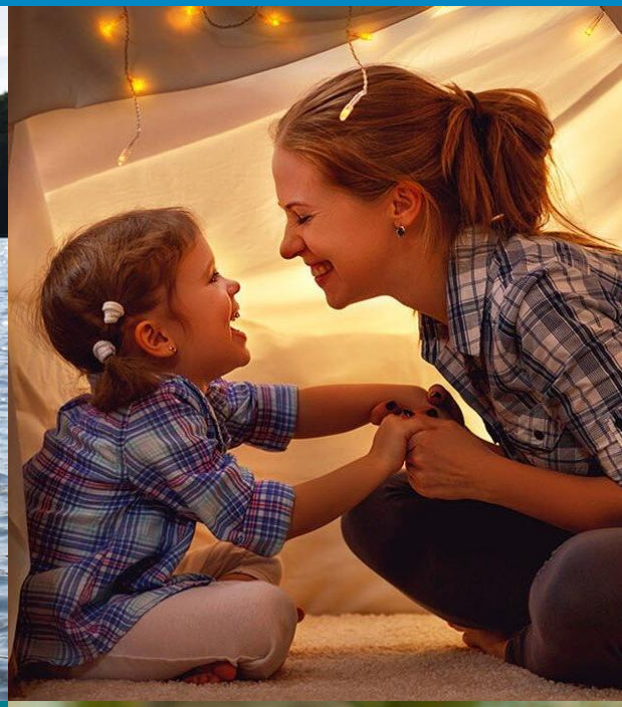
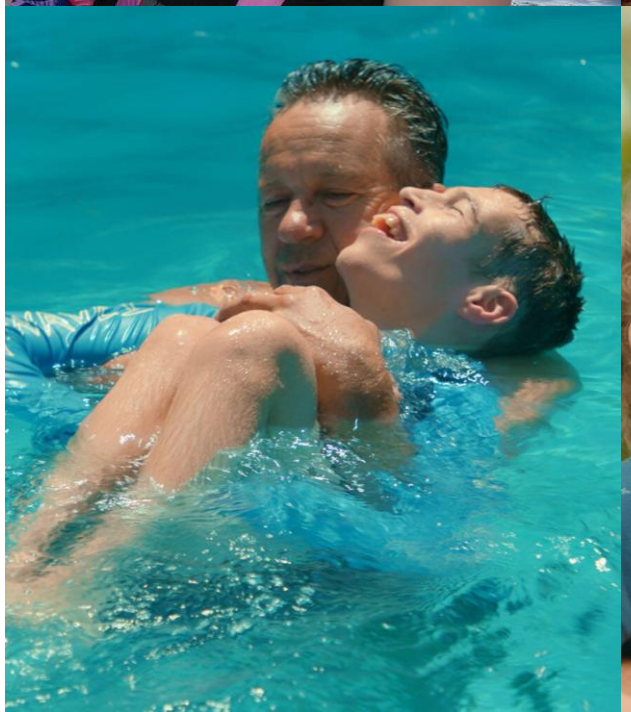
neuren pharmaceuticals

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.

neuren pharmaceuticals

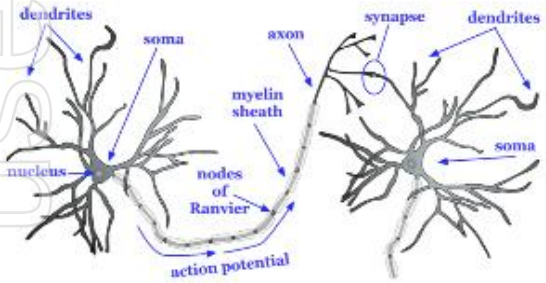
Ground-breaking impact on pediatric neurological Orphan indications

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

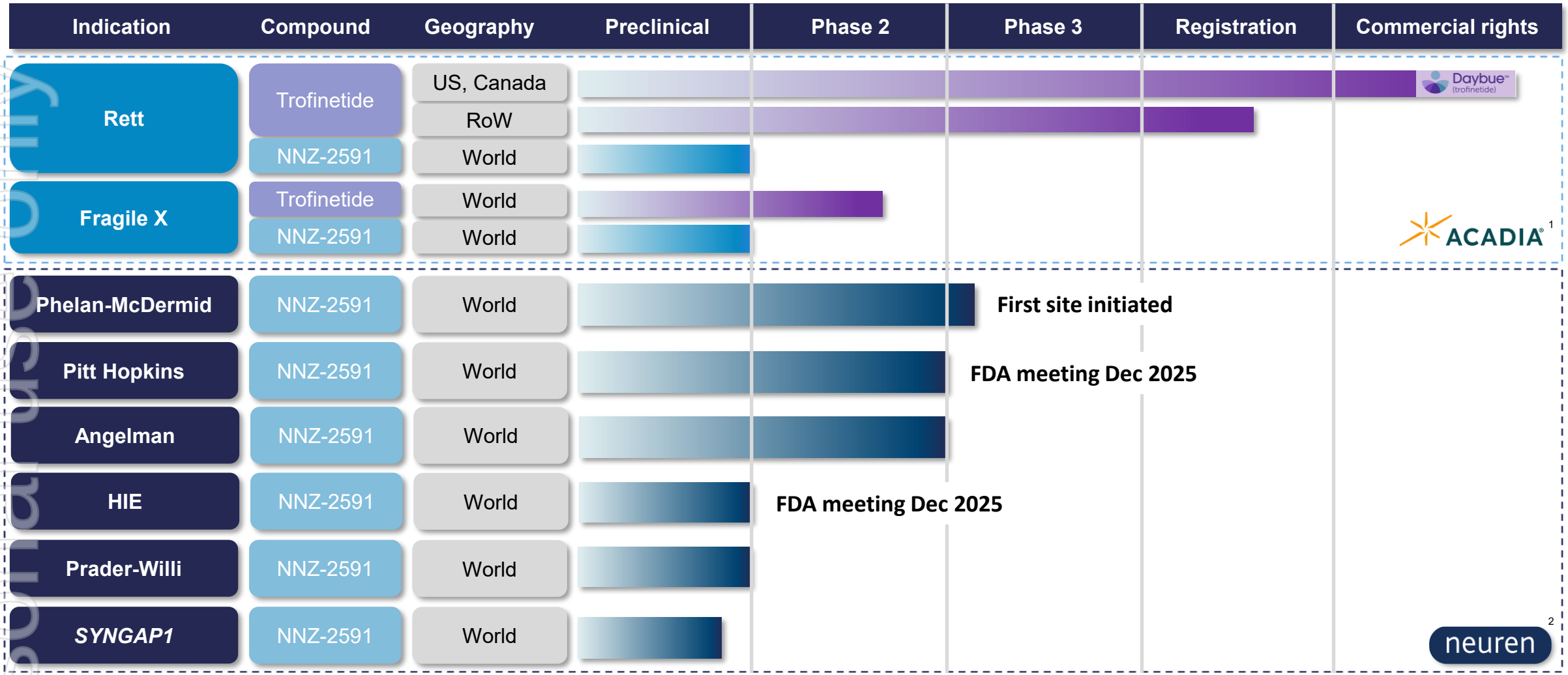
- **Walking and balance issues**
- **Anxiety and hyperactivity**
- **Seizures**
- **Impaired communication**
- **Intellectual disability**
- **Impaired social interaction**
- **Impaired hand use**
- **Sleep disturbance**
- **Gastrointestinal problems**

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
- ✓ 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 Daybue™ (trofinetide)

A$490m income from Daybue® 2023 to date

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

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

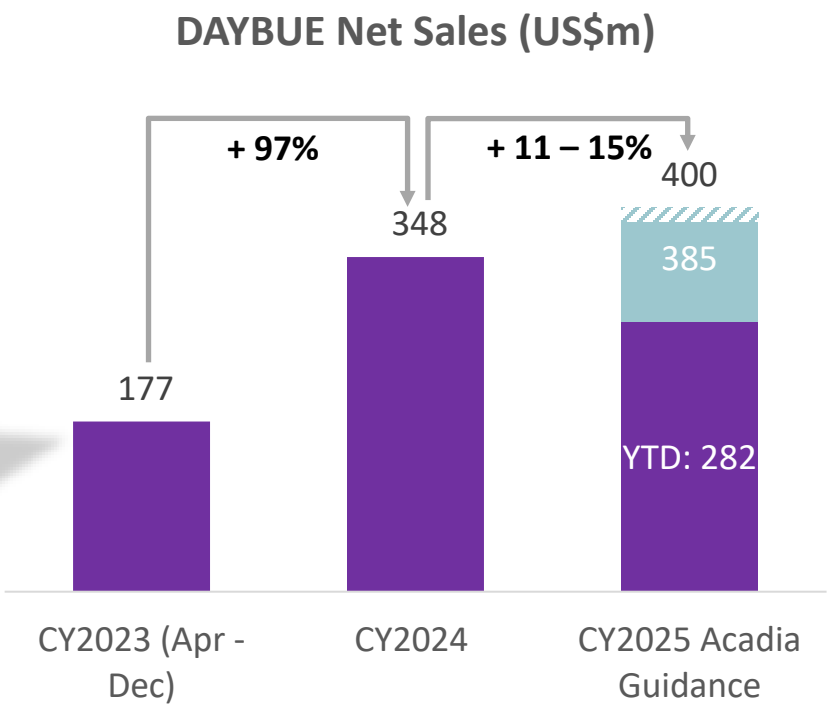
Net Sales in one calendar year	US$m
≥US$250m	✓ **50**
≥US$500m	**50**
≥US$750m	**100**
≥US$1bn	**150**

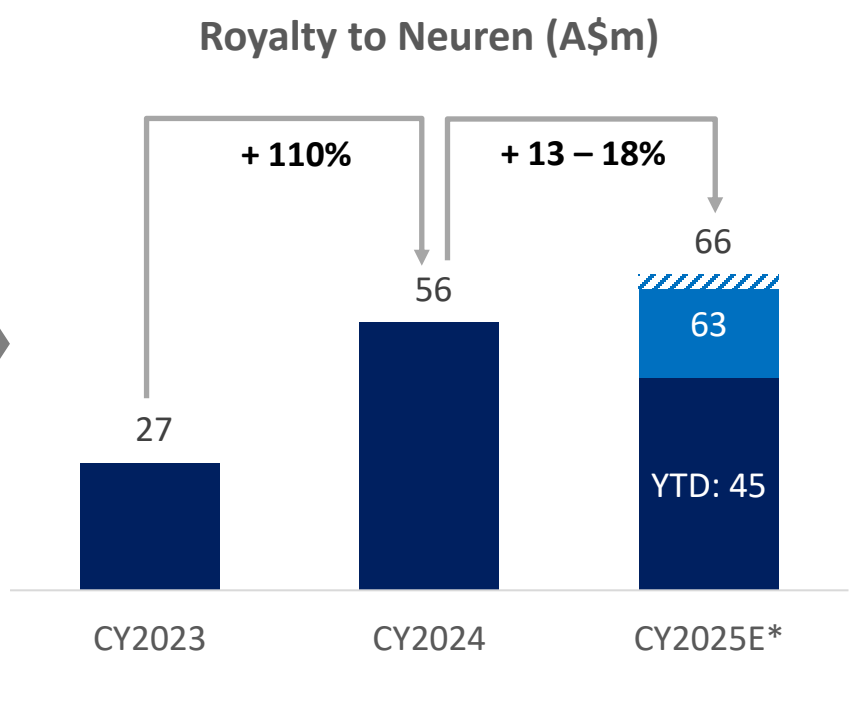
Outside North America

✓	**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)

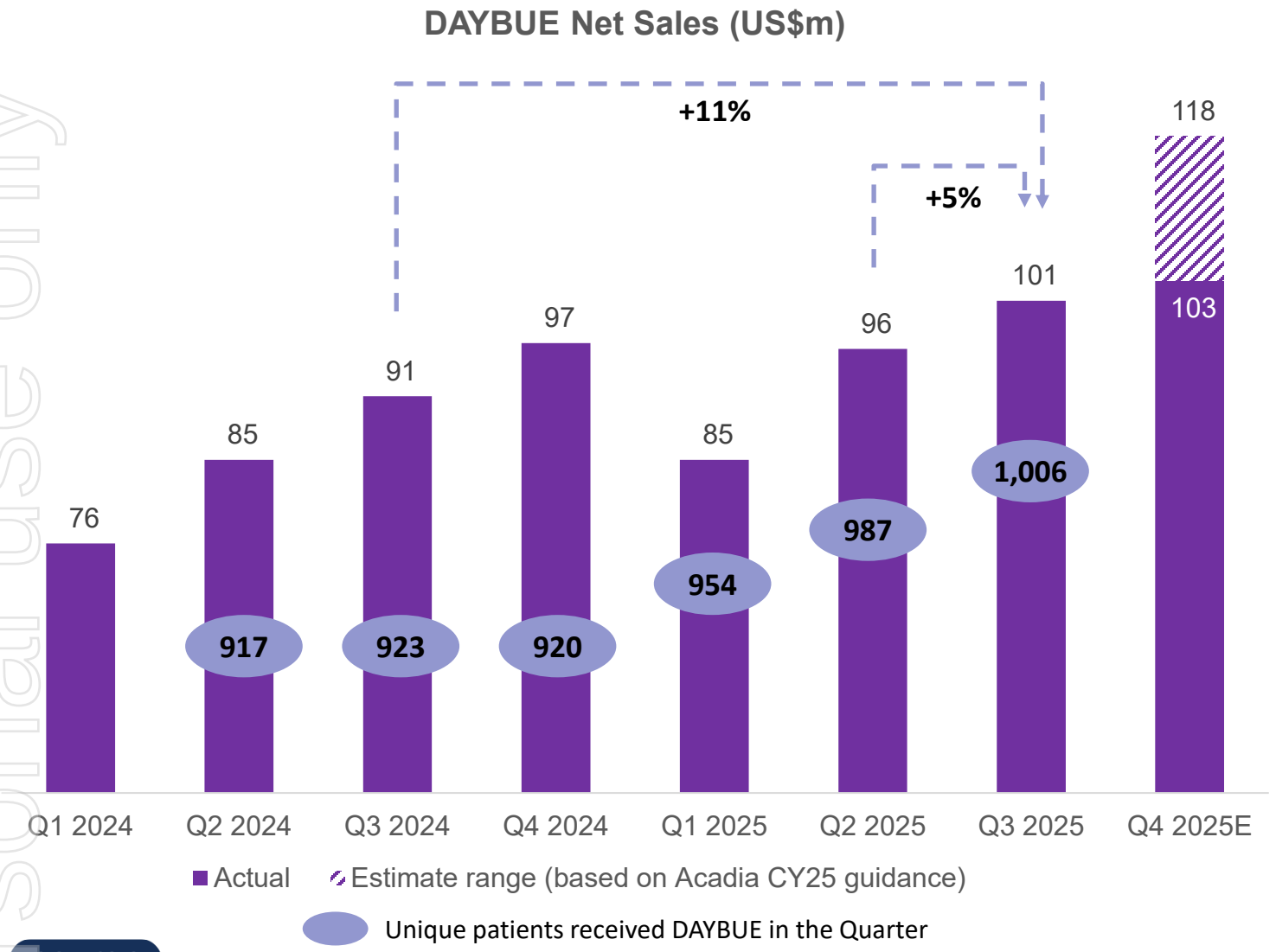




* Based on CY25 Acadia DAYBUE US Net Sales Guidance of US$385-400m, 10% of DAYBUE net sales up to US$250m and 12% of DAYBUE net sales between US$250m and US$500m, and AUDUSD of 0.65

neuren pharmaceuticals

A new phase of expansion and acceleration



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**

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 ~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

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

% 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 table comprises Neuren calculations.
Current data is based on Acadia 3Q 2025 financial results presentation 5 November 2025, 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 CHMP opinion in 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

Small clinical study commenced 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

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.*

cureSHANK

pmsf

Koala

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

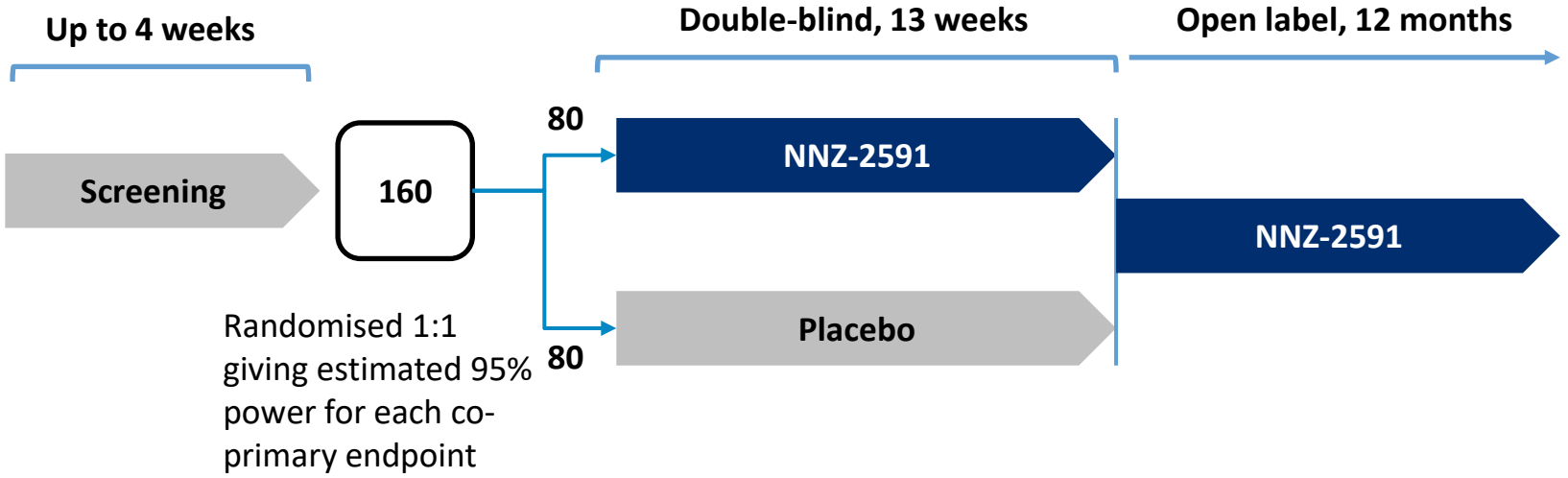
[1] Excerpts from Voice of the Patient Report of Externally-Led Patient-Focused Drug Development Meeting Nov 2022

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 2[1]**
- **~20 trial sites, mostly in US**
- **Program fully funded from existing cash**

Koala



[1] 12.5 mg/kg per day in Phase 3 vs 12 mg/kg in Phase 2, and titration period two weeks in Phase 3 vs six weeks in Phase 2

Key Phase 3 endpoints robustly positive in Phase 2 trial

Co-primary Endpoints in Koala	Phase 2 Results[1]
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[2])
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)** [3] (P = 0.0001[2]) [3]

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

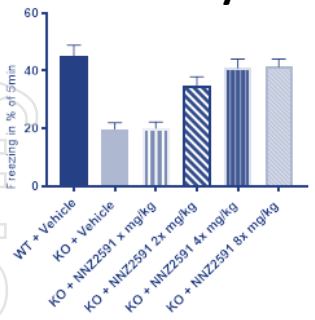
Consistency seen in Phase 2 across both clinician and caregiver reported measures and impactful symptoms, including communication

[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

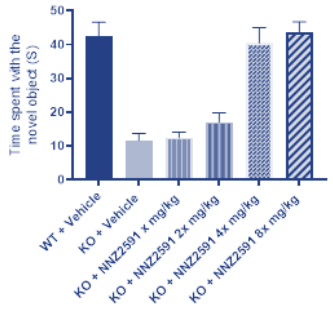
neuren pharmaceuticals

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

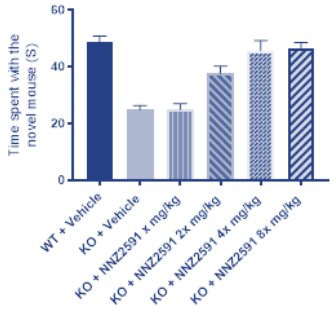
Memory



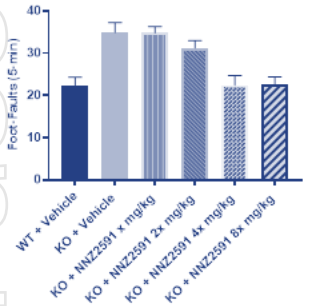
Learning



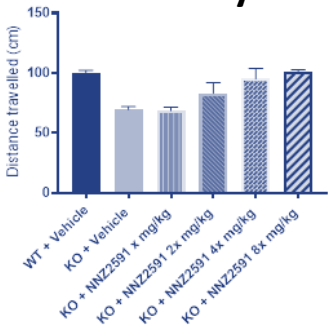
Sociability



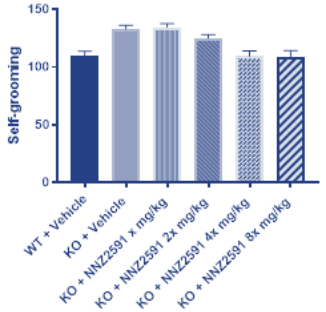
Motor function



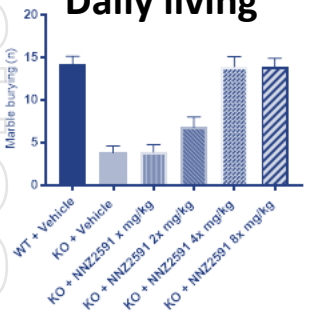
Anxiety



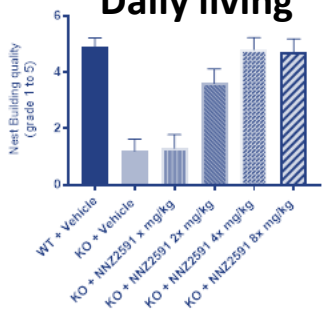
Repetitive behavior



Daily living



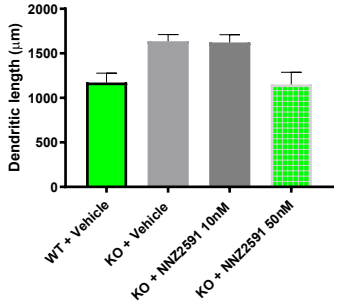
Daily living

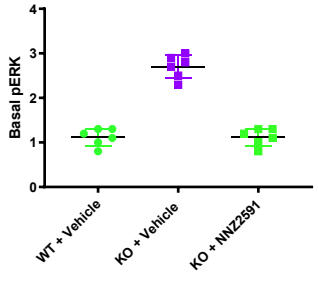


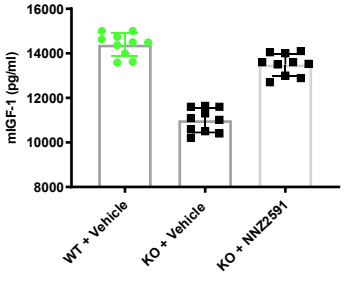
Incidence of audiogenic seizures

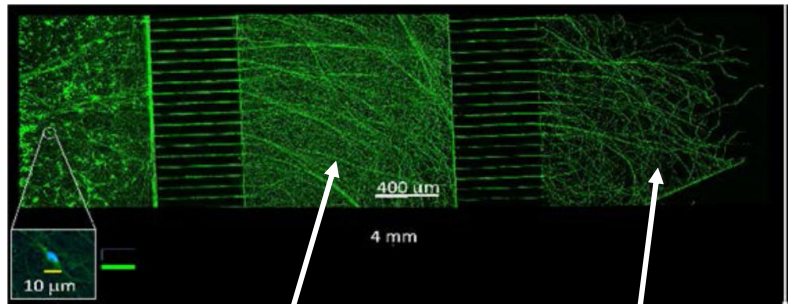
WT + vehicle	0%
KO + vehicle	60%
KO + x mg/kg	50%
KO + 2x mg/kg	30%
KO + 4x mg/kg	10%
KO + 8x mg/kg	10%

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

neuren pharmaceuticals

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

Patients stories[1]

"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."

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

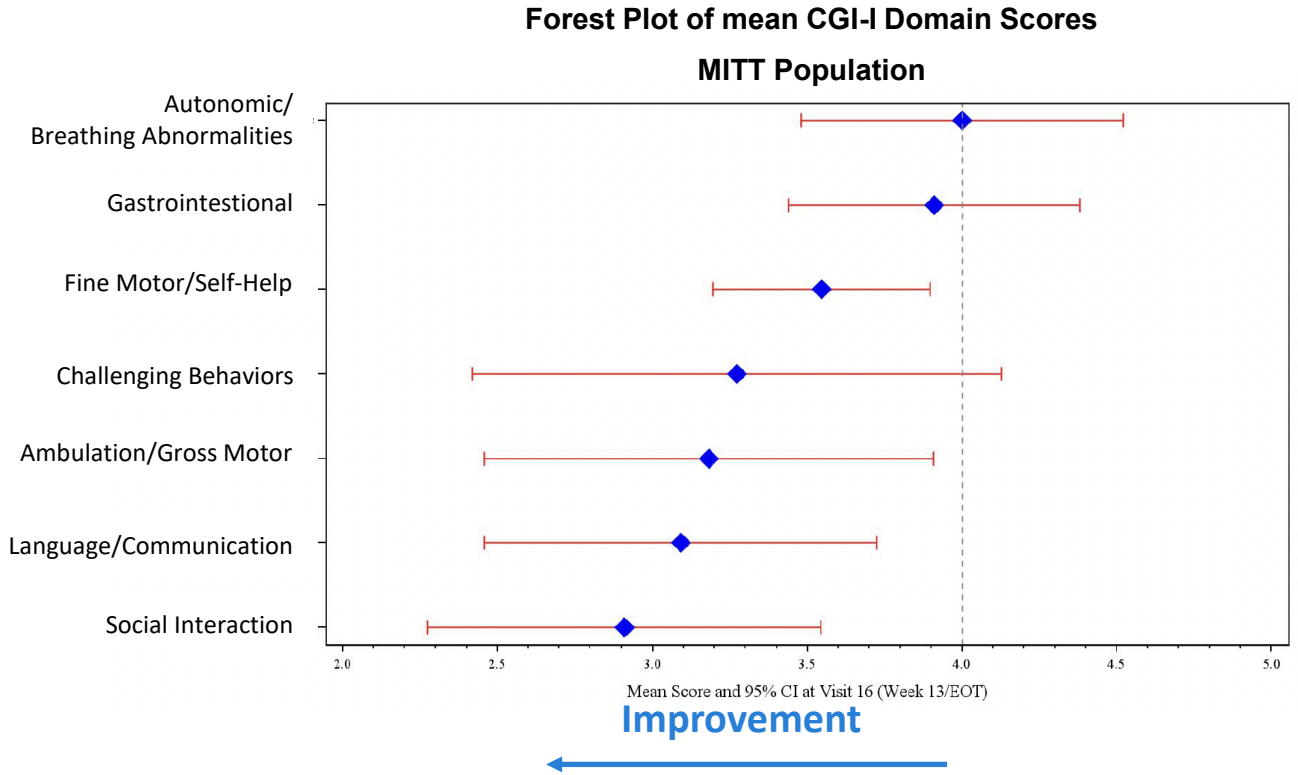
[1] Pitt Hopkins Research Foundation

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

neuren pharmaceuticals

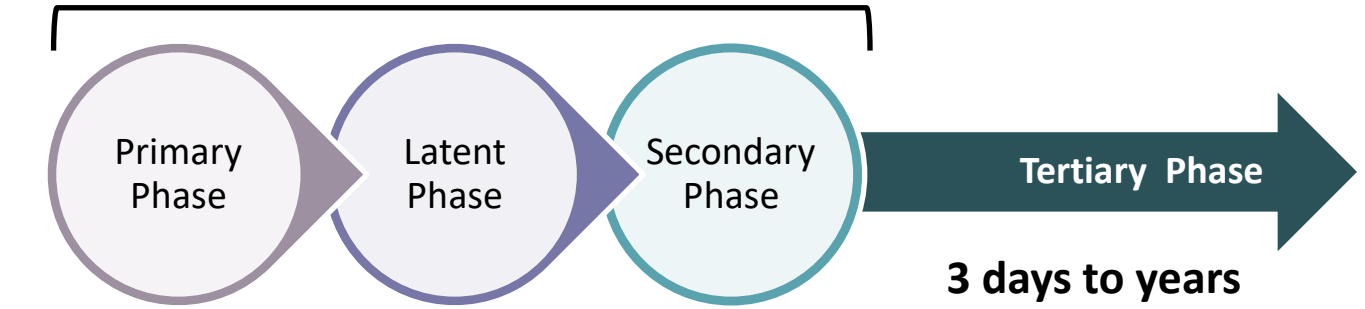
Hypoxic-Ischemic Encephalopathy (HIE)

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



Urgent unmet need for treatment to improve long-term outcomes

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

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

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

HOPE for HIE
awareness • education • support

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 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

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]	*Addressable patients*[5]		
		~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)
[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

neuren pharmaceuticals

Key milestones and catalysts

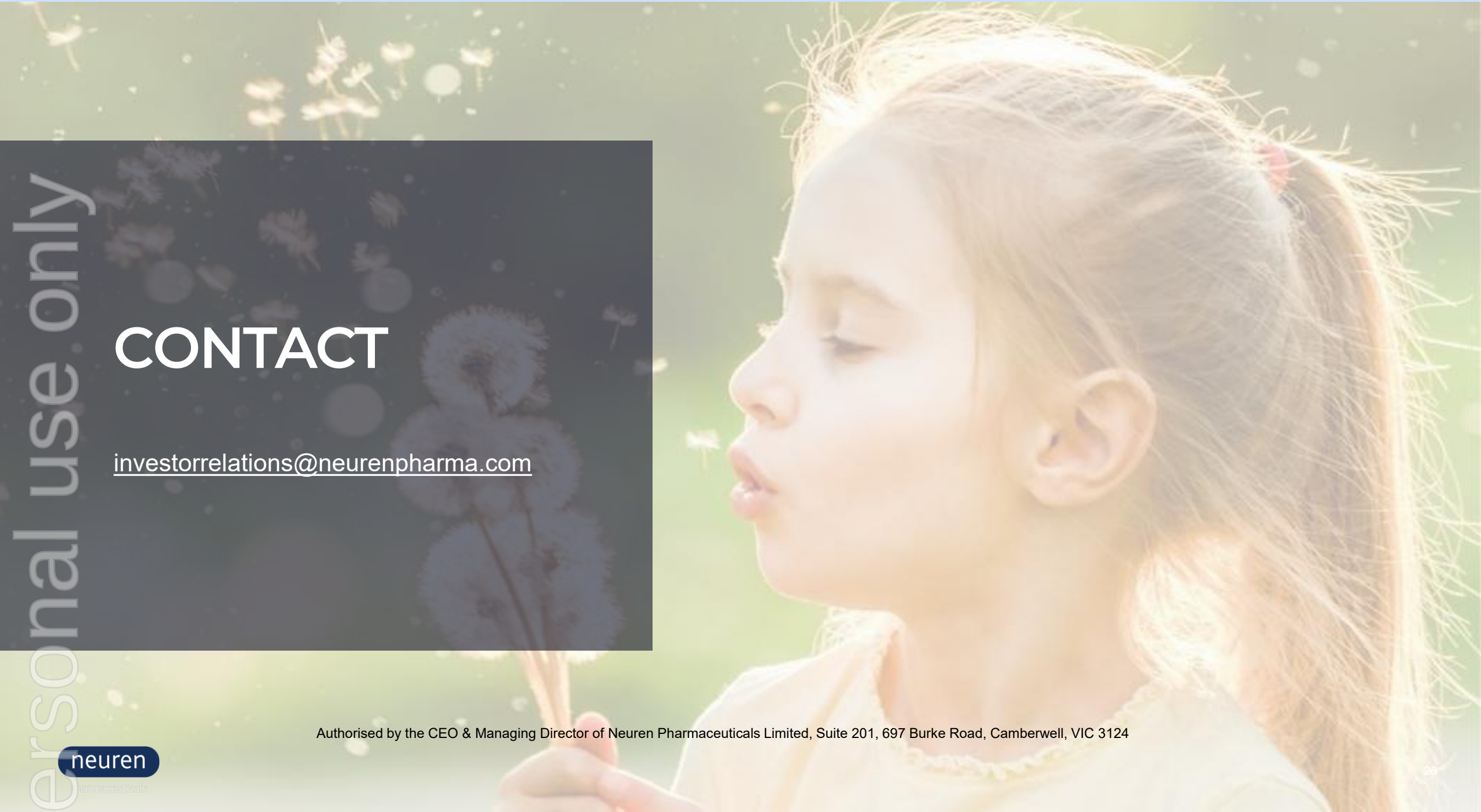
Milestones achieved 2025 to date

- ✓ 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 Neuren[1]
  - 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

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