

For personal use only

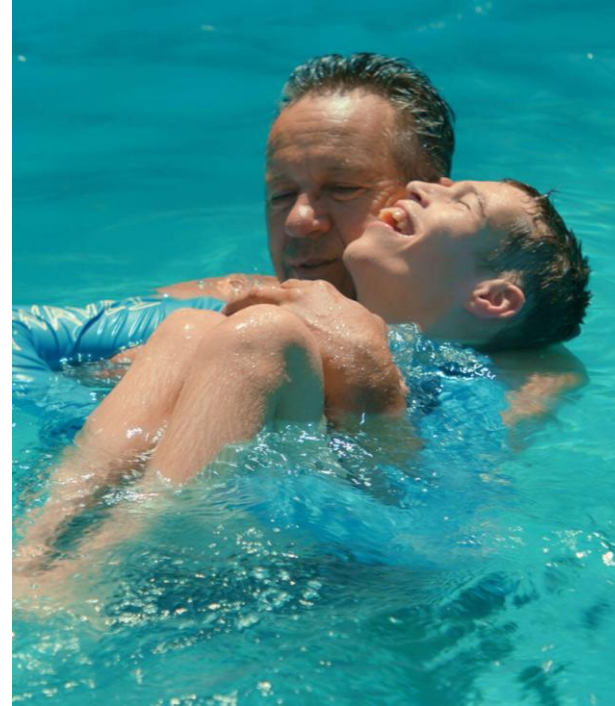


pharmaceuticals

Investor presentation

10 November 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.



Ground-breaking impact on pediatric neurological Orphan indications

Neurodevelopmental disorders

Rett
(*MECP2*)

Phelan-McDermid
(*SHANK3*)

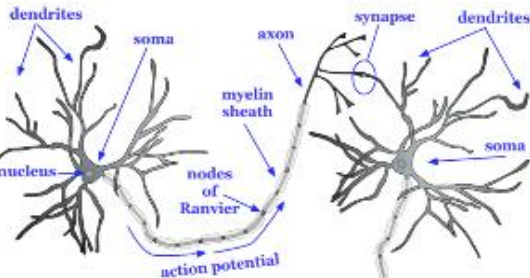
Pitt Hopkins
(*TCF4*)

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

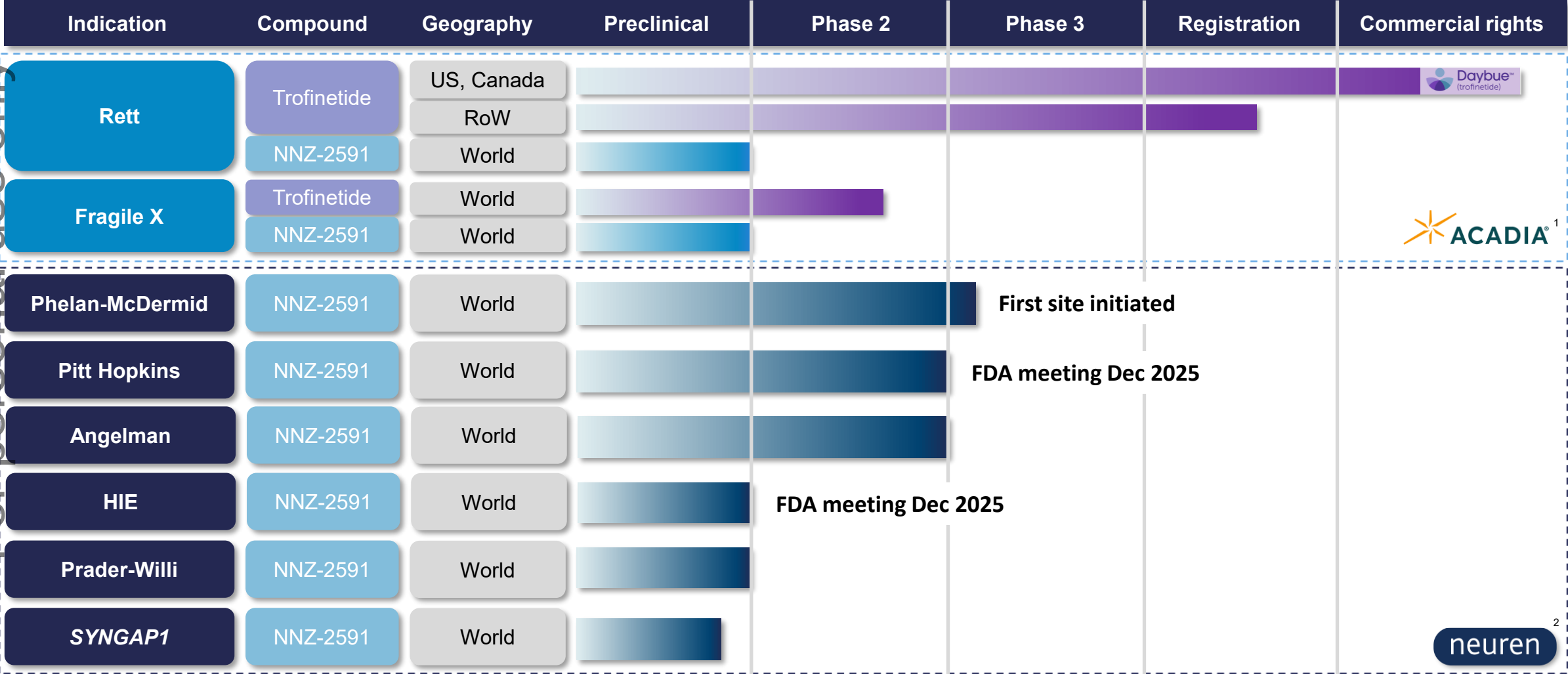
Cerebral palsy

neuren

pharmaceuticals

Multiple late-stage opportunities supported by commercial product

For personal use only



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

Large potential upside for shareholders is enabled by financial strength

For personal use only

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

- ✓ **Phelan-McDermid syndrome** in **Phase 3** study
- ✓ Advancing 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



A\$490m income from Daybue® 2023 to date

A\$310 million cash at 30 Sep 2025 (incl Q3 royalty)

Value

For personal use only

DAYBUE[®] (trofinetide)



Economics to Neuren from Acadia partnership

For personal use only

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)		Sales Milestones	
Annual Net Sales	Rates	Net Sales in one calendar year	US\$m
≤US\$250m	10%	≥US\$250m	✓ 50
>US\$250m, ≤US\$500m	12%	≥US\$500m	50
>US\$500m, ≤US\$750m	14%	≥US\$750m	100
>US\$750m	15%	≥US\$1bn	150

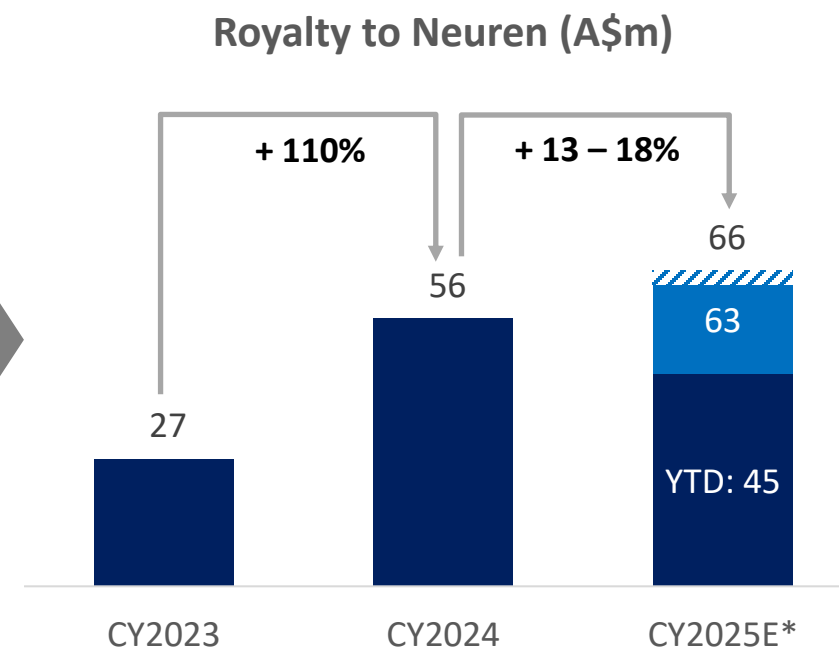
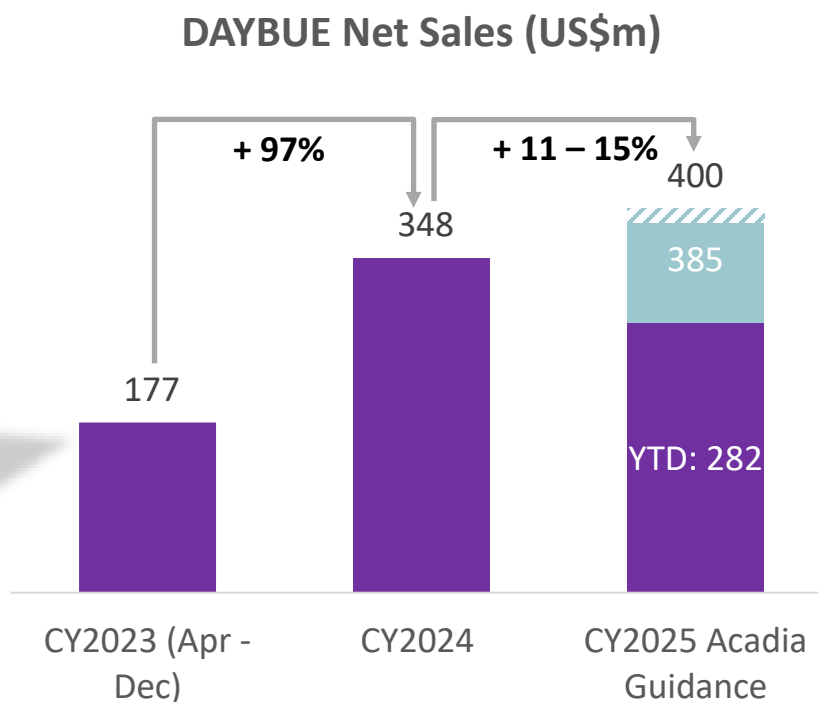
Outside North America

- ✓ **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

Growing sustainable income from DAYBUE® (trofinetide)

For personal use only



* Based on CY25 Acadia DAYBUE US Net Sales Guidance of US\$385-400m, 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

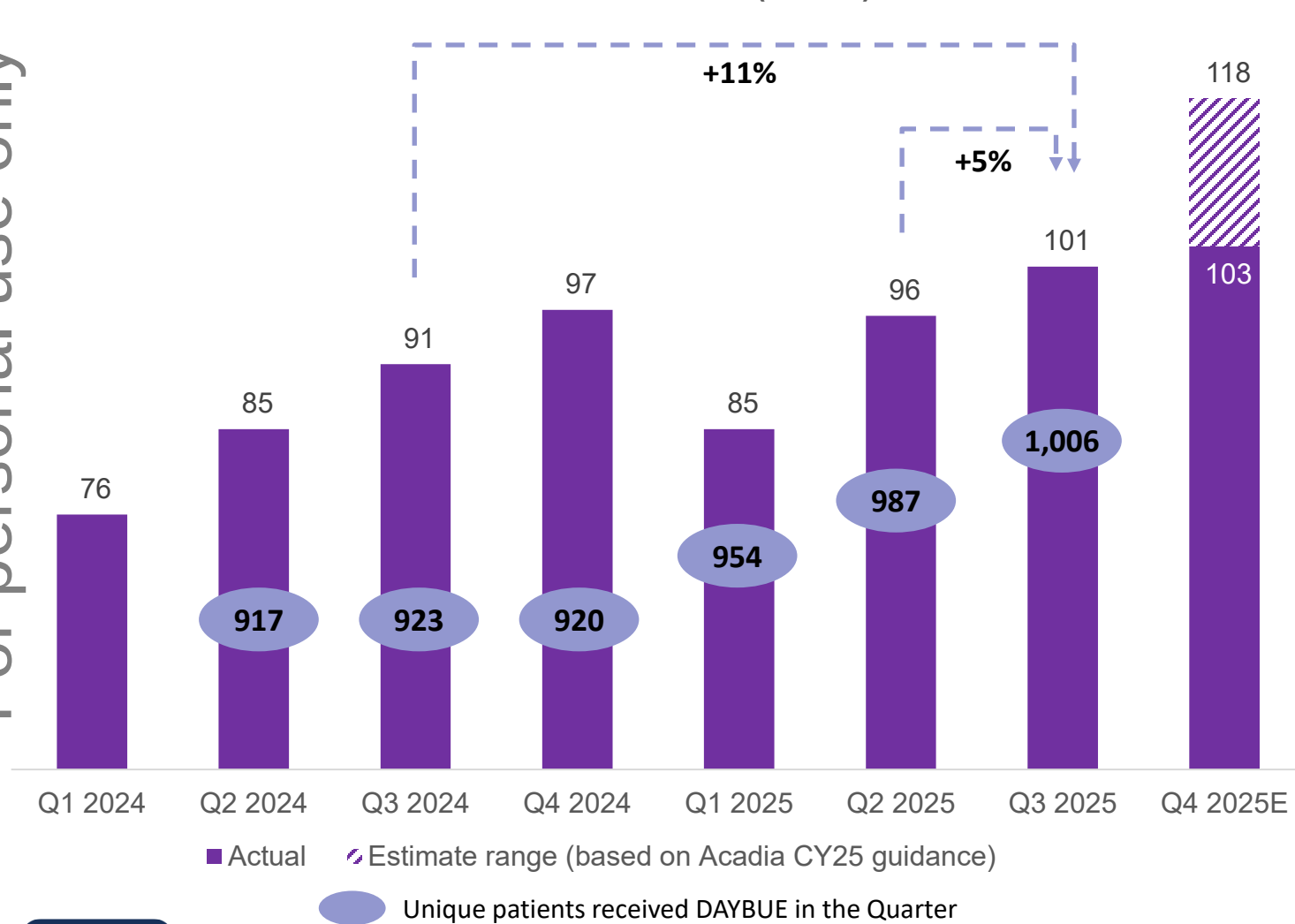
neuren

pharmaceuticals

A new phase of expansion and acceleration

For personal use only

DAYBUE Net Sales (US\$m)



Growing body of
real-world
experience

+

30% expansion in
Acadia field force,
completed **mid-2025**

Positive lead indicators in Q3 2025

Call
volumes
and
educational
programs
↑ ~20%

Highest
q-o-q ↑ in
referrals
since
launch

74% of new
patient Rx
from
outside
CoEs (↑
from 64% in
Q2)

Sales impact anticipated through **Q4 2025 and into 2026**

Key growth drivers in the US

For personal use only

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 ~40% overall
- ~27% in community (outside CoEs)

3

Maintain or improve persistency

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

% starting therapy	Number of diagnosed patients			
	5,800	7,000	8,000	9,000
40	1,160	1,400	1,600	1,800
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

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

Long term growth opportunity for trofinetide through global expansion

For personal use only



Canada

600 - 900 Rett patients¹
Approved in Oct 2024

US

6,000 - 9,000 Rett patients¹
Launched in Apr 2023

Europe

9,000 - 12,000 Rett patients¹
MAA filed with CHMP opinion in Q1 2026
Active named patient supply programs **CLINIGEN**
Acadia building commercialisation team

Japan

1,000 - 2,000 Rett patients¹
Orphan Drug Designation status granted
Small clinical study commenced to support marketing application

RoW

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



¹ Acadia estimates

For personal use only

NNZ-2591



Leading the development of a first treatment for Phelan-McDermid syndrome (PMS)

The Voice of the Patient.....¹

“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.”

“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.”*

***Developmental delay/intellectual impairment (lack of safety awareness) and communication issues** are the most troublesome concerns.*

***Improved cognitive functioning and improved communication** are the most desired outcomes.*



neuren

pharmaceuticals

NNZ-2591 development program

- ✓ Orphan Drug designation (US and EU)
- ✓ Rare Pediatric Disease designation (US)
- ✓ Meaningful improvements rated by clinicians and caregivers in open-label Phase 2 trial
- ✓ Alignment with FDA on single Phase 3 trial design and endpoints to support a New Drug Application
- ✓ Fast Track designation (US)
- ✓ Koala Phase 3 trial initiated

neuren

pharmaceuticals

¹ Excerpts from Voice of the Patient Report of Externally-Led Patient-Focused Drug Development Meeting Nov 2022

PMS Phase 3 approach consistent with positive Phase 2 trial and successful Rett program

Alignment with FDA on single Phase 3 trial design and endpoints to support a NDA

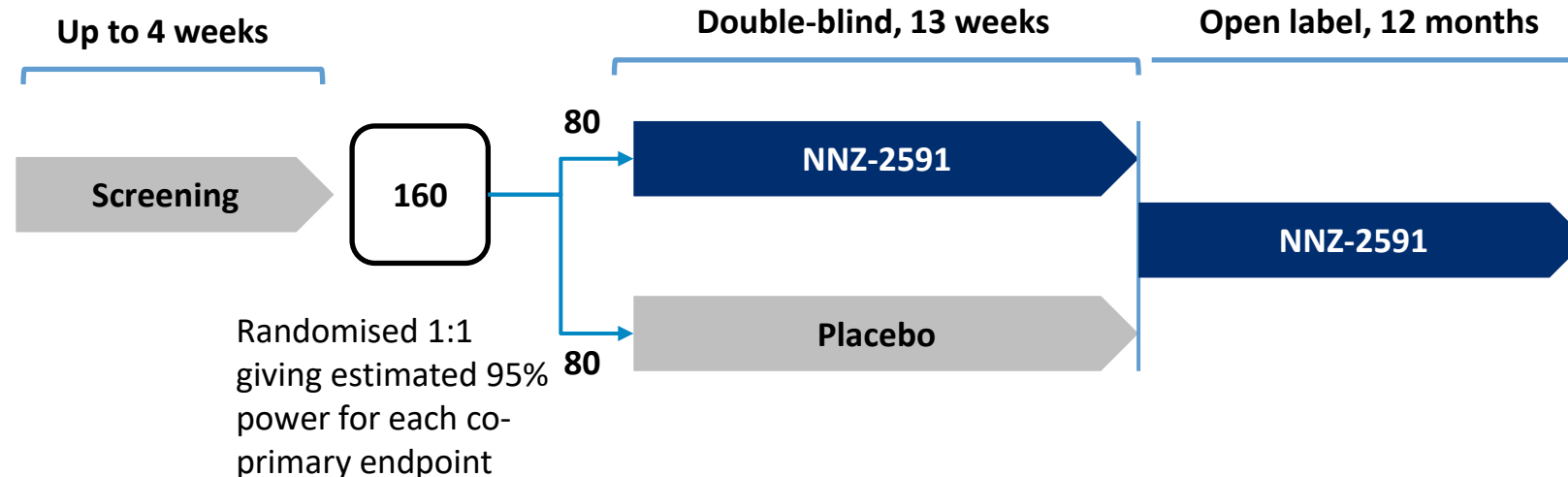


Same age range (3-12) and same length of treatment (13 weeks) as Phase 2

Target dosing equivalent to dose tested in Phase 2¹

~20 trial sites, mostly in US

Program fully funded from existing cash



Key Phase 3 endpoints robustly positive in Phase 2 trial

For personal use only

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

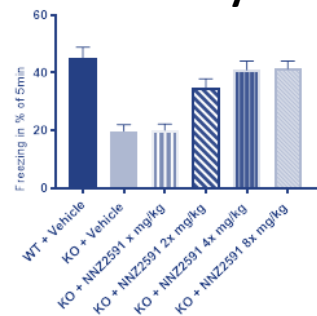
Key Secondary Endpoint in 	Phase 2 Results ¹
Caregiver Impression of Change (CIC) score	15/18 subjects showed improvement Mean score: 2.7 (P = 0.0003 ²)

Consistency seen in Phase 2 across both clinician and caregiver reported measures and impactful symptoms, including communication

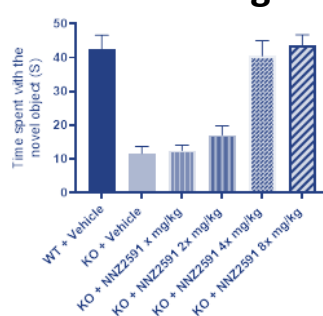
¹ NEU-2591-PMS-001: An Open-Label Study of the Safety, Tolerability, and Pharmacokinetics of Oral NNZ-2591 in Phelan-McDermid Syndrome - 13 weeks treatment of patients age 3-12 years at 4 US sites
² Wilcoxon signed rank test - p-values are nominal without type 1 error control
³ Based on post hoc analysis of overall VABS-3 secondary endpoint

Supported by clear efficacy and dose response in *shank3* model of PMS

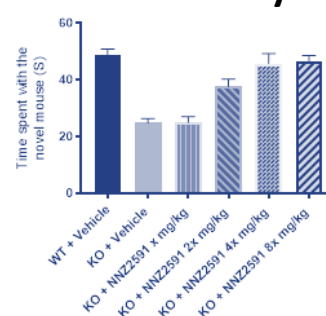
Memory



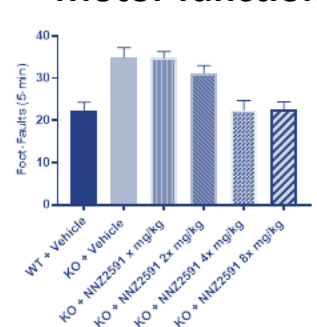
Learning



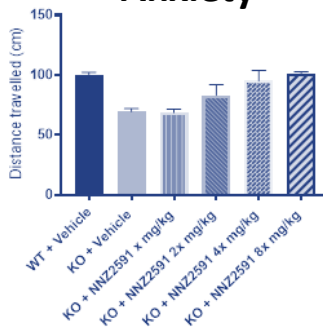
Sociability



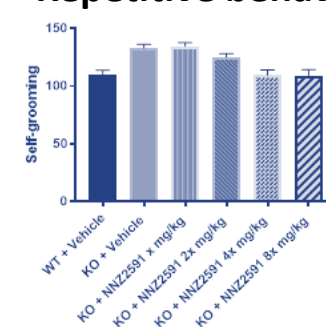
Motor function



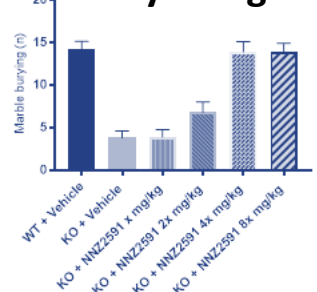
Anxiety



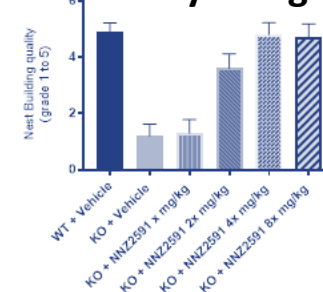
Repetitive behavior



Daily living



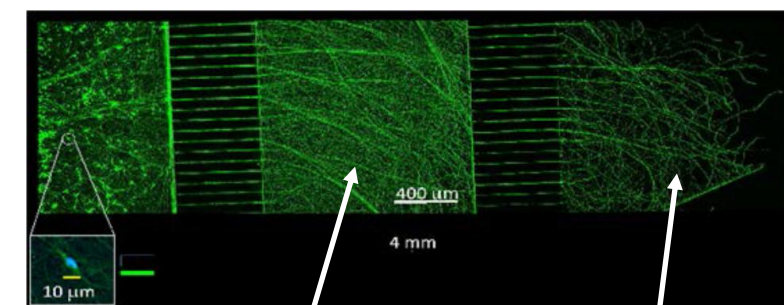
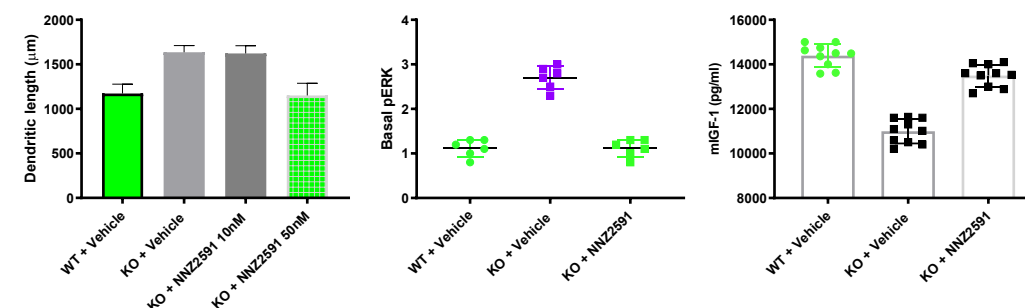
Daily living



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

Leading the development of a first treatment for Pitt Hopkins syndrome (PTHS)

Patients stories¹

"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 be 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 know 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."



**PITT HOPKINS
RESEARCH
FOUNDATION**

neuren

pharmaceuticals

NNZ-2591 development program

- ✓ Orphan Drug designation (US and EU)
- ✓ Fast Track designation (US)
- ✓ Rare Pediatric Disease designation (US)
- ✓ Consistent efficacy observed in *tcf4* model of PTHS
- ✓ Meaningful improvements rated by clinicians and caregivers in open-label Phase 2 trial
- ✓ FDA meeting in Dec 2025 to discuss next steps

neuren

pharmaceuticals

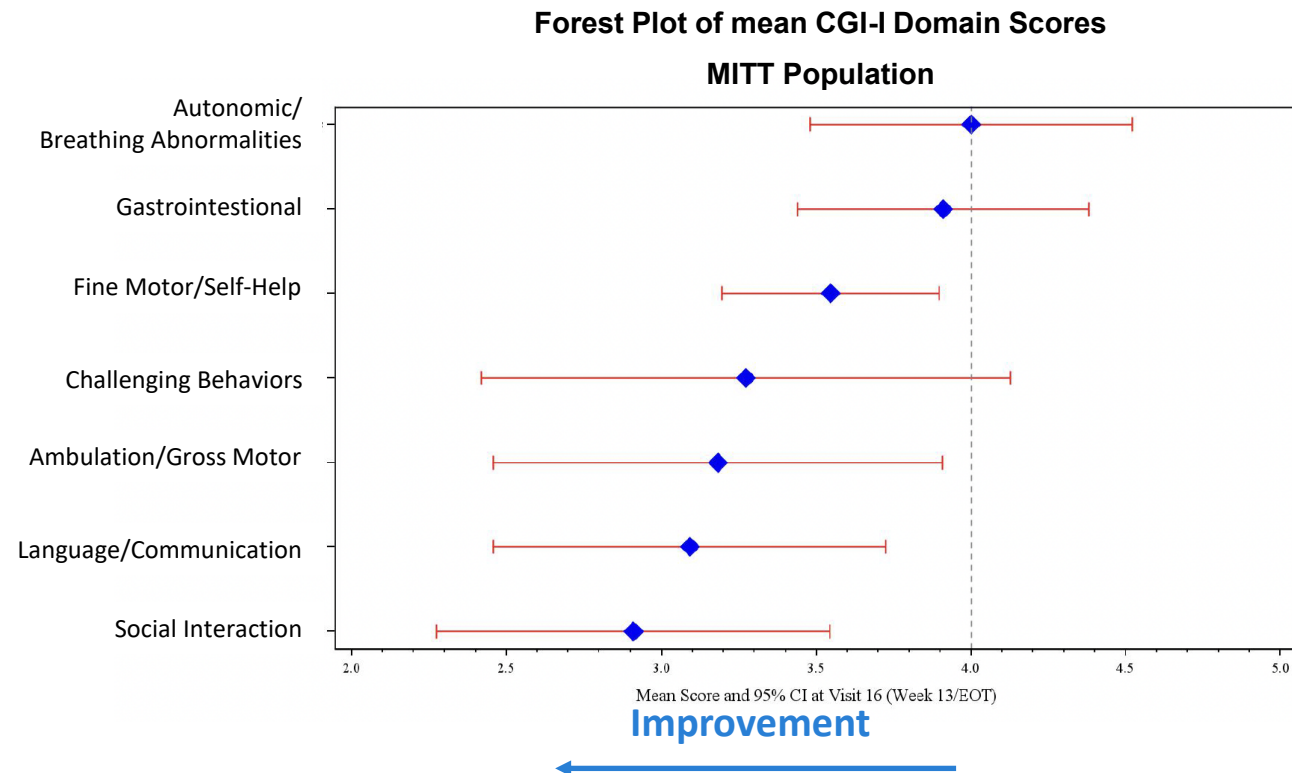
¹ Pitt Hopkins Research Foundation

Meaningful improvements observed in Phase 2 clinical trial

- 13 weeks treatment of patients age 3-12 years in open label trial at 5 US sites
- Mean **CGI-I** of **2.6** with 9 out of 11 children showing improvement ($p = 0.0039^1$)
- NNZ-2591 was safe and well tolerated, with no clinically meaningful changes in safety parameters during treatment

Improvements were seen in clinically important aspects of Pitt Hopkins syndrome, including:

- communication
- social interaction
- cognition; and
- motor abilities



¹ Wilcoxon signed rank test - p-values are nominal without type 1 error control

Hypoxic-Ischemic Encephalopathy (HIE)

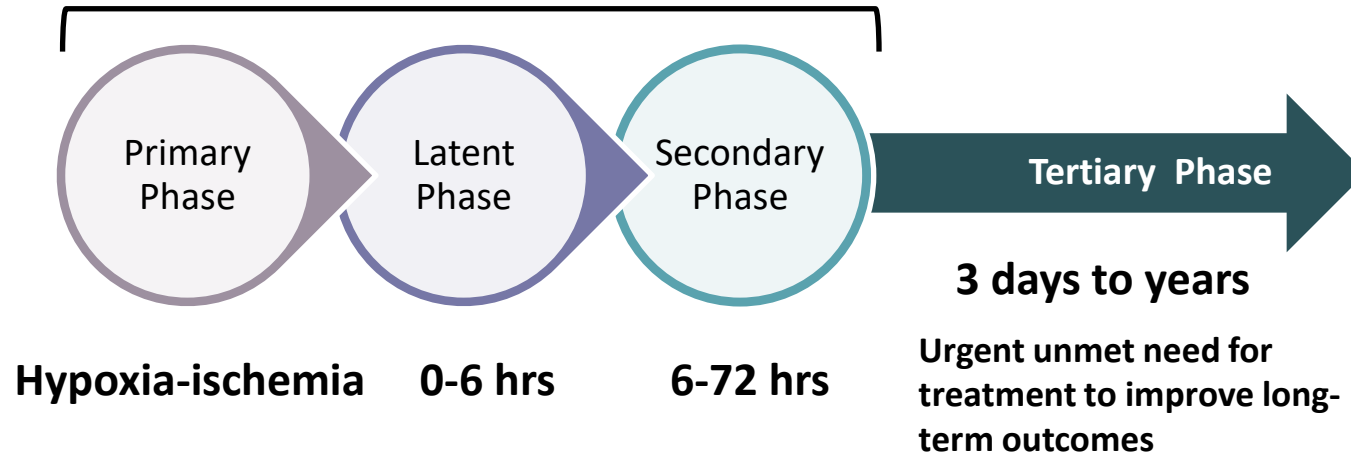
Causes of HIE

Situations where the global oxygenation of the blood flow to the brain is impacted in utero, during birth, or shortly after, that can cause fetal distress, e.g.:

- Placental issues
- Uterine rupture
- Fetal maternal hemorrhage
- Maternal infection
- Shoulder dystocia
- Cord compression and cord issues
- Sudden unexpected postnatal collapse



Standard of care is therapeutic hypothermia (TH), which reduces mortality and morbidity



40-45% of children who survive HIE have significant neurodevelopmental impairment at 2 yrs of age

Even among children not diagnosed with neurodevelopmental impairment at 2, many manifest **cognitive, behavioural** and other **functional difficulties** as they reach school age and beyond

NNZ-2591

- **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

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

For personal use only

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

- Preparing for **pre-IND** meeting with FDA in Dec 2025
- Concentration of clinical sites at large hospitals available
- Formal partnership with patient advocacy group



Commercial

- No approved drug therapy; TH and all drugs in development are for acute treatment (<7 days)
- Critical unmet need to **improve long-term outcomes**
- Planned use of NNZ-2591 acutely then for at least 1 year to leverage both **neuroprotective and neuroplasticity** effects
- **Repeating pool of patients** ~6,000 p.a. in the US¹
- 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

Substantial market opportunities in PMS, PTHS and HIE

Disorder	Published prevalence estimates	Potential patients		
		US	Europe	Japan
PMS	1/8,000 to 1/15,000 males and females ¹ ~1% of autism patients have SHANK3 mutations	19,000 - 36,000 ⁴	21,000 - 41,000 ⁴	5,000 - 9,000 ⁴
PTHS	1/34,000 to 1/41,000 males and females ²	7,000 - 8,000 ⁴	8,000 - 9,000 ⁴	1,000 - 2,000 ⁴
HIE	2-3 / 1,000 births in high income countries; 10-30 / 1,000 births in low and mid income countries ³	<i>Addressable patients⁵</i>		
		~6,000 p.a.	~7,400 p.a	~1,140 p.a.

¹ Phelan McDermid Syndrome Foundation (PMSF) (www.pmsf.org)

² Pitt Hopkins Research Foundation (PHRF) (pitthopkins.org)

³ Hope for HIE ([Hope for HIE - Hypoxic Ischemic Encephalopathy](http://HopeforHIE-HypoxicIschemicEncephalopathy))

⁴ Estimates based on United Nations population data 2024, derived by applying the estimated prevalence range to the populations under 60 years

⁵ Neuren estimates based on various published literature and company publications

Key milestones and catalysts

Milestones achieved 2025 to date

- ✓ Record number of active patients on DAYBUE in Q3 2025
- ✓ Submission by Acadia of EU marketing application for trofinetide
- ✓ Acadia initiated Managed Access Program in Europe, Israel and RoW regions
- ✓ Acadia commenced a clinical trial in Japan to support registration of trofinetide
- ✓ 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 Designations for PMS, PTHS and AS
- ✓ Announced HIE and *SYNGAP1* as new indications for NNZ-2591
- ✓ Completed A\$50m on-market share buyback

Anticipated near-term catalysts

- CY2025 DAYBUE net sales guidance US\$385 – 400m, implying A\$63 – 66m US royalties to Neuren¹
 - Acadia Q4 update
- Potential EU approval of trofinetide in 1H 2026
- US\$35m milestone payment upon 1st commercial sale in Europe
- 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\$385-400m, 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

CONTACT

investorrelations@neurenpharma.com