



Improving Lives



Rett Syndrome Clinical Trial Results

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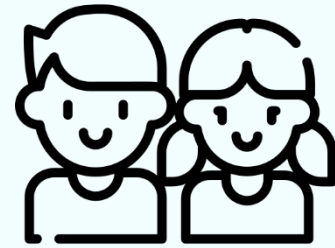
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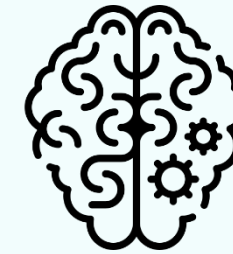
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Neurotech Four Core Strategies



**Focus on Paediatric
Patients**



**Focus On Rare
Neurological Disorders
with Neuroinflammation**



**Focus on Partnering with
Key Opinion Leaders /
Clinicians**



**Focus On Drug Product
Development**

Clinical Pipeline – 2024

Pre-Clinical

NTI164
Combination Therapies
Prednisone, Diclofenac, Other

**Other Licensed
Strains**

Phase I/II

NTI164
Cerebral Palsy

NTI164
PANDAS / PANS¹

NTI164
ASD
(90 week+ open label extension)

NTI164
Rett Syndrome

Phase II/III

NTI164
ASD



Data reported (all with statistically significant primary endpoint results)

Pipeline (2020/1)

NTI164
Combination Therapies
Prednisone, Diclofenac, Other

NTI164
Neuronal Cell Assays

**Other Licensed
Strains**

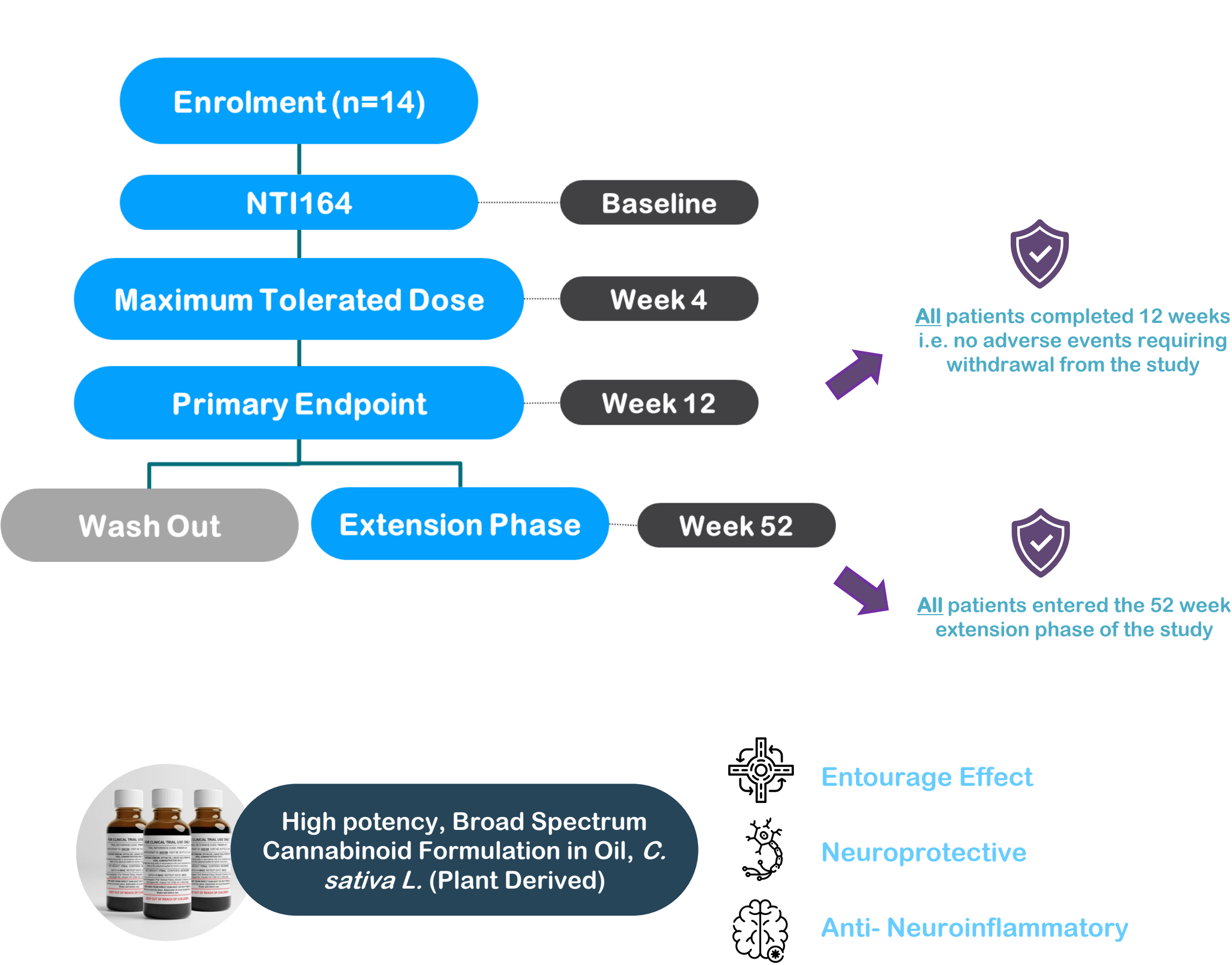
1. Paediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS) and Paediatric Acute-Onset Neuropsychiatric Syndrome (PANS)

Rett Syndrome Phase I/II Trial

“Caregivers of children with RTT experience the illness as being like an “obstacle course”, where they must continuously overcome hurdles. These include hindrances for finding responses to their symptoms and achieving a diagnosis, for managing the treatment and daily care, and for finding the essential financial resources to meet all the expenses generated by the illness.”¹



Rett Syndrome Trial Design (NTIRTT1)



Primary Endpoint

- Clinical Global Impression – Improvement (CGI-I)



Secondary Endpoints

- Rett Syndrome Behaviour Questionnaire (RSBQ)
- CGI-severity of illness (CGI-S)
- RTT- Clinician Domain Specific Concerns – Visual Analog Scale (RTT-DSC-VAS)
- Impact of Childhood Neurological Disability Scale (ICNDS)
- Overall Quality of Life Rating of the Impact of Childhood Neurological Disability Scale (ICNDS-QoL)
- Rett Syndrome: Symptom Index Score (RTT-SIS)
- RTT Caregiver Burden Inventory (RTT-CBI)
- Safety
- Communication and Symbolic Behaviour Scales Developmental Profile™ Infant-Toddler Checklist (CSBS-DP-IT Social)

* No participants received DAYBUE™ (trofinetide)¹

1. DAYBUE is a trademark of Acadia Pharmaceuticals Inc

Baseline Patient Characteristics

Characteristic		Number (%) / Mean
Age		8.8 years
Weight		27.5 kg
Sex	Female	14 (100%)
CGI-S	Mean	4.6 (100%)
	Moderate (4)	7 (50%)
	Marked (5)	5 (36%)
	Severe (6)	2 (14%)
RSBQ Total Score	Mean	44.6 (100%)
	<35	2 (14%)
	≥35	12 (86%)



A total of 14 female patients
with Rett Syndrome
participated

12 Week Safety Data

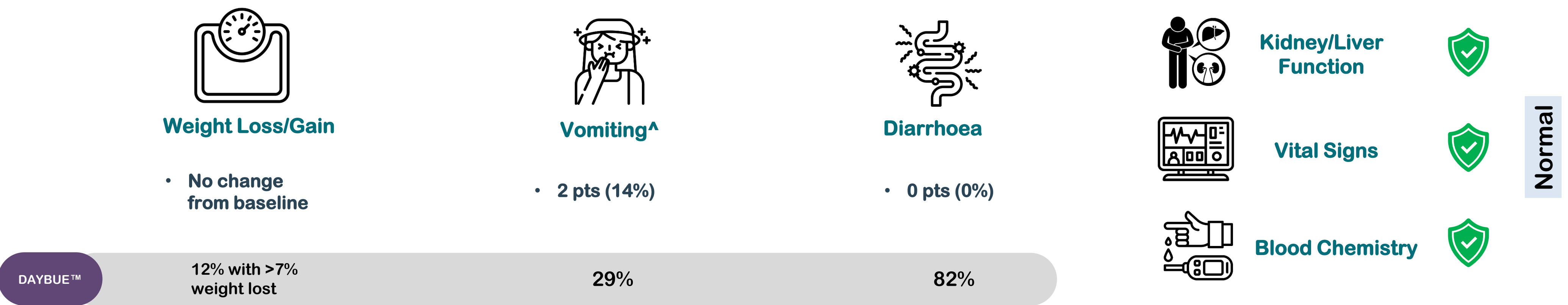
NTI164 Exhibits Excellent Safety Over 12 Weeks

A total of 14 patients evaluable at 12 weeks



One serious adverse event (SAE) recorded (Urticaria-hives) Across all doses, across entire period (12 weeks)

Adverse events (AEs) were tolerated and manageable 11 AEs*, 4 patients



Conclusion: NTI164 exhibits an excellent safety profile and minimal patient-specific side-effects
(consistent with autism and PANDAS/PANS clinical data)

*Other AEs were common cold, viral infection, pharyngitis , chest infection.
^None of these adverse events were serious and were not considered to interfere with the patient's functioning. No additional treatment was required (i.e. administration of anti-vomiting medications). DAYBUE data, source: Acadia Pharma.

Summary of Efficacy Measures

Primary Endpoint

CGI-I



Improvement of 10% from Baseline at 12 weeks ($p=0.009$) – 9 exploratory Rett-Specific Anchors
Improvement of 23% from Baseline at 12 weeks ($p=0.001$) – 4 core Rett Anchors (further development)



CGI-I
RSBQ

Co-primary endpoints used for FDA approval in trofinetide Phase 3 trial

Secondary Endpoints

RSBQ



Patients receiving NTI164 showed a 13.4 score decrease in average RSBQ total score versus baseline (30% improvement, $p<0.001$)

CGI-S



Patients receiving NTI164 showed a 0.4 decrease in CGI-S versus baseline (8.7% improvement, $p=0.009$)

ICNDS



Patients receiving NTI164 showed an 8.5 score decrease versus baseline (13% improvement, $p=0.004$)

ICNDS-QoL



Patients receiving NTI164 showed a 1.5 score increase versus baseline (60% improvement, $p<0.001$)

RTT-CBI



Patients receiving NTI164 showed a 5.0 score decrease versus baseline (16% improvement, $p=0.025$)

RTT-DSC-VAS



Patients receiving NTI164 showed a 0.6 score decrease in verbal communication (13% improvement, $p=0.014$) but no improvement in ambulation ($p=0.374$), communication choices ($p=0.374$) and hand function showed no change (NM)

RTT-SIS



No significant change ($p=0.146$) in total score

CSBS-DP-IT



Not Measured

Rett Syndrome Behavioural Questionnaire RSBQ is a caregiver-completed scale assessing a wide range of neurological and behavioural symptoms in RTT (maximum score 90). RTT Symptom Index Score RTT-SIS developed by A/Prof Ellaway examines 16 Rett-specific symptoms. RTT-Clinician Domain Specific Concerns-Visual Analog Scale RTT-DSC-VAS is a clinician-completed VAS assessing the severity of concerns in: (1) hand use; (2) ambulation; (3) seizures; (4) autonomic features; (5) behaviour; (6) attentiveness; (7) social interaction; and (8) language/communication. CGI-S is a single-item, 7-point scale by clinicians designed to assess global impression of severity (1=normal, 7 = severely ill). 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). ICNDS-QoL measures the overall quality of life of the affected individual (1 – poor, 6 –excellent). RTT-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). N/M – not measured as no difference

Clinician Expert View on Results



Associate Professor Carolyn Ellaway – Lead Investigator

“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.”

Established the Rett Syndrome Multi-Disciplinary Management Clinic, The Children's Hospital at Westmead.

Caregiver Testimonials

Caregiver #1

“She seems much more in tune to what’s going on around her, e.g. patting the dog (has NEVER done this before)”

Caregiver #2

“She uses eye pointing, sometimes brings food / drink to an adult - this has not happened before”

Caregiver #3

“Since being on the trial, she will sit and listen to music for up to an hour”

Caregiver #3

“Since being on the trial, she is now trying to get our attention ”

Primary Endpoint: CGI-I



Clinical Global Impression – Improvement (CGI-I) is a 7–point scale that reflects experts' clinical judgment of the patient based on the clinician's total experience with the Rett syndrome population graded from 1 (very much improved) to 7 (very much worse). A decrease in CGI-I score indicates improvement.

CGI-I Primary Endpoint Significantly Improved

17 April 2024 - Reported

- **Top-Line CGI-I : 4 anchors of 9 available, assessed and reported**
CGI-I versus baseline mean difference of - 0.3 (95% CI -0.015, -0.56; p = 0.04)

6 May 2024 - Reported

- **Complete CGI-I : 9 anchors of 9 available, assessed and reported**
CGI-I versus baseline mean difference of - 0.4 (95% CI -0.112, -0.681; p = 0.009)

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

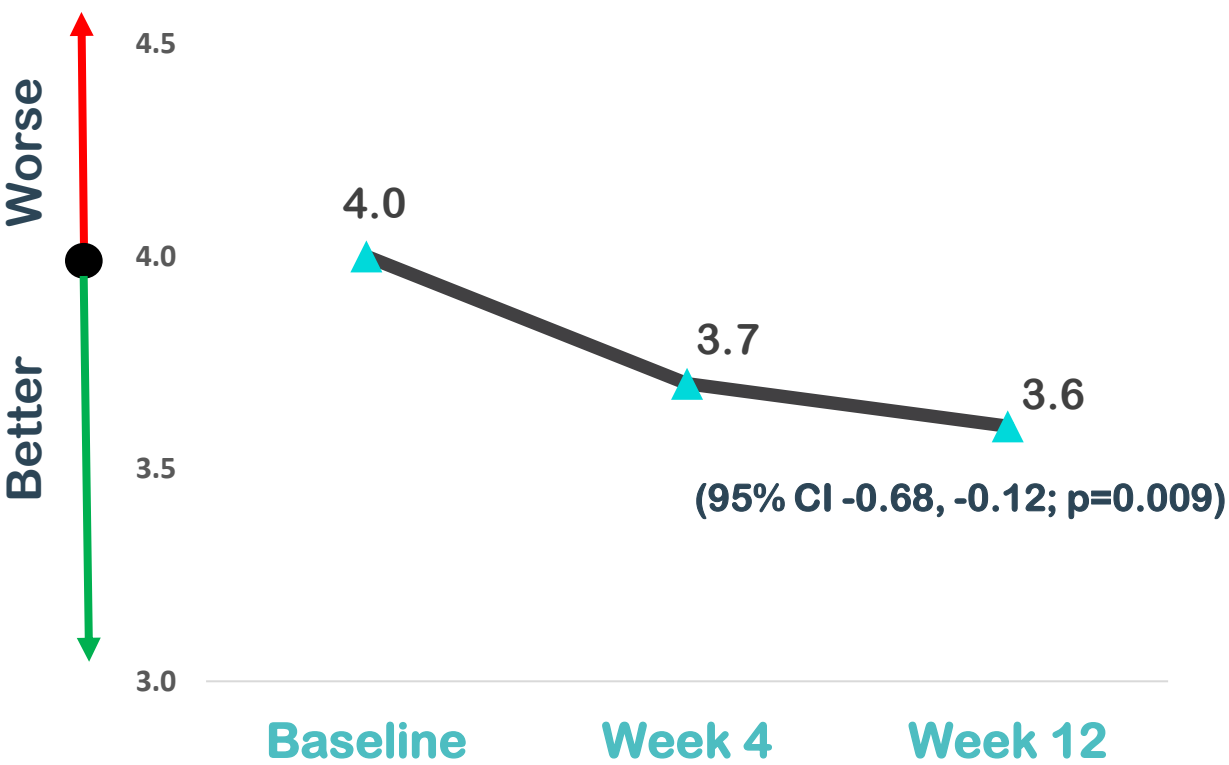
Primary Endpoint: CGI-I



Clinical Global Impression – Improvement (CGI-I) is a 7–point scale that reflects experts' clinical judgment of the patient based on the clinician's total experience with the Rett syndrome population graded from 1 (very much improved) to 7 (very much worse). A decrease in CGI-I score indicates improvement.

Scale	Very Much Improved	Much Improved	Minimally Improved	No Change	Minimally Worse	Much Worse	Very Much Worse
	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



CGI-I improved 10% at 12 weeks (p = 0.009)



Clinical Interpretation

- Significant improvement seen by the treating clinician in 7 out of 14 patients with 50% minimally improved.

CGI-I: Specific Rett Anchor Analysis

- As a first in human trial of NTI164 in Rett patients, Neurotech examined nine (9) anchors/sub-domains to further understand what domain benefits NTI164 could target for registration-directed trials
- Only 2-3 sub-domains are typically examined in Phase 3 trials for CGI-I: composite results for four (4) domains consistently cited by doctors, caregivers as important and where NTI164 showed strong improvements are shown



Communication Skills



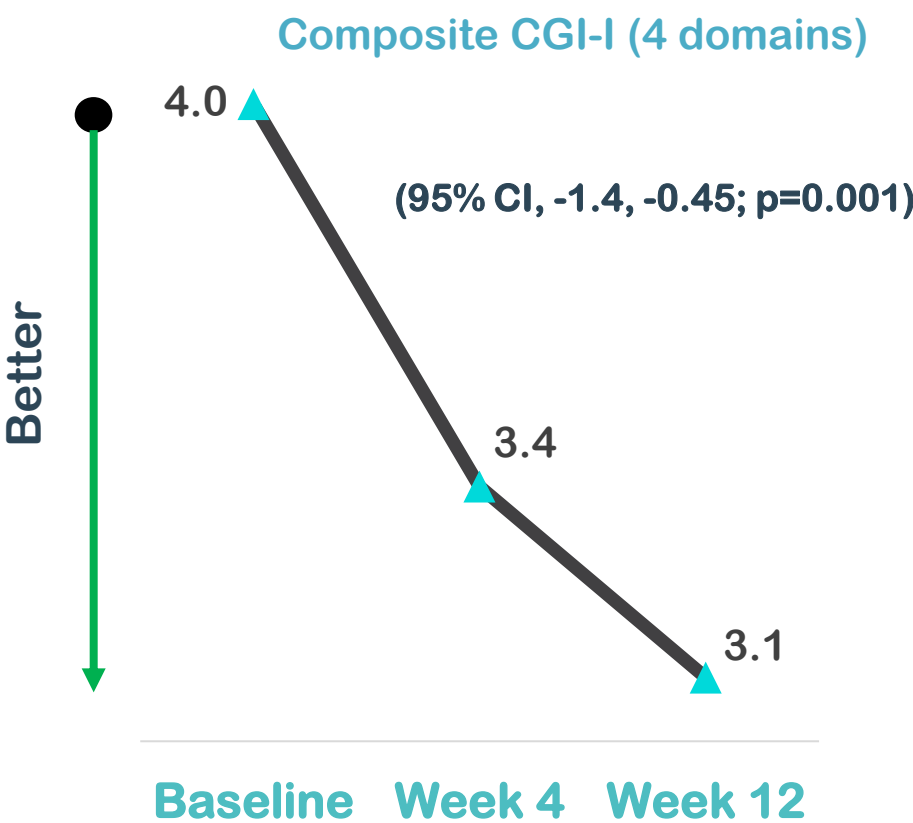
Mental Alertness



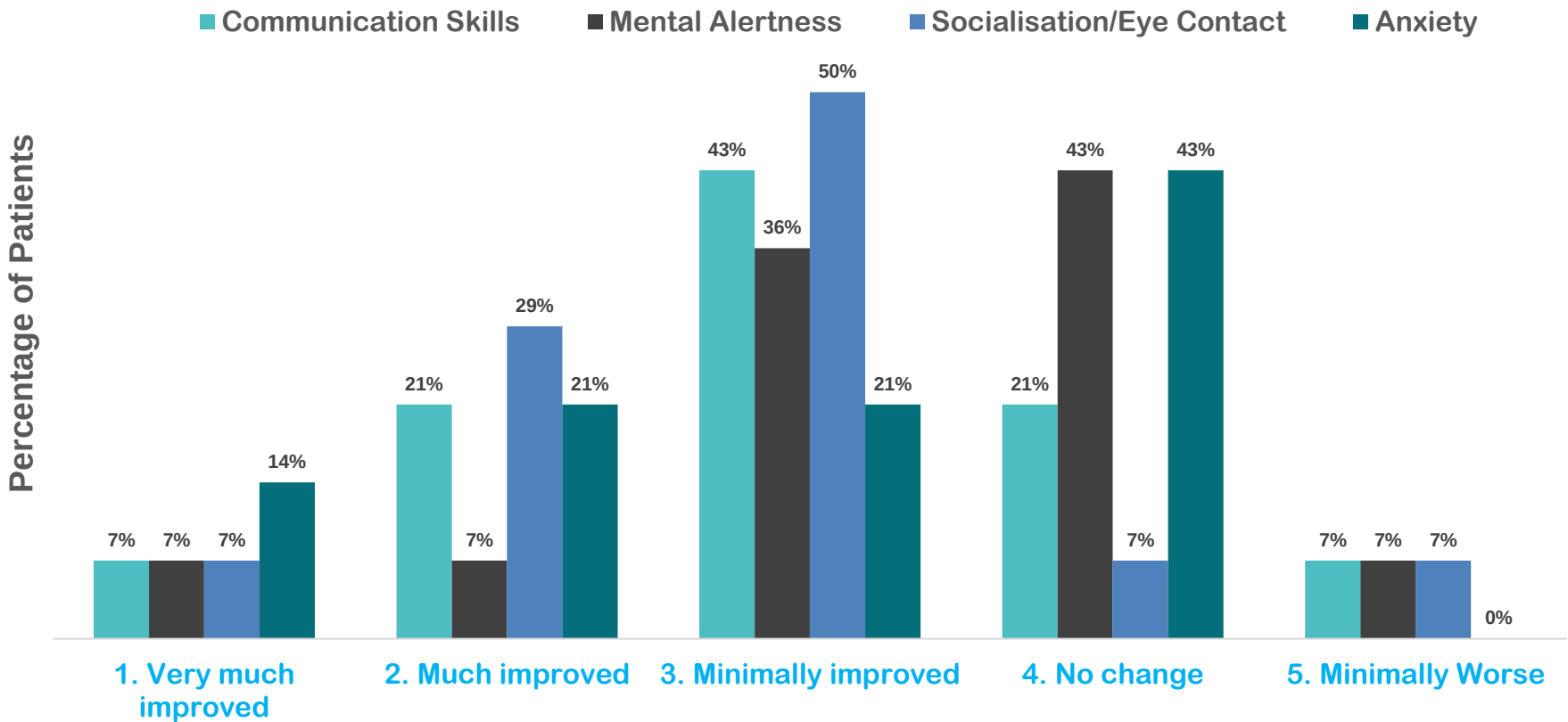
Socialisation / Eye Contact



Anxiety



CGI-I (4 domains) – 12 weeks



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

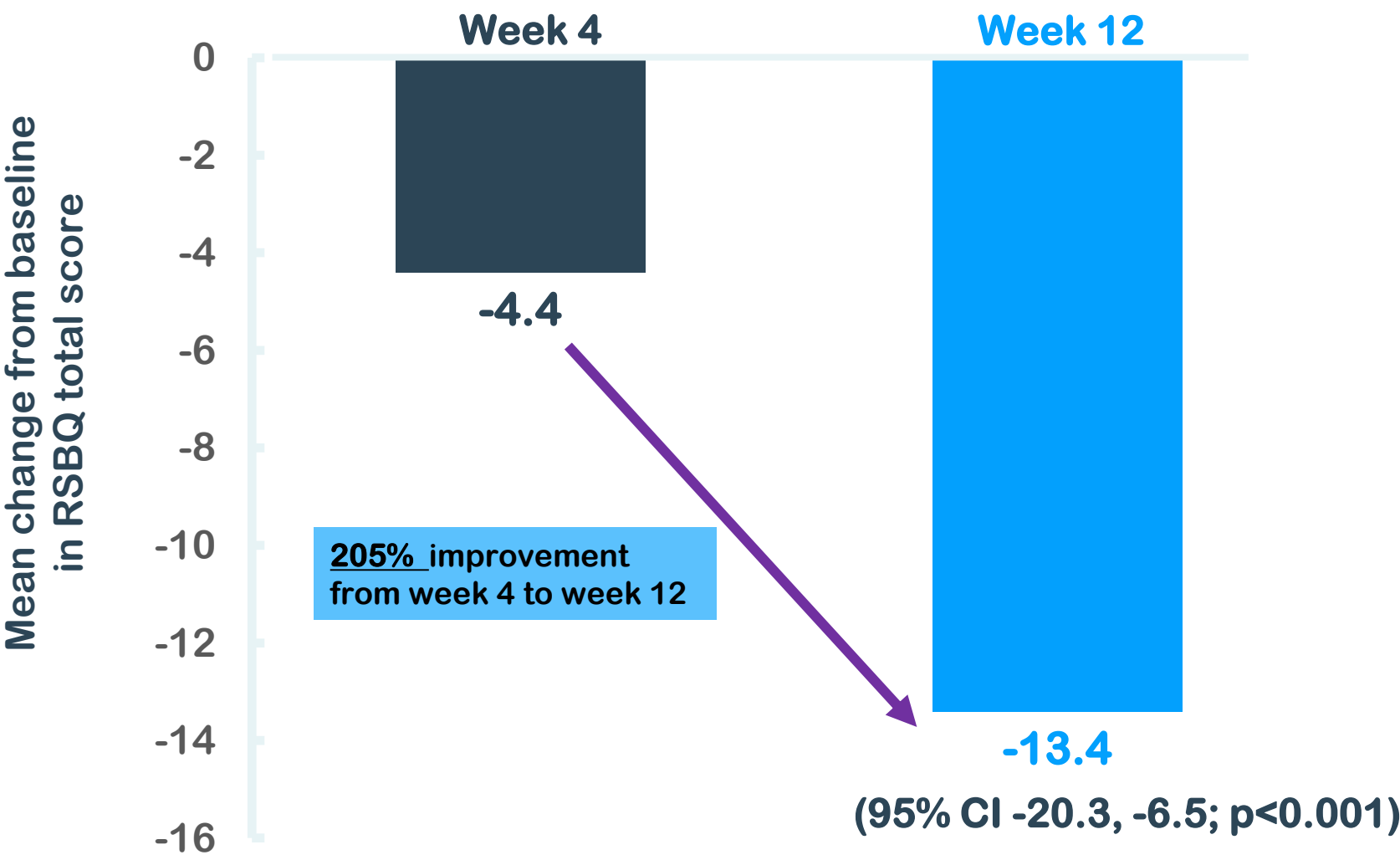
CGI-I (4 core domains) improved 23% at 12 weeks (p=0.001). 93% of patients improved

Secondary Endpoint: RSBQ



The Rett Syndrome Behaviour Questionnaire (RSBQ) assesses the severity of neurobehavioral problems from the perspective of the caregiver and is one of the most widely used measures due to the specificity of its psychometric profile to the core features of Rett and is accepted by the United States Food and Drug Administration (FDA) for use in Rett Syndrome studies

Change from Baseline RSBQ Scores¹



12 week RSBQ score improved 30% v baseline (p <0.001)

Total RSBQ Scores¹

Baseline	4 weeks	12 weeks	P value
44.6	40.2	31.2	<0.001
Improvement (v baseline) mean diff.	4.4 (10%)	13.4 (30%)	

A lower score reflects lesser severity in signs and symptoms of Rett

RSBQ Sub Domain Scores¹

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



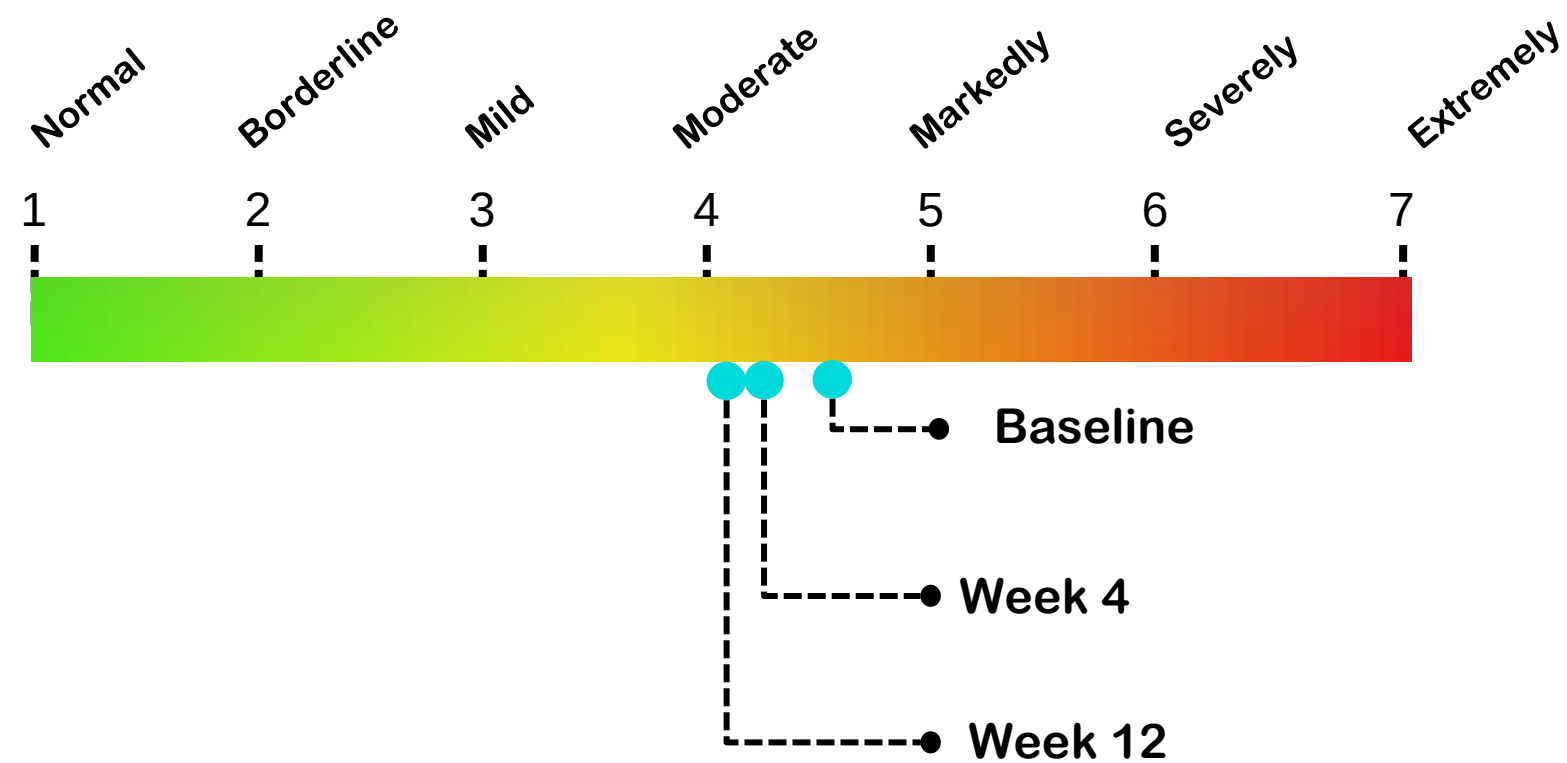
Clinical Interpretation

- Substantial 205% improvement from week 4 to week 12
- The change in RSBQ was aligned with CGI-I, implying that improvement in behavioural components may be related to overall clinical status

1. RSBQ was first shown to discriminate RTT from other intellectual disorders with good inter-rater and test-retest reliability scores. 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 examined: General Mood; Breathing Problems; Hand Behaviours; Repetitive Face Movements; Body Rocking and Expressionless Face; Nighttime Behaviours; Fear/Anxiety; and Walking/Standing. Moderate to high internal consistency has been reported for the total score and the 8 subscales, with good inter-rater and test-retest reliability scores, and significantly higher scores in a Rett population versus those with intellectual disability, thus validating its use as a diagnostic tool.

Secondary Endpoint: CGI-S

Severity of illness Scale (CGI-S)



CGI-Severity of illness¹ ($p = 0.009$)

Mean Severity of Illness (n=14)

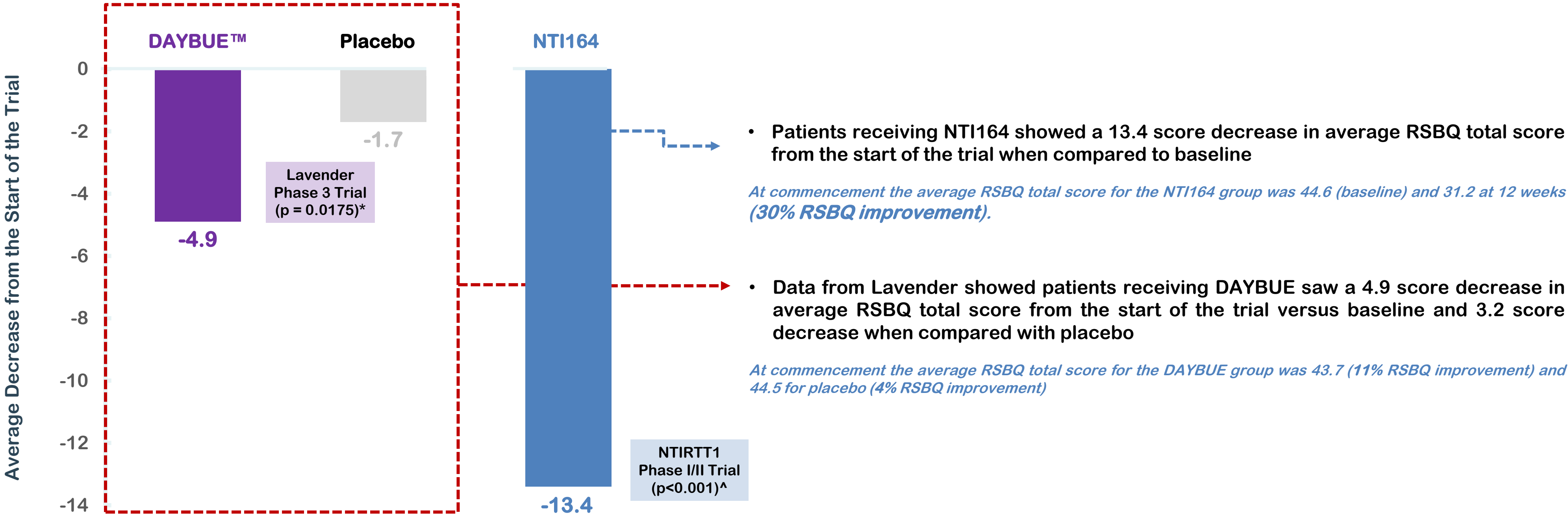


Clinical Interpretation

- CGI-S reduced to a more moderate state
- In other clinical trials to date, daily NTI164 continued to improve CGI-S beyond 12 weeks

NTI164, DAYBUE™ RSBQ – 12 weeks

Rett Syndrome Behavioural Questionnaire (RSBQ)



For basic comparison purposes only – not directly studied in the same clinical trial.

Other Secondary Endpoints



Statistical Significance Met	Not Statistically Significant	Not Measured
ICNDS p=0.004	RTT-SIS p=0.148	CSBS-DP-IT N/M
ICNDS (QoL) p<0.001	RTT-DSC-VAS Ambulation p=0.374	RTT-DSC-VAS Hand Function N/M
RTT-CBI p=0.025	RTT-DSC-VAS Communication Choices p=0.374	
RTT-DSC-VAS Verbal Communication p=0.014		

Conclusion

Met Primary Endpoint

● *NTI64 has demonstrated a statistically significant and clinically meaningful improvement in CGI-I (mean change, -0.4; $p=0.009$). When examining core domains, NTI64 showed 23% improvement at 12 weeks ($p=0.001$) and 93% of patients improved.*

Met Majority of Secondary Endpoints

● *NTI64 has demonstrated a statistically significant and clinically meaningful improvement. Key measure of RSBQ improved 205% between week 4 and week 12*

NTI64 Very Safe

● *Single serious adverse event (urticaria). Small number of adverse events, relating to vomiting, no weight loss, no diarrhoea observed. None of the adverse events were considered to significantly interfere with the patient's functioning and none of the adverse events required any additional medications (i.e. anti-vomiting)*

Huge Unmet Need

● *Single FDA approved therapy: DAYBUE™ (trofinetide); need for additional safe and effective therapies*

Key Milestones – NTI164

1H CY2024

- ✓ HREC/TGA Approval Cerebral Palsy Phase I/II Clinical Trial
- ✓ 24-week PANDAS/PANS Phase I/II Clinical Trial Data
- ✓ Rett Syndrome Phase I/II (14 girls) 52-week Extension HREC Approval
- ✓ Results of ASD Phase II/III Clinical Trial
- ✓ Top-line Rett Syndrome Phase I/II Clinical Trial data
- ✓ Results of Rett Syndrome Phase I/II Clinical Trial – full data
- Meeting outcome – TGA¹ Regulatory Advice
- Publications for ASD Phase I/II + pre-clinical NTI164 results
- Metabologenomic data from Phase I/II PANDAS/PANS Clinical Trial

2H CY2024

- Orphan Drug Designation USA – Rett Syndrome
- Orphan Drug Designation USA – PANDAS/PANS
- Orphan Drug Designation Europe – Rett Syndrome
- Orphan Drug Designation Europe – PANDAS/PANS
- Presentation of Phase I/II Rett Syndrome data at international Rett meeting
- FDA IND / EMA² toxicology
- Commence Phase I/II Cerebral Palsy Clinical Trial



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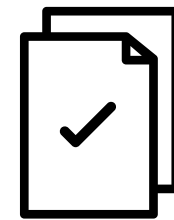
Appendices



Neurotech is a clinical-stage biopharmaceutical development company focused predominately on paediatric neurological disorders



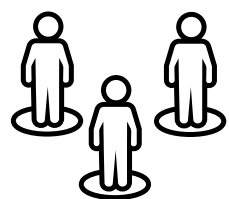
NTI164 exclusive worldwide licence for neurological disorders



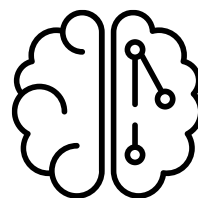
Patents Pending – Use, Composition



Novel oral biopharmaceutical cannabinoid platform (NTI164)



Focus on Paediatric Patients



Multiple Phase I/II and Phase II/III Clinical Trials



Supportive Efficacy & Safety Data in Children

About Rett Syndrome



About

- 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: **impaired brain development and function**
- Currently there is no cure for people with Rett syndrome and classified as a “rare/orphan disease” (by definition, less than 200,000 affected individuals in the US) by the Office of Rare Diseases of the National Institutes of Health

Neuroinflammation

- Numerous scientific reports support neuroinflammatory effects in Rett Syndrome
- NTI164 shown to exhibit anti-neuroinflammation and neuroprotective effects *in vitro*

MeCP2 deficiency exacerbates the neuroinflammatory setting and autoreactive response during an autoimmune challenge

M. I. Zalosnik^{1,2}, M. C. Fabio³, M. L. Bertoldi^{1,2}, C. N. Castañares³ & A. L. Degano^{1,2,3}

Chapter 14

Microglia Involvement in Rett Syndrome

Noël C. Derecki, James C. Cronk, Jonathan Kipnis

First Ever Approval

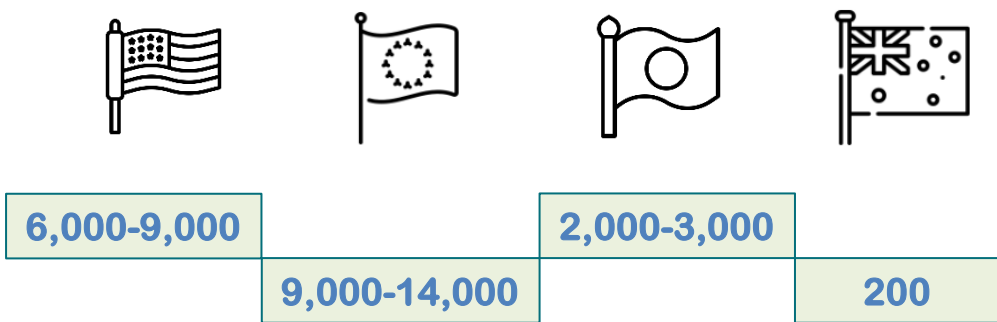


- Neuren Pharmaceuticals (ASX:NEU) / Acadia Pharmaceuticals (NASDAQ:ACAD): FDA Approval **10 March 2023**
- Sets benchmark for FDA accepted clinical endpoints, safety and tolerance

Rett Syndrome Market Dynamics



Significant Market



- 17-26k patients in USA, Europe, Japan, Australia
- Est. US\$2 billion annual market opportunity
- Narrow range of Rett specialist clinicians: focused prescriber group
- Concentrated market dynamics: 18 Rett Centres of Excellence in the US (3 in AU)
- No approved Rett drugs in Europe, Japan and Australia (USA:1)



Single Approved Therapy



- First FDA approved therapy (March 2023)
- Est. drug cost to patient ~US\$1,000 per day. US\$87 million in Q4 CY2023 (US\$177m in CY2023) net sales
- Q3: 800 patient starts (4,500 registered with Rett, ~18% penetration) – strong demand highlights urgent market need
- CY2024 sales est. US\$370m – US\$420m

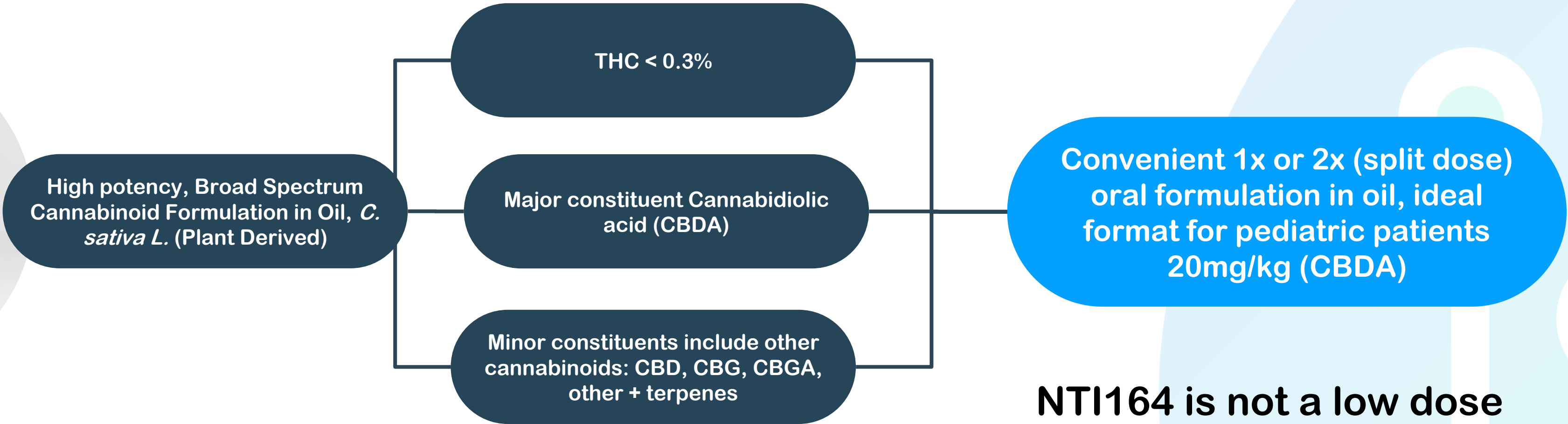


Valuation/Pricing Benchmarks

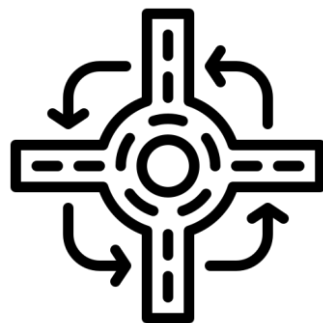


- Neuren (ASX:NEU) license deal with Acadia (NASDAQ:ACAD) close to US\$1 billion for trofinetide (*inc other indications)
- 80% covered lives for DAYBUE™ from US payers within 6 months – rapid reimbursement adoption
- Market approval via single Phase 3 clinical trial v placebo (“Lavender” – 187 pts), with open-label extension (“Lilac” – 154 pts)

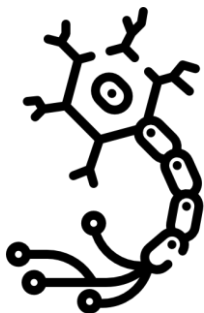
Therapeutic Agent: NTI164



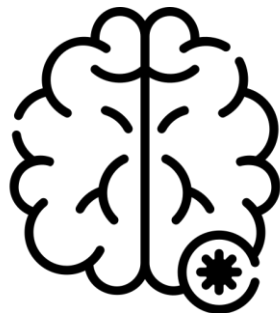
NTI164 is not a low dose CBD oil to be sold over-the-counter



Entourage Effect



Neuroprotective



Anti- Neuroinflammatory

Our Target Markets

Lack of effective therapies, significant unmet medical need

Annual Drug Therapy Market opportunity

US\$2 billion* US\$2 billion US\$1.4 billion¹ US\$4.3 billion

