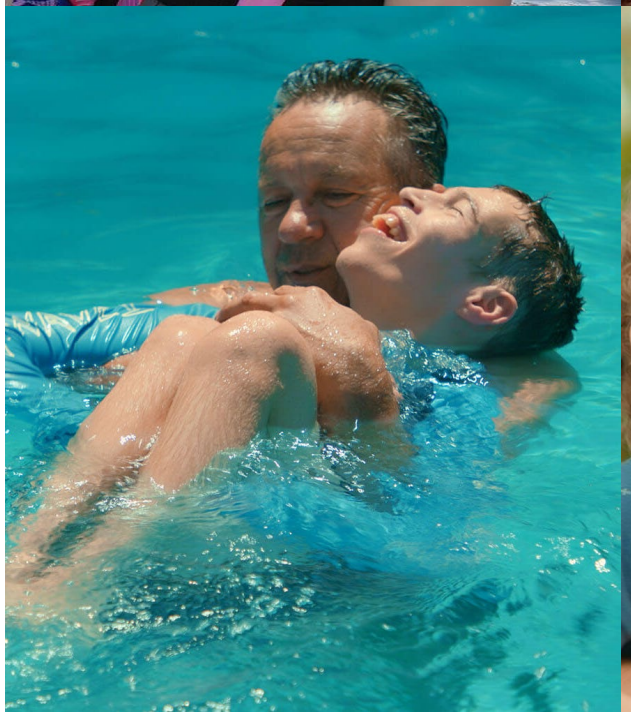
neuren pharmaceuticals

Investor presentation

27 August 2025

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.

neuren
pharmaceuticals

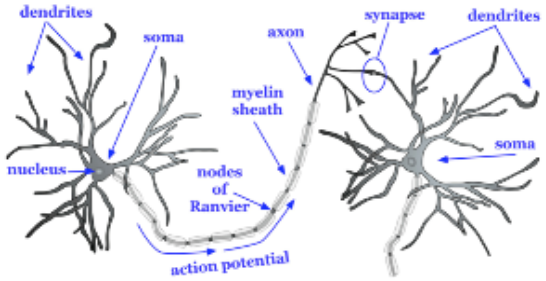
Ground-breaking impact on pediatric neurological Orphan indications

Neurodevelopmental disorders

- **Rett** *(MECP2)*
- **Phelan-McDermid** *(SHANK3)*
- **Pitt Hopkins** *(TCF4)*
- **Fragile X** *(FMR1)*
- **Angelman** *(UBE3A)* | **Prader-Willi** *(15q11-q13)* | ***SYNGAP1*-related disorder** *(SYNGAP1)*

Brain injury

- **Hypoxic-Ischemic Encephalopathy**
  (lack of oxygen or blood flow to the brain before, during or shortly after birth)



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 naturally occurring peptides that can be taken orally as liquids

Excitotoxicity, mitochondrial dysfunction, and acute & chronic inflammatory processes

Severe impact on nearly every aspect of life

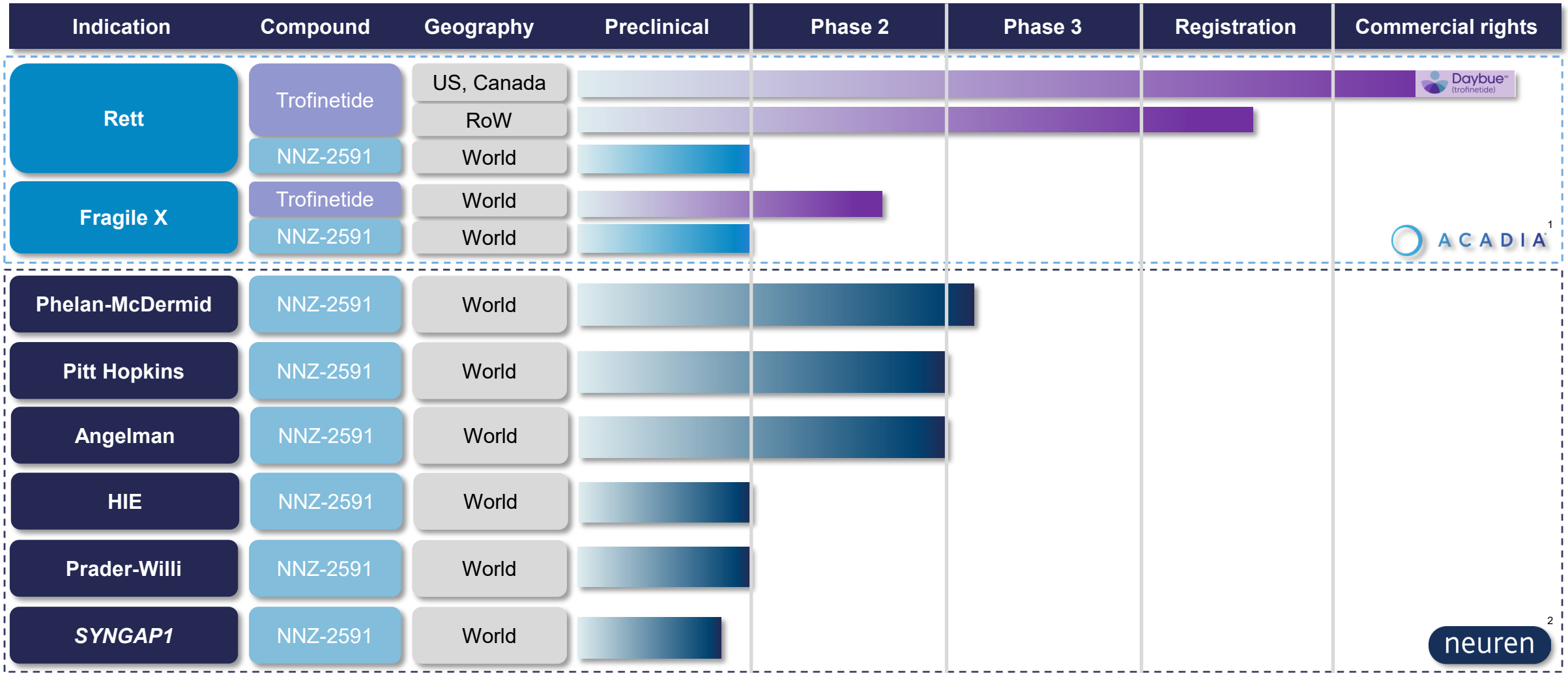
- **Walking and balance issues**
- **Anxiety and hyperactivity**
- **Seizures**
- **Impaired communication**
- **Intellectual disability**
- **Impaired social interaction**
- **Impaired hand use**
- **Sleep disturbance**
- **Gastrointestinal problems**

Long-term impact on survivors

- **Developmental delays**
- **Seizures**
- **Cognitive impairment**
- **Cerebral palsy**

neuren pharmaceuticals

Multiple late-stage opportunities supported by commercial product



[1] Exclusive license for Trofinetide and NNZ-2591 (Rett and Fragile X only) globally [2] Wholly owned by Neuren

neuren pharmaceuticals

Large potential upside for shareholders is enabled by financial strength

Maximise value of **NNZ-2591** as a multiple indication platform

- ✓ **Phelan-McDermid syndrome** in **Phase 3** study
- ✓ Accelerating development in **Pitt Hopkins syndrome** and **HIE**
- ✓ Multiple other indications in the pipeline: Angelman syndrome, Prader-Willi syndrome and *SYNGAP1*-related disorder

Long-term income growth from Acadia's successful global commercialization of Daybue™ (trofinetide)

A$473m income from Daybue® 2023 to date

A$300 million cash at 30 Jun 2025

Value

neuren pharmaceuticals

DAYBUE®
(trofinetide)

neuren
pharmaceuticals

Economics to Neuren from Acadia partnership

North America

✓ **US$10m**	**upfront in 2018**
✓ **US$10m**	**in 2022 following acceptance of NDA for review**
✓ **US$40m**	**in 2023 following 1st commercial sale in the US**
✓ **US$50m**	**In 2024 one third share of Priority Review Voucher awarded to Acadia (sold for US$150m)**
US$55m	Milestone payments related to Fragile X

Tiered Royalty Rates (% of net sales)

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

Sales Milestones

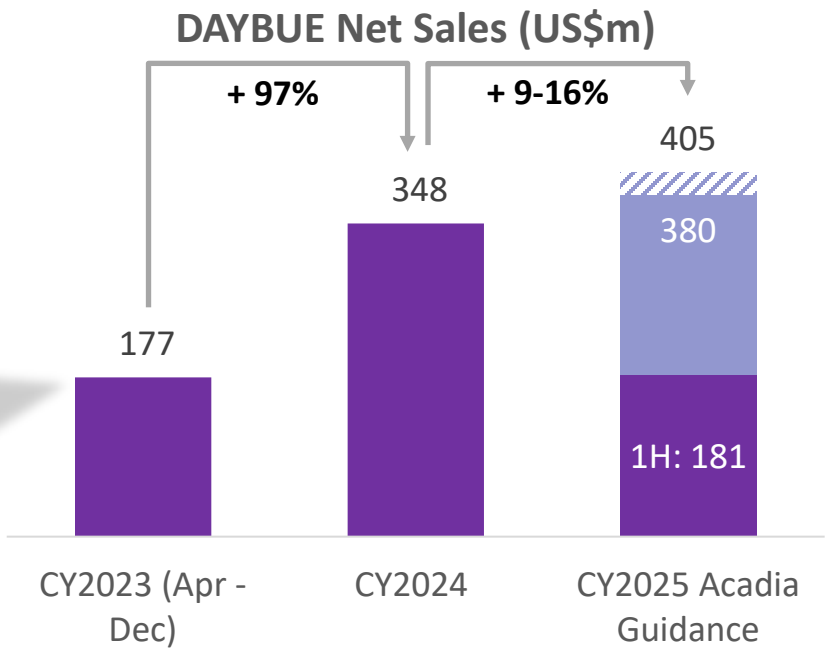
Net Sales in one calendar year	US$m
≥US$250m	✓ **50**
≥US$500m	**50**
≥US$750m	**100**
≥US$1bn	**150**

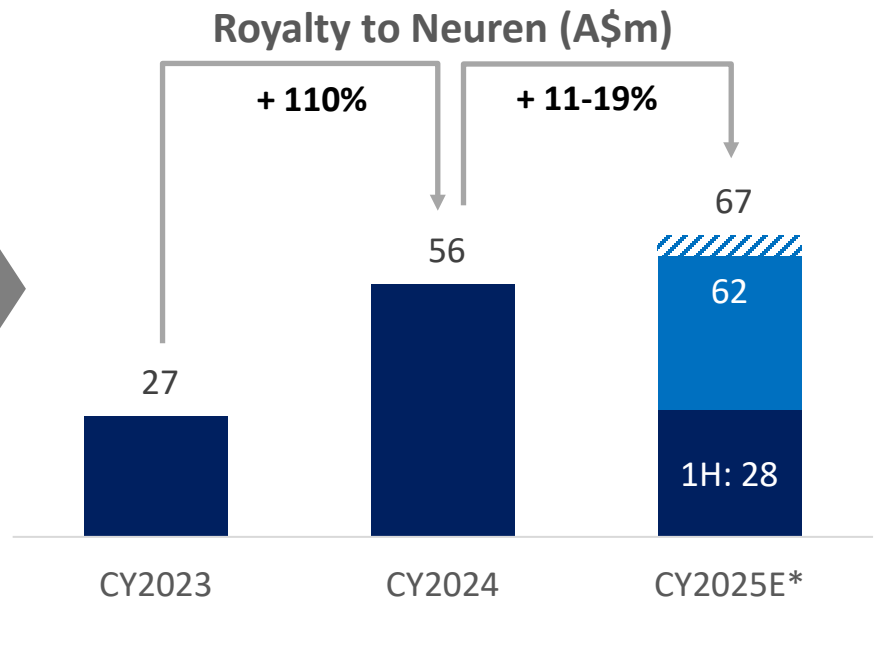
Outside North America

✓ **US$100m**	**upfront in 2023**
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

neuren pharmaceuticals

Growing sustainable income from DAYBUE® (trofinetide)

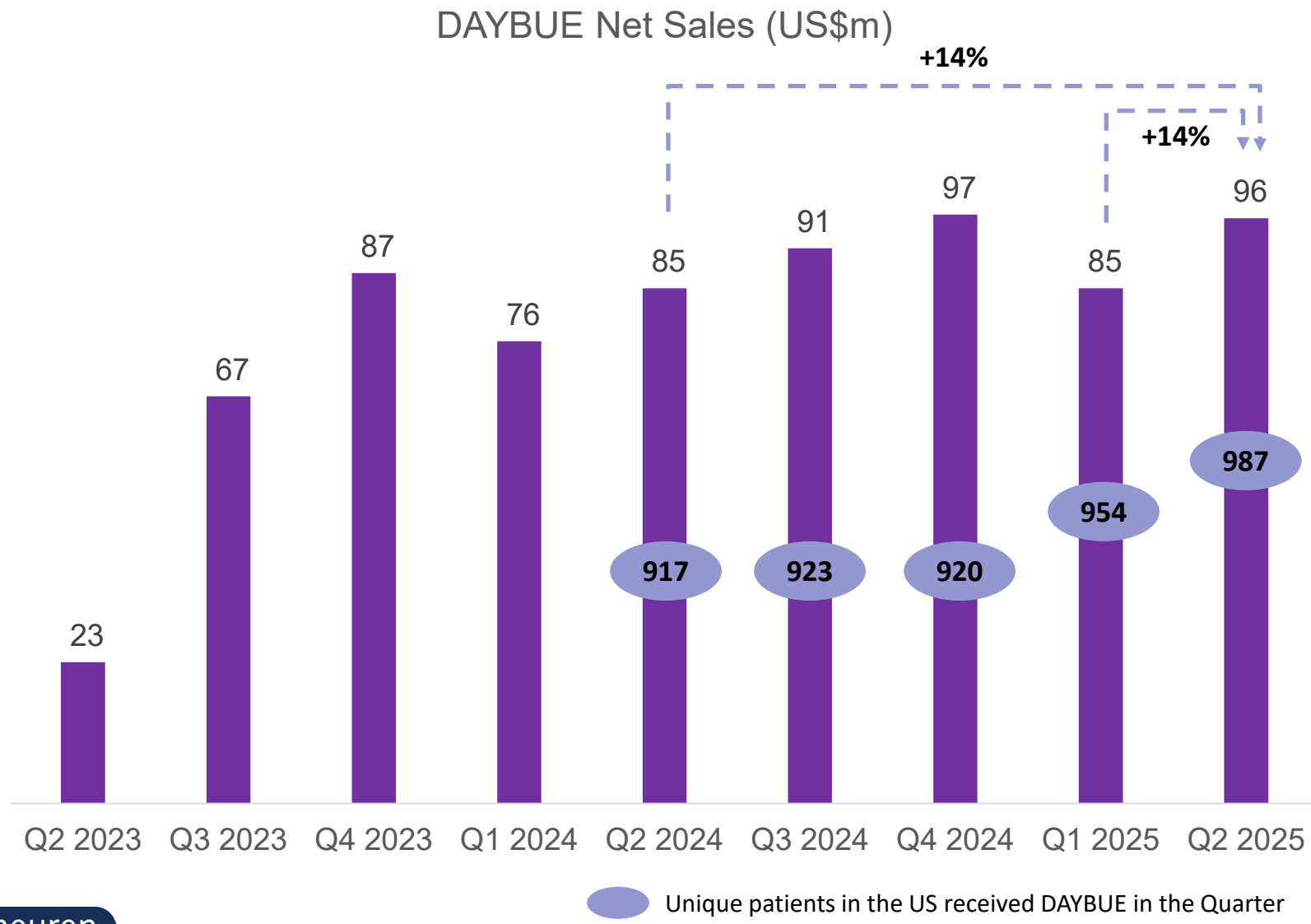




* Based on CY25 Acadia DAYBUE US Net Sales Guidance of US$380-405m, 10% of DAYBUE net sales up to US$250m and 12% of DAYBUE net sales between US$250m and US$500m, and AUDUSD of 0.65

neuren pharmaceuticals

A new phase of expansion and acceleration



- ~2/3 of US patients yet to try DAYBUE
- Completed expansion of DAYBUE US field force by ~30% to accelerate future growth outside Centers of Excellence (CoEs)
- Leveraging a growing body of real-world experience, including LOTUS study, HCP peer-to-peer program, caregiver program series
- Encouraging early signs outside CoEs, with ~3/4 of patient referrals from the community in Q2 2025
- Stable persistency with 70% of Q2 active patients on treatment >12 months

neuren pharmaceuticals

Key growth drivers in the US

1

Expand number of diagnosed patients

- Currently 5,500 – 5,800 up from 4,500 in 2023
- Theoretical prevalence 6,000 – 9,000

2

Expand % of patients starting therapy

- Currently about one third overall:
  - Median ~50% in Centers of Excellence
  - ~20% in broader community

3

Maintain or improve persistency

- Currently >50% remain on therapy after 12 months and >45% after 18 months

Illustrative potential active patient numbers assuming 50% long-term persistency

% starting therapy	Number of diagnosed patients			
	5,800	7,000	8,000	9,000
33	**Q2 2025: 987**	1,155	1,320	1,485
50	1,450	1,750	2,000	2,250
60	1,740	2,100	2,400	2,700
70	2,030	2,450	2,800	3,150

neuren pharmaceuticals

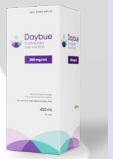
Illustrative potential active patient numbers table comprises Neuren calculations.
Current data is based on Acadia Management Discussion at Canaccord Genuity Growth Conference in Aug 2025, Acadia 2Q 2025 financial results presentation 6 August 2025, R&D Day presentation 25 Jun 2025, 1Q 2025 financial results presentation 7 May 2025, Acadia Management Discussion at Needham Healthcare Conference in Apr 2025, 4Q and full year 2024 Earnings Presentation 26 February 2025, 43rd Annual JP Morgan Healthcare Conference Presentation 14 January 2025, 2Q Second Quarter 2024 Earnings Presentation 6 Aug 2024 .

Long term growth opportunity for trofinetide through global expansion

Canada

600 - 900 Rett patients[1]

Approved in Oct 2024



US

6,000 - 9,000 Rett patients[1]

Launched in Apr 2023

Europe

9,000 - 12,000 Rett patients[1]

MAA filed with potential approval Q1 2026

Active named patient supply programs CLINIGEN

Acadia building commercialisation team

Japan

1,000 - 2,000 Rett patients[1]

Orphan Drug Designation status granted

Clinical study start in Q3 2025 to support marketing application

RoW

Active named patient supply programs in Israel and select rest of the world countries

Rafa.

FarmaMondo
RESPONSIBLE ACCESS TO SPECIALTY MEDICINES

[1] Acadia estimates

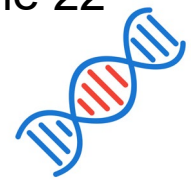
neuren pharmaceuticals

NNZ-2591

neuren pharmaceuticals

Neuren is leading development of a first treatment for Phelan-McDermid syndrome (PMS)

PMS is caused by a deletion or variation in the *SHANK3* gene on chromosome 22



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

North America	19,000 - 36,000[2]
Europe	21,000 - 41,000[2]
Japan	5,000 - 9,000[2]

~3,600 patients in PMSF membership & DataHub

ICD code assigned in **2023**

75% of PMS patients have been diagnosed with ASD

~1% of autism patients have *SHANK3* mutations

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."*

[1] Phelan McDermid Syndrome Foundation (PMSF) (www.pmsf.org)
[2] Estimates based on United Nations population data 2024, derived by applying the estimated prevalence range to the populations under 60 years

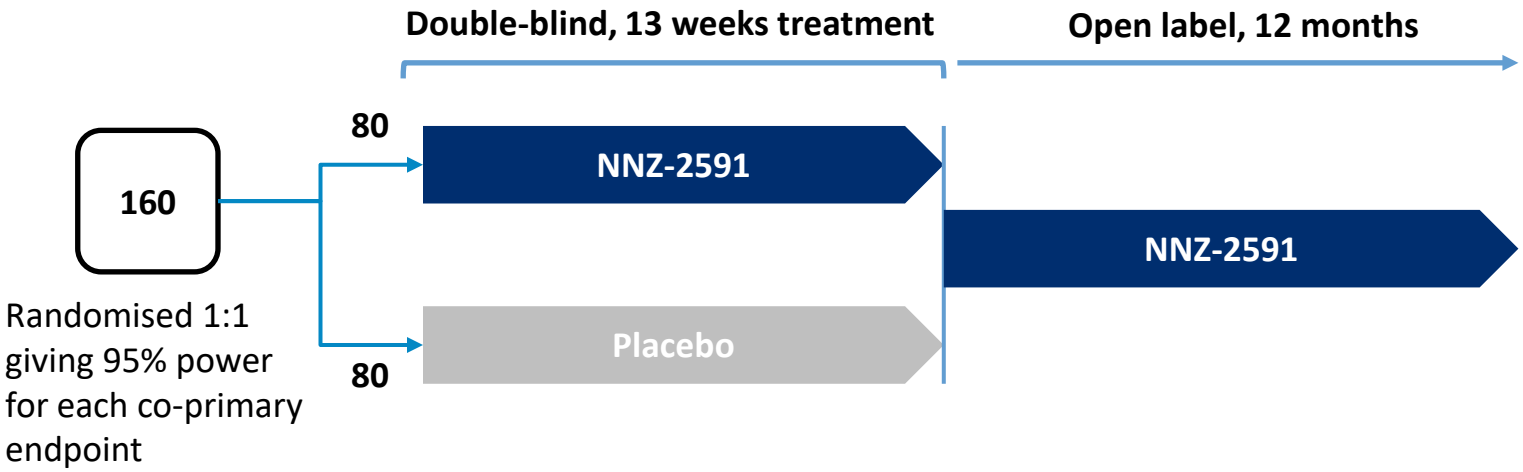
neuren pharmaceuticals

First ever Phase 3 trial in PMS underway

Same population and dose as positive Phase 2 trial, similar design to successful Rett Phase 3

Single Phase 3 trial:

- Randomised, double-blind, placebo-controlled
- 160 children aged 3-12 with Phelan-McDermid syndrome
- Target dose equivalent to dose tested in Phase 2
- Program fully funded from existing cash



Co-primary Endpoints	Phase 2 Results
Phelan-McDermid Syndrome Assessment of Change (PMSA-C), *previously referred to as CGI-I in Phase 2*	16/18 subjects showed improvement Mean score: 2.4 P < 0.0001[1]
Receptive Communication sub-domain of the Vineland Adaptive Behavior Scales, 3rd Edition (VABS-3 Receptive-Raw Score)	16/18 subjects showed improvement Mean improvement: 7.5 (from baseline of 29.0) P = 0.0001[1]

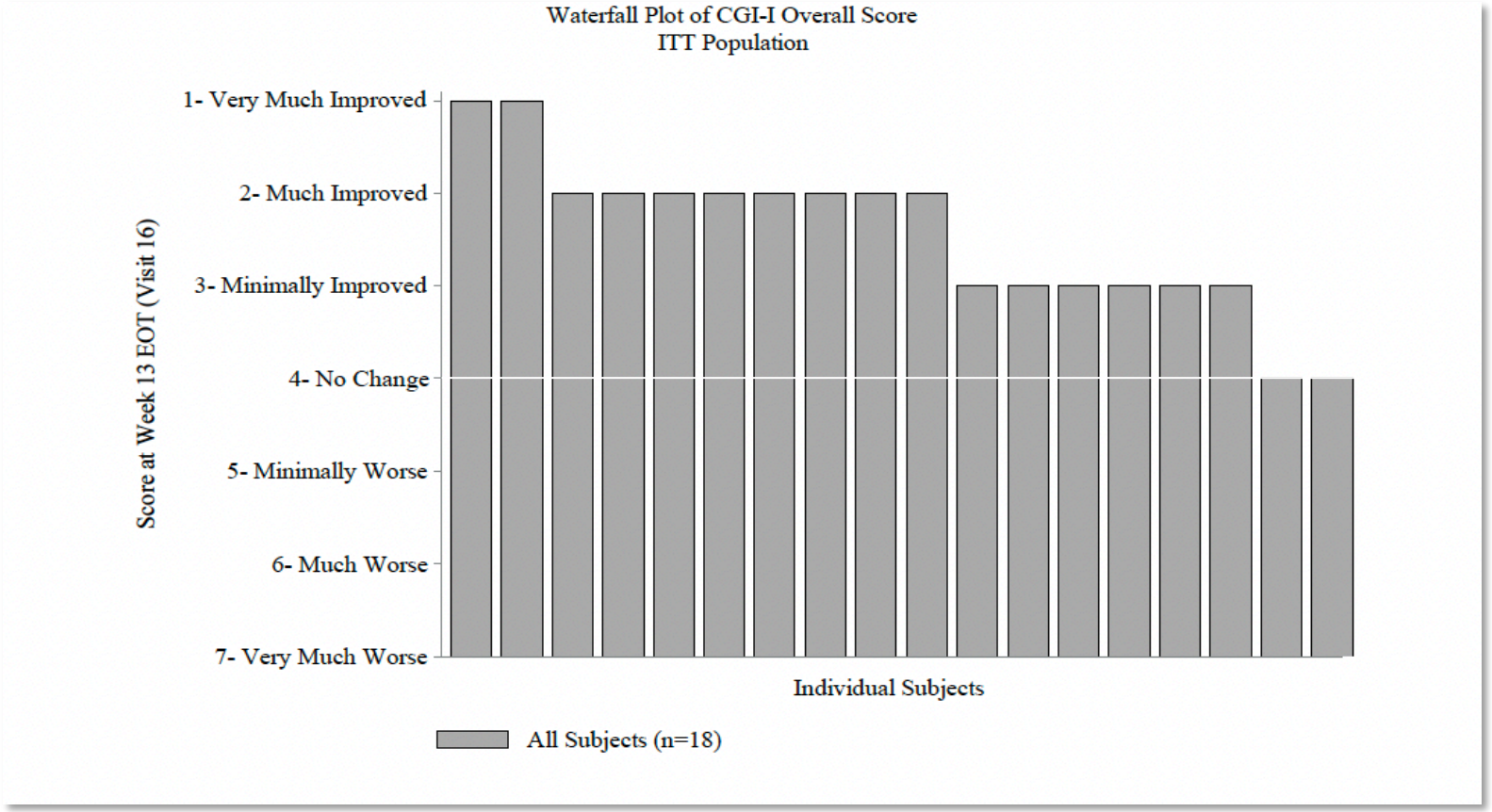
[1] Wilcoxon signed rank test

neuren pharmaceuticals

Supported by robustly positive Phase 2 trial results...

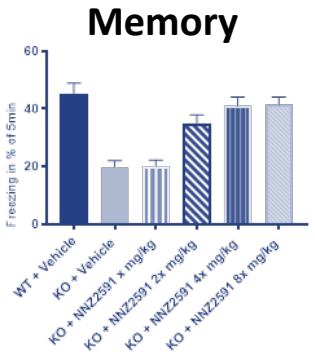
- 13 weeks treatment of patients age 3-12 years in open label trial at 4 US sites
- Significant improvement was assessed by both clinicians and caregivers across multiple efficacy measures
- **Improvements were consistently seen across clinically important aspects of PMS, including communication, behaviour, cognition/learning and socialization**
- NNZ-2591 was safe and well tolerated, with no clinically meaningful changes in safety parameters during treatment

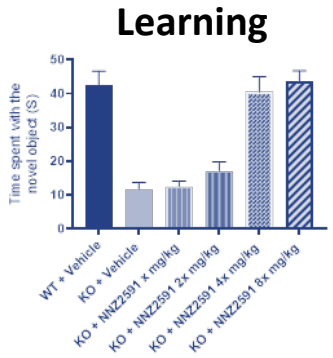
Mean **CGI-I** of **2.4** with 16 out of 18 children showing improvement

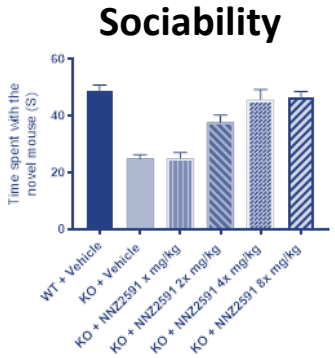


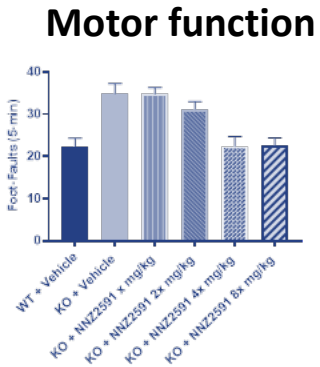
neuren pharmaceuticals

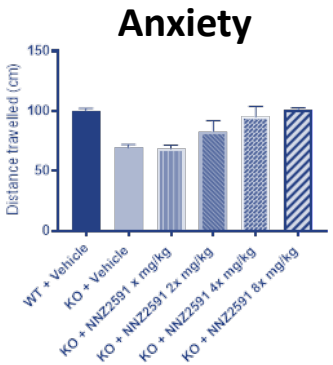
… and consistent efficacy and clear dose response in *shank3* model of PMS

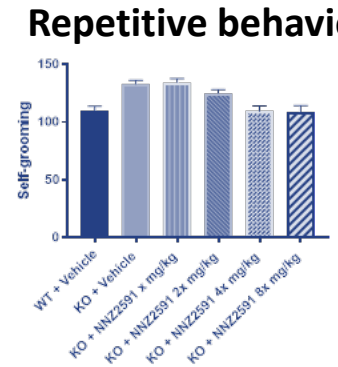


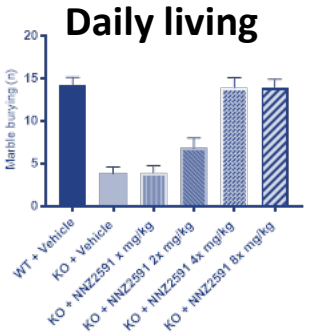


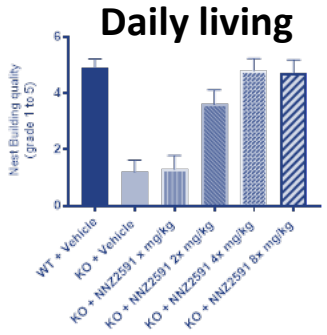








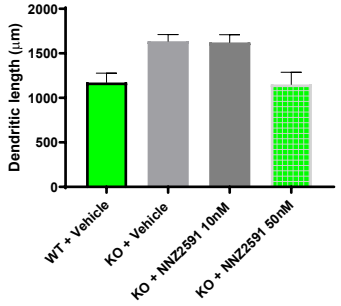


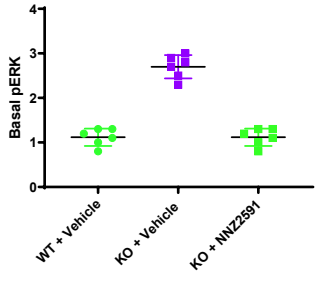


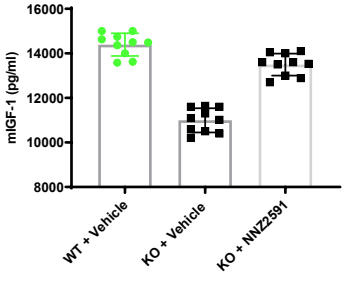
Incidence of audiogenic seizures

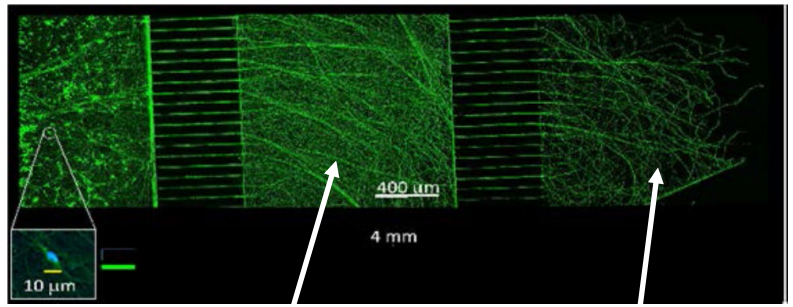
WT + vehicle	0%
KO + vehicle	60%
KO + x mg/kg	50%
KO + 2x mg/kg	30%
KO + 4x mg/kg	10%
KO + 8x mg/kg	10%

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









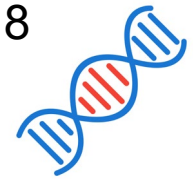
Abnormal dendrites in *shank3* knockout mice cells in culture

Normalization after treatment with NNZ-2591

neuren pharmaceuticals

Neuren is leading development of a first treatment for Pitt Hopkins syndrome (PTHS)

PTHS is caused by a deletion or variation in the *TCF4* gene on chromosome 18



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

North America	7,000 - 8,000[2]
Europe	8,000 - 9,000[2]
Japan	1,000 - 2,000[2]

~1,564 patients registered in PTHS Census

ICD code assigned in **2020**

Clinical similarities between PTHS, Rett and Angelman syndromes calling for TCF4 screening in suspected Rett or Angelman patients[3]

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."

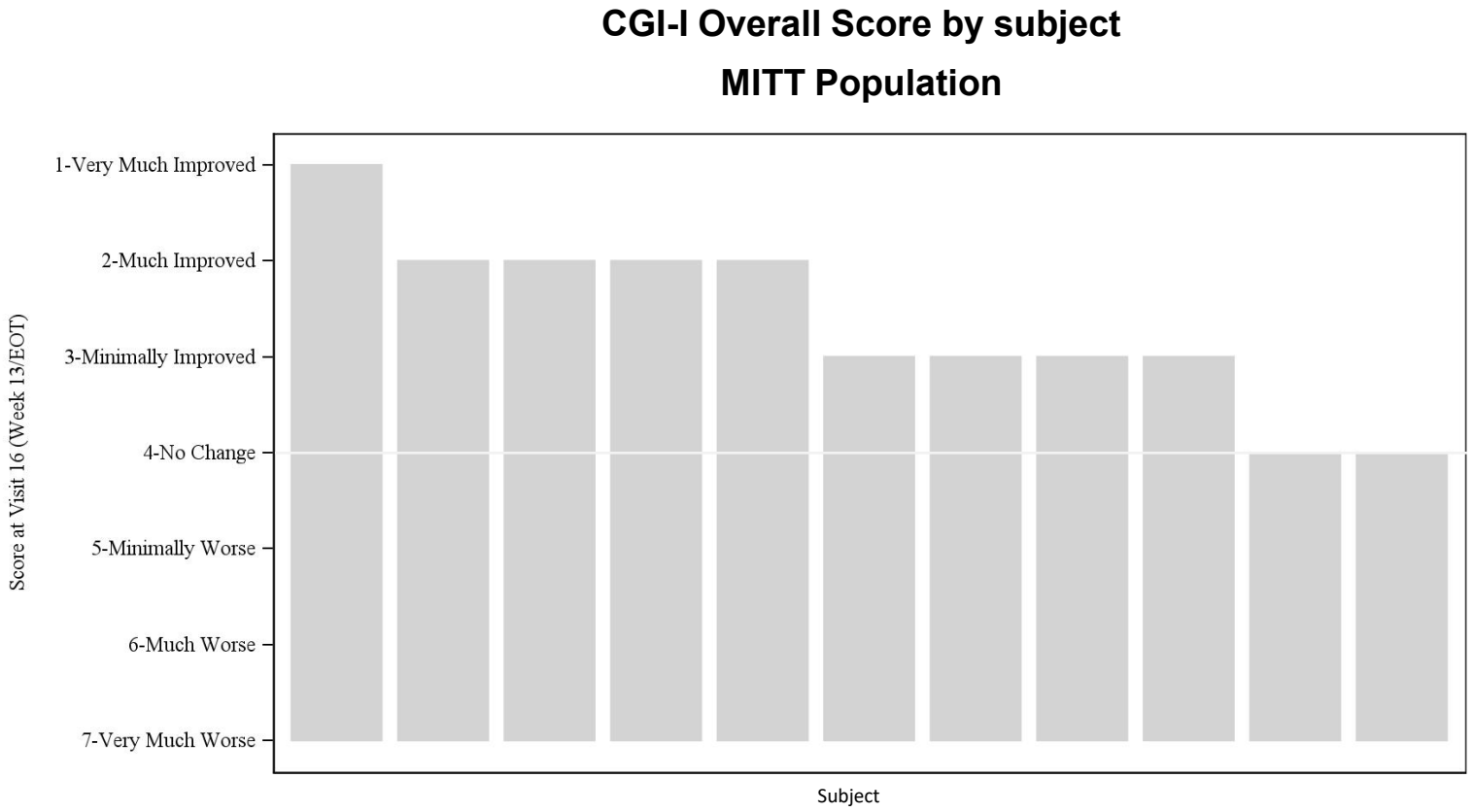
[1] Pitt Hopkins Research Foundation (PHRF) (pitthopkins.org)
[2] Estimates based on United Nations population data 2024, derived by applying the estimated prevalence range to the populations under 60 years
[3] Takano et al, "Two percent of patients suspected of having Angelman syndrome have TCF4 mutations" 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

neuren pharmaceuticals

NNZ-2591 achieved positive PTHS Phase 2 trial results…

- 13 weeks treatment of patients age 3-12 years in open label trial at 5 US sites
- Statistically significant improvement from baseline[1] assessed by both clinicians and caregivers in efficacy measures specifically designed for PTHS
- **Improvements were seen in clinically important aspects of Pitt Hopkins syndrome, including communication, social interaction, cognition and motor abilities**
- NNZ-2591 was safe and well tolerated, with no clinically meaningful changes in safety parameters during treatment

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



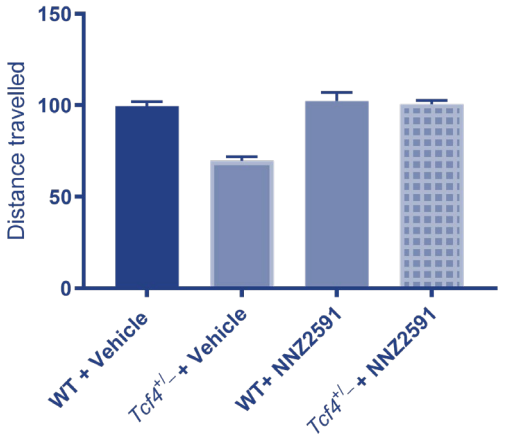
[1] Wilcoxon signed rank test

neuren pharmaceuticals

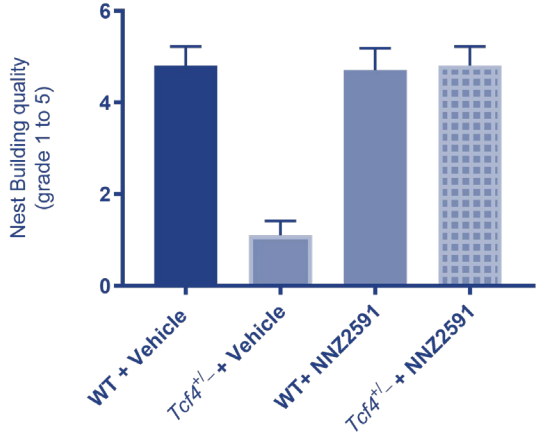
...and consistent efficacy was observed in ***TCF4*** model of PTHS

All abnormal behaviours normalised after treatment with NNZ-2591

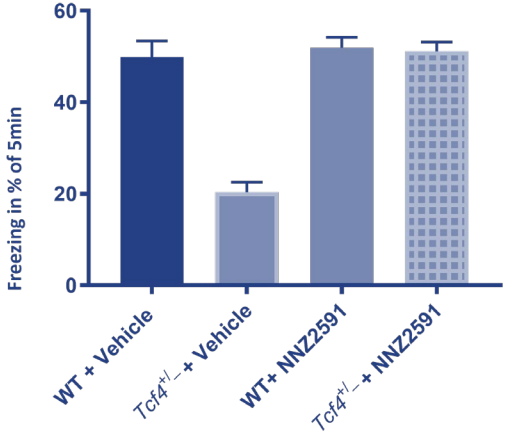
Hypoactivity



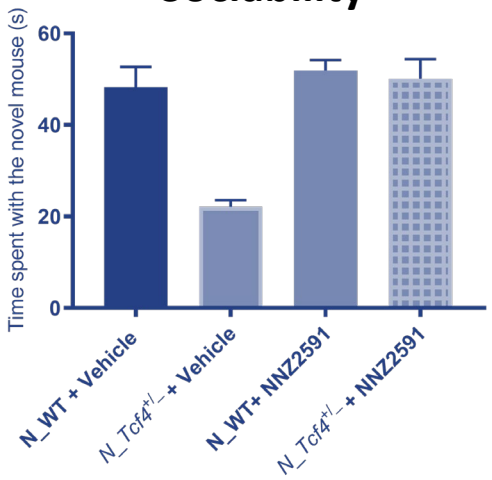
Daily living



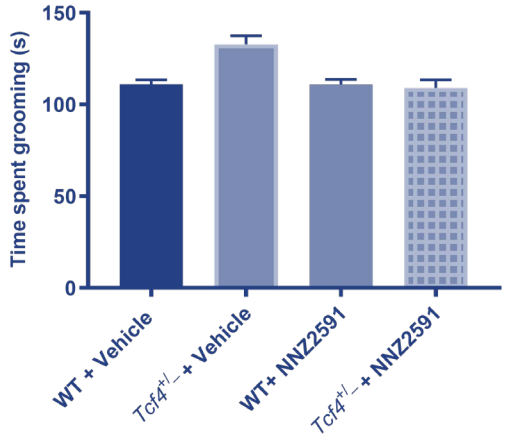
Learning & Memory



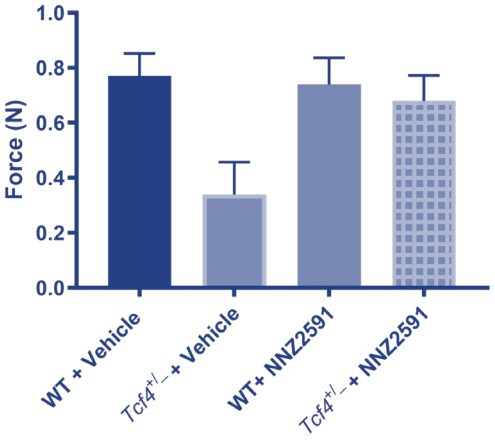
Sociability



Repetitive behavior



Motor performance



neuren pharmaceuticals

NNZ-2591 in HIE – targeting a new paradigm of treatment

HIE program retains all the advantages of the other NNZ-2591 programs:

- Orphan Drug
- Pediatric
- Urgent unmet need
- Limited competition
- Leverages the non-clinical and manufacturing platform that has been built

Clinical & Regulatory

- Exploring potential for **Phase 2/3 trial**
- Preparing for **pre-IND** meeting with FDA
- Concentration of clinical sites at large hospitals available

Scientific Foundation

- **IGF-1** promotes cell survival, modulates inflammation, and regulates synaptic transmission
- **IGF-1** levels are reduced in infants with HIE, correlating with HIE severity and outcome
- Supporting data from a range of in-vitro and in-vivo models

Commercial

- Standard of care is therapeutic hypothermia (TH), which reduces mortality and morbidity
- Critical unmet need to **improve long-term outcomes** with a neuroprotective treatment post TH
- **Repeating pool of patients** ~6,000 p.a. in the US[1]
- Addressable in ICUs - a **new in-hospital channel** for Neuren
- Eligible for **Orphan and Rare Pediatric Disease** designations

1 Neuren estimates based on various published literature

neuren pharmaceuticals

Key milestones and catalysts

Milestones achieved 2025 to date

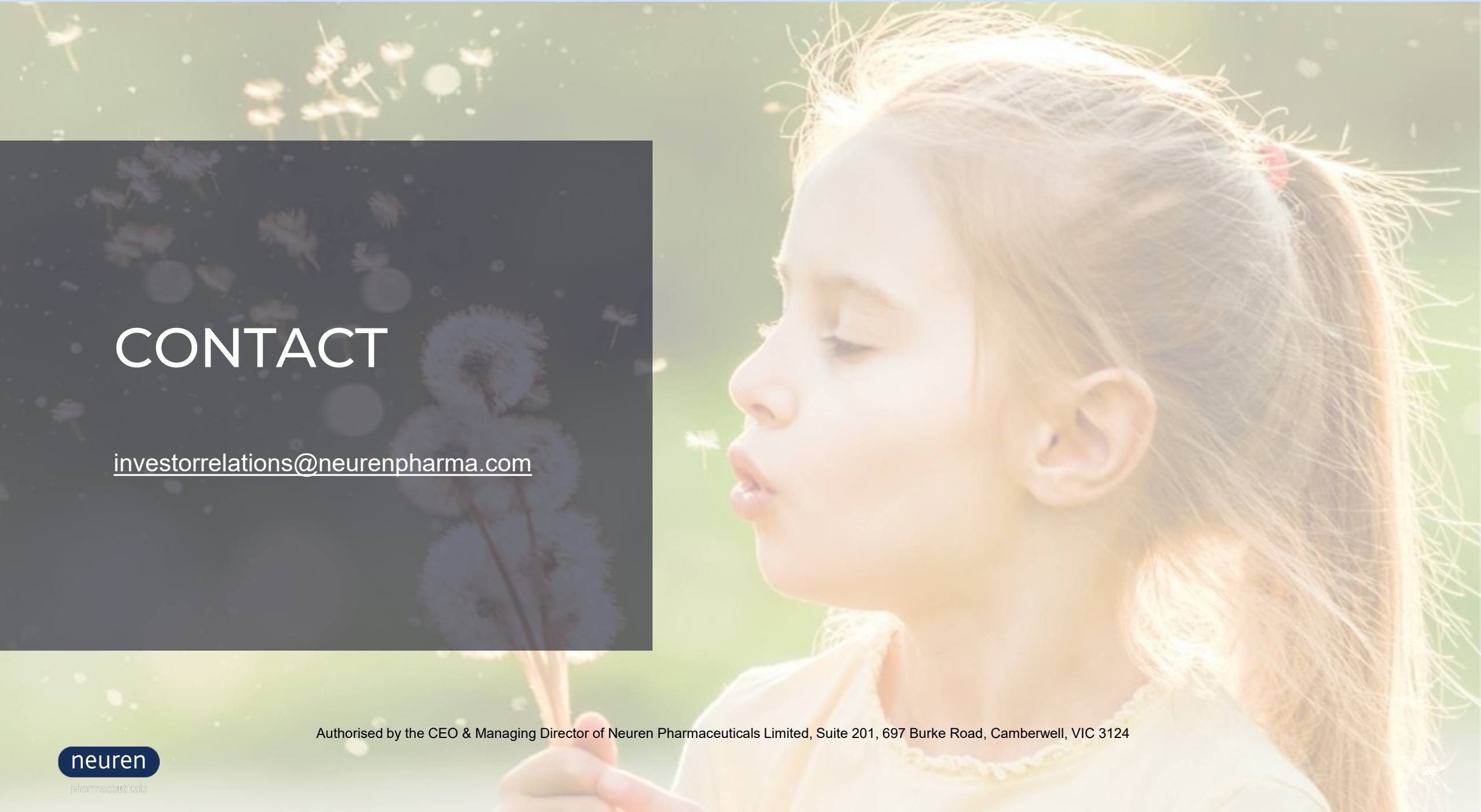
- ✓ Record number of active patients on DAYBUE in the US in Q2 2025, growing for third consecutive quarter
- ✓ Submission by Acadia of EU marketing application for trofinetide
- ✓ Acadia initiated Managed Access Program in Europe, Israel and RoW regions
- ✓ Confirmed alignment with FDA on primary efficacy assessment for PMS Phase 3 trial at Type C meeting
- ✓ First site initiated for PMS Phase 3 trial
- ✓ FDA Fast Track Designation for PTHS
- ✓ Announced HIE and *SYNGAP1* as a new indications for NNZ-2591
- ✓ Completed A$50m on-market share buyback

Anticipated near-term catalysts

- CY2025 DAYBUE US net sales guidance US$380 – 405m, implying A$62 – 67m US royalties to Neuren[1]
  - Acadia quarterly updates
- Potential EU approval of trofinetide in Q1 2026
- Acadia to commence a clinical trial in Japan in Q3 2025 to support registration of trofinetide
- PMS Phase 3 trial progress updates
- Meetings with FDA to advance development for PTHS and HIE

[1] Based on CY25 Acadia DAYBUE Net Sales Guidance of US$380-405m, 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 pharmaceuticals



CONTACT

investorrelations@neurenpharma.com

Authorised by the CEO & Managing Director of Neuren Pharmaceuticals Limited, Suite 201, 697 Burke Road, Camberwell, VIC 3124