Neuren (NEU) – ASX Announcement **28 May 2024**

Chairman's Address at 2024 Annual Meeting of Shareholders

At last year's shareholder meeting I said that the approval by the US Food and Drug Administration (FDA) of DAYBUE™ as the first ever treatment for Rett syndrome was the most important milestone in Neuren's history. One year later it is extremely pleasing to see how well DAYBUE has performed in the United States market. Acadia Pharmaceuticals generated 2023 net sales of US$177 million in a period of less than 9 months from launch of DAYBUE and earlier this month they reported 2024 Q1 net sales of US$75.9 million and gave guidance for full year 2024 net sales of US$370 to US$420 million. By any comparison this is an excellent new product launch and Acadia is to be congratulated for their efforts to deliver these results.

Following an extensive competitive partnering process, we expanded our partnership with Acadia in July 2023 by way of an exclusive licence to develop and commercialise trofinetide globally. This was an important step forward to allow Acadia to bring DAYBUE to new markets across the world and they are in a unique position of being able to leverage knowledge of all aspects of the development, marketing and distribution of DAYBUE. The expanded agreement delivered to Neuren US$100 million up-front and very attractive future economics linked to launches and sales in key territories.

In April 2024 Health Canada accepted for review the New Drug Submission (NDS) of trofinetide for the treatment of Rett Syndrome that was submitted by Acadia. Health Canada has granted a priority Review for this submission which brings the potential for approval of the product in that market by the end of this year. In addition, Acadia is making good progress with both the European Medicines Agency and the Japanese regulatory agency as they work towards bringing DAYBUE to these key regions.

We are still in the early stages of the commercial life of trofinetide but already Neuren has received A$271.6 million in royalties, milestones and up-front payments from this product alone. It has been wonderful to see trofinetide come to life as DAYBUE, a commercially available product in the United States and with positive action being taken to enable future international expansion in many countries across the world there is much more to look forward to in the years ahead. Neuren will benefit from an attractive stream of royalties and milestone payments that will flow to us from Acadia as they expand sales of DAYBUE in the United Sates and internationally. In addition we are entitled to a one third share of the market value of the Rare Pediatric Disease Priority Review Voucher that was awarded to Acadia by the FDA.

For many years we have held high hopes that NNZ-2591 could be another extremely attractive prospect for the treatment of rare neurological illnesses. In December 2023 we announced highly encouraging results from our Phase 2 clinical trial of NNZ-2591 in Phelan-McDermid syndrome. These results exceeded our expectations, both in the consistency of the findings and

the magnitude of improvements seen across clinically important aspects of Phelan-McDermid syndrome, including communication, behaviour, cognition/learning and socialisation.

In news released yesterday we were excited to announce positive results from our Phase 2 trial of NNZ-2591 in Pitt Hopkins syndrome. Once again we saw meaningful improvements in important aspects of Pitt Hopkins syndrome, consistently observed by both clinicians and caregivers.

In both of these complex and debilitating indications there is such urgent unmet need and Neuren is currently leading the way in striving to achieve the first approved treatment for these communities. We expect to have our end of Phase 2 meeting with the FDA for Phelan-McDermid syndrome in quarter 3 of this year to agree the next steps.

We are excited by the progress that we have made in the last 12 months with NNZ-2591 and there is much more to be done as we look forward to the Phase 2 trial results for Angelman syndrome in quarter 3 this year and we are evaluating other undisclosed indications whilst continuing the manufacture of drug supplies and other preparatory activities required for a Phase 3 program.

We continue to have a very active focus on investor relations and together with our inclusion in the S&P/ASX 200 index in September 2023 we now have many more institutional shareholders and a high level of interest and engagement from the financial markets community. We continue to seek higher interest and investment, both in Australia and overseas, assisted by a wide range of intermediaries as we share the Neuren story widely.

For those who have been shareholders of Neuren for a while it goes without saying that our financial performance last year was different to anything we have ever produced before. We have noted previously that Neuren has no cost attached to the royalty and milestone revenue we receive from Acadia, which therefore flows straight into pre-tax profit. The impact of this was evident in our financial results for 2023, the highlight of which was profit after tax of A$157 million. This reflected revenue from Acadia of A$232 million, comprising royalties of A$27 million, a milestone payment of A$59 million and A$146 million upfront from the expanded worldwide agreement.

Following this financial transformation we have received confirmation from ASX that Neuren is no longer required to file quarterly cash flow and activity reports. This will enable us to align any quarterly commentary that we choose to provide with the timing of Acadia's quarterly reporting.

Neuren is in a very strong financial position, with cash and short-term investments at 31 March 2024 of A$243.1 million up from A$228.5 million at 31 December 2023, and the ongoing revenue stream from DAYBUE. This supports our commitment to achieving the best outcome for shareholders by pursuing value-adding opportunities to their fullest potential. For NNZ-2591, we will continue to evaluate all options to achieve this as the events of this year unfold.

We are grateful to our shareholders, both longstanding and new, and all the patient communities for the support that is so critical for our success. I extend my thanks and that of the Board to Jon and the Neuren team for their achievements and dedication, assisted by our many valued business partners.

It is a pleasure to work with my fellow Directors and I'm thankful for their support and commitment to Neuren. It's with some sadness that I inform you that Trevor Scott intends to retire as a director of Neuren at the end of June 2024 after a period of some 22 years on the Board during which time he has made an immeasurable impact, especially during the most challenging times on Neuren's journey. It has been a delight to work with Trevor and I wish him every possible happiness as he enjoys his well-earned free time post 30 June and thank him for his extraordinary contribution to Neuren.

I will come back to this matter and ask Trevor to say a few words at the end of today's meeting but for now I'd invite Neuren's CEO Jon Pilcher to address the meeting.

About Neuren

Neuren is developing new drug therapies to treat multiple serious neurological disorders that emerge in early childhood and have no or limited approved treatment options. Recognising the urgent unmet need, all programs have been granted "orphan drug" designation in the United States. Orphan drug designation provides incentives to encourage development of therapies for rare and serious diseases.

DAYBUE™ (trofinetide) is approved by the US Food and Drug Administration (FDA) for the treatment of Rett syndrome in adult and pediatric patients two years of age and older. Neuren has granted an exclusive worldwide licence to Acadia Pharmaceuticals Inc. for the development and commercialisation of trofinetide.

Neuren's second drug candidate, NNZ-2591, is in Phase 2 development for multiple neurodevelopmental disorders, with positive results achieved in Phase 2 clinical trials in Phelan-McDermid syndrome and Pitt Hopkins syndrome.

Contact:
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ASX Listing Rules information

This announcement was authorized to be given to the ASX by the board of directors of Neuren Pharmaceuticals Limited, Suite 201, 697 Burke Road, Camberwell, VIC 3124

Forward-looking Statements

This announcement contains forward-looking statements that are subject to risks and uncertainties. Such statements involve known and unknown risks and important factors that may cause the actual results, performance or achievements of Neuren to be materially different from the statements in this announcement.

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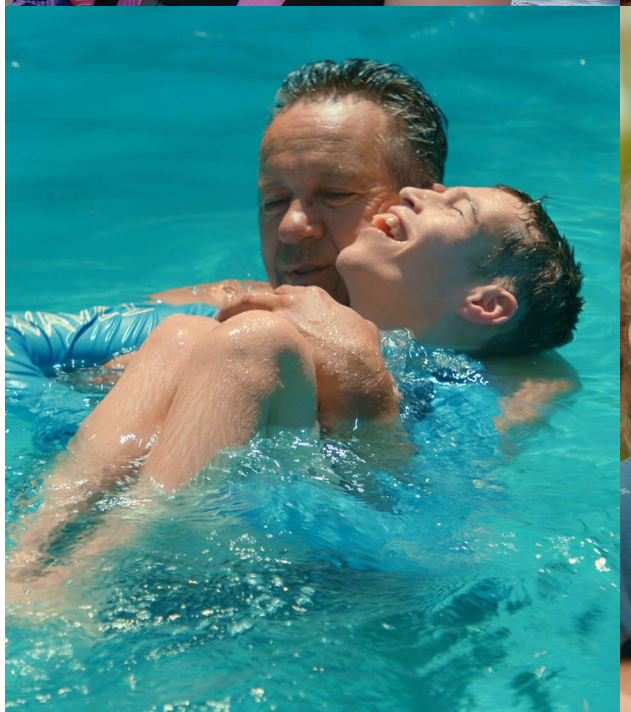
Annual Shareholders' Meeting

28 May 2024

IMPROVING THE LIVES OF PEOPLE WITH NEURODEVELOPMENTAL DISABILITIES






Forward looking statements

This presentation contains forward looking statements that involve risks and uncertainties. Although we believe that the expectations reflected in the forward looking statements are reasonable at this time, Neuren can give no assurance that these expectations will prove to be correct. Actual results could differ materially from those anticipated. Reasons may include risks associated with drug development and manufacture, risks inherent in the regulatory processes, delays in clinical trials, risks associated with patent protection, future capital needs or other general risks or factors.

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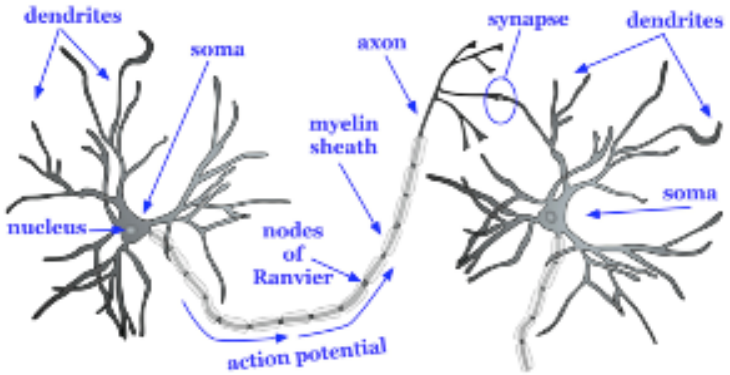
Seeking a ground-breaking impact on neurodevelopmental disorders

Rett	Fragile X	Phelan-McDermid	Angelman	Pitt Hopkins	Prader-Willi
MECP2	*FMR1*	*SHANK3*	*UBE3A*	*TCF4*	*15q11-q13*



Impaired communication between neurons, abnormal formation/pruning of dendrites & chronic inflammation

Neuren's drugs

target the critical role of IGF-1 in this upstream process, using analogs of peptides that can be taken orally as liquids

Severe impact on nearly every aspect of life		
walking and balance issues	anxiety and hyperactivity	seizures
Impaired communication	intellectual disability	Impaired social interaction
impaired hand use	sleep disturbance	gastrointestinal problems

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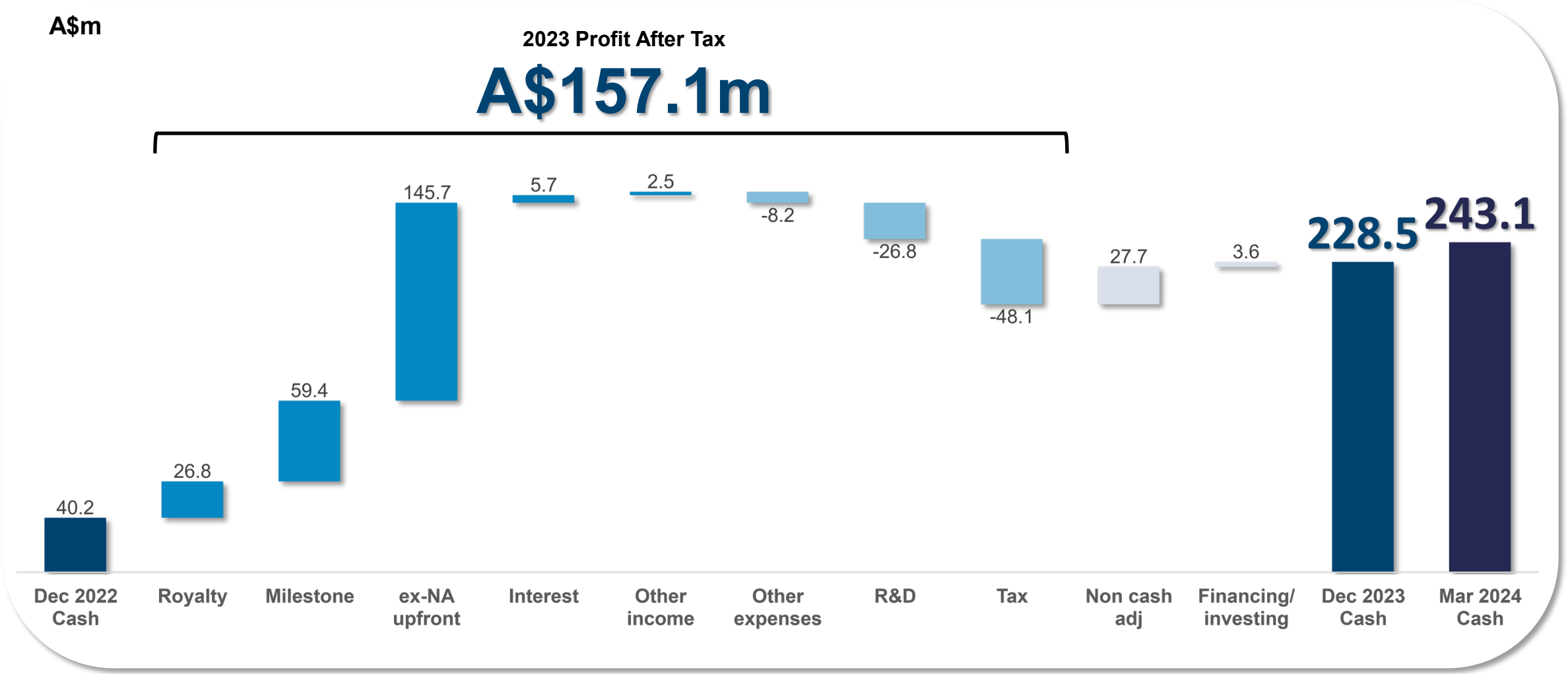
Financial strength to maximise growth opportunities



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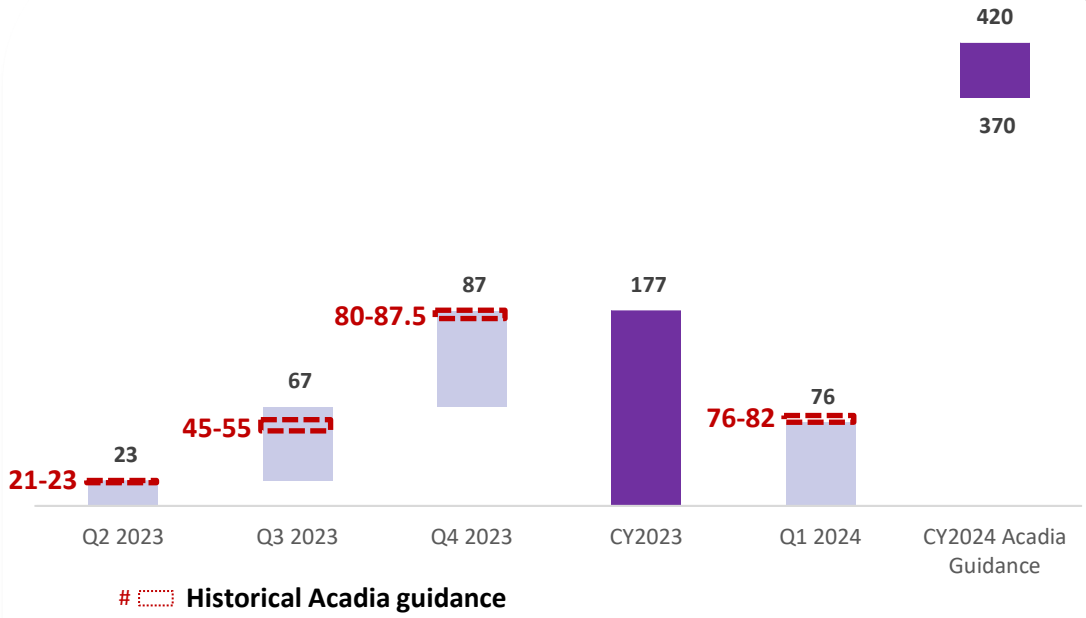
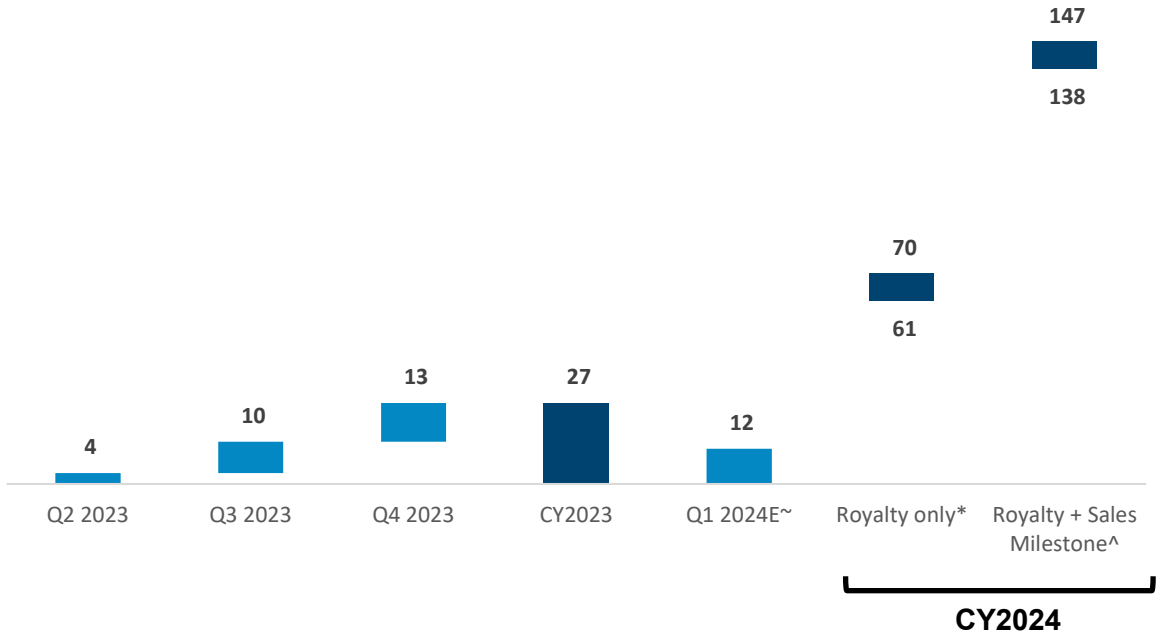
Growing sustainable income from commercialised product

DAYBUE Net Sales (US$m)



2023 net sales of US$177m
2024E net sales of US$370 – 420m

Royalty and Sales Milestone Payments to Neuren (A$m)



2023E royalty of A$27m
2024E royalty of A$61 – 70m, plus A$77m sales milestone

~ Based on 10% of DAYBUE net sales and AUDUSD of 0.652294
* Based on 10% of DAYBUE net sales up to US$250m and 12% of DAYBUE net sales between US$250m and US$500m, and AUDUSD of 0.65
^ Neuren will be entitled to US$50m sales milestones (receivable in Q1 2025) if CY2024 DAYBUE net sales reaches US$250m; assumes AUDUSD of 0.65

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Three key drivers transforming near term value

1 Realise Neuren's share of **trofinetide value in the US** through Acadia's successful commercialization of

Daybue™ (trofinetide)

2 Realise Neuren's share of **trofinetide ex-US** value through expanded global partnership with Acadia

3

Confirm efficacy of **NNZ-2591** in Phase 2 trials for multiple indications, with global rights retained by Neuren

- ✓ Positive top-line results for **Phelan-McDermid syndrome**
- ✓ Positive top-line results for **Pitt Hopkins syndrome**
- Top-line results for **Angelman syndromes** in **Q3 2024**

DAYBUE / Trofinetide

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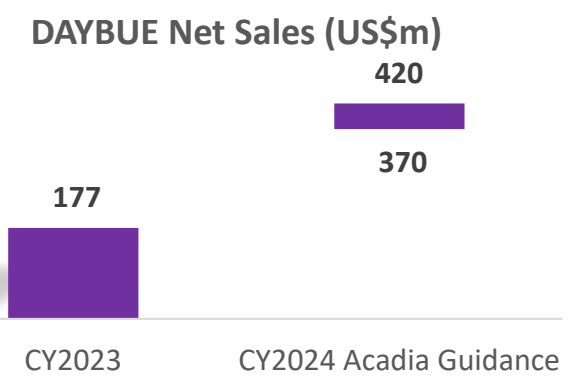
North America – DAYBUE™ US launch in April 2023

	US	Canada
Potential Rett patients	6,000 - 9,000[1]	600 - 900[1]
Currently identified Rett patients	5,000[1]	NDS accepted for priority review, potential approval around year-end 2024[3]

As of 3 May 2024: >1,300 patients initiated therapy, 862 active on therapy



Economics to Neuren:

- ✓ **US$10m** **upfront in 2018**
- ✓ **US$10m** **in 2022 following acceptance of NDA for review**
- ✓ **US$40m** **in Q2 2023 following 1st commercial sale in the US**
- **US$33m** one third share of Priority Review Voucher awarded to Acadia (assuming market value US$100m)
- **US$55m** Milestone payments related to Fragile X

Tiered Royalty Rates (% of net sales)[2]

Annual Net Sales	Rates
≤US$250m	**10%**
>US$250m, ≤US$500m	**12%**
>US$500m, ≤US$750m	**14%**
>US$750m	**15%**

Sales Milestones

Net Sales in one calendar year	US$m
≥US$250m	**50**
≥US$500m	**50**
≥US$750m	**100**
≥US$1bn	**150**

[1] Acadia estimates
[2] Royalty rates payable on the portion of annual net sales that fall within the applicable range
[3] Acadia First Quarter 2024 Earnings Call presentation in May 2024

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Meaningful real world benefits reported

LILAC-2 Caregiver Exit Interviews[1]

Area/type of improvement with trofinetide reported by ≥15% of caregivers, n (%)	Caregivers N=25 (%)
Engagement with others	*11 (42.3)*
Hand use	*10 (38.5)*
Eye gaze	*8 (30.8)*
Attention/focus/concentration	*7 (26.9)*
Tobii eye trackers use	*7 (26.9)*
Ability to make sounds	*6 (23.1)*
Happier mood or disposition	*6 (23.1)*
Ability to walk	*5 (19.2)*
Alertness	*5 (19.2)*
New words	*5 (19.2)*
Seizures	*4 (15.4)*
Aware of environment	*4 (15.4)*
Repetitive hand movements	*4 (15.4)*

Real World Experience[1]

"It was her engagement level with the world outside of her – to me and to friends in school; it just blossomed, and it was like a light was turned on."

"Her verbalization definitely improved, and she started saying more things."

"Picking up things a lot more (mostly her cup), happens daily and she is now trying to drink by herself."

"Improved cognitive ability, and [the parents] are hearing new words or words they have not heard in a while."

[1] Acadia Fourth Quarter and Full Year 2023 Earnings Call presentation in Feb 2024

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Outside North America

	Europe	Japan	Other
Potential Rett patients	9,000 - 14,000[1]	1,000 - 2,000[1]	~30,000[2]
Currently identified Rett patients	~4,000[2]	~800 - 1,000[2]	~2,000[2]

- **Europe:** Pediatric investigation plan (PIP) filed with and accepted by EMA, with a potential Marketing Authorisation Application filing in Q1 2025[3]
- **Japan:** Formal meeting with Japanese regulatory agency (PMDA) scheduled in 2Q24 to discuss clinical plan[3]

Economics to Neuren:

✓	**US$100m**	**upfront**
	US$35m	following 1st commercial sale in Europe
	US$15m	following 1st commercial sale in Japan
	US$10m	following 1st commercial sale of a 2nd indication Europe
	US$4m	following 1st commercial sale of a 2nd indication Japan

Sales milestones	On achievement of escalating annual net sales thresholds: Europe: up to **US$170m** Japan: up to **US$110m** RoW: up to **US$83m**
Tiered royalties	**Mid-teens to low-20s %** of net sales

[1] Acadia estimates
[2] Neuren estimates based on prevalence studies and patient organisations
[3] Acadia First Quarter 2024 Earnings Call presentation in May 2024

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NNZ-2591

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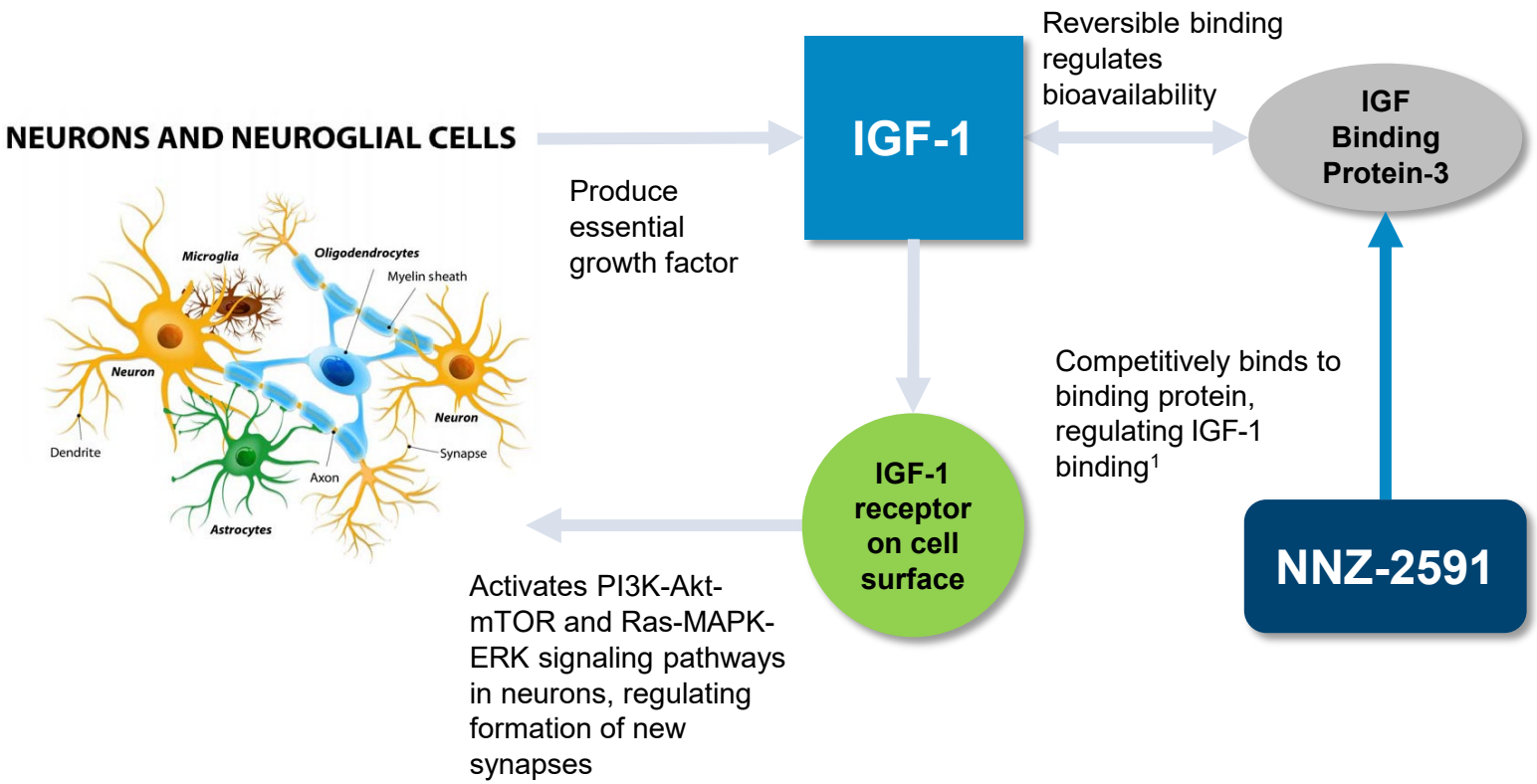
Regulating IGF-1 in the brain



- **NNZ-2591** is a synthetic analog of cyclic glycine proline, a peptide that occurs naturally in the brain, designed to be more stable, orally bioavailable and readily cross the blood-brain barrier
- **NNZ-2591** can regulate the amount of IGF-1 that is available to activate IGF-1 receptors
- The effects of **NNZ-2591** are “state-dependent” – correcting impairment, but not impacting normal cells

[1] doi: 10.1038/srep04388: Guan et al, 2017: Cyclic glycine-proline (cGP) regulates IGF-1 homeostasis by altering the binding of IGFBP-3 to IGF-1

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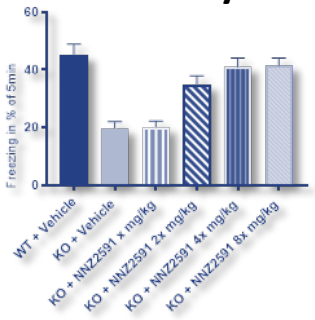
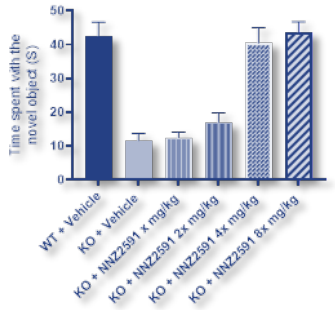
Clear efficacy and dose response in Phelan-McDermid syndrome model

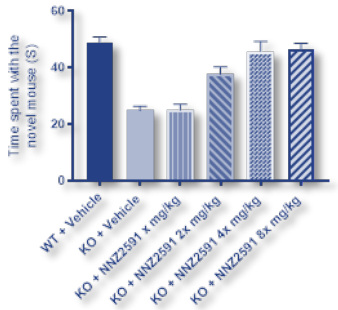
Memory



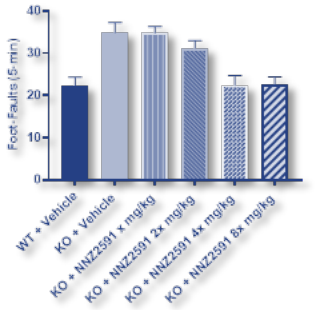
Learning



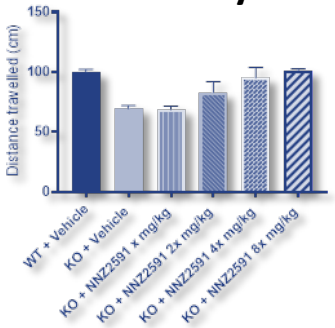
Sociability



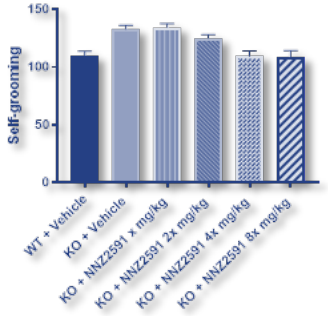
Motor function



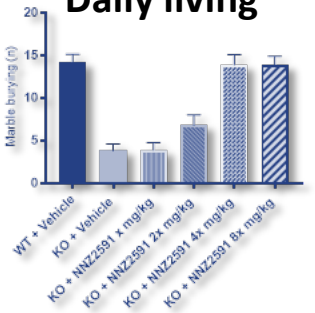
Anxiety



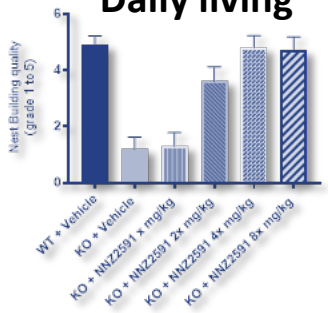
Repetitive behavior



Daily living



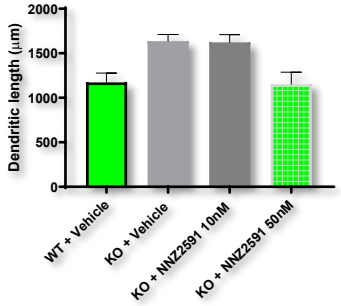
Daily living

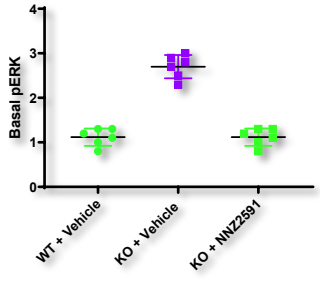


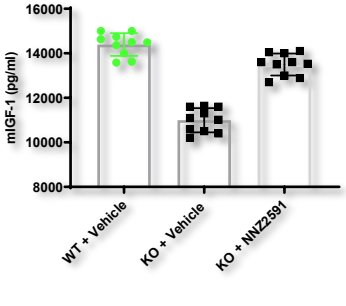
Incidence of audiogenic seizures

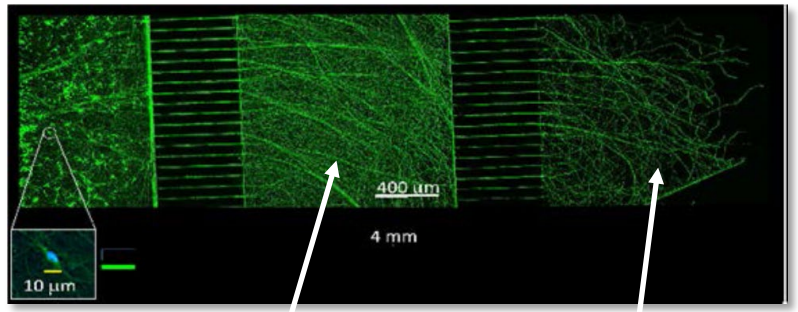
WT + vehicle	0%
KO + vehicle	60%
KO + x mg/kg	50%
KO + 2x mg/kg	30%
KO + 4x mg/kg	10%
KO + 8x mg/kg	10%

In biochemical testing, NNZ-2591 was shown to normalize the abnormal length of dendritic spines that form the synapse, the excess activated ERK protein (pERK) and the depressed level of IGF-1 in *shank3* knockout mice









Abnormal dendrites in *shank3* knockout mice cells in culture

Normalization after treatment with NNZ-2591

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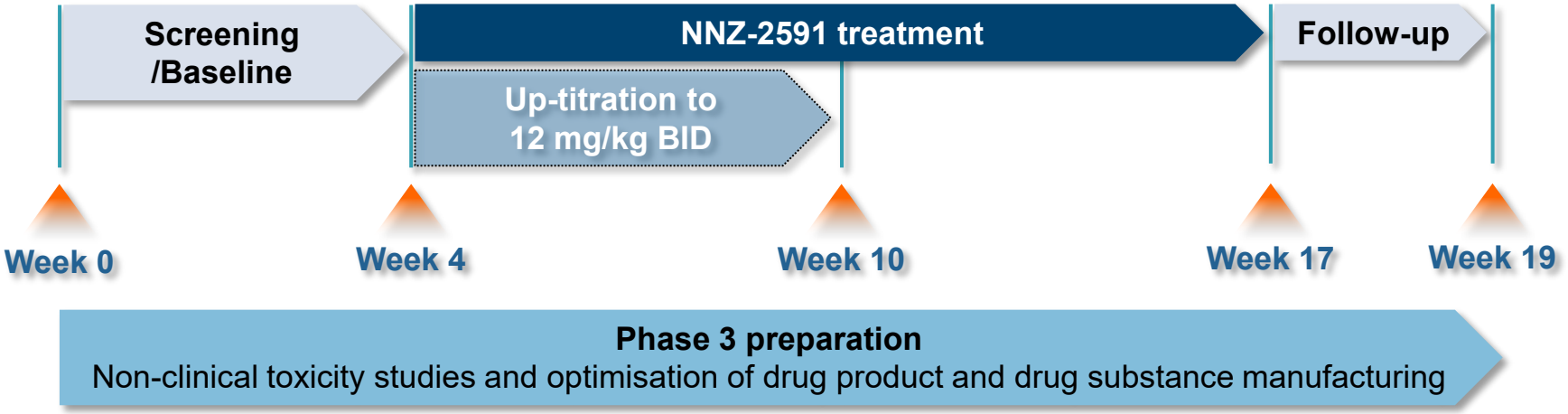
Key features of first Phase 2 trials

Overall aim – expedite data that informs the design of subsequent registration trials and prepare for Phase 3 in parallel



- Prioritising speed to data and maximising opportunity to demonstrate effects
- Confirm safety and PK in pediatric patients
- Assess treatment impact across multiple efficacy measures to select primary endpoint for registration trial
- **Positive results for Phelan-McDermid syndrome and Pitt Hopkins syndrome**
- **Top-line result for Angelman syndrome in Q3 2024**
- Manufacturing for Phase 3 commenced

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Phelan-McDermid syndrome (PMS)

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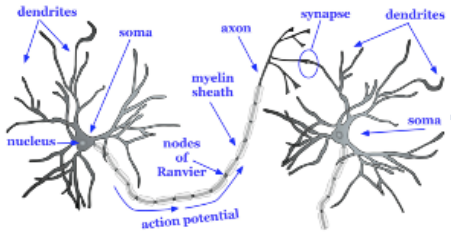
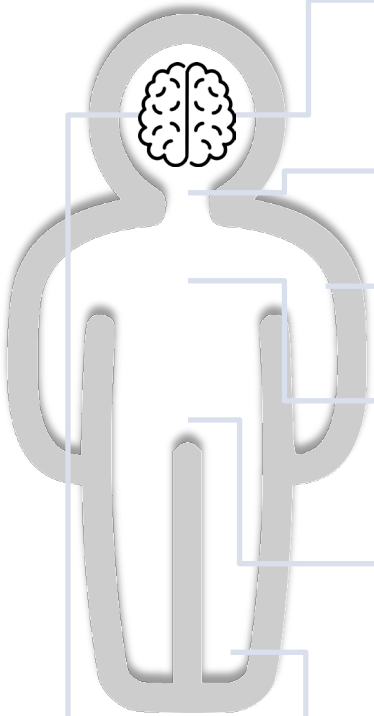
PMS has overwhelming unmet medical need

Cause of the syndrome

Deletion or variation in the *SHANK3* gene on chromosome 22

SHANK3 protein plays a role in the formation, maintenance and function of dendrites and synapses





Broad and severe impact on life

Intellectual impairment
Behavioural issues
Sleep disorders
Seizures (~40% of patients)

Language deficits
Feeding difficulties

Motor delays
Low muscle tone

Sweat less, risk of overheating
High pain tolerance

Difficulties toilet training (~3/4 of patients)
GI dysfunction (most commonly constipation)

Walking abnormalities

Frequent hospitalization and heightened risk of accidents

From Voice of the Patient Report

Externally-Led Patient-Focused Drug Development Meeting 8 Nov 2022

"PMS has an overwhelming unmet medical need. *There are no FDA approved treatments for PMS despite its severely debilitating manifestations. Parents and caregivers are open to trying almost anything to try to relieve their child's suffering; most have tried an incredibly high number of treatments and approaches for symptom management, with very little success. Some received medications that caused more harm than good"*

"PMS has severe quality of life impacts on those living with the disease, as well as on parents and siblings. *Most activities of daily life, including communicating needs or wants, self-care (bathing, dressing, toileting) and socializing with peers/siblings are affected. Most individuals living with PMS rely on their parents and caregivers for all their daily needs, and many require 24-hour care."*

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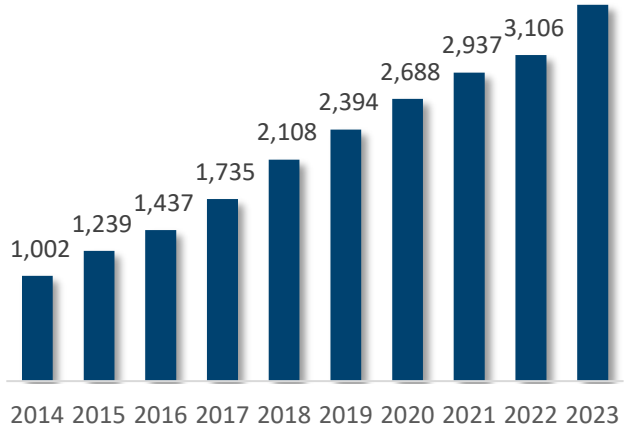
PMS is historically under-diagnosed, but this is changing

Estimated prevalence is 1% of people with autism - 1/8,000 to 1/15,000 males and females[1]

	US	Europe	Japan	China	Other[2]
Potential PMS patients	17,000 – 32,000[3]	21,000 – 41,000[3]	5,000 - 9,000[3]	51,000 – 95,000[3]	16,000 - 31,000[3]

Phelan-McDermid Syndrome Foundation members



Currently 1,739 US members

75% of PMS patients have been diagnosed with an ASD

~1% of autism patients have *SHANK3* mutations

Opportunity to accelerate diagnosis

Autism

US ADDM tracks 440k children with autism spectrum disorder

- Rising awareness
- EL-PFDD meeting with FDA in 2022
- ICD code assigned in 2023
- Enhanced genetic testing technologies
- Expanding ADDM network sites

[1] Phelan McDermid Syndrome Foundation (PMSF) (www.pmsf.org)
[2] Brazil, Israel, South Korea, Australia and New Zealand
[3] Estimates based on United Nations population data 2022, derived by applying the estimated prevalence range to the populations under 60 years (urban population only for China)

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Neuren is leading development of a first approved treatment for PMS

Phase 2 Program Status

- Phase 2 clinical development in the US under an IND
- End of Phase 2 Meeting with FDA planned Q3 2024
- Orphan Drug designation in US and EU
- Eligible for Rare Pediatric Disease Designation Priority Review Voucher program

Limited products in development

Company	Product Development Stage
neuren pharmaceuticals	**Positive Phase 2 trial**
#2	Phase 2 trial closed Jan 2021
#3	Phase 1
#4	Phase 1
#5	Pre-clinical

Neuren engaging with all stakeholders

pmsf

cureSHANK

Leading clinicians

FDA

Phase 2 clinical trial results highlights

- **NNZ-2591 was safe and well tolerated, with no clinically significant changes in laboratory values or other safety parameters during treatment**
- **Significant improvement was assessed by both clinicians and caregivers across multiple efficacy measures**
- **Improvements were consistently seen across clinically important aspects of Phelan-McDermid syndrome, including communication, behaviour, cognition/learning and socialisation**
- **Clinician and caregiver global efficacy measures showed a level of improvement typically considered clinically meaningful:**
  - **PMS Clinical Global Impression of Improvement (CGI-I) – mean score of 2.4 with 16 out of 18 children showing improvement assessed by clinicians**
  - **PMS Caregiver Overall Impression of Change (CIC) – mean score of 2.7 with 15 out of 18 children showing improvement assessed by caregivers**
- **For 10 out of 14 efficacy endpoints, improvement from baseline on overall/total scores was statistically significant ($p<0.05$)[1]**

[1] Wilcoxon signed rank test

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Safety and tolerability summary

NNZ-2591 was safe and well tolerated

- ✓ Well tolerated
- ✓ Most Treatment Emergent Adverse Events (TEAE) were mild to moderate
  - 1 Serious TEAE (gastroenteritis) not related to study drug, occurred during safety follow-up period after end of treatment
  - 3 discontinuations due to TEAEs not related to study drug: 2 due to testing positive for COVID-19 and 1 due to seizures
- ✓ No clinically significant changes in laboratory values, electrocardiogram (ECG) or other safety parameters were observed during treatment

TEAEs in 2 or more subjects

Event	N=18 n (%)	Event	N=18 n (%)
Constipation	2 (11.1)	Somnolence	3 (16.7)
Diarrhea	2 (11.1)	Pyrexia	3 (16.7)
Nausea	2 (11.1)	Fatigue	2 (11.1)
Vomiting	2 (11.1)	Aggression	2 (11.1)
COVID-19	3 (16.7)	Insomnia	2 (11.1)
Nasopharyngitis	2 (11.1)	Decreased Appetite	3 (16.7)
Otitis Media	2 (11.1)	Rhinorrhea	2 (11.1)
Psychomotor Hyperactivity	4 (22.2)		

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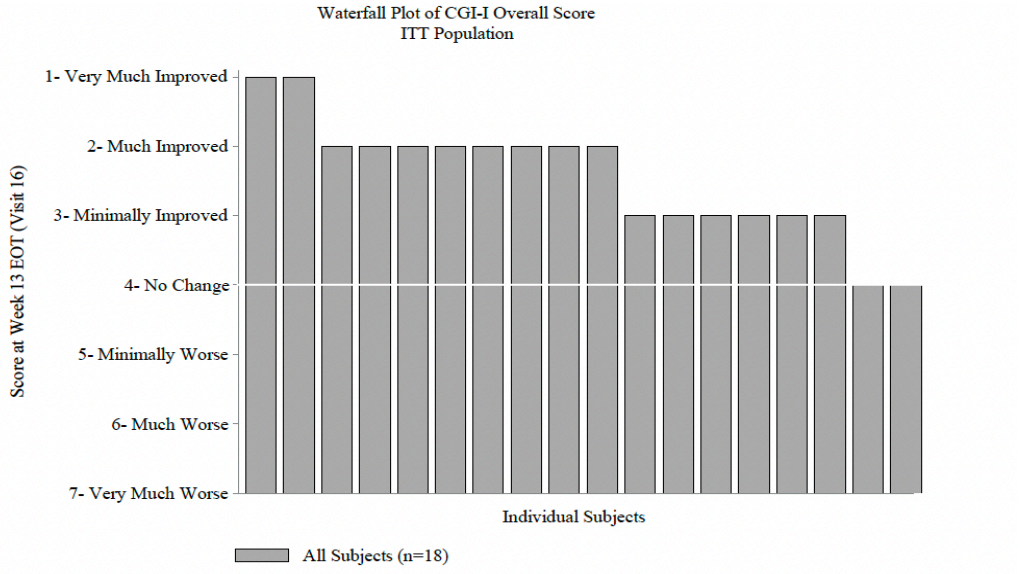
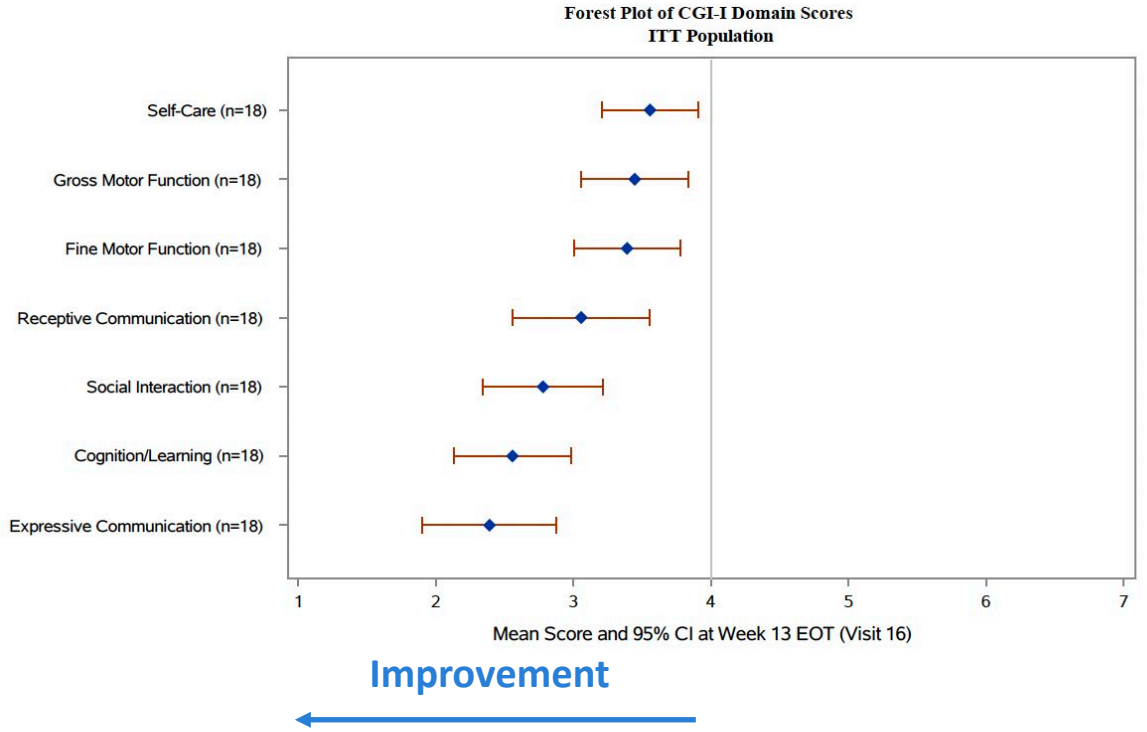
PMS CGI-I (clinician) results by subject and by domain

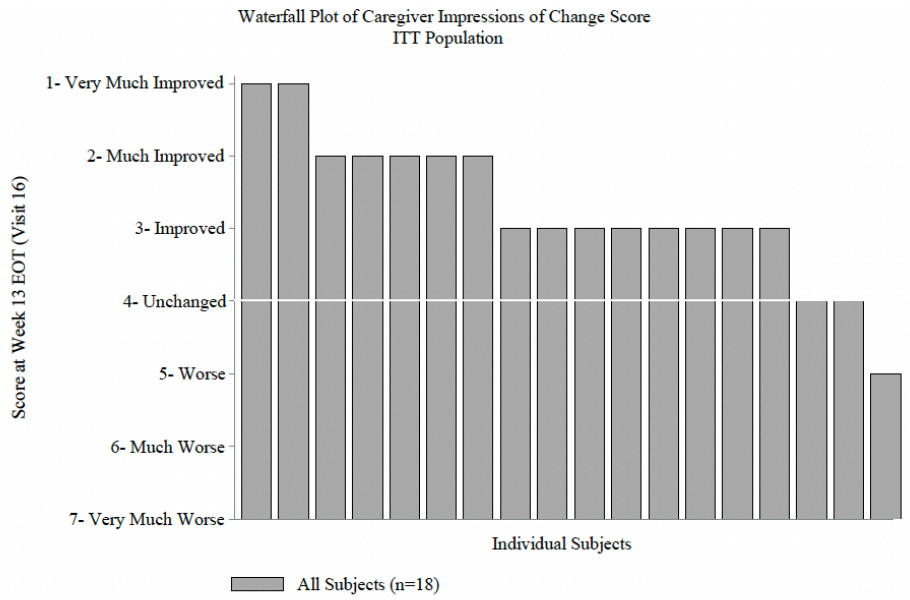
Mean CGI-I score of 2.4 with 16 out of 18 children showing improvement

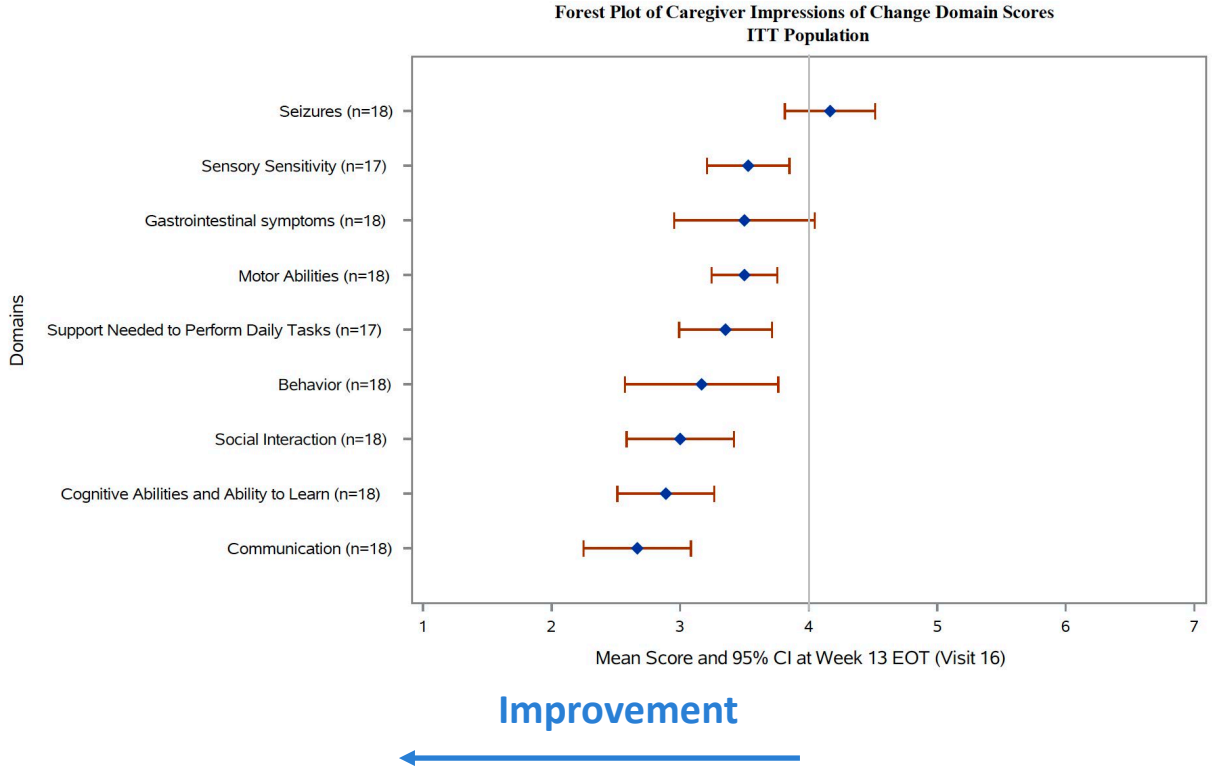




PMS CIC (caregiver) results by subject and by domain

Mean CIC score of 2.7 with 15 out of 18 children showing improvement



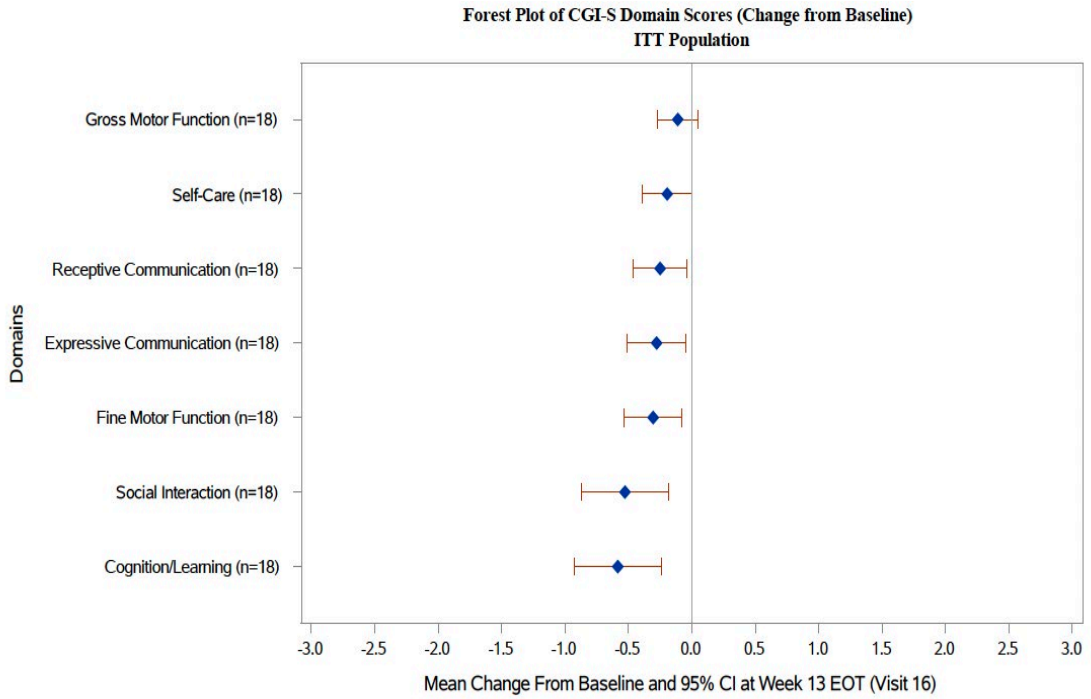


Improvement

PMS Clinical Global Impression of Severity (CGI-S) and Caregiver Top 3 Concerns results by domain

7 subjects improved by one point on the overall CGI-S score after 13 weeks of treatment and improvement was observed in the most common concerns of caregivers (communication, behaviour, social interaction, self-care)

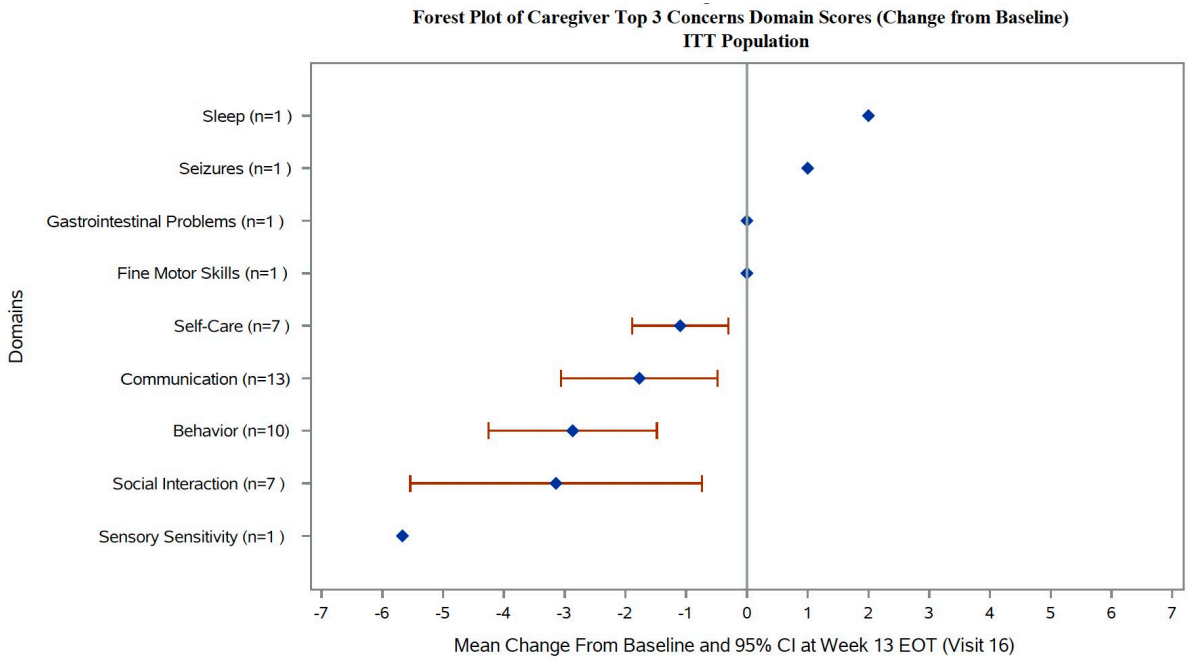
CGI-S domains



Improvement

Caregiver Top 3 Concerns

(Domains based on frequency of nomination)



Improvement

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Clinician and caregiver testimonials

Clinicians

"Marked improvement in expressive language and moderate improvement in socialization."

"Teachers noted improvement in learning new skills."

"Able to focus work at school, both to the things they always enjoy and new tasks."

"Expressive communication- significant improvement in using more complex phrases, better back and forth communication. Better expressing needs. Some commentary on how mom is feeling, "I want you to be happy"."

"Expressive communication- babbling much more than baseline."

"A few 1-2 word phrases that were not at baseline "oh boy", "Hi Mama", "I love you", "oh my"."

"Gross motor- Stronger climbing ladders, comes downstairs which never did before, Walks upstairs without help (needed help at baseline)."

Caregivers

"Using more words while retaining eye contact… Improved pretend play… Initiating eye contact"

"Less scripting, less stimming… More flexible with changes… In general, they are more safe-even at bus stop"

"More focused , engaged, aware of their environment, people."

"So much happier, not throwing self to ground when can't get his way"

"More attentive and it makes for an easy learner, Now can focus better on what we are trying to teach."

"Attention span is great right now… He can focus long enough to complete tasks and try new things."

"Can now run instead of walking fast… Good balance, not needing assistance on stairs."

Pitt Hopkins syndrome (PTHS)

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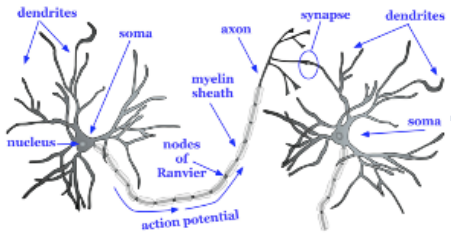
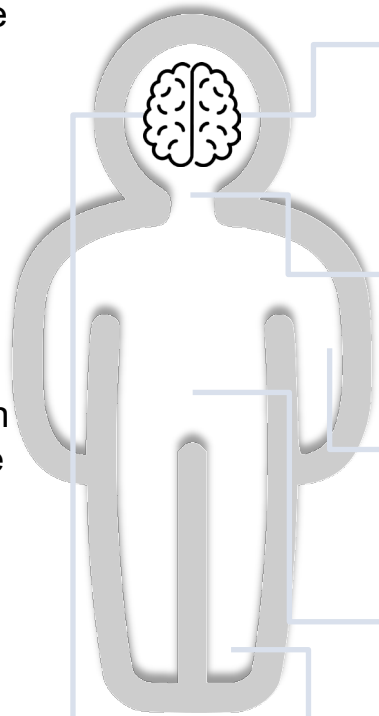
PTHS overview

Cause of the syndrome

Deletion or variation in the *TCF4* gene on chromosome 18

TCF4 protein plays a role in the formation, maintenance and function of dendrites and synapses





Broad and severe impact on life

Intellectual impairment
Behavioural issues
Sensory processing disorder
Sleep disorders
Seizures
Vision impairment (severe myopia)

Language deficits
Breathing problems (hyperventilation, apnea, breath-holding)
Feeding difficulties

Motor impairments including hypotonia (low muscle tone) and gross and fine motor delays

GI dysfunction (gastroesophageal reflux and constipation)

Walking abnormalities

Patients stories

Pitt Hopkins Research Foundation

"She was tested earlier for Angelman and Rett Syndrome, but they were of course negative. I had a strange feeling that something was wrong with her already when she was a newborn…I started to see different doctors with her, but they just told me nothing was wrong, until we met a Neurologist who told us that she had Cerebral Palsy and that she would not able to walk, ever…She doesn't talk but when she was about one year old she was saying a few words that never ever came back..."

"Caleb is currently 10 months old and he does not sit or roll yet and is not really interested in toys. He is currently in an early intervention program and is going through physical therapy, and sees a vision teacher and special education teacher…It has not been an easy journey thus far. I still do not how and where I get all my strength from. I know things will only get harder as he gets older but I am ready to accept the challenge and take each day as it comes."

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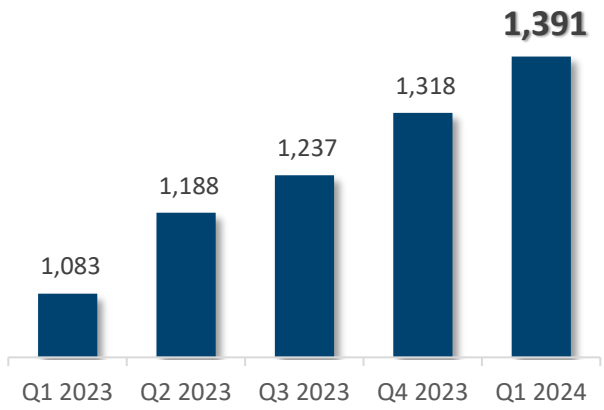
PTHS is historically under-diagnosed, but this is changing

Estimated prevalence is 1/34,000 to 1/41,000 males and females[1]

	US	Europe	Japan	China	Other[2]
Potential PTHS patients	6,000 – 7,000[3]	8,000 – 9,000[3]	1,000 - 2,000[3]	18,000 – 22,000[3]	6,000 - 7,000[3]

Pitt Hopkins Syndrome Census – initiated Q1 2023[1]



Currently 497 in US & Canada, 329 in EMA & UK, 248 in China, 60 in ANZ

Clinical similarities between PTHS, Rett and Angelman syndromes calling for TCF4 screening in suspected Rett or Angelman patients[4]

Opportunity to accelerate diagnosis

Autism

US ADDM tracks 440k children with autism spectrum disorder

- Rising awareness
- ICD code assigned in 2020
- Enhanced genetic testing technologies
- Expanding ADDM network sites

[1] Pitt Hopkins Research Foundation (PHRF) (pitthopkins.org)
[2] Brazil, Israel, South Korea, Australia and New Zealand
[3] Estimates based on United Nations population data 2022, derived by applying the estimated prevalence range to the populations under 60 years (urban population only for China)
[4] Takano et al, "Two percent of patients suspected of having Angelman syndrome have TCF4 mutations" Clin Genet. 2010 Sep;78(3):282-8; Armani et al, "Transcription factor 4 and myocyte enhancer factor 2C mutations are not common causes of Rett syndrome" Am J Med Genet A. 2012;158A(4):713–9

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Neuren is leading development of a first approved treatment for PTHS

Neuren Program Status

- Positive Phase 2 trial
- Clinical development in the US under an IND
- Orphan Drug designation in US and EU
- Eligible for Rare Pediatric Disease Designation Priority Review Voucher program

Limited products in development

Company	Product Development Stage
neuren pharmaceuticals	**Successful Phase 2**
#2	Phase 2 *(research institute sponsored, focusing on GI symptoms)*
#3	Phase 1/2a trial *(not yet recruiting)*
#4	*Preclinical*

Neuren engaging with all stakeholders

PITT HOPKINS RESEARCH FOUNDATION

Leading clinicians

FDA

Phase 2 clinical trial results highlights

- **NNZ-2591 was safe and well tolerated, with no meaningful trends in laboratory values or other safety parameters during treatment**
- **Statistically significant improvement from baseline assessed by both clinicians and caregivers in all 4 efficacy measures specifically designed for Pitt Hopkins syndrome ($p<0.05$)[1]**
- **Clinician and caregiver global efficacy measures showed a level of improvement considered clinically meaningful:**
  - **PTHS Clinical Global Impression of Improvement (CGI-I) – mean score of 2.6 with 9 out of 11 children showing improvement assessed by clinicians**
  - **PTHS Caregiver Overall Impression of Change (CIC) – mean score of 3.0 with 8 out of 11 children showing improvement assessed by caregivers**
- **Improvements were seen in clinically important aspects of Pitt Hopkins syndrome, including communication, social interaction, cognition and motor abilities**

[1] Wilcoxon signed rank test

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Safety and tolerability summary

NNZ-2591 was safe and well tolerated

- ✓ Well tolerated
- ✓ All Treatment Emergent Adverse Events (TEAE) were mild to moderate, mostly not drug related
  - 0 Serious TEAE
  - 4 discontinuations due to TEAEs, all mild/moderate, all resolved
- ✓ No meaningful trends in laboratory values, electrocardiogram (ECG) or other safety parameters were observed during treatment

TEAEs in 2 or more subjects

Event	N=16 n (%)		Event	N=16 n (%)	
Constipation	3 (19)	2 mild, 1 mod	Contusion	2 (13)	all mild
Diarrhea	4 (25)	all mild	Gastroenteritis-viral	2 (13)	1 mild, 1 mod
Vomiting	2 (13)	all mild	Nasopharyngitis	3 (19)	all mild
Fatigue	4 (25)	3 mild, 1 mod	Cough	2 (13)	all mild
Somnolence	2 (13)	all mild	Rhinorrhea	2 (13)	all mild
Irritability	2 (13)	all mild	Decreased appetite	2 (13)	all mild

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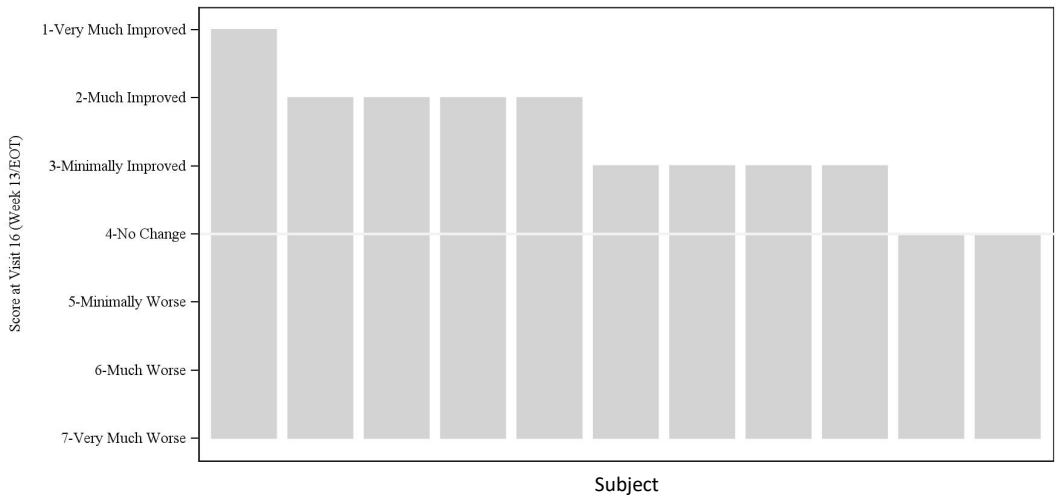
PTHS CGI-I (clinician) results by subject and by domain

Mean CGI-I score of 2.6 with 9 out of 11 children showing improvement

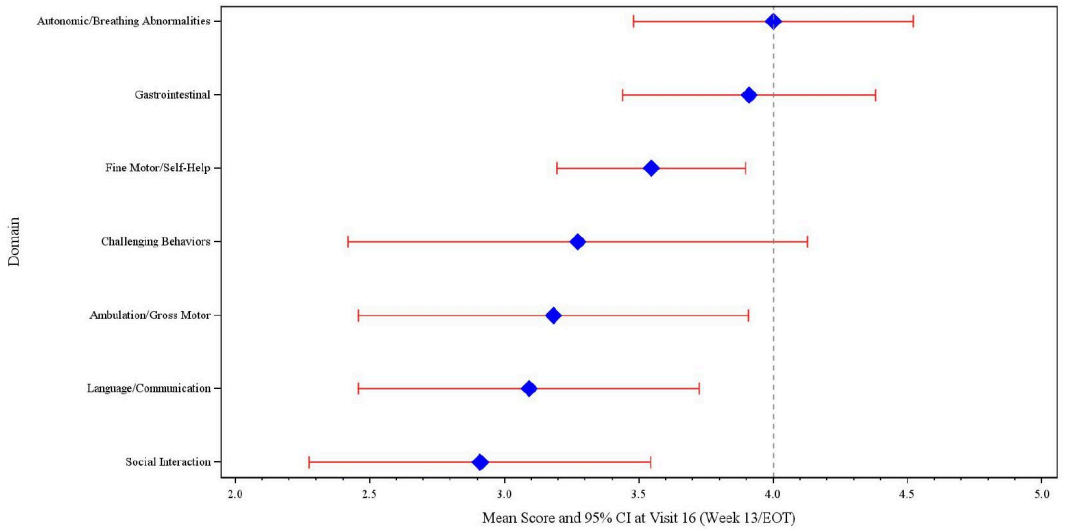
CGI-I Overall Score by subject

MITT Population



Forest Plot of mean CGI-I Domain Scores

MITT Population



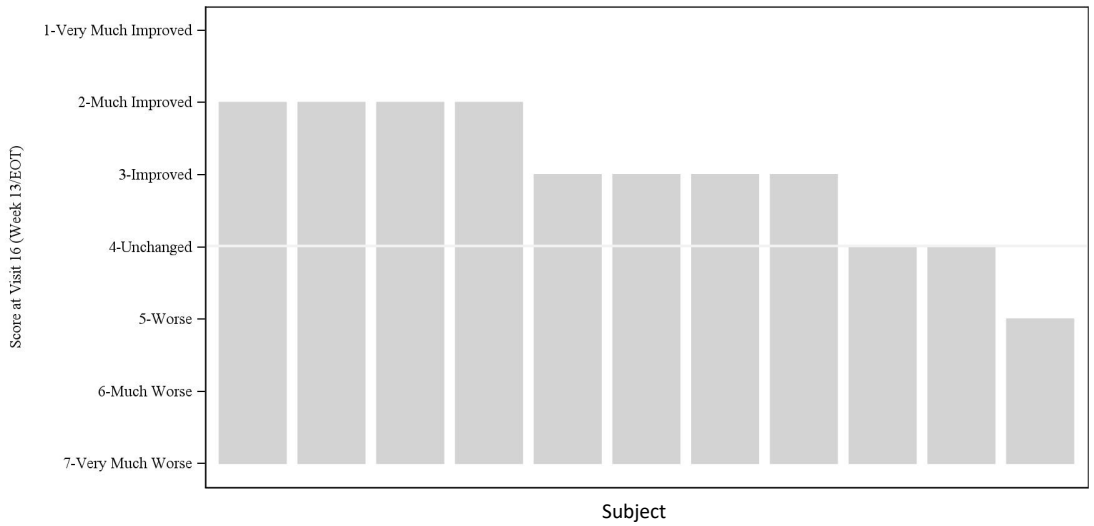
Improvement

PTHS CIC (caregiver) results by subject and by domain

Mean CIC score of 3.0 with 8 out of 11 children showing improvement

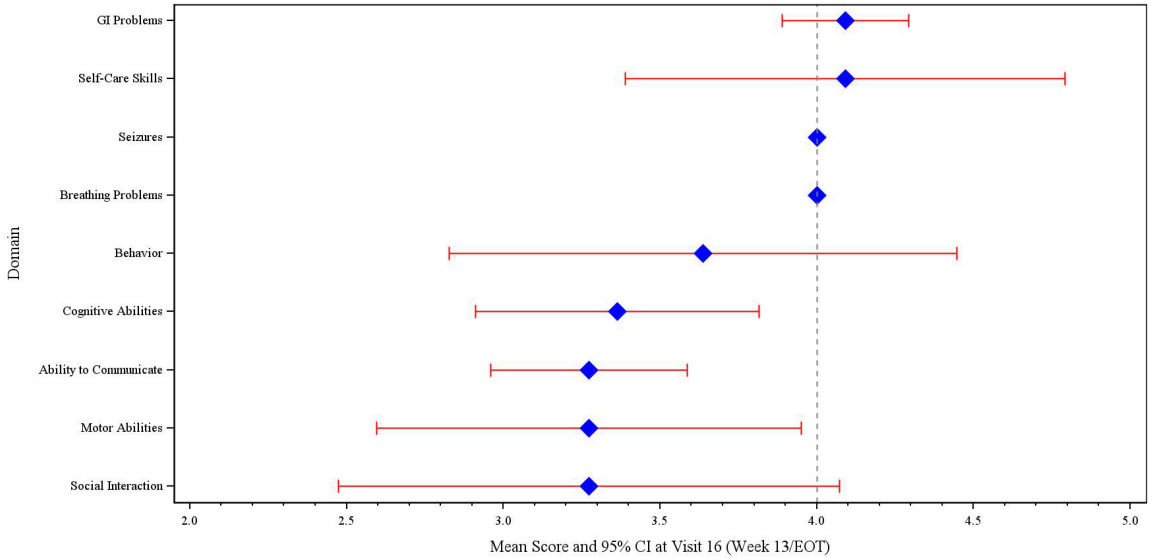
CIC Overall Score by subject

MITT Population



Forest Plot of mean CIC Domain Scores

MITT Population

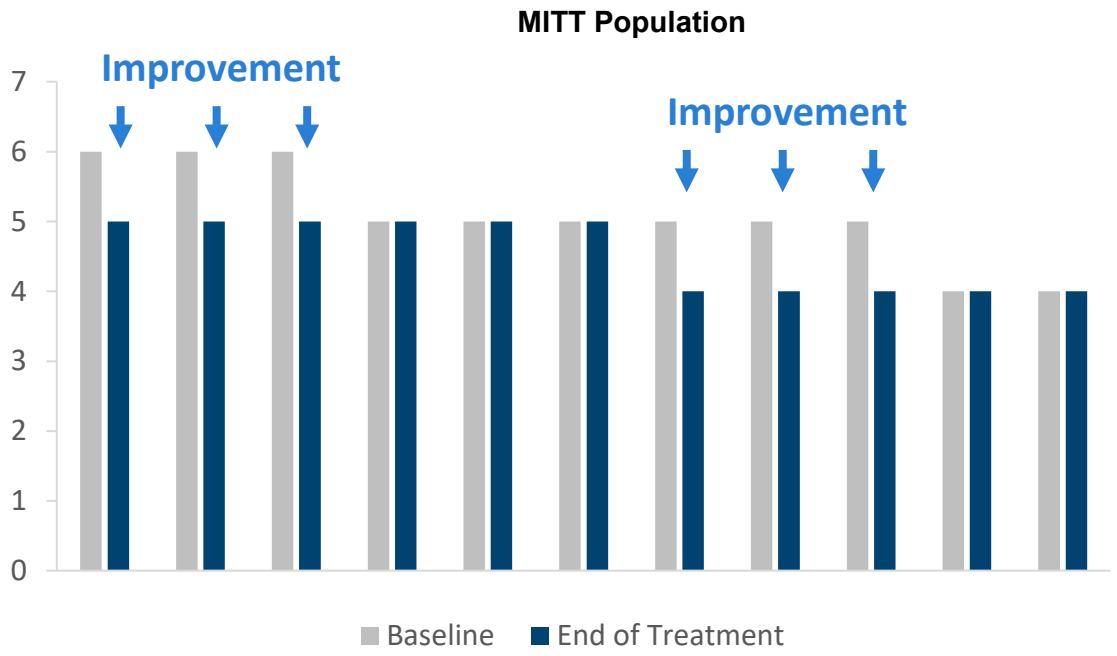


Improvement

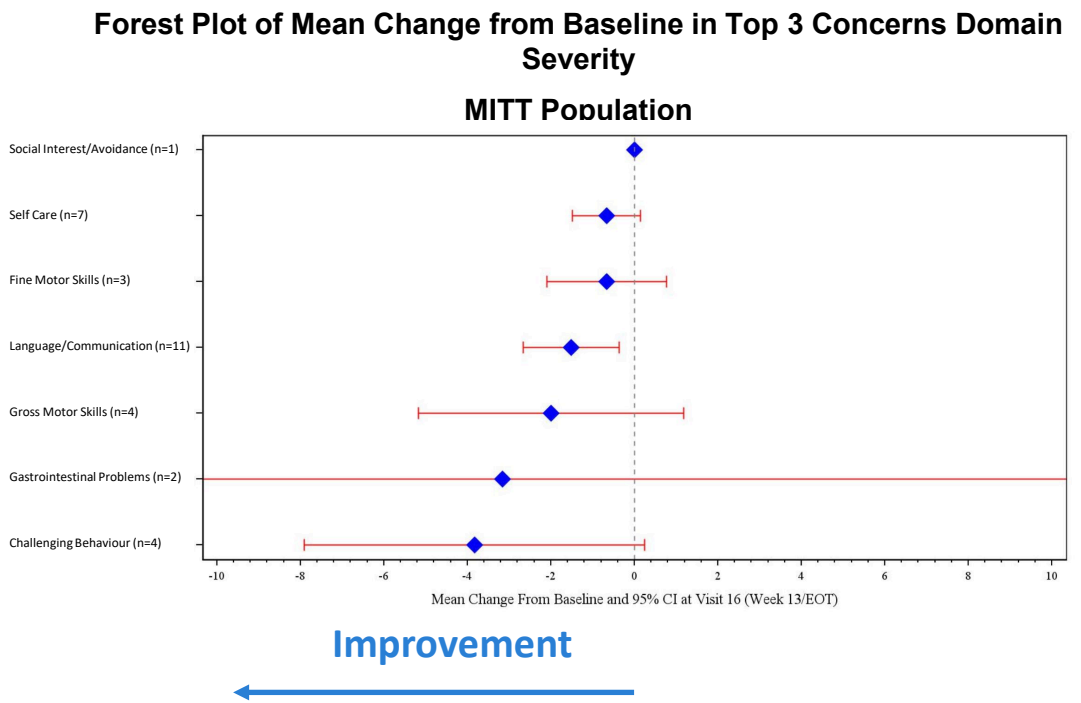
PTHS Clinical Global Impression of Severity (CGI-S) and Caregiver Top 3 Concerns results by domain

6 subjects improved by one point on the overall CGI-S score after 13 weeks of treatment and improvement was observed in the most common concerns of caregivers (communication, self care, behaviour, motor skills)

CGI-S Scores



Caregiver Top 3 Concerns
(Domains and frequency of nomination)



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Clinician and caregiver testimonials

Clinicians

"Increased babbling and jargoning….More inflections with eye contact and consonant sounds rather than just noises."

"Decreased frequency and intensity of smacking and hairpulling."

"Supported stepping increased over last few months…Now taking steps without trainer with parent support."

"Improved expressive communication: 2 additional words, uses AAC device to ask for food. Increase vocalization."

"Less breath holding. More opinionated. More social interest."

"Able to match items/pictures…moved from 4 pictures to 6 pictures."

"Improved motor skills. Better motor coordination getting in car."

Caregivers

"Is now able to explore environment… can move towards people to initiate contact and… can seek out whatever … wants to play with."

"Can seem to hold on to things for longer periods without letting go."

"Stability when walking improved."

"Listen to conversation + follow some discussions, able to understand when we're talking about…"

"Far less hyper and easily able to concentrate better… is able to concentrate and master tasks that … has been working on for years (getting in and out of car independently, catching a ball)."

"More intentional movements… been more gentle with almost all interactions."

"Almost constant babbling and even has said "hi" and "more.""

"More calm and attentive, especially looking at faces and eyes."

Phase 2 trial results validating multi-indication platform

	Phelan-McDermid syndrome N=18, 13 weeks	Pitt Hopkins syndrome N=11, 13 weeks
General safety & tolerability	Safe and well tolerated, with no meaningful trends in laboratory values or other safety parameters during treatment	Safe and well tolerated, with no meaningful trends in laboratory values or other safety parameters during treatment
Serious TEAEs	1 unrelated to drug	0
Mean CGI-I	2.4 (89% shown improvement)	2.6 (82% shown improvement)
Mean CIC	2.7 (83% shown improvement)	3.0 (73% shown improvement)
# patients had CGI-S improvement of 1	7 (39%)	6 (55%)
# syndrome-specific efficacy measures statistically significant[1]	5/5	4/4

[1] Wilcoxon signed rank test

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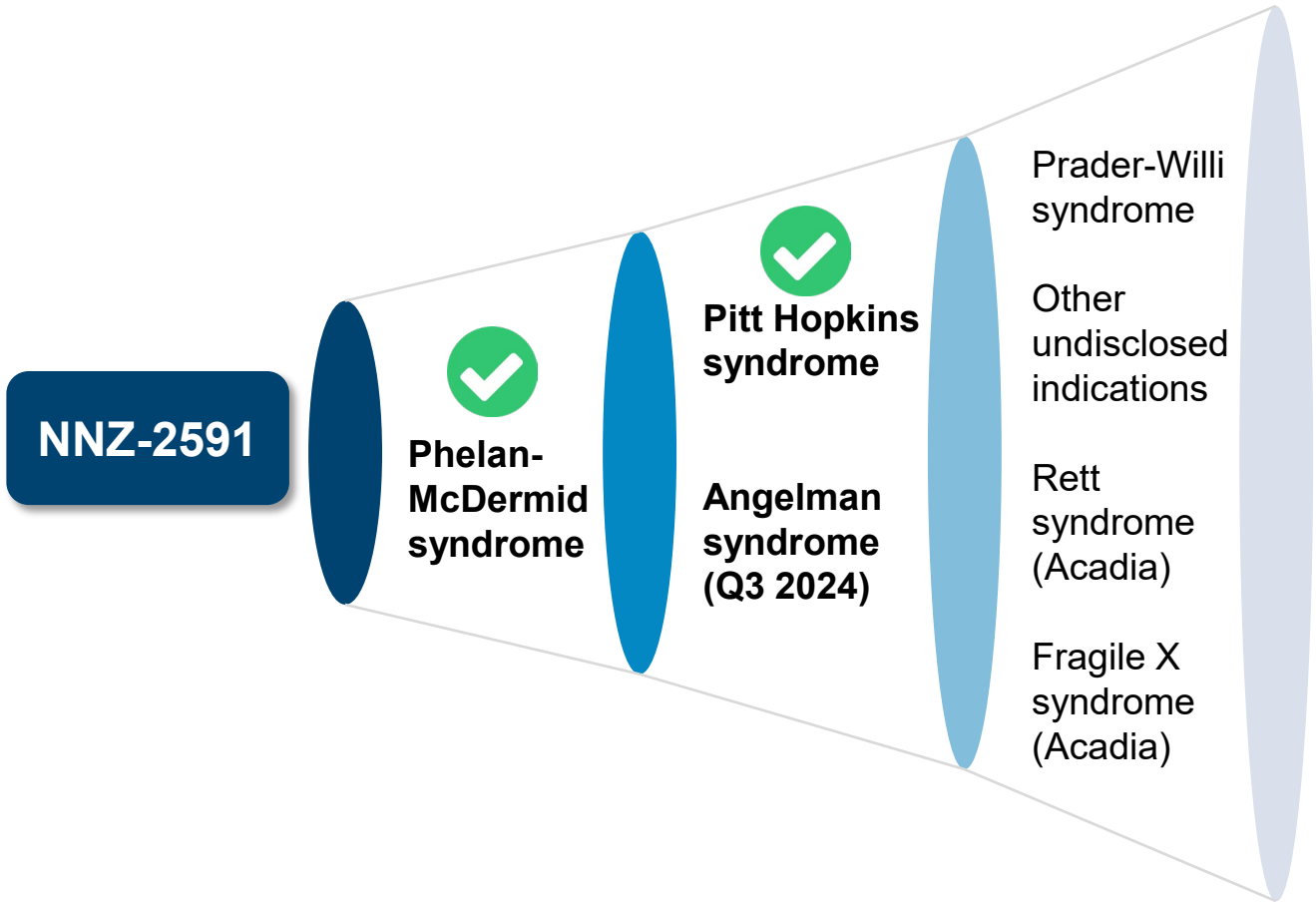
Multiple indications opportunity for NNZ-2591



- **Positive results from Phelan McDermid syndrome and Pitt Hopkins syndrome Phase 2 trials**
- **Top-line results from Angelman syndrome Phase 2 trial expected in Q3 2024**
- **End of Phase 2 meeting with FDA for Phelan McDermid syndrome planned Q3 2024**
- The mechanism of action of NNZ-2591 is relevant for many other neurodevelopmental synaptopathies
- Rett and Fragile X syndromes are licensed to Acadia, with same economics to Neuren as trofinetide; Neuren retains worldwide rights to all other indications

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Highlights

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Highlights

1

DAYBUE™ (trofinetide) approved by US FDA as the first and only treatment for Rett syndrome, launched by partner Acadia in Apr 2023

2

Total economics to Neuren from global trofinetide partnership with Acadia up to US$1bn[1] plus 10 to low 20s % royalties

3

Successful DAYBUE US launch, with 2023 net sales of US$177m and 2024E net sales of US$370-420m[2]

4

Accelerating Phase 2 development of NNZ-2591 in multiple indications. Positive results for Phelan-McDermid syndrome and Pitt Hopkins syndrome

5

NNZ-2591 novel mechanism of action has many more potential applications, with Rett and Fragile X licensed to Acadia

6

A$243m cash at 31 Mar 2024 – well positioned to maximize the benefits of all value creating opportunities

[1] Including payments already received and future payments
[2] Acadia guidance reiterated in First Quarter 2024 Financial Results announcement in May 2024

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