

neuren

Corporate Presentation

2 September 2026

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.



Large potential upside for shareholders is enabled by financial strength

A\$287
million cash
as at 30 Jun
2026

Long-term income growth
from **DAYBUE®**
(trofinetide)¹



A\$543m income from DAYBUE
since launch in 2023

NNZ-2591² indications prioritised for
maximum commercial impact

Phelan-McDermid syndrome (PMS)

**Pitt Hopkins syndrome
(PTHS)**

**Hypoxic Ischemic
Encephalopathy (HIE)**

Angelman syndrome, Prader-Willi Syndrome, *SYNGAP1*,
Rett syndrome (Acadia)*, Fragile X syndrome (Acadia)*

*Rett and Fragile X syndromes are licensed to Acadia, with same economics to Neuren as trofinetide; Neuren retains worldwide rights to all other indications

¹ Refer to www.acadia.com for DAYBUE (trofinetide) US prescribing and important safety information. Trofinetide is approved in the EU, Canada and Israel. Trofinetide is not approved in Australia

² NNZ-2591 is an investigational medicine and is currently not approved for sale in any country

A uniquely positioned ASX biotech company

Sustainable **growing royalty income from DAYBUE**, driven by strong momentum in US and ongoing global expansion

Recurring royalty **supplemented by significant milestone payments**

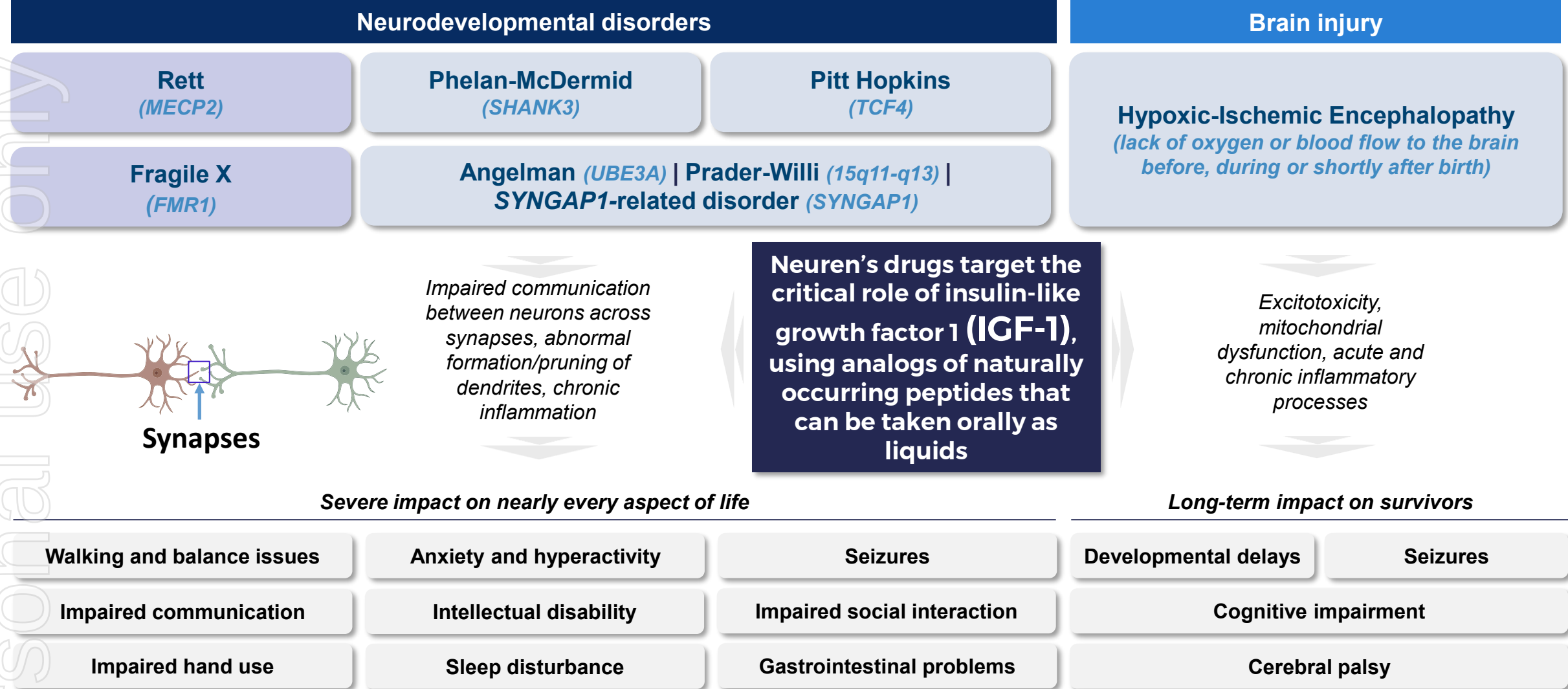
Attractive DAYBUE commercial model with 100% pretax profit margin for Neuren

NNZ-2591 value potential to be unlocked through successful execution of PMS Phase 3 study

Multiple potential indications beyond PMS, with development prioritised for maximum commercial impact

Prioritised pipeline **fully funded**, with **surplus cash** enabling opportunities to optimise total shareholder return

Targeting serious neurodevelopmental conditions with urgent unmet need



DAYBUE (trofinetide)

Exclusively licensed to Acadia
Pharmaceuticals globally

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Strong DAYBUE sales momentum driving sustainable royalty growth

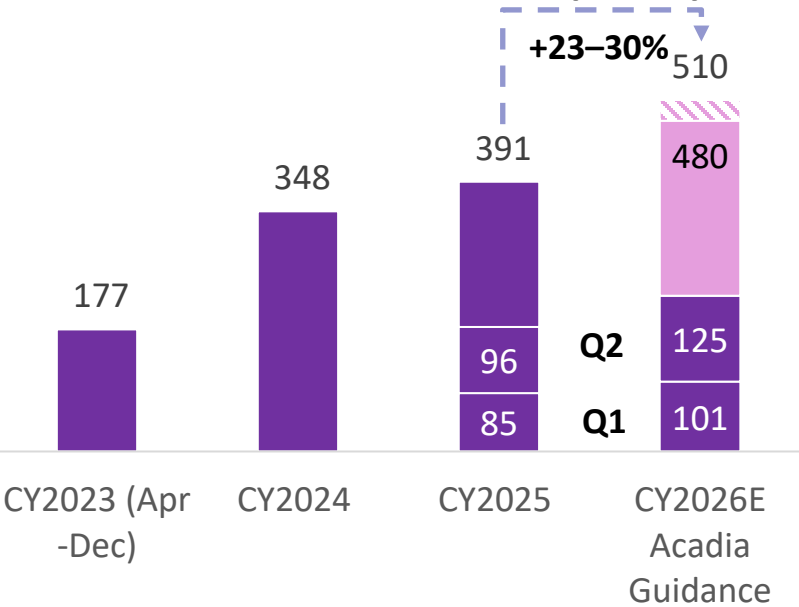


Strong adoption of new powder formulation STIX in the US exceeding expectations

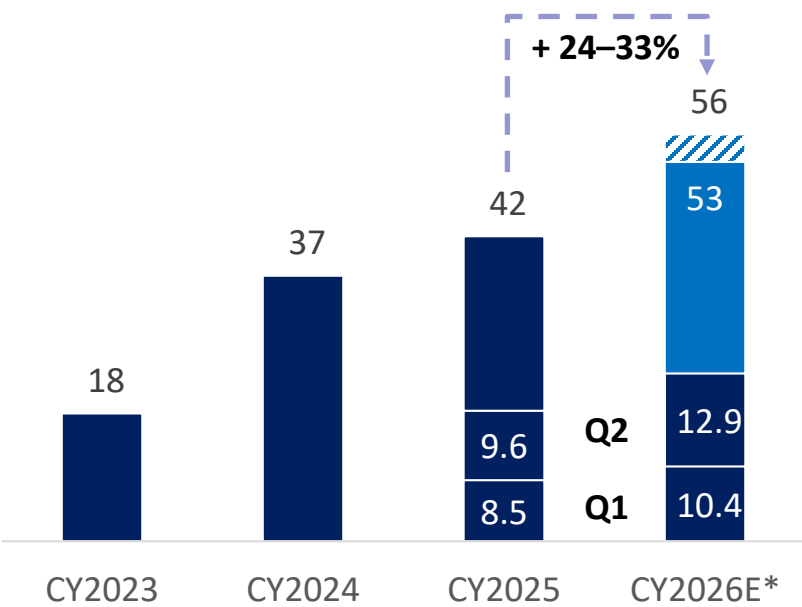
DAYBU® launch in Germany anticipated in early Q4 2026

The only approved treatment for Rett syndrome in US, EU, Canada and Israel

DAYBUE Global Net Sales (US\$m)



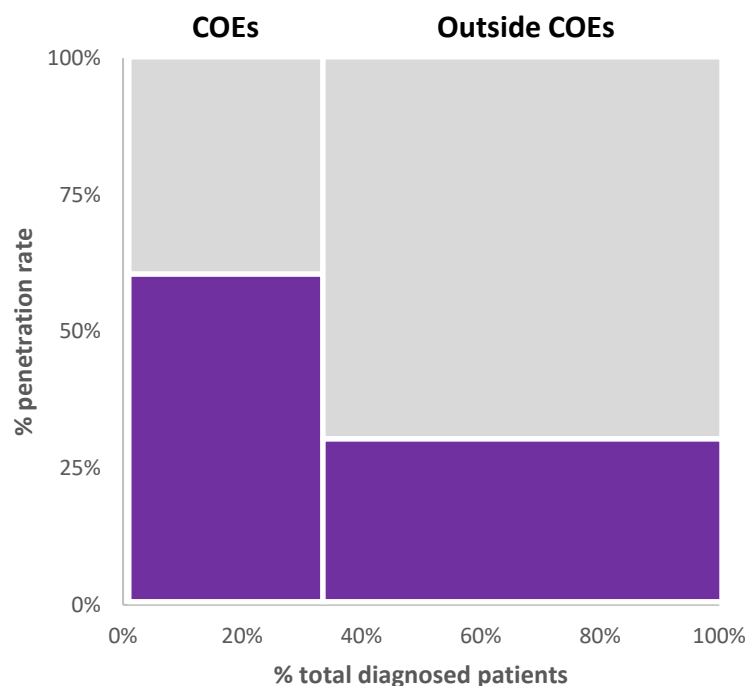
Royalty to Neuren (US\$m)



Significant upside potential in the US

Delphi expert consensus panel recently recommended DAYBUE as part of the standard of care for eligible patients with Rett syndrome¹

US Penetration Rate²



DAYBUE STIX accelerating engagement with new and returning patients

- Limited launched in Q1 2026 focusing on Centers of Excellence (COEs)
- Broadly available from early Q2 2026
- 40% of all US DAYBUE patients now receiving STIX
- 45% of STIX demand in Q2 were from new or returning patients

Refer to www.acadia.com for DAYBUE (trofinetide) US prescribing and important safety information. Trofinetide is approved in the EU, Canada and Israel. Trofinetide is not approved in Australia

¹ Prange EO, Beisang A, Pehlivan D, et al. Expert Consensus on Real-World Use of Trofinetide for Rett Syndrome Using a Modified Delphi Method. Ann Child Neurol. 2026; 4:38-51.

² Acadia Q1 2026 Earnings Call

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Long term growth opportunity through global expansion



Approved Mar 2023

6,000 - 9,000 Rett patients¹

Future Development
Milestones²

Future Sales
Milestones²

Tiered Royalty Rates
(% of net sales)³

Net Sales in a CY	US\$m
≥US\$500m	50
≥US\$750m	100
≥US\$1bn	150

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



Approved Aug 2026

9,000 - 12,000 Rett patients¹

US\$35m following 1st
commercial sale in Europe

Up to **US\$170m** on
achievement of escalating
annual net sales thresholds

Mid-teens to low-20s % of
net sales



Phase 3 results Sep–Nov 2026

1,000 Rett patients¹

US\$15m following 1st
commercial sale in Japan

Up to **US\$110m** on
achievement of escalating
annual net sales thresholds

Mid-teens to low-20s % of
net sales

¹ Acadia estimates

² Each milestone payment is payable once only

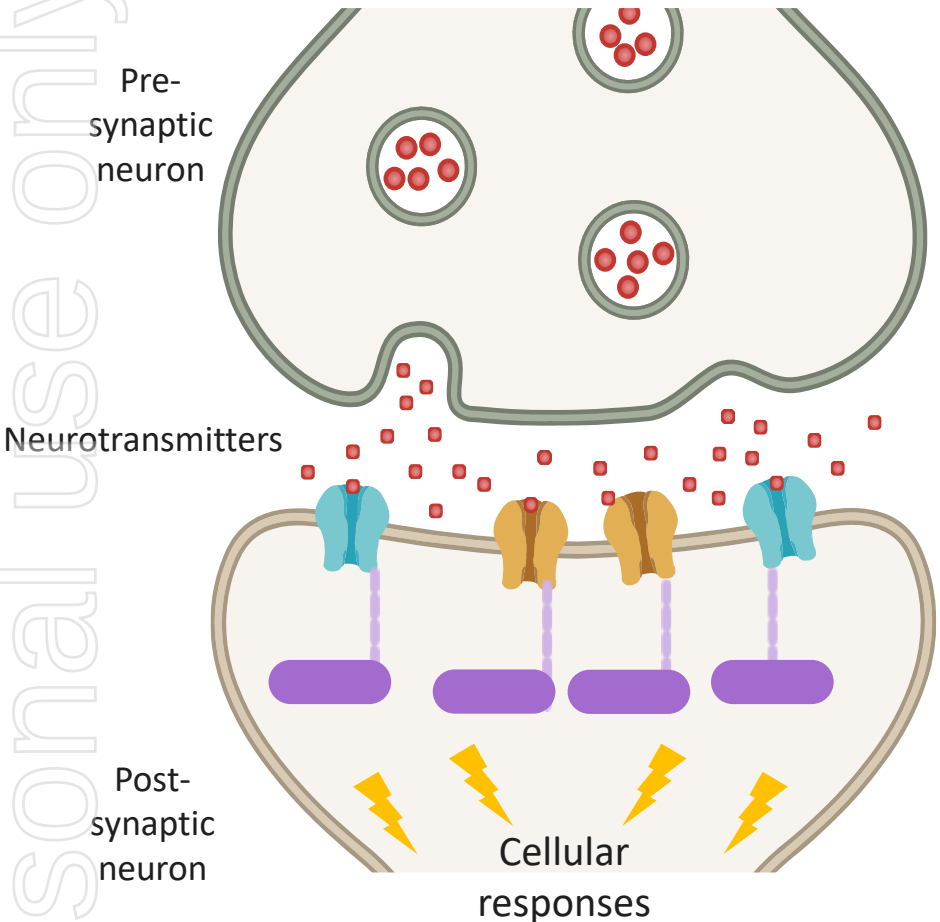
³ Royalty rates payable on the portion of annual net sales that fall within the applicable range

NNZ-2591 (ercanetide)



NNZ-2591 targets the critical role of IGF-1 in synapses

Synapses

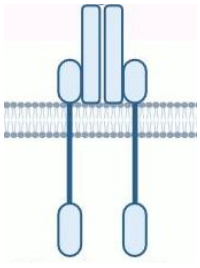
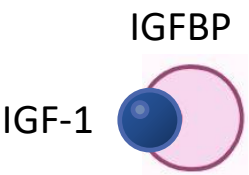


IGF-1 regulates synaptic transmission

IGF-1 regulates synaptic vesicle dynamics. By enhancing neurotransmitter release, IGF-1 increases synaptic transmission

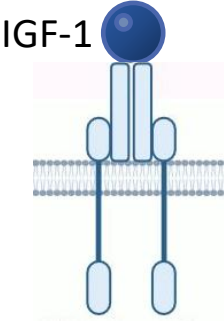
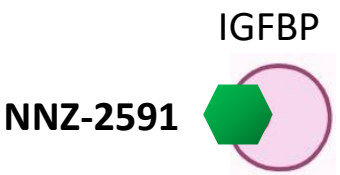
IGF-1 promotes the delivery of neurotransmitter receptors into the membrane. This directly increases the amplitude of the postsynaptic response

NNZ-2591 increases IGF-1 availability¹ and attenuates neuroinflammation²



IGF-1R

IGF-1 activity is regulated by binding proteins (IGFBPs) that bind IGF-1 and prevent it from acting at its receptor (IGF-1R), reducing signaling



IGF-1R

NNZ-2591 increased the availability of IGF-1 to trigger signaling at IGF-1R in vitro¹, increasing the amount of signaling

¹ Guan et al. Sci. Rep. 2014;4:4388. doi: 10.1038/srep04388

² Evaluation of the neuroprotective effects of NNZ-2591 in a mouse model of neonatal hypoxic-ischemic encephalopathy. University of Nebraska Medical Center, 2025. Unpublished data on file

NNZ-2591 is the first investigational medicine in Phase 3 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.*



NNZ-2591 program

- ✓ Alignment with FDA on single Phase 3 trial design and endpoints to support a New Drug Application
- ✓ Koala Phase 3 trial enrolling in US and Canada
- ✓ Meaningful improvements rated by clinicians and caregivers in open-label Phase 2 trial²
- ✓ Supported by positive effects and dose response in *shank3* model of PMS³
- ✓ Orphan Drug designation (US and EU)
- ✓ Rare Pediatric Disease designation (US)
- ✓ Fast Track designation (US)

NNZ-2591 is an investigational medicine and is currently not approved for sale in any country

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

² 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

³ The impact of NNZ-2591 on the phenotype of the *shank3* KO mouse model of Phelan-McDermid syndrome. GeN.DDi, 2019. Unpublished data on file

Koala - the first ever Phase 3 trial in PMS

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

4 - 6 weeks

Screening

160

Randomised 1:1 giving estimated 95% power for each co-primary endpoint

80

80

NNZ-2591

Placebo

NNZ-2591

Koala

Double-blind, 13 weeks

Open label, 12 months

ClinicalTrials.gov

Study Title	NCT Number	Status	Interventions	Phase	Enrollment
A Study of NNZ-2591 in Pediatric Participants With Phenylketonuria	NCT07281079	Recruiting	• Drug: NNZ-2591 • Drug: Placebo	Phase 3	160

Study Title	NCT Number	Status	Interventions	Phase	Enrollment
An Open-Label Study of NNZ-2591 in Pediatric Participants With Phenylketonuria	NCT07593391	Recruiting	• Drug: NNZ-2591	Phase 3	180



Key Phase 3 endpoints robustly positive in Phase 2 trial

RESEARCH ARTICLE OPEN ACCESS

NNZ-2591 in Children and Adolescents With Phelan-McDermid Syndrome

Single-Group, Open-Label, Phase 2 Trial Results

Anni M. Neumeier,¹ Siddharth Srivastava,² J. Lloyd Holder, Jr.,³ Mark A. Milad,⁴ Liza Squires,⁵ Nancy Elizabeth Jones,⁶ Larry Glass,⁷ and Elizabeth Berry-Kravis⁸

Neurol Genet 2026;12:e200338. doi:10.1212/NXG.000000000200338

Abstract

Background and Objectives

Phelan-McDermid syndrome (PMS) is a rare genetic neurodevelopmental disorder with no currently approved treatments. NNZ-2591, a synthetic analog of the insulin-like growth factor 1 metabolite cyclic glycine-proline, was evaluated in children and adolescents with PMS in a phase 2, multisite, open-label clinical trial.

Methods

Participants aged 3–12 years at screening received twice-daily oral NNZ-2591 for 13 weeks; doses were uptitrated from 4 mg/kg to 12 mg/kg over 6 weeks (NCT05025241). Safety and pharmacokinetic profiles were primary end points; 14 efficacy assessments were secondary end points, which included global and symptom-specific PMS assessments, quality of life, communication, behavior, adaptive behavior/self-care, gastrointestinal health, and sleep assessments. Wilcoxon signed-rank tests evaluated change from or observed change relative to baseline vs the null median, with $p < 0.05$ indicating significance.

Results

Eighteen participants received NNZ-2591 (mean [SD] age 8.6 years, mean [SD] weight: 30.4 [10.8] kg). NNZ-2591 was well tolerated; most treatment-emergent adverse events were mild to moderate. Significant improvements from baseline were observed in 10 of 14 efficacy assessments at week 13, including global and symptom-specific PMS assessments, quality of life, behavior, gastrointestinal symptoms, and sleep. At week 13, the PMS-specific Clinical Global Impression (CGI) of Improvement mean (SD) score was 2.4 (0.9) and the median (range) score was 2.0 (1.0, 4.0) ($p < 0.0001$), with 16 of 18 participants showing improvement; the PMS-specific Caregiver Impression of Change mean (SD) score was 2.7 (1.0) and the median (range) score was 3.0 (1.0, 5.0) ($p = 0.0003$), with 15 of 18 participants showing improvement. PMS-specific assessment subdomains of communication, cognition/learning, and socialization showed consistent improvements. A 24-hour steady-state area under the curve (AUC_{24hr}) was estimated for each participant using a one-compartment, linear, population pharmacokinetic model where clearance and volume of distribution parameters were scaled by body weight. Participants with an NNZ-2591 $AUC_{24hr} > 300 \mu\text{g} \cdot \text{h/mL}$ experienced improvements in the PMS-specific CGI of Improvement scores.

Discussion

For children and adolescents with PMS, NNZ-2591 appeared generally safe, with clinicians and caregivers reporting meaningful improvements in important symptoms of PMS. The benefit-risk and pharmacokinetic profiles support continued evaluation of NNZ-2591 for PMS.

Trial Registration Information

ClinicalTrials.gov; NCT05025241. Submitted August 24, 2021. First participant enrolled on August 8, 2022.

¹Lurie Center for Autism, Massachusetts General Hospital, Lexington, MA; ²Department of Neurology, Rosamund Stone Zander Translational Neuroscience Center, Boston Children's Hospital, Boston, MA; ³Department of Pediatrics, Baylor College of Medicine, Houston, TX; ⁴Milad Pharmaceutical Consulting, Plymouth, MI; ⁵Neuren Pharmaceuticals, Camberwell, Australia; ⁶Department of Pediatrics, Rush University Medical Center, Chicago, IL.

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e200338(1)



Co-primary Endpoints in

Phase 2 Results¹

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

Phase 2 Results¹

Caregiver Impression of Change (CIC) score

15/18 subjects showed improvement
Mean score: 2.7
($P = 0.0003^{2}$)

NNZ-2591 was well tolerated in Phase 2, with no clinically meaningful changes in safety parameters during treatment

NNZ-2591 is an investigational medicine and is currently not approved for sale in any country

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

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Neuren's leadership in science and community for PMS

Koala Phase 3 study¹ continues to gain momentum



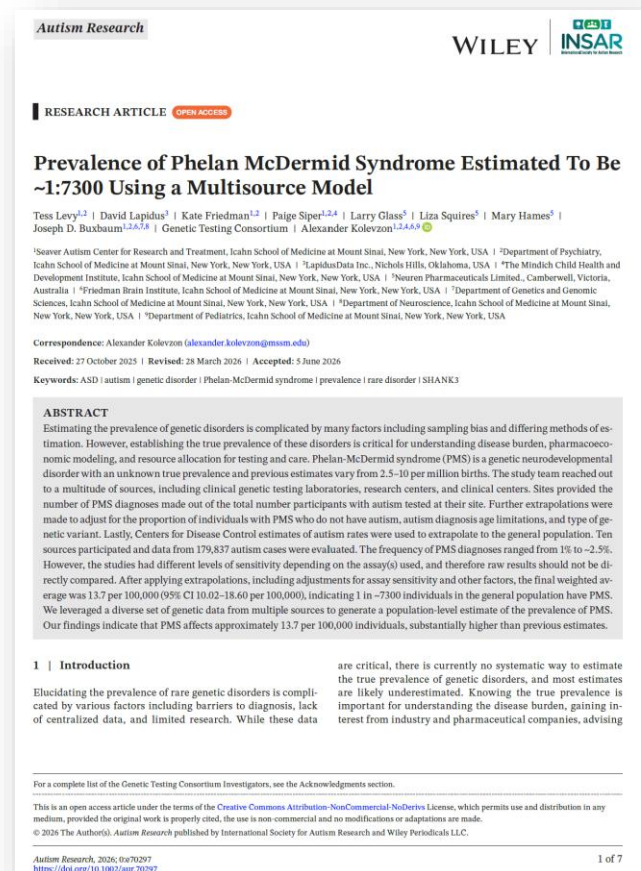
16 trial sites in US/Canada activated

100+ patients referred to sites or await site activation

8 sites activated in OLE for completers of 13-weeks study

First patient from Phase 2 study enrolled in OLE

Recent published study supported by Neuren estimating the prevalence of PMS to be **1 in 7,300** people (~**39,000** in North America²)



Honoured to support and participate in the biannual **PMSF Family Conference** as the Presenting Sponsor



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¹ Koala is a randomised, double-blind, placebo-controlled clinical trial evaluating the safety and efficacy of NNZ-2591 for 13 weeks in approximately 160 children aged 3 to 12 years and a 52-week open-label extension study

² Estimate based on United Nations population data 2025, derived by applying the estimated prevalence rate to the populations under 60 years

Aiming for the first investigational medicine in Phase 3 for Pitt Hopkins syndrome (PTHS)

NNZ-2591 program

- ✓ Type B End of Phase 2 meeting with FDA scheduled for Oct 2026 to align Phase 3 study
- ✓ Clinical improvements observed by clinicians and caregivers in Phase 2 trial¹
- ✓ Positive effects observed in *tcf4*^{+/-} model of PTHS²
- ✓ Orphan Drug designation (US and EU)
- ✓ Fast Track designation (US)
- ✓ Rare Pediatric Disease designation (US)



Phase 2 trial highlights¹

- 13 weeks treatment of patients age 3-17 years in open label trial at 5 US sites
- Mean CGI-I of 2.6 with 9 out of 11 children showing improvement ($p = 0.0039^3$)

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

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

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¹ NEU-2591-PTHS-001: An Open-Label Study of the Safety, Tolerability, and Pharmacokinetics of Oral NNZ-2591 in Pitt Hopkins syndrome - 13 weeks treatment of patients age 3-17 years at 5 US sites

² Drug Validation Initiative. Gen.DDi, 2019. Unpublished data on file

³ Wilcoxon signed rank test - p-values are nominal without type 1 error control

Multiple late-stage opportunities wholly owned by Neuren

INDICATION	COMPOUND	GEOGRAPHY	PRECLINICAL / PHASE 1	PHASE 2	PHASE 3	REGISTRATION
Phelan-McDermid	NNZ-2591	World				
Pitt Hopkins	NNZ-2591	World				
HIE	NNZ-2591	World				
Angelman	NNZ-2591	World				
Prader-Willi	NNZ-2591	World				
SYNGAP1	NNZ-2591	World				

NNZ-2591 is an investigational medicine and is currently not approved for sale in any country

A milestone-rich roadmap

DAYBUE (trofinetide)¹

NNZ-2591 (ercanetide)²

Acadia Q3 26 results

Acadia Q4 26 results

Commercial launch in
Germany

US\$35m 1st EU
commercial sale
milestone payment

Japan trial top-line results

Japan NDA submission

Q3 2026

Q4 2026

2027

Periodic updates on Koala progress

Commencement of
juvenile animal toxicity
study to support HIE IND

End of Phase 2 meeting with FDA
to align PTHS Phase 3 study

PTHS Externally-Led Patient-Focused
Drug Development (EL-PFDD) Meeting
with the FDA

IND application and
FDA meeting for HIE

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¹ Refer to www.acadia.com for DAYBUE (trofinetide) US prescribing and important safety information. Trofinetide is approved in the EU, Canada and Israel. Trofinetide is not approved in Australia

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