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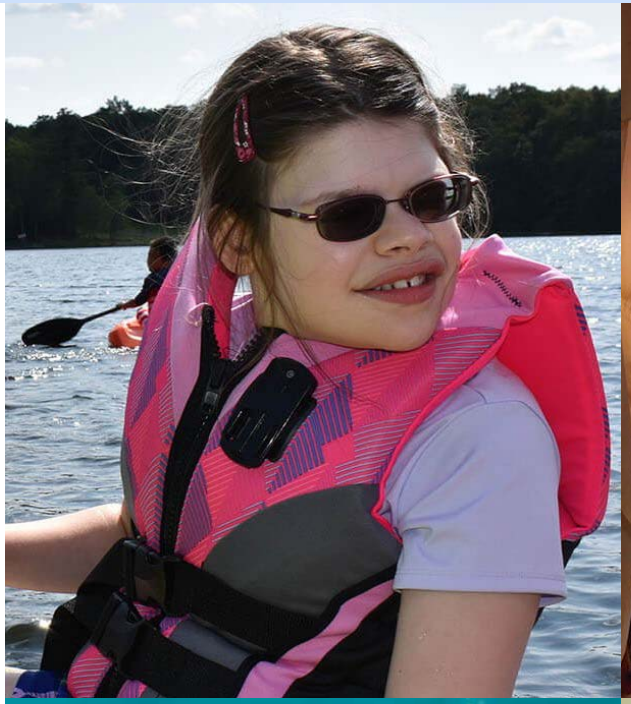
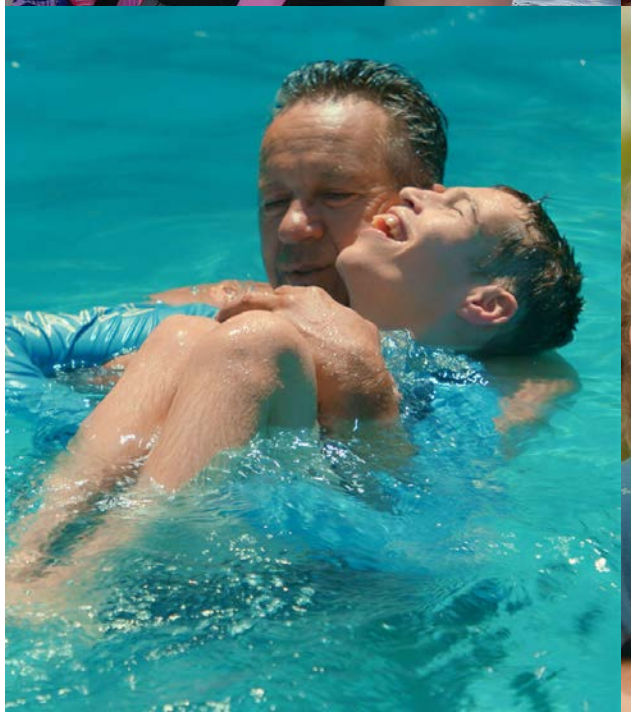
Investor Presentation

8 November 2023

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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Leadership in neurodevelopmental disorder therapy development

Developing new therapies for debilitating neurodevelopmental disorders that emerge in early childhood and are characterised by impaired connections and signalling between brain cells

Daybue™ (trofinetide)

World's **1st and only** approved therapy for **Rett** Syndrome[1]

Clinical development in **5 more** neurodevelopmental disorders, all with **Orphan Drug** designation, with no existing approved therapies[2]

no royalties payable to 3rd parties

Incorporated in New Zealand, based in Melbourne, Australia, listed on ASX (Code: NEU)

[1] Currently approved in US only
[2] Except growth hormone to treat some aspects of Prader-Willi syndrome

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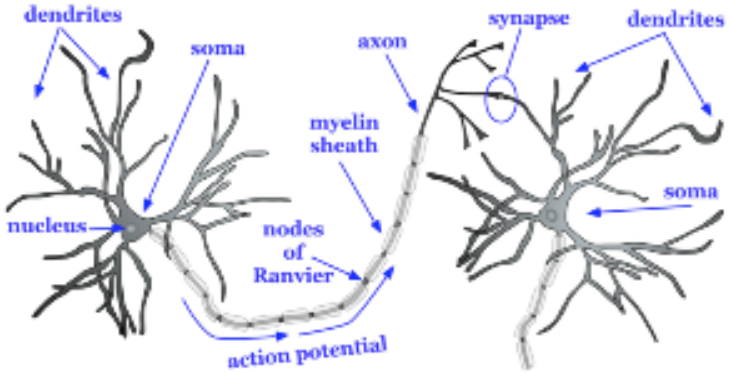
Seeking a ground-breaking impact on neurodevelopmental disorders

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
speech impairment	intellectual disability	breathing irregularities
impaired hand use	sleep disturbance	gastrointestinal problems

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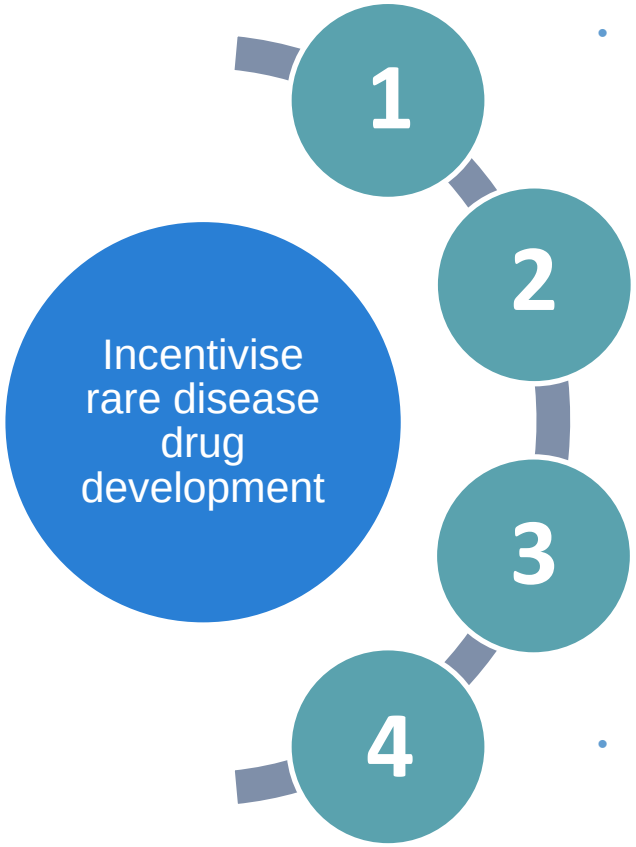
Attractiveness of Orphan Drug model

Neuren is targeting multiple “rare diseases”, but they are not “ultra-rare”



- Marketing exclusivity periods protect against generics independent of patents (7.5 years in US, 12 years in EU, 10 years in Japan, South Korea and Taiwan, China has proposed to introduce 7 years)
- Priority review by regulators (e.g. 6 months in US instead of 10 months) and higher probability of approval
- Urgent unmet need results in strong engagement from patient community and leading physicians, and immediate access to known patients
- Attractive pricing environment

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Commercial and late-stage pipeline

Indication	Compound	Geography	Preclinical	Phase 1	Phase 2	Phase 3	Registration	Commercial rights
Rett	Trofinetide	US						Daybue (trofinetide)
		RoW						
	NNZ-2591	World						ACADIA
Fragile X	Trofinetide	World						
	NNZ-2591	World						
Phelan-McDermid	NNZ-2591	World				Phase 2 top-line results in Dec 2023		neuren
Pitt Hopkins	NNZ-2591	World						
Angelman	NNZ-2591	World						
Prader-Willi	NNZ-2591	World						

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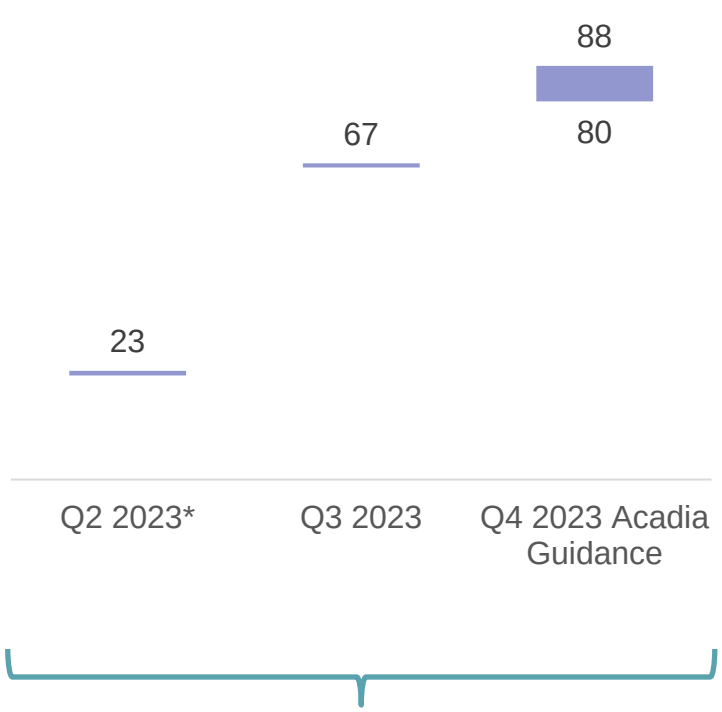
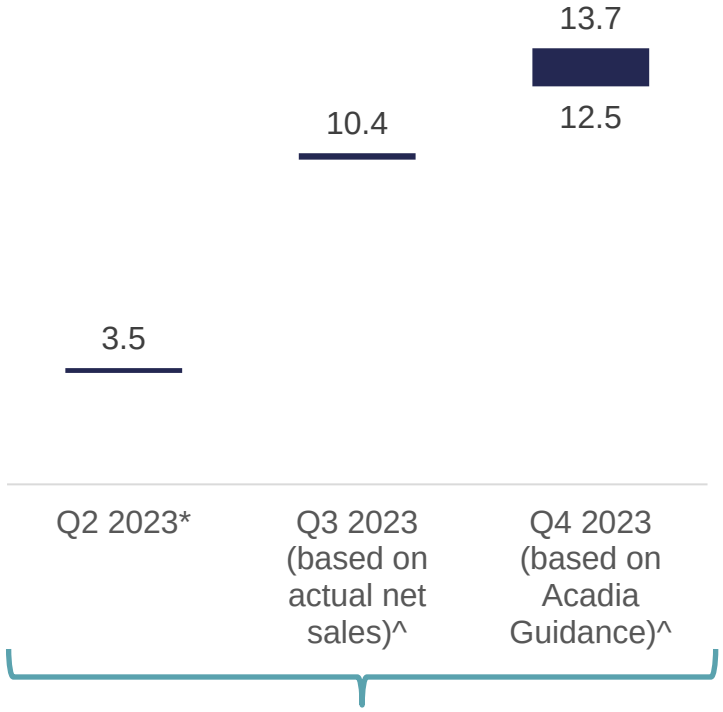
Financial strength to maximise growth opportunities

DAYBUE Net Sales (US$m)



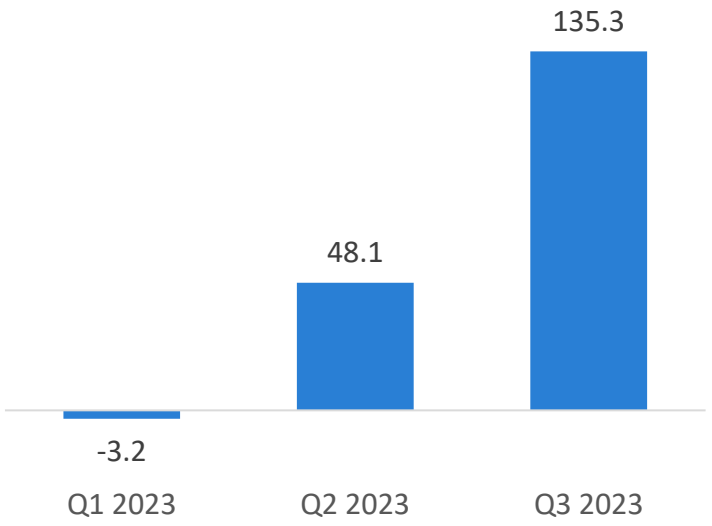
2023E net sales of US$170m – US$178m

Royalty to Neuren (A$m)



2023E royalty of A$26m – A$28m

Neuren cash flows from operating activities (A$m)



Cash balance 30 Sep

A$230m

* Since launch to 30 Jun 2023

^ Based on 10% of DAYBUE net sales and AUDUSD of 0.6433 for Q3 and 0.6400 for Q4

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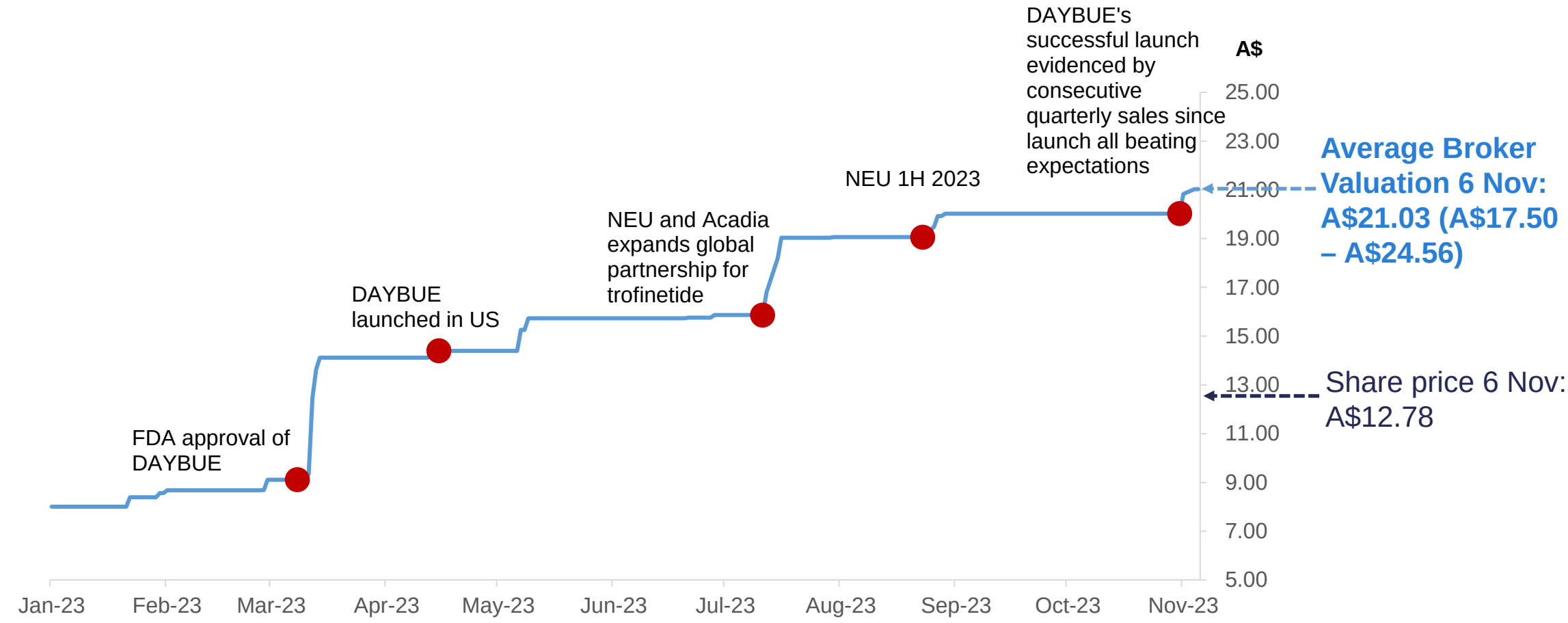
Ongoing value creation with significant upside



Historical average broker valuation include Bell Potter, E&P, Jefferies, MST (until 14 Jul 2023), Petra and Wilsons (since 2 Mar 2023)

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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 four valuable indications, with global rights retained by Neuren

   First top-line results in **Dec 2023** for **Phelan-McDermid syndrome**

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Trofinetide

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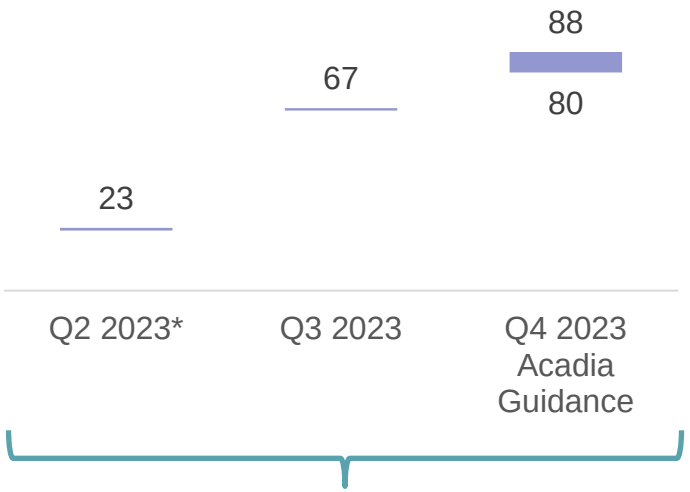
Trofinetide North America – DAYBUE™ US launch in April 2023

	US
Potential Rett patients	6,000 - 9,000[1]
Currently identified Rett patients	4,500[1]

DAYBUE Net Sales (US$m)



2023E net sales of US$170m – US$178m

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

* Since launch to 30 Jun 2023
[1] Acadia estimates
[2] Royalty rates payable on the portion of annual net sales that fall within the applicable range

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Exceptional DAYBUE US launch – as of Acadia Q3 results announcement

Strong and broad-based demand

- **800** patients on DAYBUE as at 30 Sep 2023[1]
- Surge in initial demand has exceeded pre-launch expectations
- **81%** of patients remain on therapy 4 months after starting treatment[2]
- Clinical efficacy, medical education and GI management measures have produced significant benefits
- **75-80%** compliance to labeled dose at 3 months
- **80%** of covered lives covered by formal plans, up from
  - 70%+ in September
  - ~33% in August
  - 20% in July

Positive caregiver testimonials

"Her feet are much closer together with a more normal gait… When she's standing her feet are at less than a 45 degree angle now, so even in one day, there was a great improvement in the way she walks."

"She is using her right hand more. She's able to raise her right arm and help caregivers put on her shirt, and touch her nose and head using her right hand when previously she did not use this hand at all."

"Her speech has improved and she's able to communicate with people more, as well as make better eye contact."

"[She] is able to communicate more with her eyes. She will look at her cup and then back at caregiver, and when given water will gulp it down. She also looked at her empty tray as if to ask for food."

"She is more alert, communicates better and her motor skills have improved."

[1] Net of any discontinuations
[2] Measured by confirmed discontinuations only

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Trofinetide outside North America – expansion of Acadia partnership

Transaction in July 2023 leverages Acadia's unique knowledge and expertise from successful DAYBUE development and commercialization in the US and the established supply chain; Acadia responsible for all costs

	Europe	Japan	Other
Potential Rett patients	9,000 - 14,000[1]	2,000 - 3,000[1]	~30,000[2]
Currently identified Rett patients	~4,000[2]	~1,000[2]	~2,000[2]

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

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NNZ-2591

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5x larger opportunity for NNZ-2591

Disorder	Gene mutation	Published prevalence estimates	Potential patients		
			US[1]	Europe[1]	RoW[1, 2]
Phelan-McDermid	*SHANK3*	1/8,000 to 1/15,000 males and females	24,000	31,000	103,500
Pitt Hopkins	*TCF4*	1/34,000 to 1/41,000 males and females	6,000	8,000	28,000
Angelman	*UBE3A*	1/12,000 to 1/24,000 males and females	16,000	20,000	66,000
Prader-Willi	*15q11-q13*	1/10,000 to 1/30,000 males and females	17,000	21,000	72,000
			63,000	**80,000**	**270,000**

- Current opportunity for NNZ-2591 is more than 5 times the Rett Syndrome opportunity[3]
- There are many other neurodevelopmental disorders potentially relevant for NNZ-2591 mechanism of action
- 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] Estimates derived by applying the mid-point of the prevalence estimate range to the populations under 60 years
[2] RoW comprises Japan, China (urban population), Brazil, Israel, South Korea, Australia and New Zealand
[3] Based on number of potential patients globally

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NNZ-2591 has ideal attributes leading into Phase 2

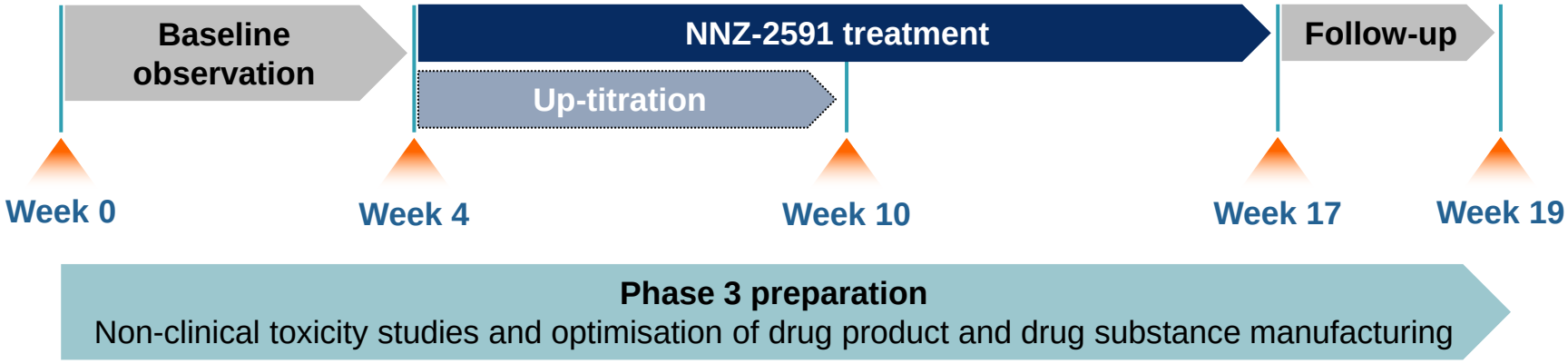
- ✓ Novel mechanism of action
- ✓ Clear and consistent efficacy in mouse models of each syndrome
- ✓ Biochemical effects in the brain confirmed
- ✓ Optimum dose identified
- ✓ Demonstrated high oral bioavailability and blood-brain barrier penetration
- ✓ IND-enabling program of non-clinical toxicology and CMC studies completed
- ✓ Proprietary drug substance manufacturing process with exceptional purity and high yield, administered as patient-friendly liquid dose
- ✓ Safe and well tolerated in Phase 1 trial
- ✓ Orphan designations from FDA and EMA
- ✓ INDs approved by FDA for Phelan-McDermid, Angelman, Pitt Hopkins and Prader-Willi syndromes

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
- 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
- **First top-line results in Dec 2023 for Phelan-McDermid syndrome**

	Phelan-McDermid	Pitt Hopkins	Angelman	Prader-Willi
n subjects	Up to 20	Up to 20	Up to 20	Up to 20
Age range	3 to 12	3 to 17	3 to 17	4 to 12
Location	US	US	Australia	US



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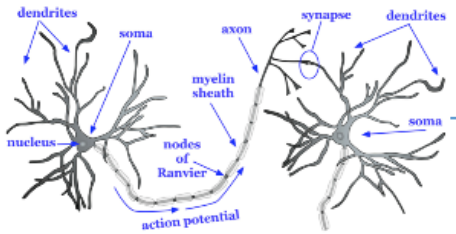
Phelan-McDermid syndrome has an overwhelming unmet medical need

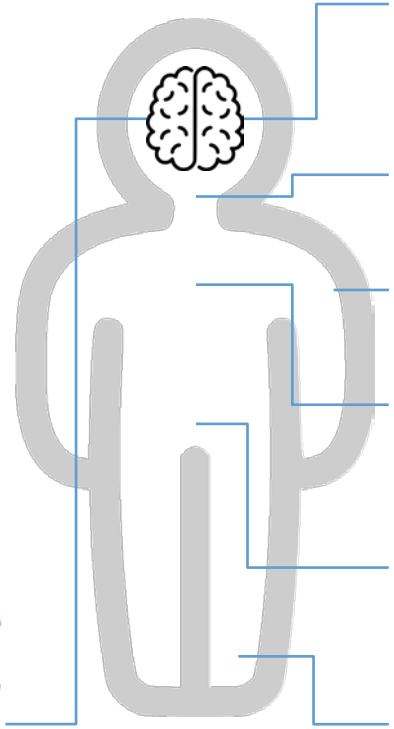
Cause of the syndrome

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)

Absent or delayed speech
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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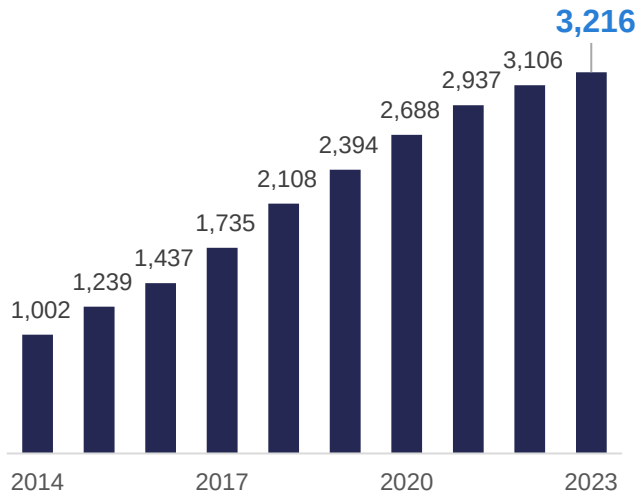
Historically under-diagnosed, but this is changing

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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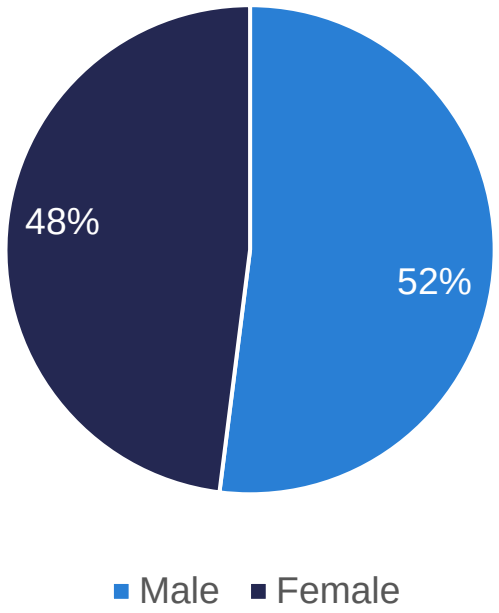
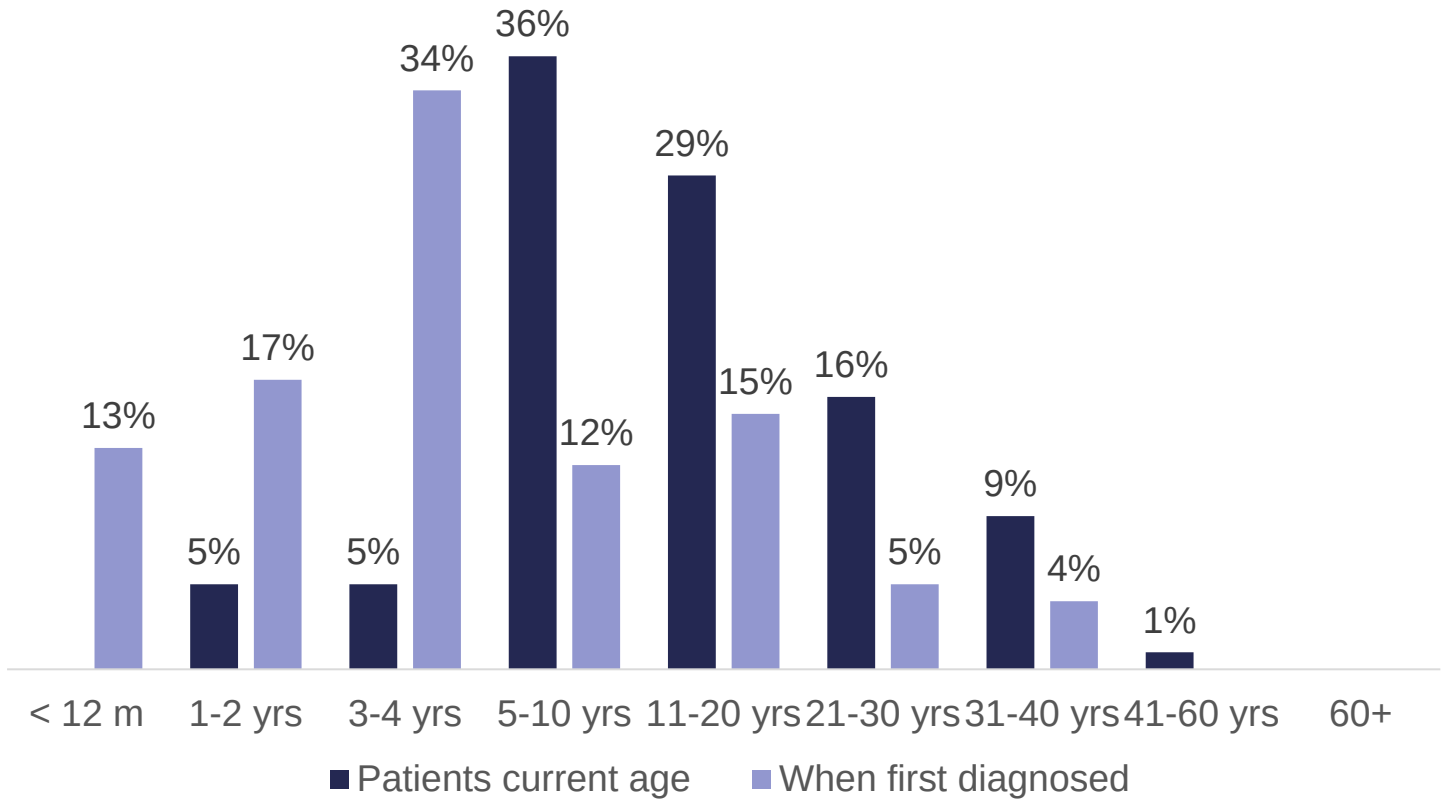
Phelan McDermid syndrome affects all genders and ages

% currently diagnosed patients by gender[1]



% currently diagnosed patients by age group[1]



[1] Estimates based on survey of participants in the Externally-Led Patient Focused Drug Development (EL-PFDD) meeting on Phelan-McDermid Syndrome 8 Nov 2022

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Neuren has opportunity to achieve first approved treatment in PMS

Phase 2 data imminent

- Results expected in December 2023
- Orphan Drug designation in US and EU
- Phase 2 clinical development in the US under an IND
- Eligible for Rare Pediatric Disease Designation Priority Review Voucher program

Limited products in development

Company	Product Development Stage
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#2	Phase 2 terminated early
#3	Phase 1
#4	Pre-clinical
#5	Pre-clinical

Neuren collaborating with all stakeholders

pmsf

cureSHANK

Leading clinicians

FDA

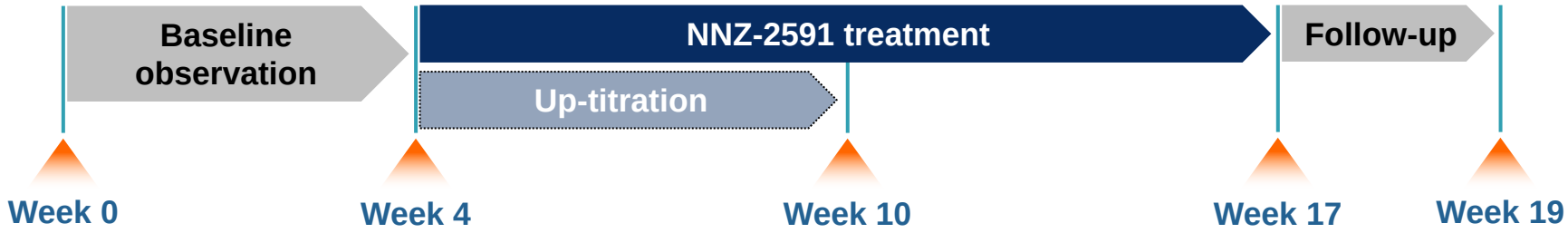
Neuren's Phase 2 trial in children with Phelan-McDermid syndrome

First study in pediatric patients, collecting the data needed to design a registration study

4 US sites: Rush University, Massachusetts General Hospital, Boston Children's Hospital and Texas Children's Hospital

n subjects: Up to 20

Age range: 3 to 12



Primary endpoints

Safety, tolerability and PK

+

Secondary endpoints

Range of efficacy measures collecting information from clinicians and caregivers on overall change in PMS (e.g. CGI-I), change in specific aspects of PMS (e.g. communication and behaviour) and quality of life

Enables selection of the best primary efficacy end-point or end-points for a registration study

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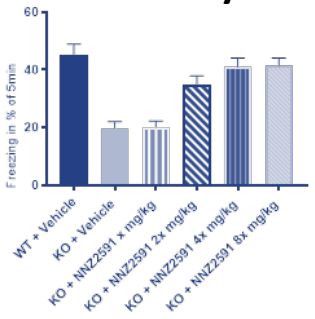
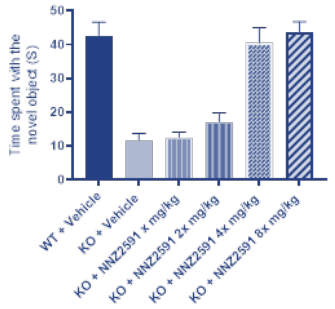
Consistent efficacy & clear dose response for NNZ-2591 in shank3 model

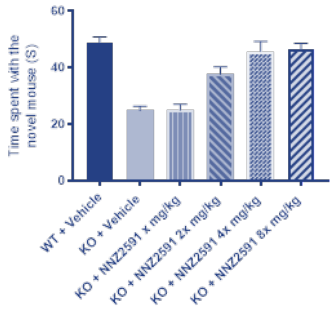
Memory



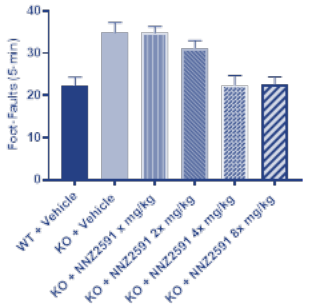
Learning



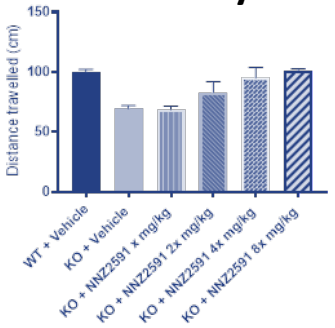
Sociability



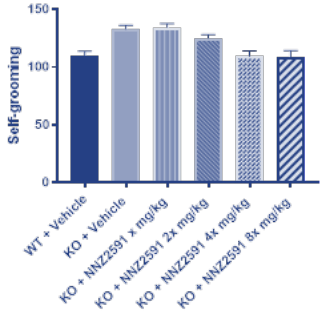
Motor function



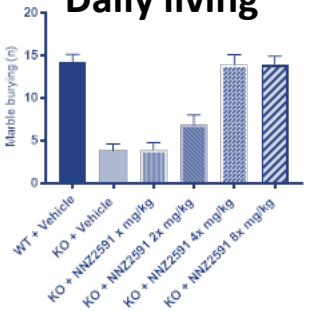
Anxiety



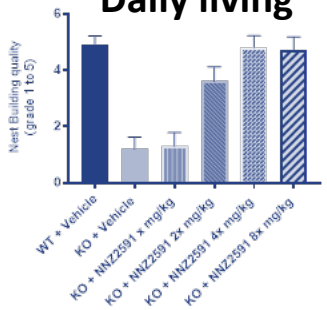
Repetitive behavior



Daily living



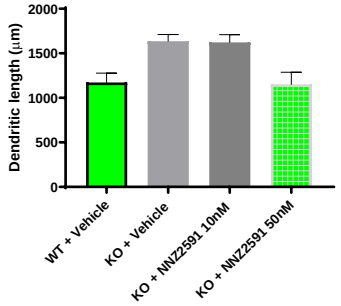
Daily living

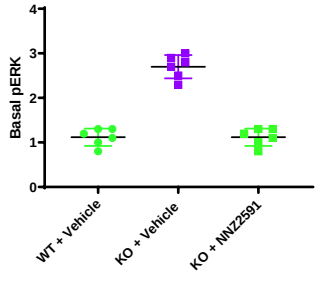


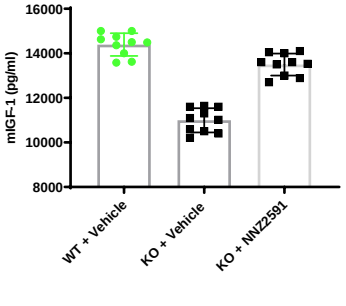
Incidence of seizures

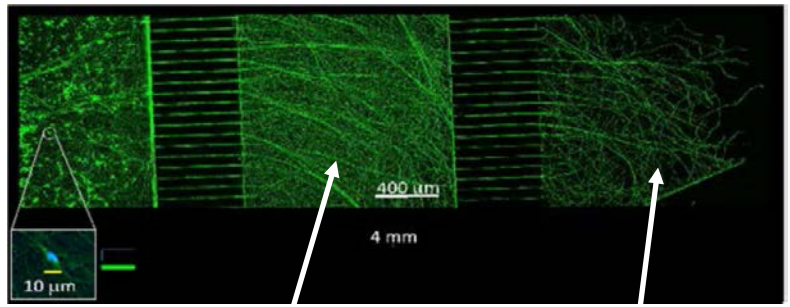
WT + vehicle	0%
KO + vehicle	60%
KO + x mg/kg	50%
KO + 2x mg/kg	30%
KO + 4x mg/kg	10%
KO + 8x mg/kg	10%

In biochemical testing, NNZ-2591 was shown to normalise the abnormal length of dendrite spines between brain cells, 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

Normalisation after treatment with NNZ-2591

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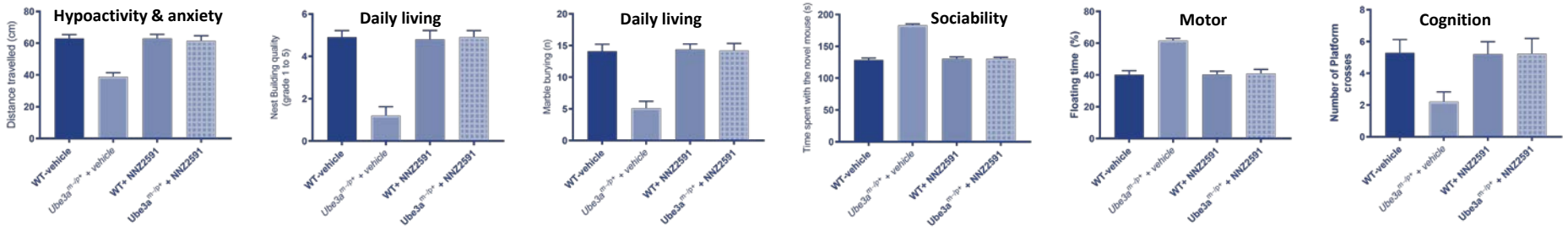
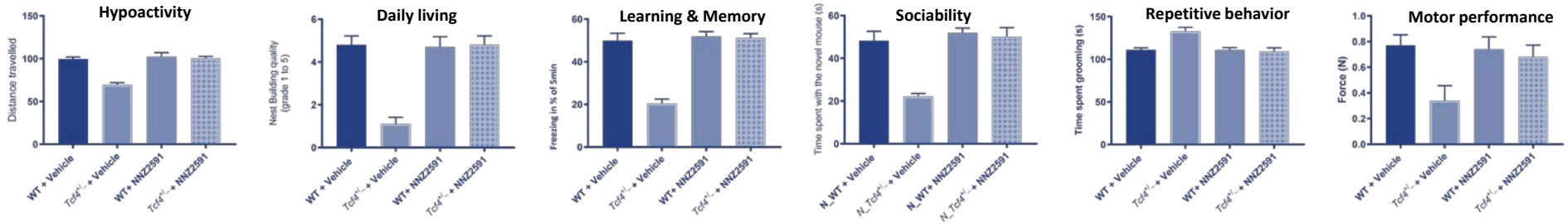
Consistent efficacy in models of Pitt Hopkins, Angelman and Prader-Willi

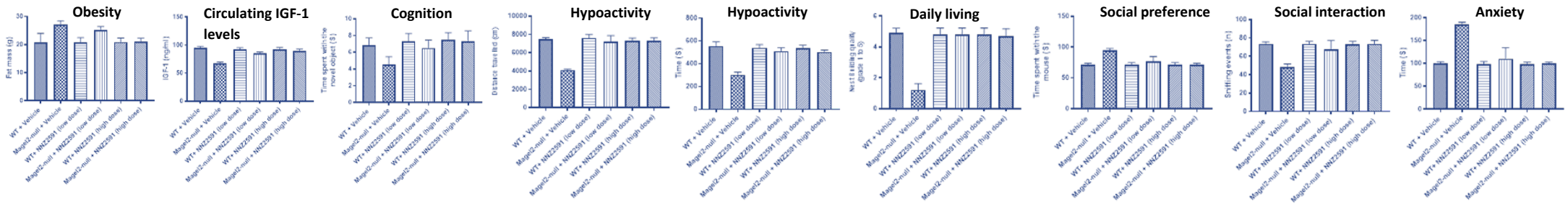
Angelman



Pitt Hopkins



Prader-Willi



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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 expected net sales of US$170m–178m[2] in 2023

4. Accelerating Phase 2 development of NNZ-2591 in 4 indications, with potential markets 5x Rett syndrome. First top-line results in Dec 2023

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

6. A$230m cash at 30 Sep 2023 – well positioned to maximize the benefits of all value creating opportunities

[1] Including payments already received and future payments
[2] Q2 actual net sales of US$23m, Q3 actual net sales of US$67m and Q4 net sales guidance of US$80m – US$88m

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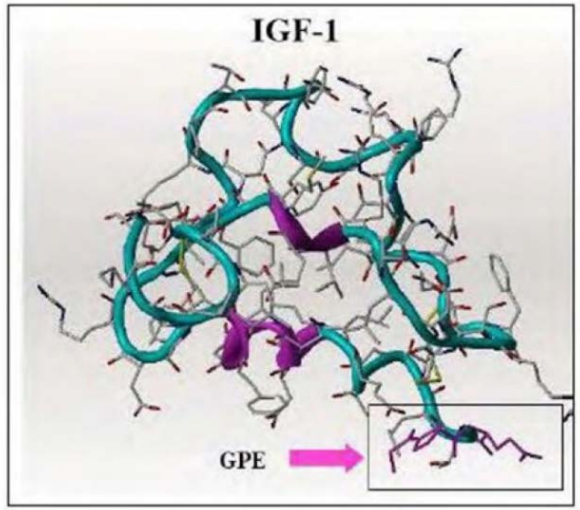
Novel mechanisms of action - trofinetide

Trofinetide

- Trofinetide is an investigational drug and a novel synthetic analog of GPE, the amino-terminal tripeptide of IGF-1



GPE=glycine-proline-glutamate; IGF-1= Insulin-like growth factor 1

Proposed Mechanism of Action[1]

Rett syndrome features:

- Insufficient formation of new synapses by neurons
- Excessive pruning of existing synapses by overactive microglia

Trofinetide is thought to:

- Improve synaptic function and restore synaptic structure
- Inhibit overactivation of inflammatory microglia and astrocytes
- Increase the amount of IGF-1 in the brain

[1] Chahrour, Science, 2008; Itoh, J Neuropath Exp Neurol, 2007; Bourguignon, Brain Res, 1999; Tropea, PNAS, 2009
Source: Acadia Lavender Study Results Presentation https://ir.acadia-pharm.com/static-files/84457c64-60ab-4b2f-a166-edc1d465f4a8

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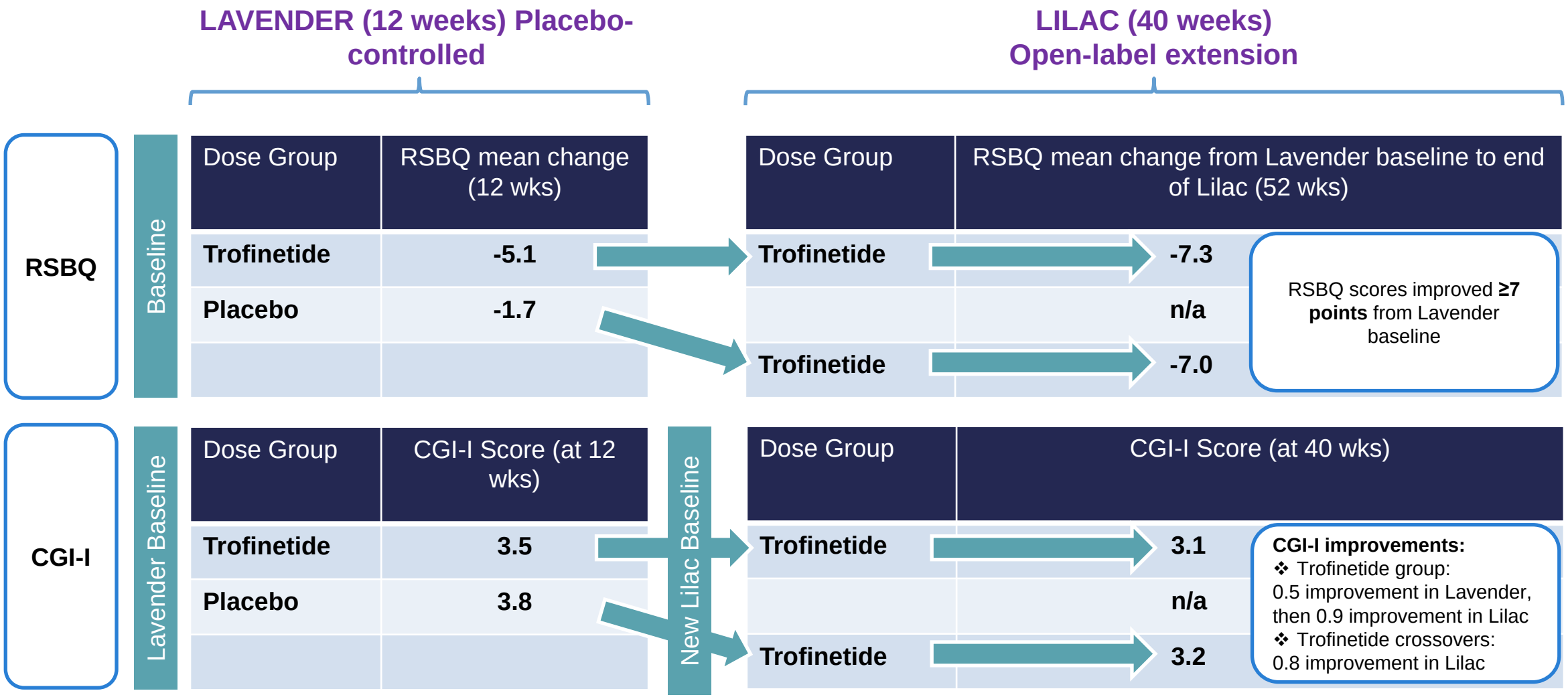
Sustained and continued improvement observed in trials



Source: Acadia presentation (Acadia Corporate Presentation (4Q22 Earnings), Lavender Study Results (acadia.com))
RSBQ: n=161 for Lavender at 12 weeks; n=88 for Lilac at 40 weeks.
CGI-I: n=163 for Lavender at 12 weeks; n=91 for Lilac at 40 weeks. CGI-I uses a 7-point Likert scale; a score of 4 = no improvement; >4 = worsening and <4 = improvement.

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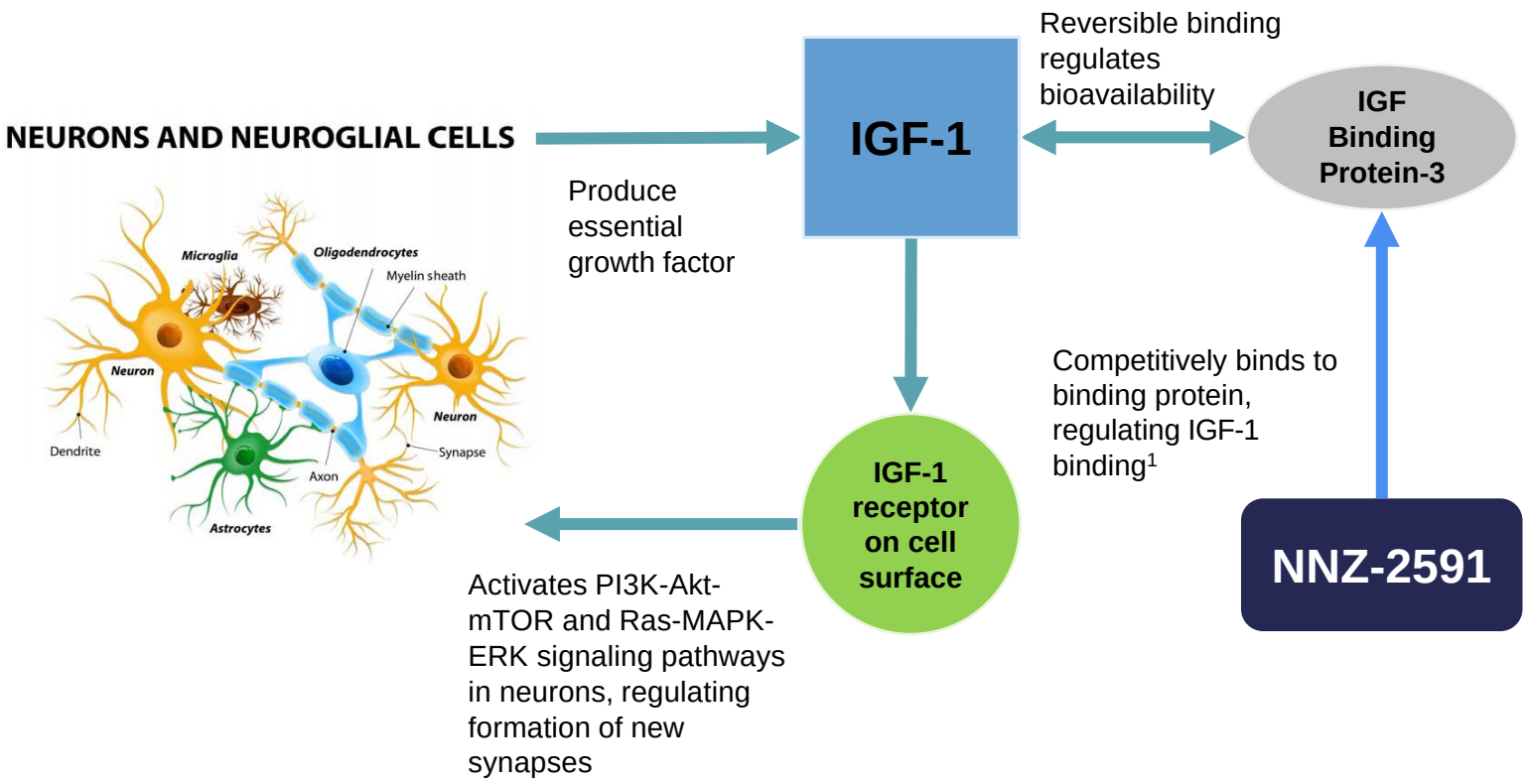
Novel mechanisms of action – NNZ-2591



- **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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