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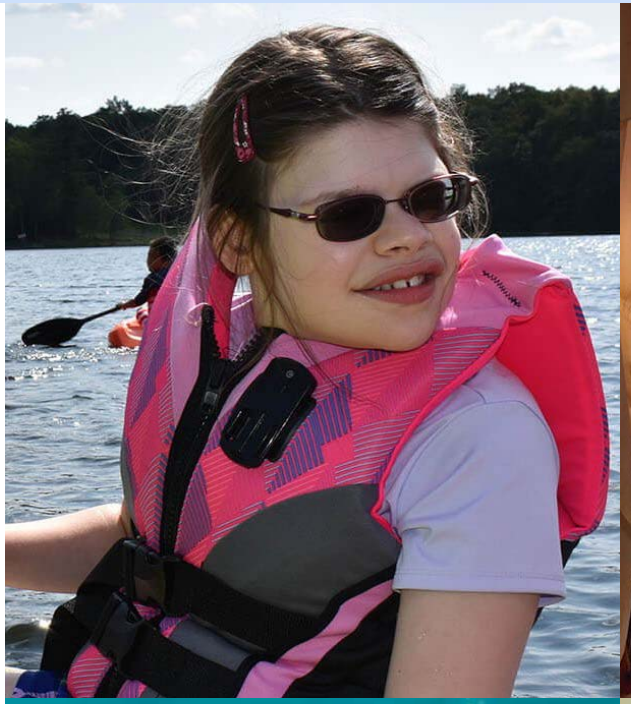
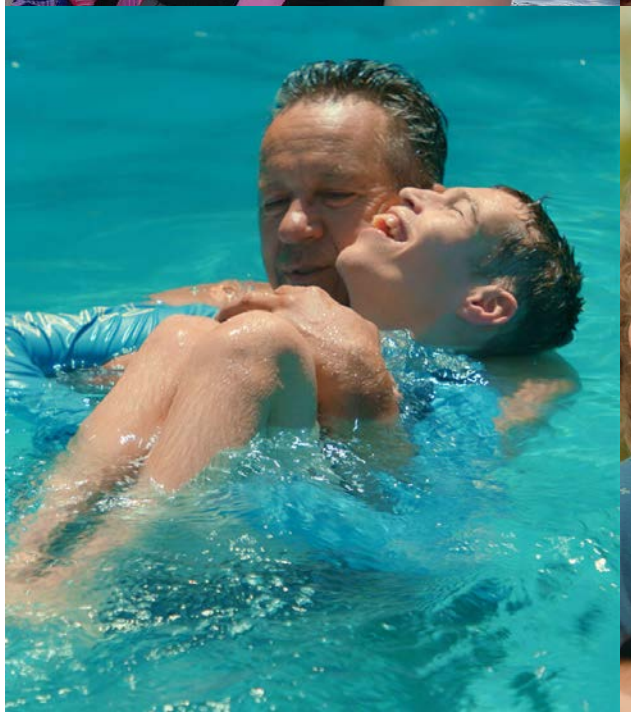
Bioshares

25 July 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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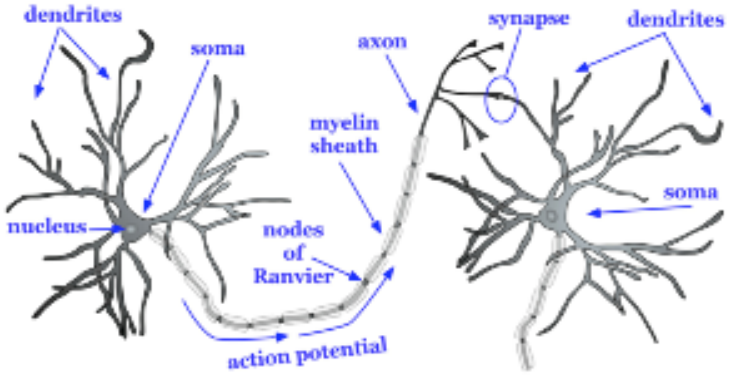
Seeking a ground-breaking impact on neurodevelopmental disorders

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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Highlights

1. DAYBUE™ (trofinetide) approved by US FDA as the 1st and only treatment for Rett syndrome, launched by Acadia on 17 April 2023

2. Neuren's potential revenue for Rett syndrome in the US alone of US$33m[1] plus up to US$350m sales milestones plus 10-15% royalties

3. Partnership with Acadia for trofinetide expanded from North America to worldwide on 13 July 2023 including US$100m up-front payment

4. Neuren's potential revenue ex-NA for trofinetide up to US$427m milestones (launch plus sales) plus mid-teen to low 20's % royalties

5. Accelerating Phase 2 development of NNZ-2591 in 4 indications, with potential markets 5x Rett syndrome

6. NNZ-2591 novel mechanism of action has many more potential applications

[1] Assuming US$33m is received as one third share of the value of a Rare Pediatric Disease Priority Review Voucher

Ex-NA transaction maximizes value of trofinetide and NNZ-2591

1. Expands Acadia's exclusive trofinetide licence to worldwide, for up to additional US$527m to Neuren (including US$100m up-front) plus mid-teens to low-20s % royalties on net sales outside North America

2. 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

3. Unlocks NNZ-2591's potential application in Rett and Fragile X globally, with separate sales milestones and royalties to Neuren identical to trofinetide inside and outside North America

4. Significantly strengthens Neuren's position to explore all strategic options, with cash at 30 June 2023 plus the up-front payment[1] A$226 million

[1] Assuming AUD/USD exchange rate of 0.68 and US withholding tax of 5% for the up-front payment

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Economics to Neuren for trofinetide

	US	Europe	Japan	Other	Total
Potential Rett patients[1]	6,000 - 9,000	~13,000	~3,000	~30,000	
Currently identified Rett patients	4,500	~4,000	~1,000	~2,000	
Average net price per patient p.a.[2]	US$375,000	n.a.	n.a.	n.a.	
Payments already received	US$60m				**US$60m**
1/3 PRV	US$33m[3]				**US$33m**
Upfront	*paid*	……US$100m……			**US$100m**
Dev and launch milestones - Rett	*paid*	US$35m	US$15m	-	**US$50m**
Dev and launch milestones – Fragile X / 2nd indication	US$55m	US$10m	US$4m	-	**US$69m**
Sales milestones	US$350m	US$170m	US$110m	US$83m	**US$713m**
Total payments before royalties					**US$1,025m**
Tiered royalties % of net sales[4]	**10-15%**	**Mid-teen to low 20s %**			

[1] Potential patient estimates derived by applying the mid-point of the published prevalence estimate range to the populations under 60 years
[2] 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
[3] Assuming Rare Pediatric Disease Priority Review Voucher market value of US$100m
[4] Royalty rates payable on the portion of annual net sales that fall within the applicable range

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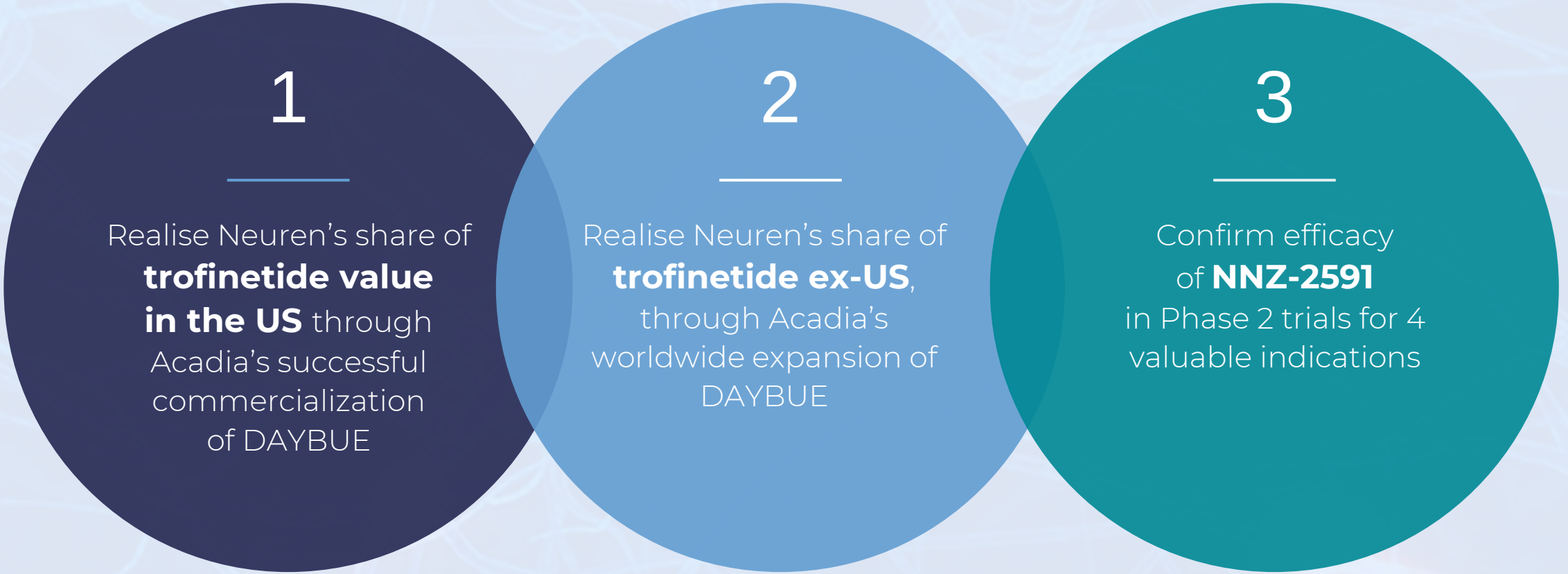
Three key drivers transforming near term value



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The 3-year journey for 10x.....

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The 10-year journey for Rett syndrome.....

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NNZ-2591 - leveraging all the learnings from the Rett syndrome journey

Doing the same things……..

- Build deep relationships with patient communities and key physicians
- Test a range of efficacy endpoints to identify the best primary endpoint(s) for registration trial
- Collaborative approach to regulators
- Flexible thinking as data emerges

Doing things better…….

- Test children in first trial in patients
- Treat for longer period in first trial
- Build better package of non-clinical studies before first trials
- Prioritise keeping CMC development ahead of the plan
- Avoid early false-negative result
- Involve Europe earlier in the program
- Progress multiple indications in parallel
- Ensure funding enables best approach

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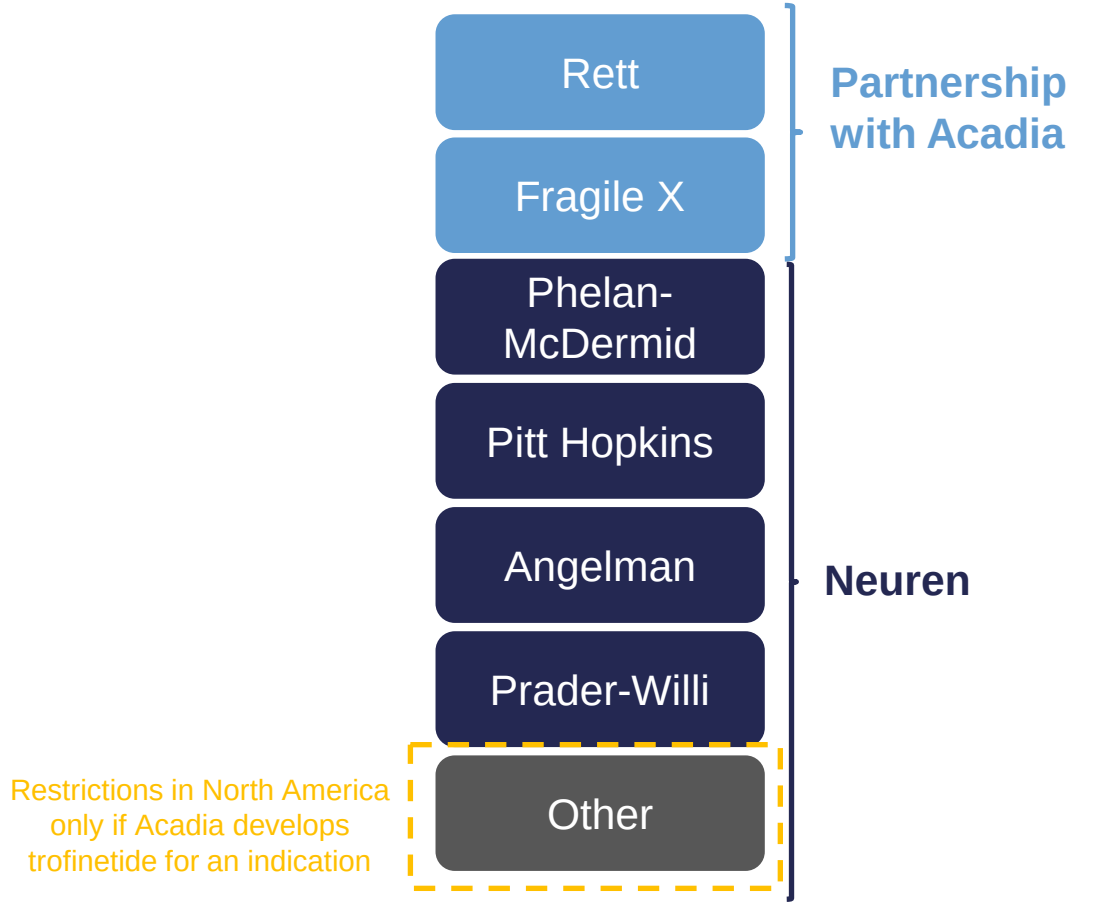
Value of NNZ-2591 further enhanced by Acadia partnership expansion



- Exclusive worldwide licence to Acadia for Rett and Fragile X syndromes only
- 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

- Neuren retains worldwide rights to NNZ-2591 in all other indications
- Ongoing Phase 2 clinical trials in Phelan-McDermid, Pitt Hopkins, Angelman and Prader-Willi syndromes
- First top-line results expected in Dec 2023

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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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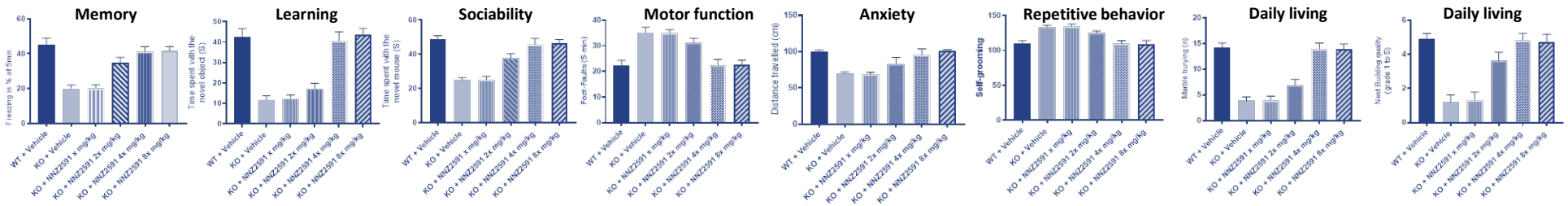
NNZ-2591 has ideal attributes leading into Phase 2

- ✓ 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

Clear and consistent efficacy in animal models

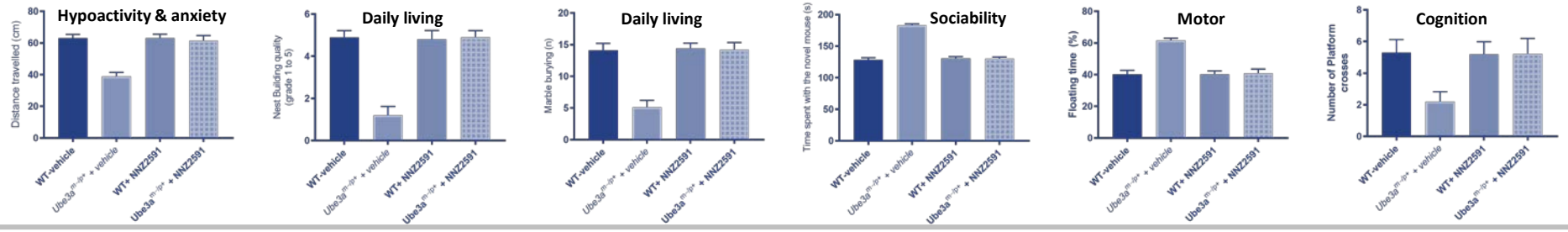
Phelan-McDermid



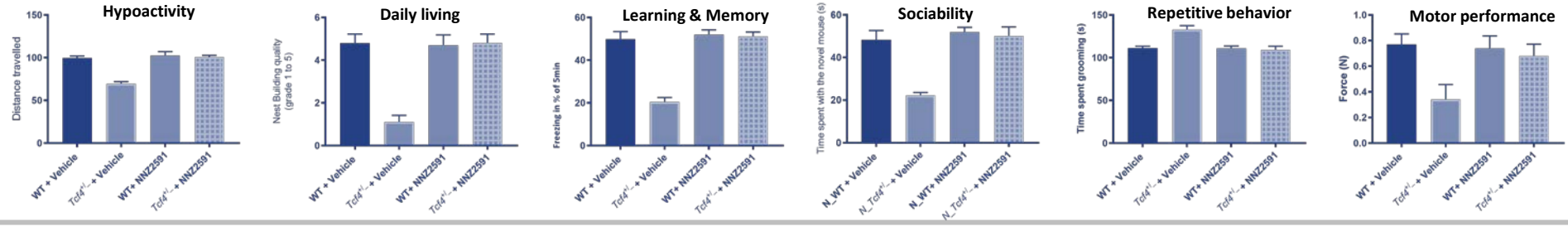
Incidence of seizures

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%

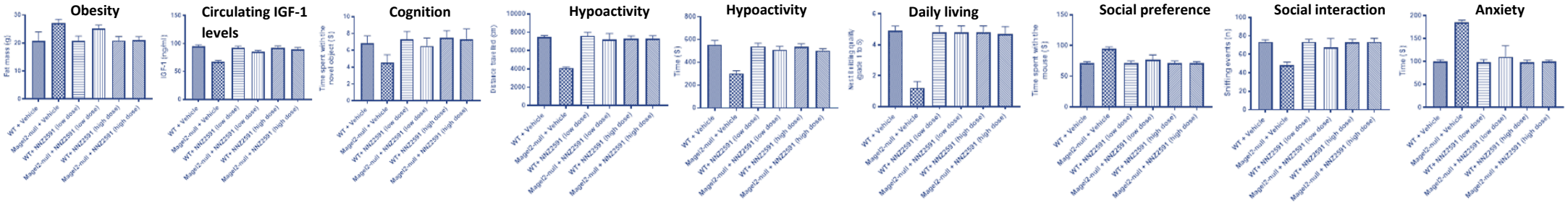
Angelman



Pitt Hopkins



Prader-Willi



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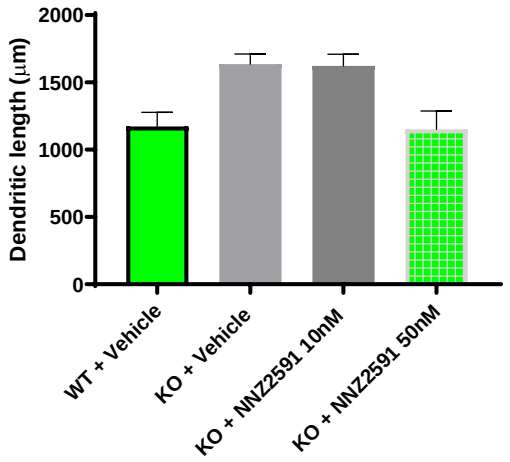
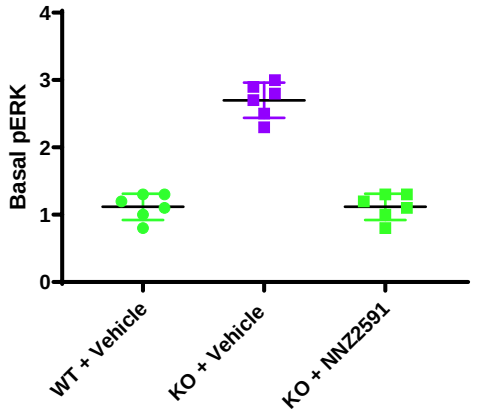
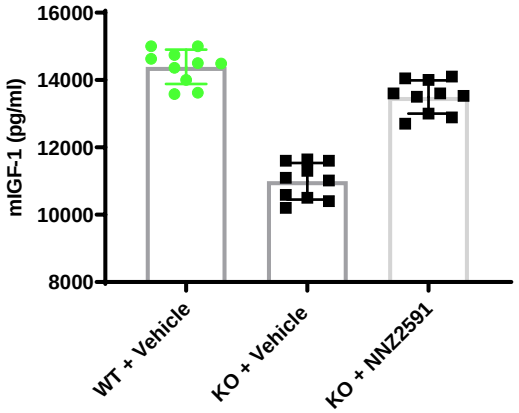
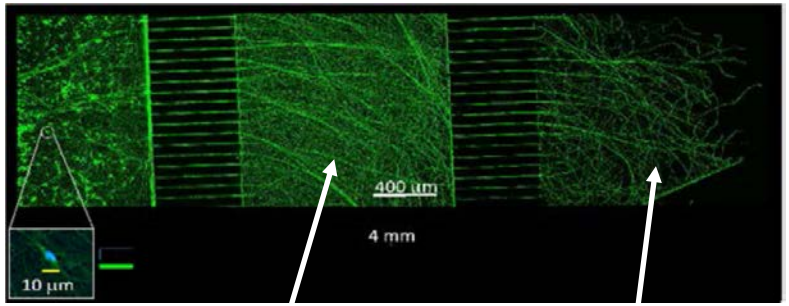
Biochemical effects confirmed

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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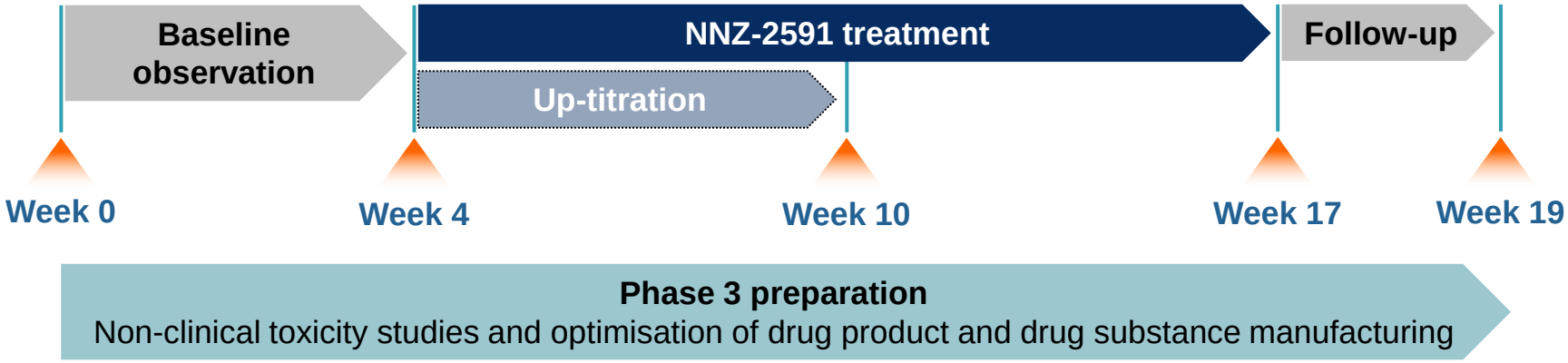
Key features of first Phase 2 trials

Overall aim – expedite data that enables subsequent trials to be designed as 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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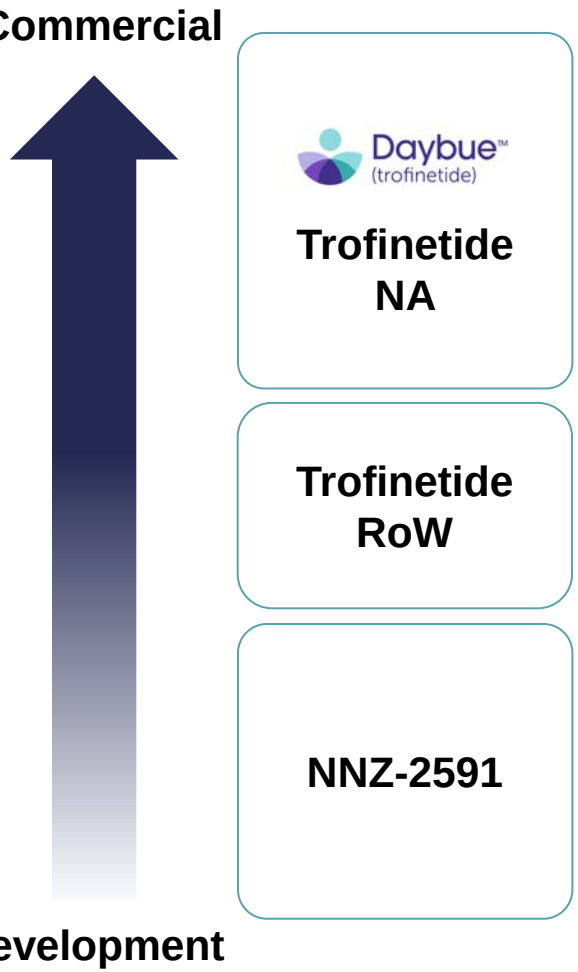
Transforming catalysts in 2023



Trofinetide NA

- ✓ DAYBUE for Rett syndrome approved by FDA
- ✓ Priority Review Voucher awarded to Acadia
- ✓ First US commercial sale - US$40m milestone payment
- Quarterly royalties on net sales
- 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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