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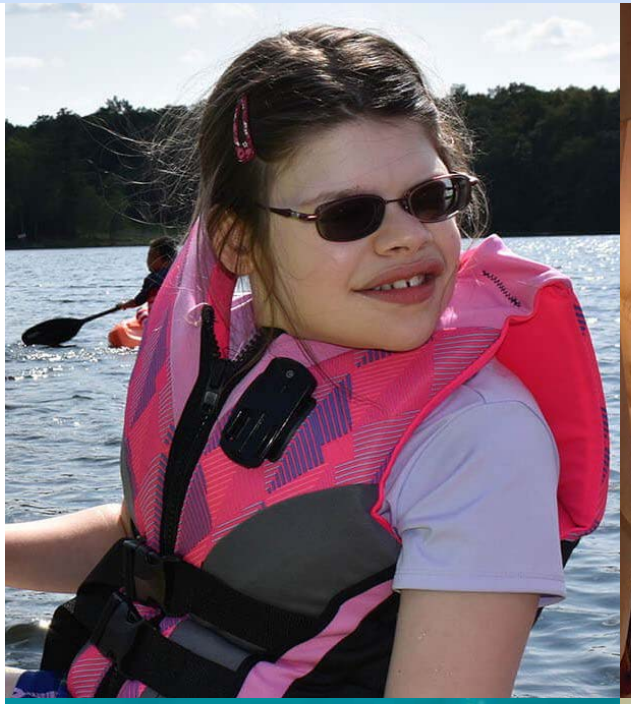
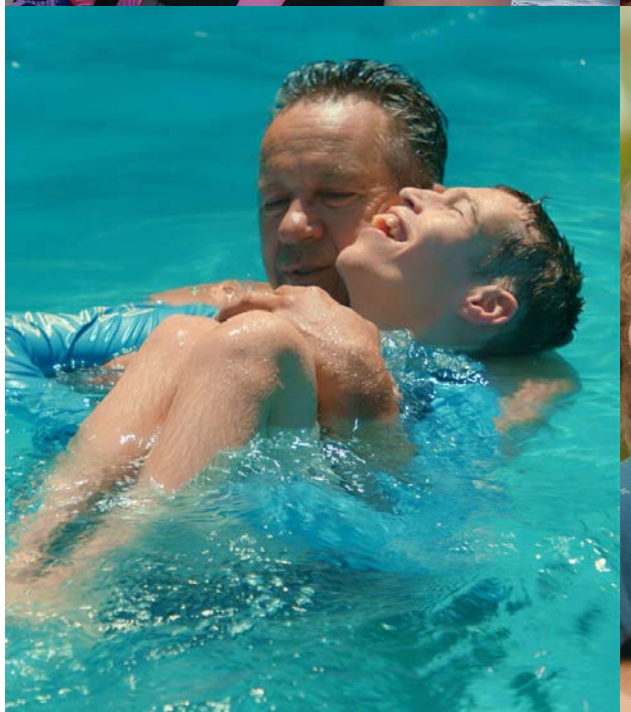
Investor Presentation

28 Aug 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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Global leader 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)

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

Highlights

1. DAYBUE™ (trofinetide) approved by US FDA as the 1st and only treatment for Rett syndrome, launched by partner Acadia in April 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 Q2 2023 net sales of US$23m and Q3 2023 net sales guidance of US$45-55m
4. Accelerating Phase 2 development of NNZ-2591 in 4 indications, with potential markets 5x Rett syndrome
5. NNZ-2591 novel mechanism of action has many more potential applications, with Rett and Fragile X licensed to Acadia
6. A$224m pro forma cash at 30 June 2023[2] – well positioned to maximize the benefits of all value creating opportunities

[1] Including payments already received and future payments

[2] Including US$100 million up-front payment received in July 2023

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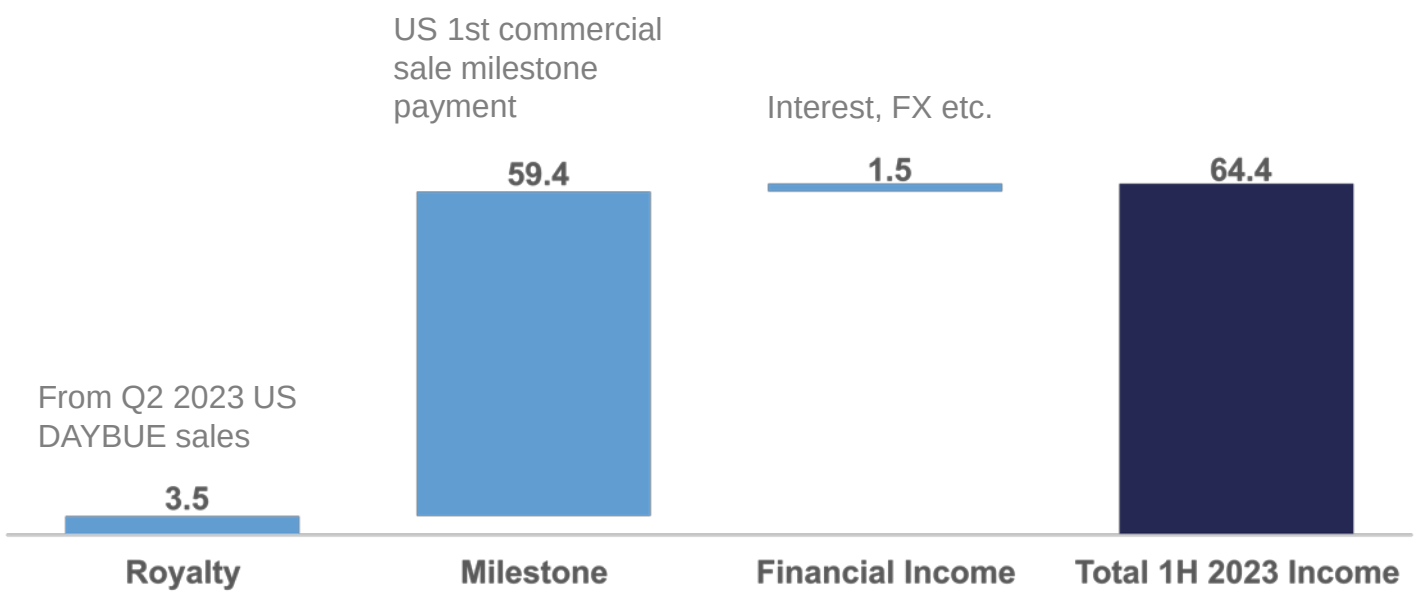
Transformation underway



	Royalty	Milestone	Financial Income	Total 1H 2023 Income
FY 2022	-	14.6	1.8[1]	16.3[1]

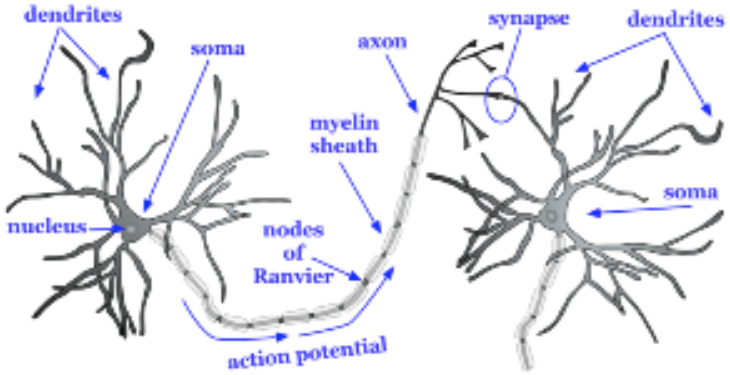
H1 2023 Net Profit After Tax

A$47.8m

[1] Reported income less loss on financial derivative

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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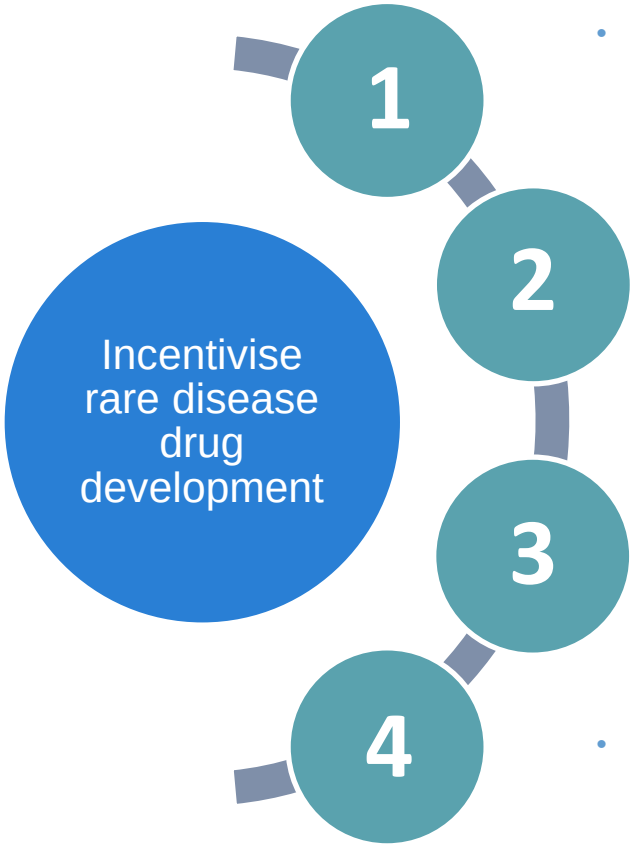
Attractiveness of Orphan Drug model

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) ACADIA
		RoW						
	NNZ-2591	World						
Fragile X	Trofinetide	World						
	NNZ-2591	World						
Phelan-McDermid	NNZ-2591	World						neuren
Pitt Hopkins	NNZ-2591	World						
Angelman	NNZ-2591	World						
Prader-Willi	NNZ-2591	World						

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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Economics to Neuren from trofinetide partnership with Acadia

	US	Europe	Japan	Other	Total
Potential Rett patients	6,000 - 9,000[1]	9,000 - 14,000[1]	2,000 - 3,000[1]	~30,000[2]	
Currently identified Rett patients	4,500[1]	~4,000[2]	~1,000[2]	~2,000[2]	
Average net price per patient p.a.	US$375,000[3]				
Payments already received	**US$60m**	**……US$100m……**			**US$160m**
Future payments before royalties	**US$438m[4]**	**US$215m**	**US$129m**	**US$83m**	**US$865m**
Tiered royalties % of net sales[5]	**10-15%**	**Mid-teen to low 20s %**			

[1] Acadia estimates
[2] Neuren estimates based on prevalence studies and patient organisations
[3] Acadia estimate, includes assumptions for average weight of expected patient population, compliance rates to therapy and mandatory government discounts; the list price will be US$21.10 per mL
[4] Including 1/3 share of Rare Pediatric Disease Priority Review Voucher assuming market value of US$100m
[5] Royalty rates payable on the portion of annual net sales that fall within the applicable range

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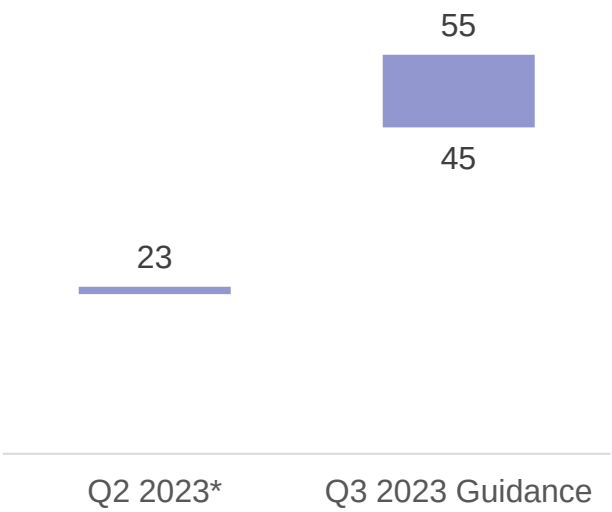
Trofinetide North America

DAYBUE commercial launch in US 17 April 2023

- 1st and **only** treatment for Rett syndrome

Acadia Net Sales (US$m)



** Since launch to 30 Jun 2023*

Economics to Neuren:

Rett Syndrome only

✓	**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)

Aggregate of all indications

Tiered Royalty Rates (% of net sales)[1]

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

[1] Royalty rates payable on the portion of annual net sales that fall within the applicable range

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Successful DAYBUE US launch – update from Acadia Q2 earnings call

Strong and broad based demand

- **400+** prescribers have written subscriptions
- Enrollment forms from **all sectors**
- As of 2 Aug 2023, **7 out of 10** written prescriptions from 2Q had converted to paid
- Patient mix is consistent with the **broad label**

Accelerating payer coverage

- **1/3** of covered lives already covered by formal plans, and coverage is accelerating
- **2/3** through medical exception or letter of medical necessity
- **Payer mix consistent** with expectations (60% Medicaid, 25% commercial plans, remainder Medicare & other)
- **Re-authorizations consistent** with expectation and other rare disease products

Positive caregivers testimonials

"She is more alert, will move her head back and forth following a conversation between two people, she laughs appropriately during conversations."

"She is more alert and focused and was able to sit and play cards. At a therapy session today, she was able to complete several exercises."

"One of the noticeable changes was more purposeful hand use. She is able to point at and touch her tablet and even use a spoon."

"Mom reported that hand wringing had decreased and that her daughter reached for food at dinner."

"I want to share the consistent and up-to date communication we have received from our FAM and Acadia Connect… We are so grateful for the Acadia team, the communication and engagement."

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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

✓	**US$100m**	**upfront payment**
	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
	US$164m	

Total payments unrelated to sales performance

Sales milestones	Europe: up to **US$170m** Japan: up to **US$110m** RoW: up to **US$83m**	On achievement of escalating annual net sales thresholds
Tiered royalties	**Mid-teens to low-20s**	% of net sales

If Acadia sub-licenses any region within the first 2 years, Neuren is entitled to a share of any upfront and development milestones received by Acadia. Creditable against future payments to Neuren in the sub-licensed region.

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5x larger opportunity for NNZ-2591

Disorder	Gene mutation	Published prevalence estimates	Potential patients		
			US[1]	Europe[1]	Asia[1, 2]
Phelan-McDermid	*SHANK3*	1/8,000 to 1/15,000 males and females	22,000	28,000	81,000
Angelman	*UBE3A*	1/12,000 to 1/24,000 males and females	14,000	18,000	52,000
Pitt Hopkins	*TCF4*	1/34,000 to 1/41,000 males and females	7,000	9,000	25,000
Prader-Willi	*15q11-q13*	1/10,000 to 1/30,000 males and females	13,000	16,000	47,000
			56,000	**71,000**	**205,000**

- 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

[1] Estimates derived by applying the mid-point of the prevalence estimate range to the populations under 60 years
[2] Asia comprises Japan, Korea, Taiwan, Israel and urban populations of China and Russia
[3] Based on number of potential patients globally

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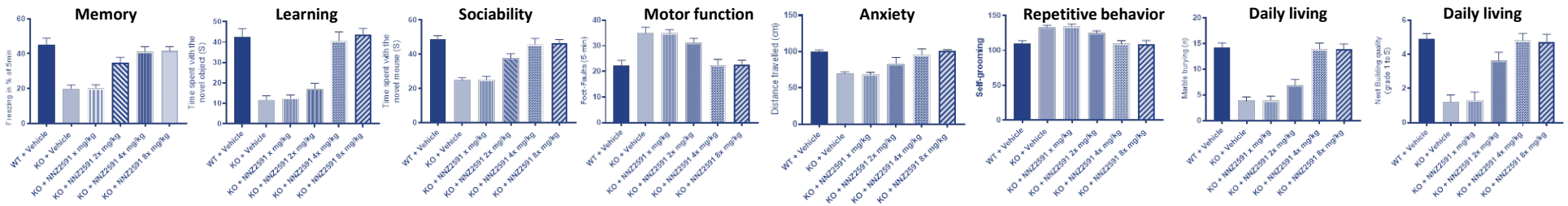
Clear and consistent efficacy in animal models

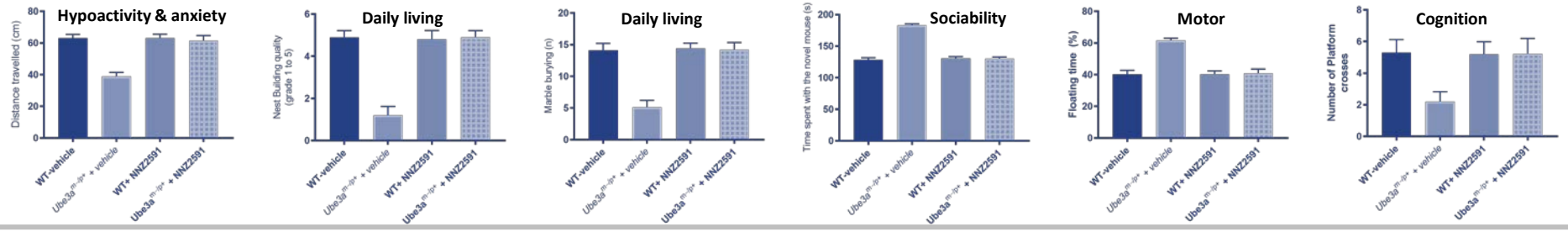
Phelan-McDermid



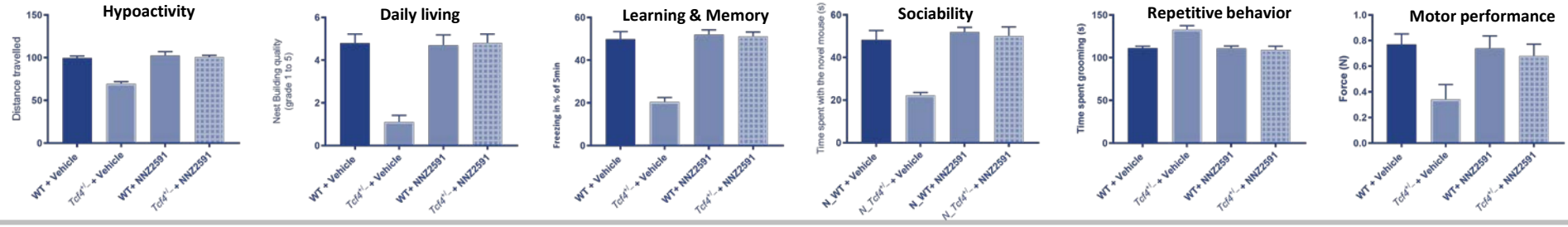
Incidence of seizures

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%

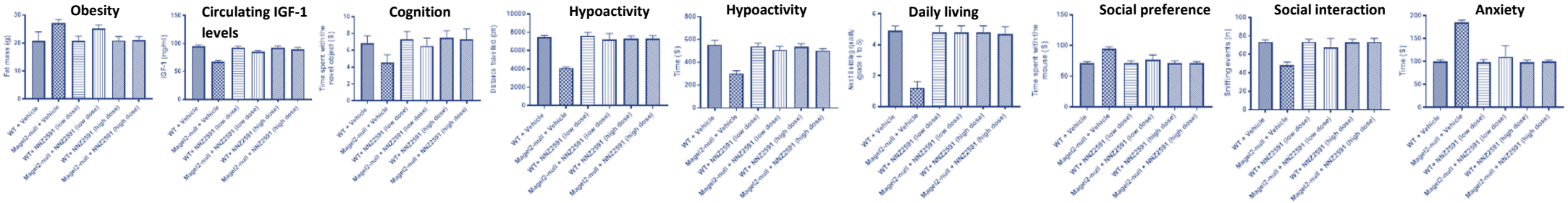
Angelman



Pitt Hopkins



Prader-Willi



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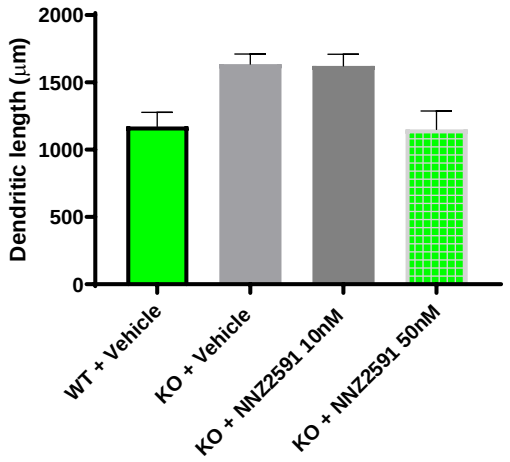
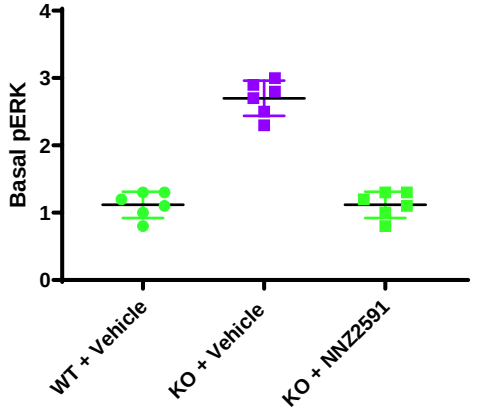
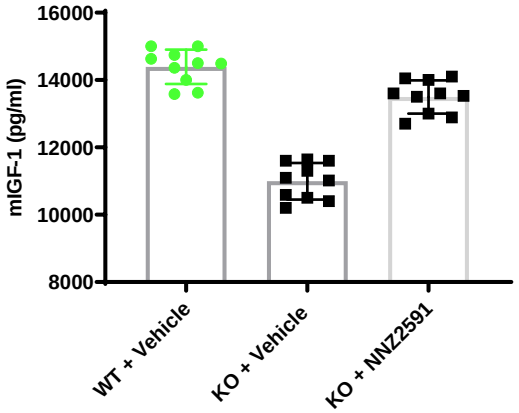
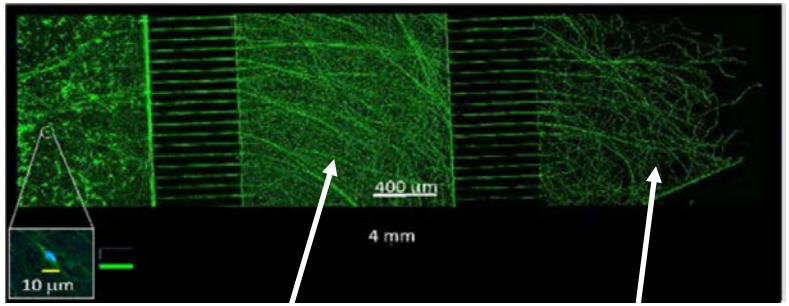
Biochemical effects confirmed

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

Normalisation after treatment with NNZ-2591

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NNZ-2591 has ideal attributes leading into Phase 2

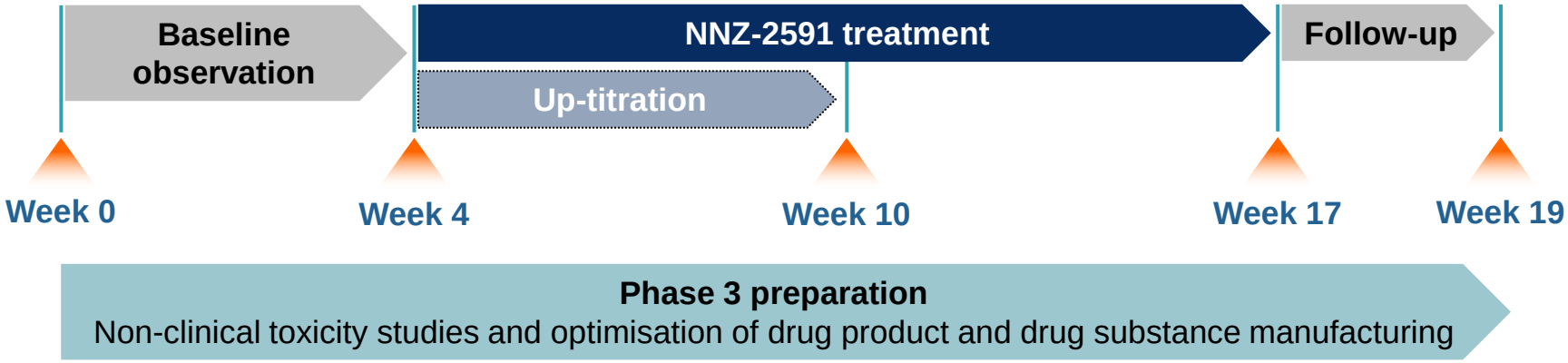
- ✓ Novel mechanism of action
- ✓ Clear and consistent efficacy in mouse models of each syndrome
- ✓ Biochemical effects in the brain confirmed
- ✓ Optimum dose identified
- ✓ Demonstrated high oral bioavailability and blood-brain barrier penetration
- ✓ IND-enabling program of non-clinical toxicology 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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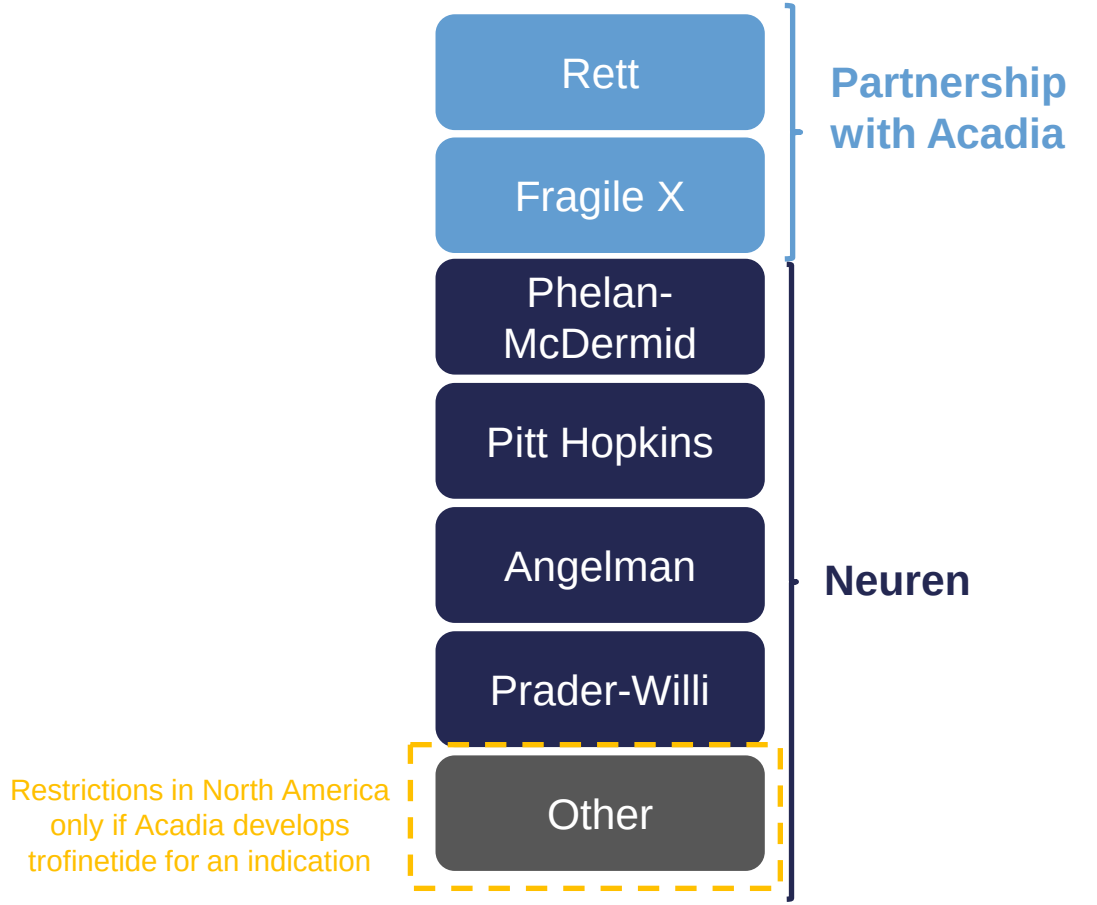
Value of NNZ-2591 further enhanced by Acadia partnership expansion



- Exclusive worldwide licence to Acadia for Rett and Fragile X syndromes only - which couldn't be developed by Neuren independently
- Neuren retains worldwide rights to NNZ-2591 in all other indications
- Potential future payments to Neuren for NNZ-2591 in Rett and Fragile X syndromes identical to the payments for trofinetide inside and outside North America

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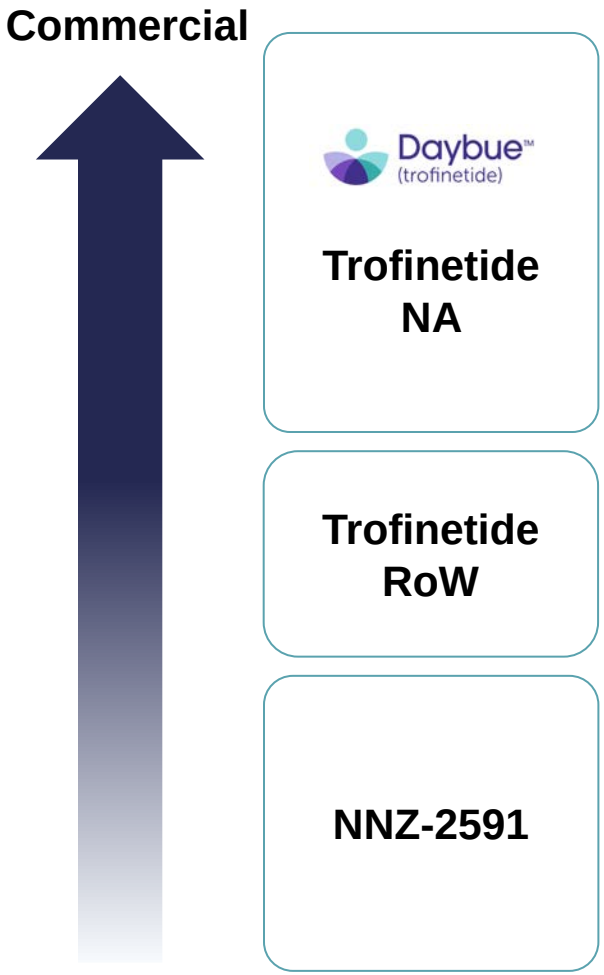
Transforming catalysts in 2023



Trofinetide NA

- ✓ DAYBUE for Rett syndrome approved by FDA
- ✓ Priority Review Voucher awarded to Acadia
- ✓ First US commercial sale - US$40m milestone payment
- ✓ First royalty on net sales
- Ongoing quarterly royalties
- Priority Review Voucher value one third share – estimated as US$33m

Trofinetide RoW

- ✓ Global trofinetide partnership with Acadia
- ✓ Receive US$100m upfront payment from Acadia

NNZ-2591

- ✓ Initiate Prader-Willi syndrome Phase 2 trial
- ✓ Complete enrolment in Phelan-McDermid syndrome Phase 2 trials
- Complete enrolment in Pitt Hopkins and Angelman syndrome Phase 2 trials
- Top-line results for Phelan-McDermid syndrome in Dec 2023

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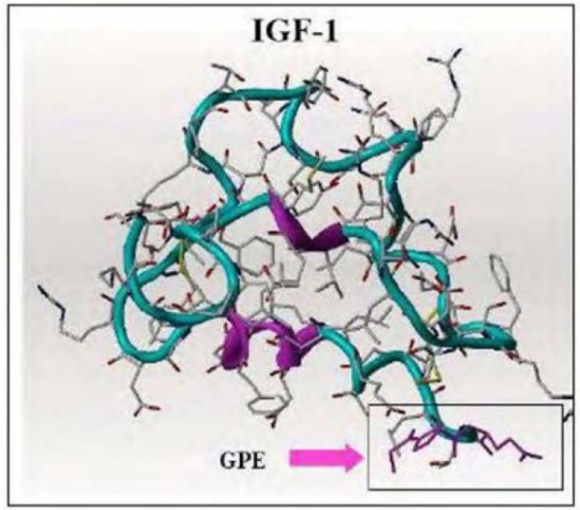
Novel mechanisms of action - trofinetide

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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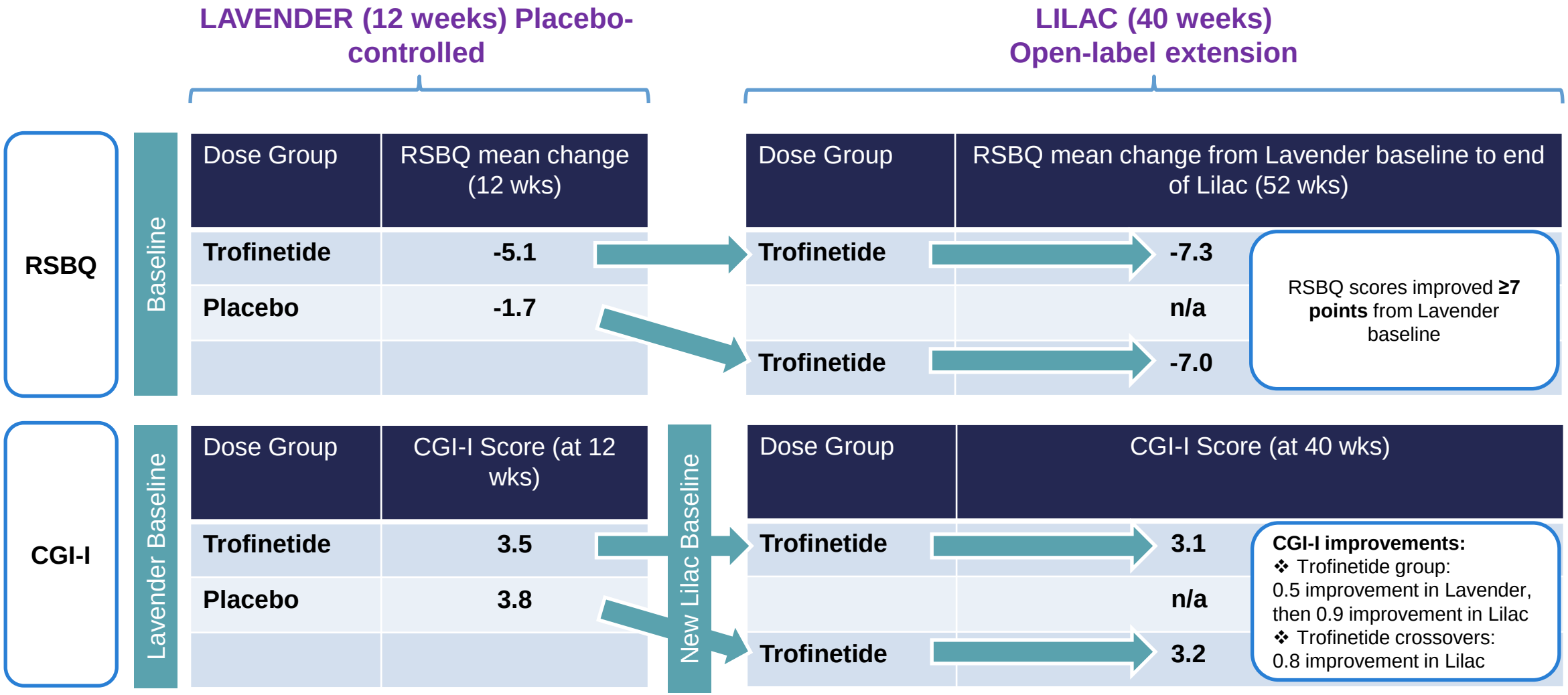
Sustained and continued improvement observed in trials



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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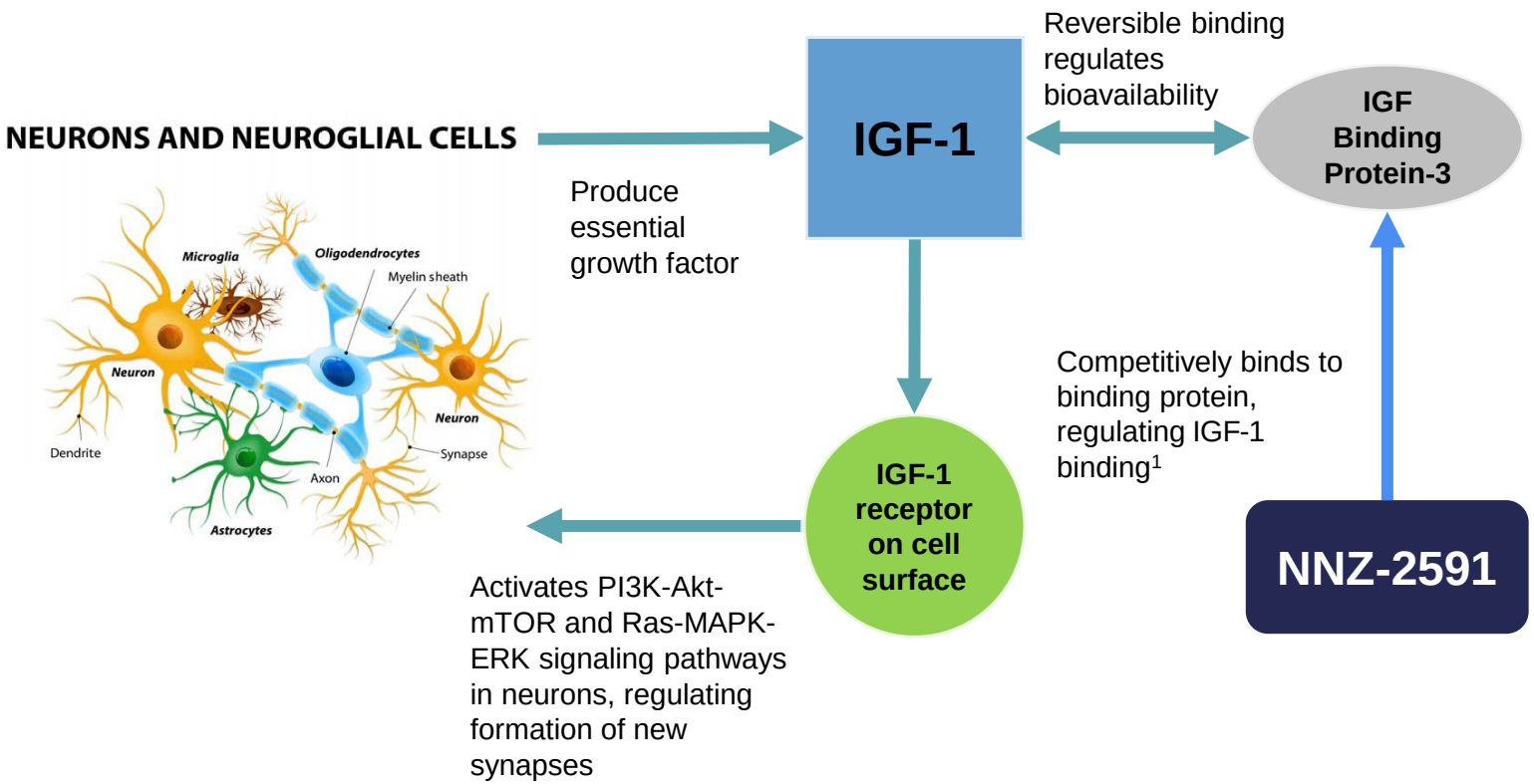
Novel mechanisms of action – NNZ-2591



- **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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