoms associated with ASD have untoward side effects including weight gain, sedation and hormonal imbalance. Given that NTI164 was well-tolerated without weight gain or sedation, NTI164 shows promise compared to these treatments[1].**
- **Recently completed and published paediatric ASD studies utilising CBD and/or THC do not show any statistical efficacy and had minimal effects after three plus months and (with a THC component) had 'sedation' as a significant side effect[2,3]. NTI164 measures favourably when compared to these treatments.**
- **The results open up opportunities for a potential treatment pathways outside of ASD including a wide range of neurological disorders such as Attention Deficit Hyperactivity Disorder ("ADHD"), Multiple Sclerosis, Motor Neuron Disease, Rett's Syndrome, Concussion and Cerebral Palsy.**
- **Conference Call with CEO, Dr Alexandra Andrews to be held at 11am WST today – details to follow.**

Neurotech International Limited (ASX: NTI) ("Neurotech" or "the Company") is pleased to announce the successful outcomes relating to the safety, tolerability, and efficacy of NTI164 and on key behavioural parameters that impact ASD patients. NTI164 is one of NTI's proprietary cannabis strains, exclusively licenced from Dolce Cann Global (Ltd), in respect of neurological applications and is the world's first full-spectrum

[1] *Al-Huseini, S. et al., (2022). Effectiveness and Adverse Effects of Risperidone in Children with Autism Spectrum Disorder in a Naturalistic Clinical Setting at a University Hospital in Oman. Autism research and treatment, 2022, 2313851. https://doi.org/10.1155/2022/2313851*

[2] *Thomas, M. & Frampton, C., (2022) HOPE® 1 demonstrates improvements in Clinical Global Impression (CGI) in patients with Autism Spectrum Disorder.* https://zeliratx.com/wp-content/uploads/2022/04/ZEL040-White-Paper_Hope_FA.pdf

[3] *Shani Poleg, et al (2019). Cannabidiol as a suggested candidate for treatment of autism spectrum disorder. Progress in Neuro-Psychopharmacology and Biological Psychiatry. https://www.sciencedirect.com/science/article/abs/pii/S0278584618304445*

medicinal cannabis product (less than 0.3% THC) to be successfully studied in children with Autism Spectrum Disorder (ASD). The study was conducted by Professor Michael Fahey, Head of Paediatric Neurology at Monash Children's Hospital in Melbourne.

The Phase I/II study was designed to rigorously assess the safety of NTI164 in a dose-escalation regime and to detect a signal for efficacy on the behaviour, focus and related cognitive parameters using a range of validated neuro-psychological tools. This study was designed to form the foundation for follow-up studies in therapies relating to the treatment of a wide range of neurological disorders such as Attention Deficit Hyperactivity Disorder ("ADHD"), Multiple Sclerosis, Motor Neuron Disease, Rett Syndrome and Cerebral Palsy.

Overall Study Design and Outline:

- Open-label study.
- The study population: Children aged between eight years through to seventeen years that have a medical diagnosis of Level II and III Autism Spectrum Disorder (ASD) as confirmed by the Autism Diagnostic Observational Schedule (ADOS-2) criteria.

Study Primary Endpoints:

- Safety and tolerability - across dose regime (5mg/kg, 10mg/kg, 15mg/kg and 20 mg/kg).
- Safety was monitored and measured by clinical examination, full blood examinations, liver and renal function tests in addition to parent/carer and physician questionnaires.

Study Behavioural Endpoints:

- Efficacy was measured through parent/carer and physician questionnaires to assess parameters including, but not limited to:
  - Anxiety
  - Participation
  - Irritability
  - Hyperactivity
  - Mood, and
  - Self-stimulation

In total, over 2,250 assessment points were created through the landmark study.

KEY STUDY RESULTS

SAFETY AND TOLERABILITY

- **The safety data concluded that NTI164 at 5, 10, 15 and 20mg/kg administered in two doses daily, is safe and well-tolerated in this study population**
- **No changes were observed in patients' full blood examination, liver function or kidney function tests. There were no changes observed in the patients' vital signs or weight.**

EFFICACY

- **Statistical analysis of key assessments, including Clinical Global Impression of Severity of Illness (CGI-S) demonstrated statistical significance at 28 days of treatment. Paired t-test: the mean difference of CGI-S between 28 days of treatment and baseline was -0.714, 95% Confidence Interval = -1.332, - 0.097, p value=0.027.**
- **93% (13 out of 14 active patients) showed symptom improvement relating to severity of illness after 28 days of daily treatment with NTI164.**

- **Most importantly, parental/carer observations also indicated consistent improvement in the trial participant's 'overall functioning' when compared to baseline at the commencement of the trial. The average rating for the severity of illness at baseline was 4.4 (out of a score of 7 meaning extremely ill and 1 meaning, not ill) and this score was reduced to 3.6 after 28 days of NTI164 treatment.**

Specific instances of markedly improved behaviours (i.e. reduction in fear, agitation and anxiety) were observed. These key areas of neuro-behavioural change will also be the key focus of the upcoming Phase II/III registration trials due to commence in calendar Q3 in 2022.

Chief Investigator Professor Fahey, Monash Children's Hospital said, *"I am very encouraged with these results. We have designed a rigorous study on all fronts to assess the potential application of NTI164 for the treatment of ASD. We are encouraged by the efficacy shown by NTI164 in this trial and we are looking forward to the extension of this trial, in addition to the planned initiation of a Phase II/III trial, to further assess the long-term safety and efficacy of NTI164 with the potential to lead to drug registration."*

The only drug currently approved by the FDA for children with ASD is Risperidone. It is prescribed for children to assist with irritability. Common side effects include; headaches, drowsiness, anxiety and uncontrollable muscle movements. Given the NTI trial results show no serious adverse side effects and high patient compliance, the Company is well placed to make significant inroads into the ASD market expected to be around US$5.5bn by 2028[3].

Neurotech International Chairman, Brian Leedman said, "*We cannot underestimate the significance of the results from our world-first landmark trial. NTI is now a significant step closer in the drug development timeline to introducing to the market a treatment option for paediatric ASD which is natural, safe and based on the results to date, offers substantial behavioural improvements in ASD. The fact that the results are based on a 28 day trial period with further significant results from patients who have remained on the treatment, the Company is very excited that it is genuinely opening up a new treatment pathway for not just ASD, but a wide range of neurological disorders such as Attention Deficit Hyperactivity Disorder ("ADHD"), Multiple Sclerosis, Motor Neuron Disease, Rett's Syndrome and Cerebral Palsy which are targeted for both NTI and Strategic Partner trials moving forward."*

Neurotech International CEO, Dr Alexandra Andrews, said, *"We are extremely pleased with these breakthrough results for NTI164. The fact that 93% of participants have shown notable improvements without any serious side effects is an outstanding outcome. We are incredibly grateful for the generous participation of patients and their families as well as the team of staff and clinicians at Monash Children's Hospital who have made this landmark trial possible. It is heart-warming to think we are in a position to effectively support children with autism and their caregivers by providing a new therapeutic option that may improve their quality of life."*

Neurotech International Director, Professor Allan Cripps AO commented, *"This study has shown substantial benefit across a range of clinical measures in most children who participated in the trial. Based on these results, a significant advantage shown is that the treatment essentially has no side effects. These exciting clinical results and the extensive pre-clinical data that we have available pave the way for an upcoming phase II/III trial in children with ASD and potential trials in patients with many neuroinflammatory disorders."*

Update on Provisional Patent Applications

The Company has previously announced that it has submitted key, provisional patents applications relating to the composition and use of NTI164 to treat various neurological disorders, including ASD[4]. NTI, through its

[3] https://www.globenewswire.com/news-release/2021/12/14/2351376/0/en/Autism-Spectrum-Disorder-Therapeutics-Market-Size-2021-2028-is-Expected-to-be-Worth-USD-5-15-Billion.html)

[4] 14 October 2021 Provisional Patent Lodgements

patent attorneys, recently completed international type searches conducted by IP Australia (Canberra) on both NTI 164 patents which demonstrated that there is no prior art concerning the inventions.

This shows that the Company's patent strategy is on track so far. If granted, its patents could add significant commercial value to the future commercialisation of NTI164 across ASD and other neurological disorders.

Regulatory Pathway

The Company has also initiated discussions with the Therapeutics Good Administration (TGA) to assess product scheduling and classification for the Australian Market. In collaboration with regulatory experts, the Company is now mapping out a full regulatory development roadmap/pathway for the registration and commercialisation of NTI164 for ASD and other neurological indications. The Company has initiated pre–IND **("Investigational New Drug")** discussions with the FDA and is the process of developing a clear roadmap for product registration and commercial development in the USA with an initial face to face pre-IND meeting set for end of August 2022.

Board Appointment

The Company is pleased to announce the appointment of Mr Gerald Quigley as a non-executive director. Mr Quigley is a pharmacist and consumer health commentator based in Melbourne. Mr Quigley has published extensively across multiple fields relating to natural extracts and their role in the regulation of inflammation and is a leading media health commentator heard each week on television and radio stations across Australia. He has extensive knowledge relating to pharmaceutical/nutraceutical product development, dispensing and marketing in addition to product positioning within the relevant regulatory landscapes (eg. TGA, FDA).

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

Further Information
Dr Alexandra Andrews
CEO
aa@neurotechinternational.com
+61 (0)405 339 788

Brian Leedman
Chairman
b.leedman@neurotechinternational.com
+61 (0)41 228 1780

Media:
Amalie Schreurs
White Noise Communications
amalie@whitenoisecomms.com
+61 (0)431 636 033

Monash Media
For all enquires Monash Media and Communications
media@monashhealth.org or (03) 9594 7722.

About Neurotech

Neurotech International Limited (ASX:NTI) is a biopharmaceutical company focused on the development and commercialisation of neurological solutions that improve quality of life. Neurotech is currently conducting world-first clinical trials to assess the potential application of NTI164 for the treatment of Autism Spectrum Disorder (ASD). Results of Phase I/II 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 Phase II/III of the trial to further assess the long-term safety and efficacy of NTI164, with the potential to lead to drug registration.

The Company has also submitted key, provisional patents relating to the composition and use of NTI164 to treat various neurological disorders, including ASD.

For more information about Neurotech and Mente Autism, please visit **www.neurotechinternational.com**.

APPENDIX 1 - Study Details

This study is 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 at screening, defined as serum alanine aminotransferase (ALT) or aspartate aminotransferase (AST) > 2 Å~ upper limit of normal (ULN) or total bilirubin (TBL) > 2 Å~ 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.

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.

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.

APPENDIX 2 - SYNOPSIS

Name of Sponsor	Neurotech International	Individual Study Table Referring to Part of the Dossier	*(For National Authority Use only)*
Finished Product Name	NTI164	**Volume** n/a	
Name of Active Ingredient	Cannabinoids	**Page** n/a	

Title of Study	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 – Part I. ANZCTR Registration Number: ACTRN12621000760875P
Investigator	Professor Michael Fahey Head of Paediatric Neurology Monash Children's Hospital 246 Clayton Road, Clayton VIC Australia 3168 +61 3 9594 6666
Study centre	Monash Children's Hospital 246 Clayton Road, Clayton VIC Australia 3168 +61 3 9594 6666
Publication (reference)	n/a
Study period	*Date of first enrolment* May 2021 *Date of last enrolment* February 2022
Phase of Development	Phase I / II
Objectives	To assess the safety and efficacy of NTI164 after 28 days of daily treatment.
Methodology	The principal investigator assessed each patient to determine the most efficacious and tolerable dose for that individual and made changes to their treatment schedule as required.
Number of patients planned and analysed	20 patients planned; 14 patients analysed.

Name of Sponsor	Neurotech International	Individual Study Table Referring to Part of the Dossier	*(For National Authority Use only)*
Finished Product Name	NTI164	**Volume** n/a	
Name of Active Ingredient	Cannabinoids	**Page** n/a	

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 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.

Investigational product

53mg/ml of NTI164 administered daily at weekly doses of 5mg/kg, 10mg/kg, 15mg/kg and 20mg/kg.

Duration of treatment

28 days.

Reference therapy

Extensive published research review and evaluation was used to determine the dose, duration and route of administration.

Safety Evaluation

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

Efficacy Evaluation

Parent/caregiver-led questionnaires, physician-led questionnaires:

- Clinical Global Impression of Improvement for the Caregiver (CGI-I-Ca)
- CGI of Improvement for the Clinician (CGI-I-C)
- CGI of Change in Target Behaviour (CGI-C)
- CGI of Change in Attention (CGI-CA)
- CGI of Severity of Illness (CGI-S)
- Anxiety Scale for Children – Child version (ASD-ASC-C)
- Anxiety Scale for Children – Parent version (ASD-ASC-P)
- Sleep Disturbances Scale for Children (SDSC)

Statistical methods

- Wilcoxon Signed-Rank Test and the Paired t-test were used to assess the statistical significance.

Name of Sponsor	Neurotech International	Individual Study Table Referring to Part of the Dossier	*(For National Authority Use only)*
Finished Product Name	NTI164	**Volume** n/a	
Name of Active Ingredient	Cannabinoids	**Page** n/a	

SUMMARY - CONCLUSIONS

Efficacy Results

Paired t-test: the mean difference of CGI-S between 28 days of treatment and baseline was -0.714, 95% confidence interval = -1.332, -0.097, p value=0.027.

The Wilcoxon Signed-Rank Test statistic was: -15, the corresponding p-value was 0.047.

13 of the 14 patients (93%) showed symptom improvement relating to severity of illness after 28 days of daily treatment with NTI164.

Safety Results

A total of 21 adverse events were reported by ten participants. 28% of these reports were digestive related (n=6) ie., abdominal 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.

Conclusion

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 autism spectrum disorder after 28-days of daily therapy. Side effects reported were not serious or severe and did not significantly interfere with patients' functioning. No 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.

Date of this report

July 2022

1. Clinical Global Impression – Severity (CGI-S)

The CGI-S scale was used to analyse the therapeutic effect 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 NTI164 treatment).
- *Efficacy Index:* rated based on drug effect only. This is a calculated score based on the degrees of therapeutic effect and side effects.

1.1. Global Improvement

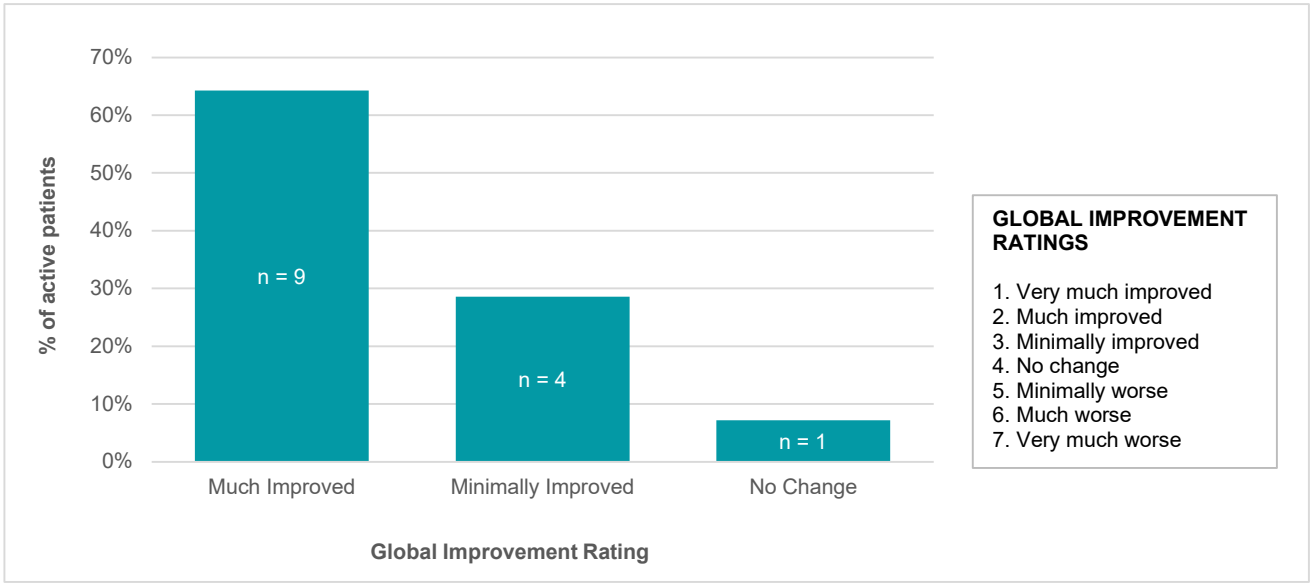
93% of active patients showed improvement after 28 days of daily treatment with NTI164. 64% of these patients had a global improvement of 'Much improved', 29% had a global improvement of 'Minimally improved' and only one patient (7%) had 'No change' (Figure 1).

The Wilcoxon Signed-Rank Test and the Paired t-test were used to assess the statistical significance:

Paired t-test: the mean difference of CGI-S between 28 days of treatment and baseline was -0.714, 95% confidence interval = -1.332, -0.097, p value=0.027.

The Wilcoxon Signed-Rank Test statistic was: -15, the corresponding p-value was 0.047.

Figure 1 - CGI-S | Global Improvement at 28 days of NTI164 treatment



1.2. Severity of Illness

The average rating for the severity of illness at baseline was 4.4 (Figure 2). This reduced to an average rating of 3.6 after 28 days of NTI164 treatment (Figure 3)

Figure 2 - CGI-S | Severity of Illness after 28 days of treatment.

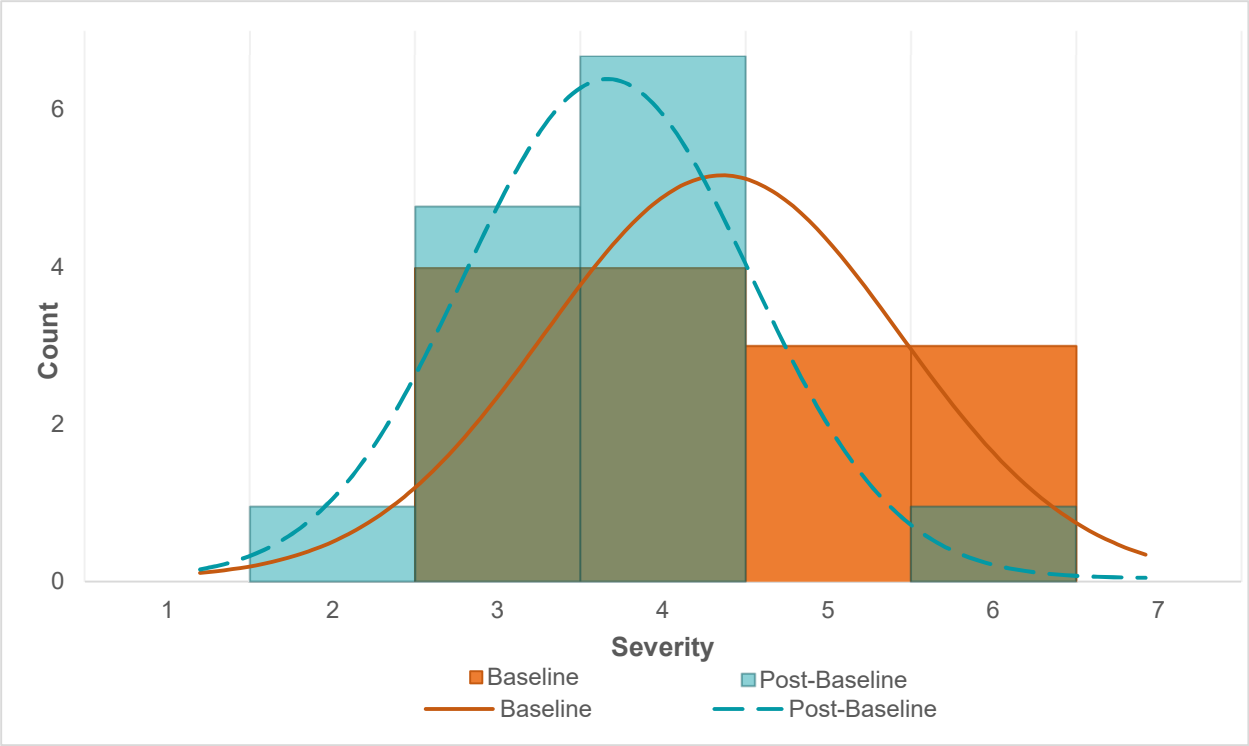
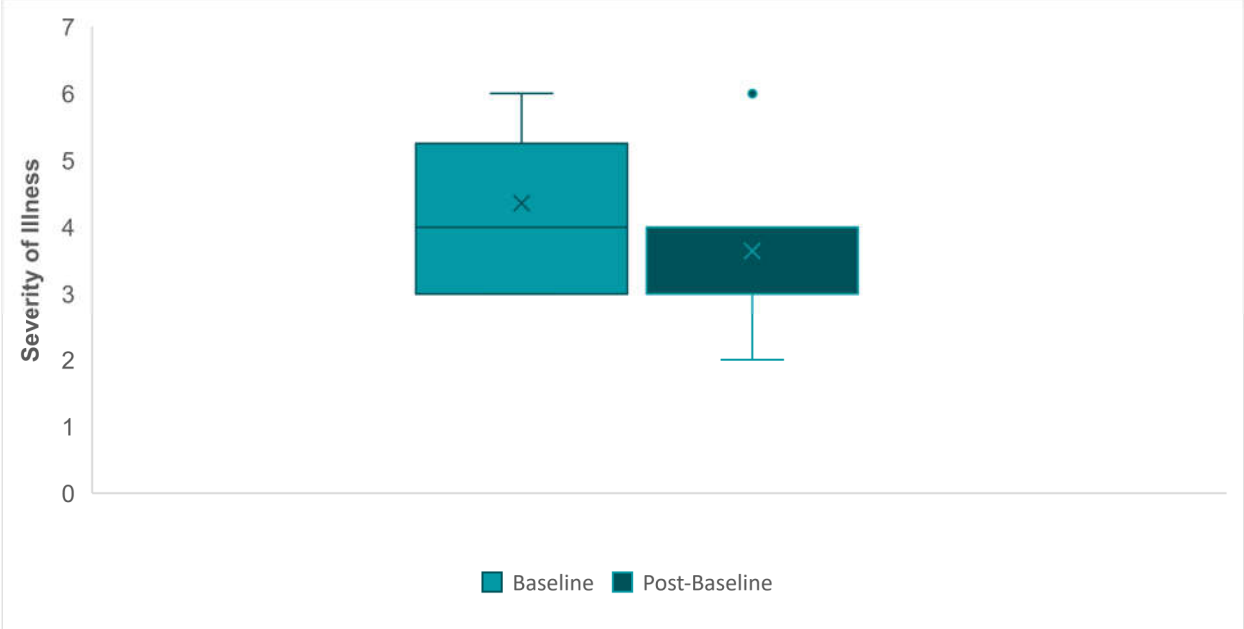


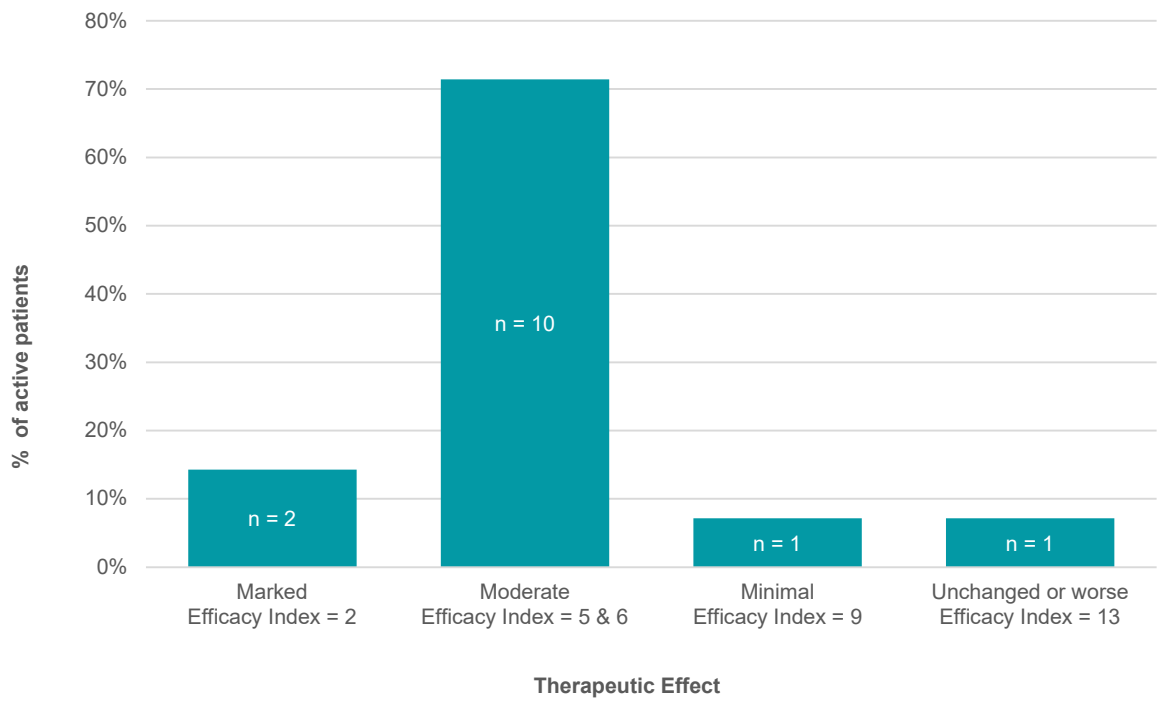
Figure 3 - CGI-S | Severity of Illness after 28 days of treatment.



1.3. Therapeutic Effect

After 28-days of daily treatment with NTI164, 14% of active patients demonstrated the second highest possible efficacy index of *2: Marked therapeutic effect with side effects that do not significantly interfere with patient's functioning.* 72% of active patients had an efficacy index of either *5* or *6: Moderate therapeutic effect* 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*, 7% had an efficacy index of *9*: *Minimal therapeutic effect with no side effects* and only one patient, 7%, had an efficacy index based on seeing no change in condition, *13: Unchanged or worse with no side* effects (Figure 4).

Figure 4 - CGI-S | Therapeutic Effect



EFFICACY INDEX SCORES

2 = Marked Therapeutic Effect, Vast improvement. Complete or nearly complete remission of all symptoms.
Side Effects: Do not significantly interfere with patient's functioning.
5 = Moderate Therapeutic Effect, Decided improvement. Partial remission of symptoms.
Side Effects: None.
6 = Moderate Therapeutic Effect, Decided improvement. Partial remission of symptoms.
Side Effects: Do not significantly interfere with patient's functioning.
9 = Minimal Therapeutic Effect, Slight improvement which doesn't alter status of care of patient.
Side Effects: None.
13 = Unchanged or worse.
Side effects: None.

1.4. Tabulation of Individual Response Data

Table 1 – Tabulation of individual response data

Participant ID	Severity of Illness Baseline	Severity of Illness Post-Baseline	Global Improvement	Therapeutic Effect	Side Effects	Efficacy Index
S00102	5. Markedly ill	4. Moderately ill	3. Minimally improved	Moderate	Do not significantly interfere with patient's functioning	6
S00103	5. Markedly ill	4. Moderately ill	2. Much improved	Moderate	Do not significantly interfere with patient's functioning	6
S00104	4. Moderately ill	3. Mildly ill	2. Much improved	Moderate	None	5
S00106	6. Severely ill	4. Moderately ill	2. Much improved	Moderate	Do not significantly interfere with patient's functioning	6
S00110	3. Mildly ill	3. Mildly ill	2. Much improved	Marked	Do not significantly interfere with patient's functioning	2
S00111	3. Mildly ill	4. Moderately ill	3. Minimally improved	Minimal	None	9
S00112	6. Severely ill	3. Mildly ill	2. Much improved	Marked	Do not significantly interfere with patient's functioning	2
S00113	3. Mildly ill	3. Mildly ill	3. Minimally improved	Moderate	Do not significantly interfere with patient's functioning	6
S00114	5. Markedly ill	3. Mildly ill	3. Minimally improved	Moderate	Do not significantly interfere with patient's functioning	6
S00115	4. Moderately ill	4. Moderately ill	2. Much improved	Moderate	None	5
S00116	4. Moderately ill	4. Moderately ill	2. Much improved	Moderate	None	5
S00117	4. Moderately ill	4. Moderately ill	2. Much improved	Moderate	None	5
S00118	6. Severely ill	6. Severely ill	4. No change	Unchanged or worse	None	13
S00119	3. Mildly ill	2. Borderline mentally ill	2. Much improved	Moderate	None	5

END--------