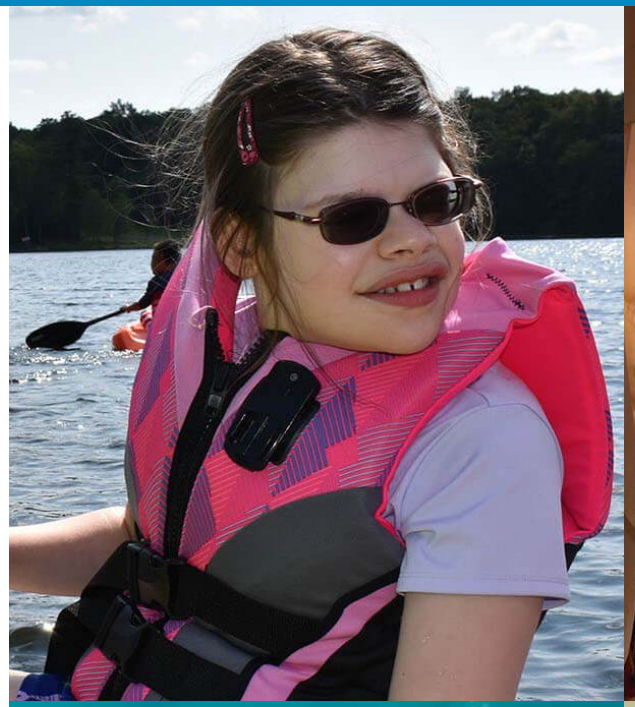
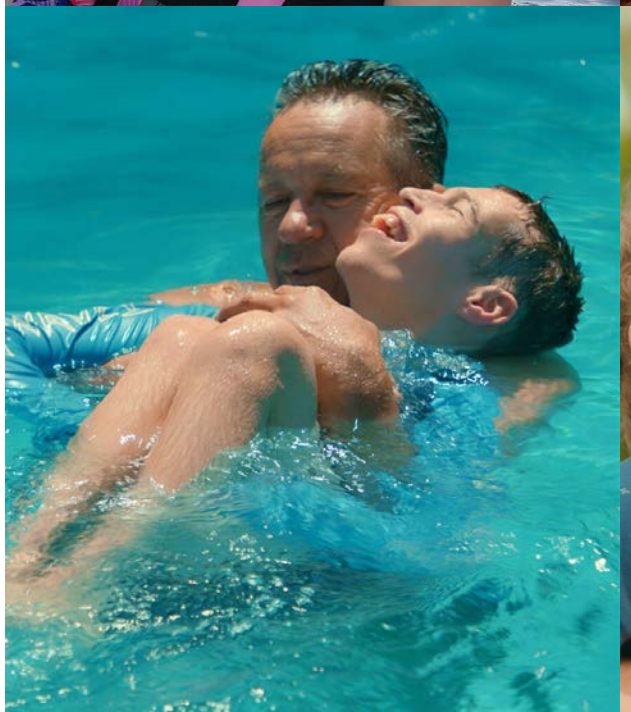
neuren pharmaceuticals

Bioshares

12 July 2024

IMPROVING THE LIVES OF PEOPLE WITH NEURODEVELOPMENTAL DISABILITIES





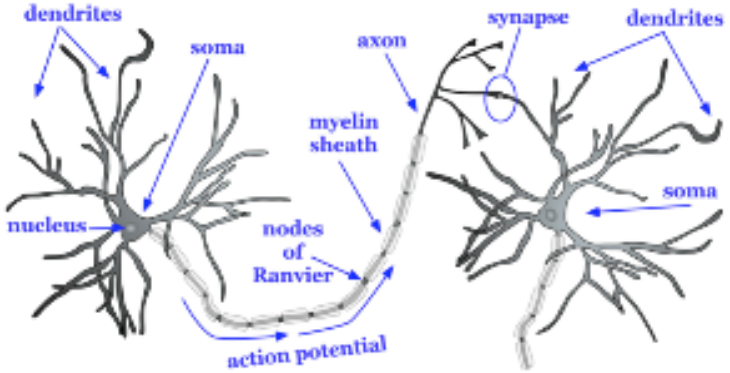

Forward looking statements

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

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

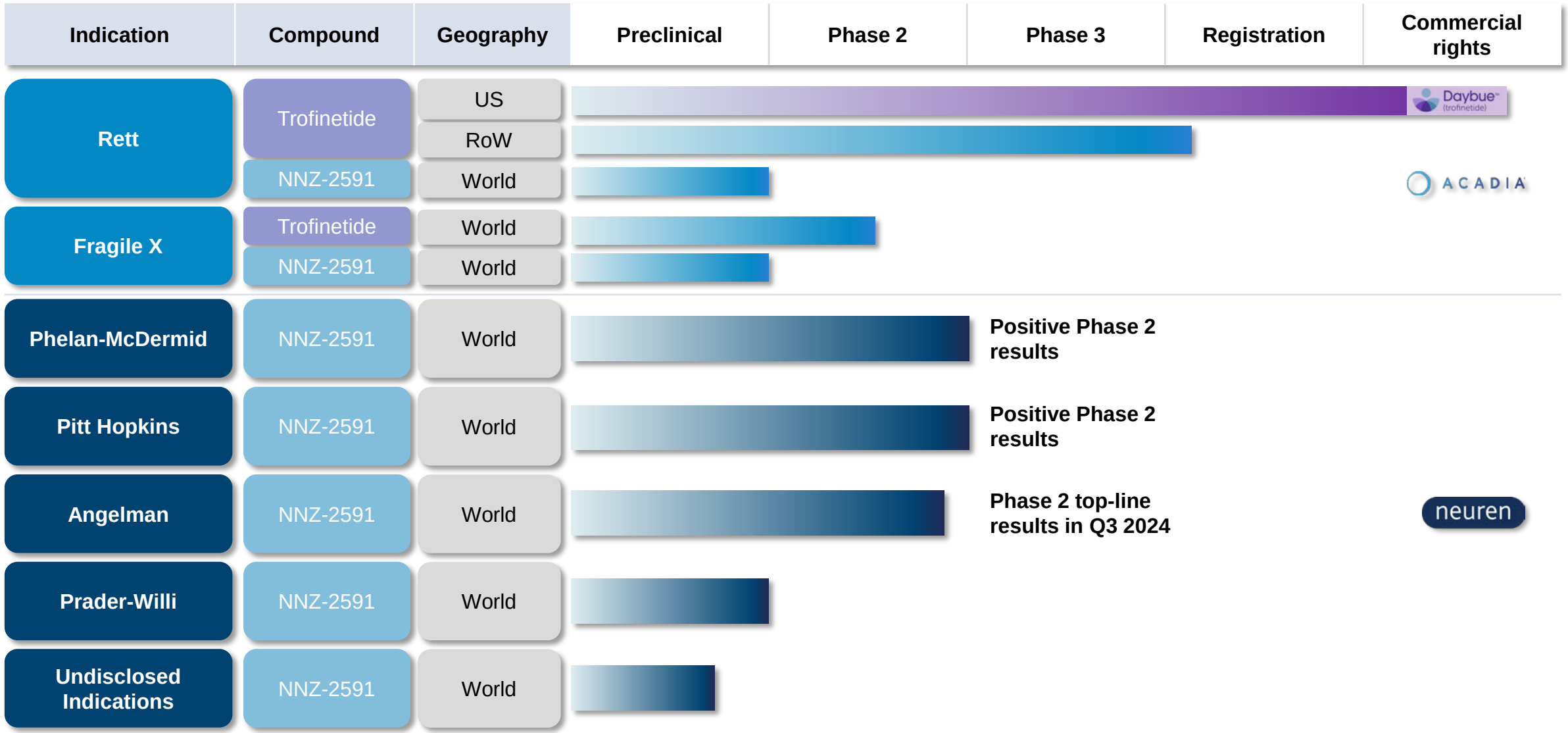
Neuren's drugs

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
Impaired communication	intellectual disability	Impaired social interaction
impaired hand use	sleep disturbance	gastrointestinal problems

neuren pharmaceuticals

Commercial and late-stage pipeline



neuren pharmaceuticals

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 multiple indications, with global rights retained by Neuren

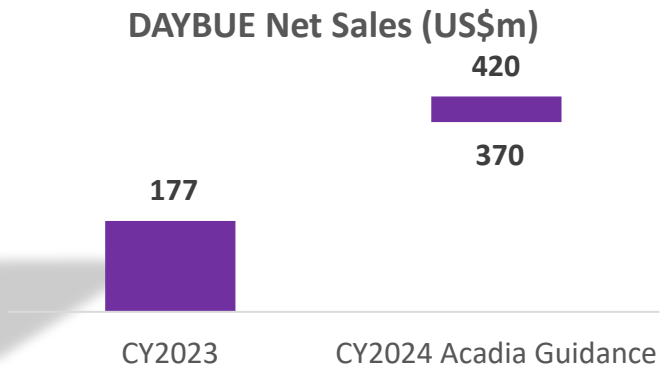
- ✓ Positive top-line results for **Phelan-McDermid syndrome**
- ✓ Positive top-line results for **Pitt Hopkins syndrome**
- Top-line results for **Angelman syndrome** in **Q3 2024**

neuren pharmaceuticals

DAYBUE™ (trofinetide) North America – US launch in April 2023

	US	Canada
Potential Rett patients	6,000 - 9,000[1]	600 - 900[1]
Currently identified Rett patients	5,000[1]	NDS accepted for priority review, potential approval around year-end 2024[3]

As of 3 May 2024: >1,300 patients initiated therapy, 862 active on therapy



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**

[1] Acadia estimates
[2] Royalty rates payable on the portion of annual net sales that fall within the applicable range
[3] Acadia First Quarter 2024 Earnings Call presentation in May 2024

neuren pharmaceuticals

Trofinetide outside North America

	Europe	Japan	Other
Potential Rett patients	9,000 - 14,000[1]	1,000 - 2,000[1]	~30,000[2]
Currently identified Rett patients	~4,000[2]	~800 - 1,000[2]	~2,000[2]

- **Europe:** Pediatric investigation plan (PIP) filed with and accepted by EMA, with a potential Marketing Authorisation Application filing in Q1 2025[3]
- **Japan:** Formal meeting with Japanese regulatory agency (PMDA) scheduled in 2Q24 to discuss clinical plan[3]

Economics to Neuren:

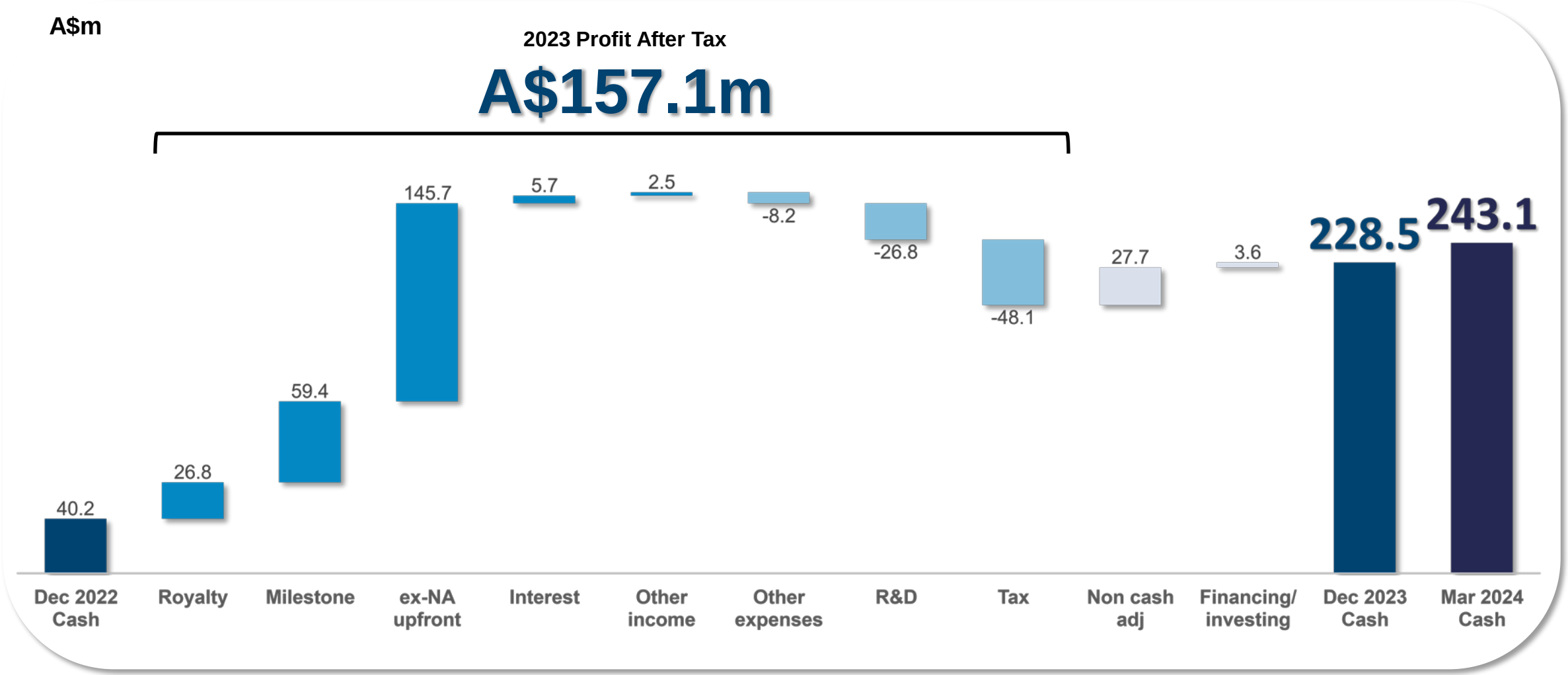
✓	**US$100m**	**upfront**
	US$35m	following 1st commercial sale in Europe
	US$15m	following 1st commercial sale in Japan
	US$10m	following 1st commercial sale of a 2nd indication Europe
	US$4m	following 1st commercial sale of a 2nd indication Japan

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
[3] Acadia First Quarter 2024 Earnings Call presentation in May 2024

neuren pharmaceuticals

Revenues provide financial strength to maximise growth opportunities



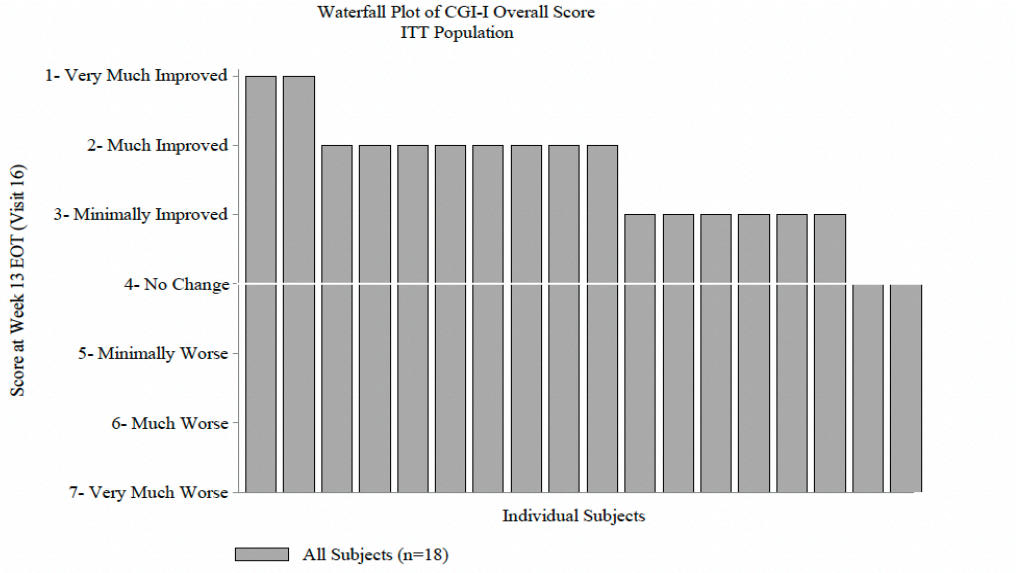
neuren pharmaceuticals

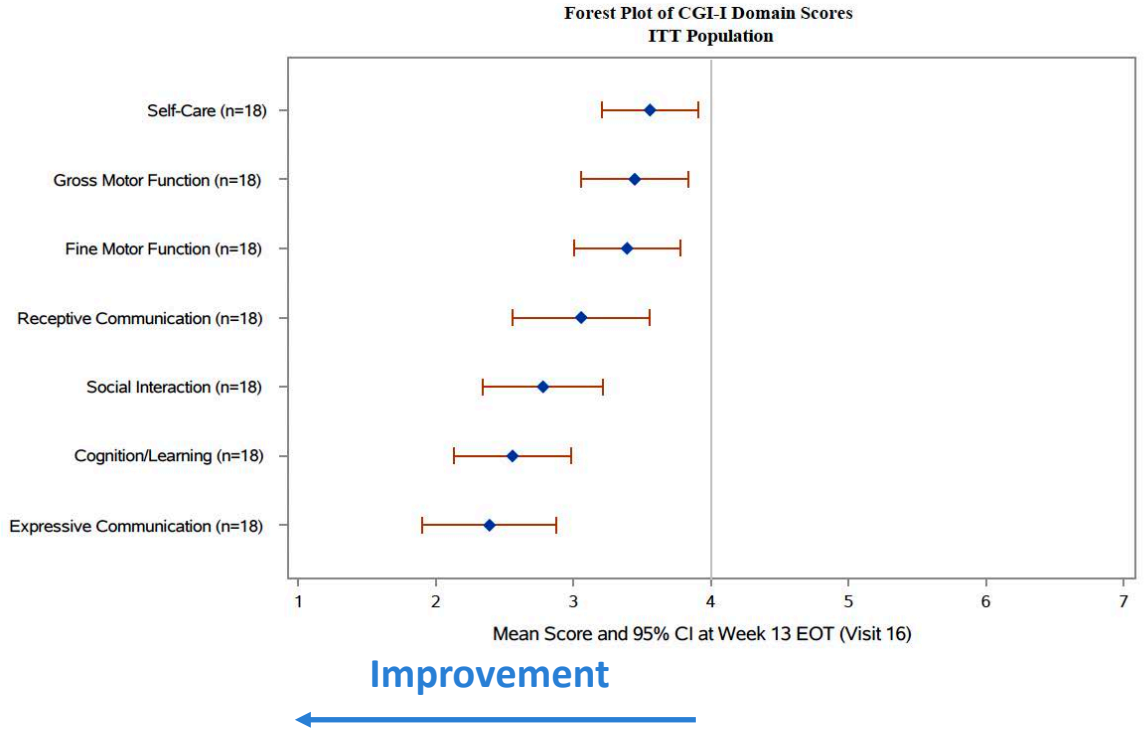
NNZ-2591

neuren pharmaceuticals

PMS CGI-I (clinician) results by subject and by domain

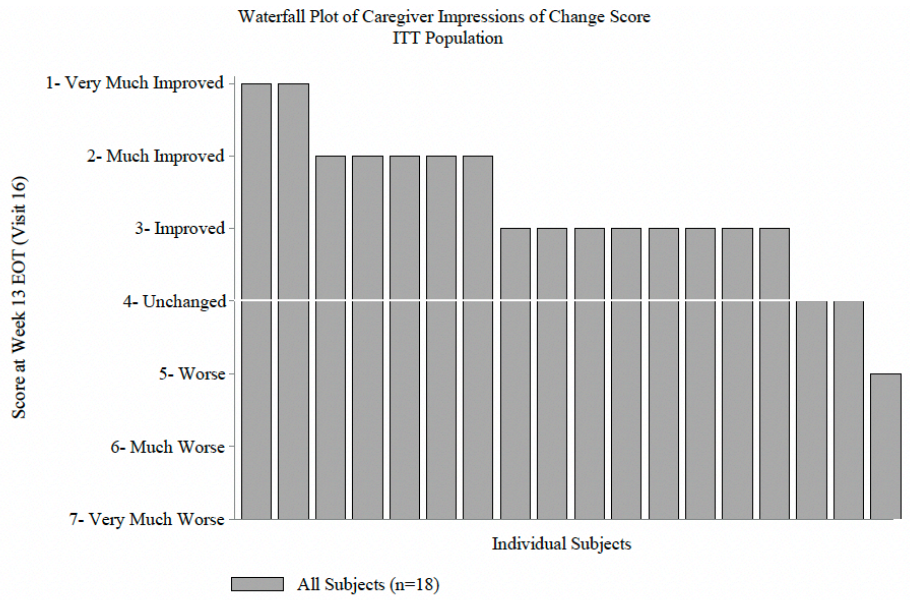
Mean CGI-I score of 2.4 with 16 out of 18 children showing improvement

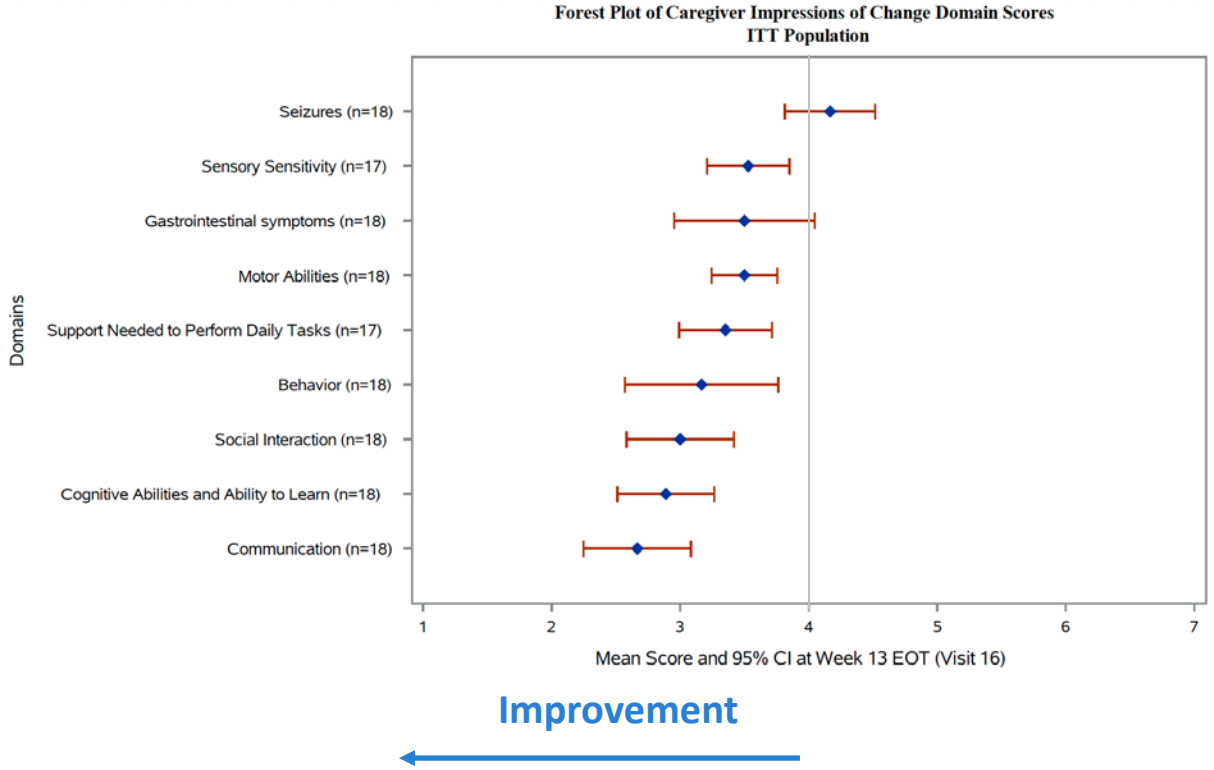




PMS CIC (caregiver) results by subject and by domain

Mean CIC score of 2.7 with 15 out of 18 children showing improvement





Improvement

Clinician and caregiver testimonials

Clinicians

"Marked improvement in expressive language and moderate improvement in socialization."

"Teachers noted improvement in learning new skills."

"Able to focus work at school, both to the things they always enjoy and new tasks."

"Expressive communication- significant improvement in using more complex phrases, better back and forth communication. Better expressing needs. Some commentary on how mom is feeling, "I want you to be happy"."

"Expressive communication- babbling much more than baseline."

"A few 1-2 word phrases that were not at baseline "oh boy", "Hi Mama", "I love you", "oh my"."

"Gross motor- Stronger climbing ladders, comes downstairs which never did before, Walks upstairs without help (needed help at baseline)."

Caregivers

"Using more words while retaining eye contact… Improved pretend play… Initiating eye contact"

"Less scripting, less stimming… More flexible with changes… In general, they are more safe-even at bus stop"

"More focused , engaged, aware of their environment, people."

"So much happier, not throwing self to ground when can't get his way"

"More attentive and it makes for an easy learner, Now can focus better on what we are trying to teach."

"Attention span is great right now… He can focus long enough to complete tasks and try new things."

"Can now run instead of walking fast… Good balance, not needing assistance on stairs."

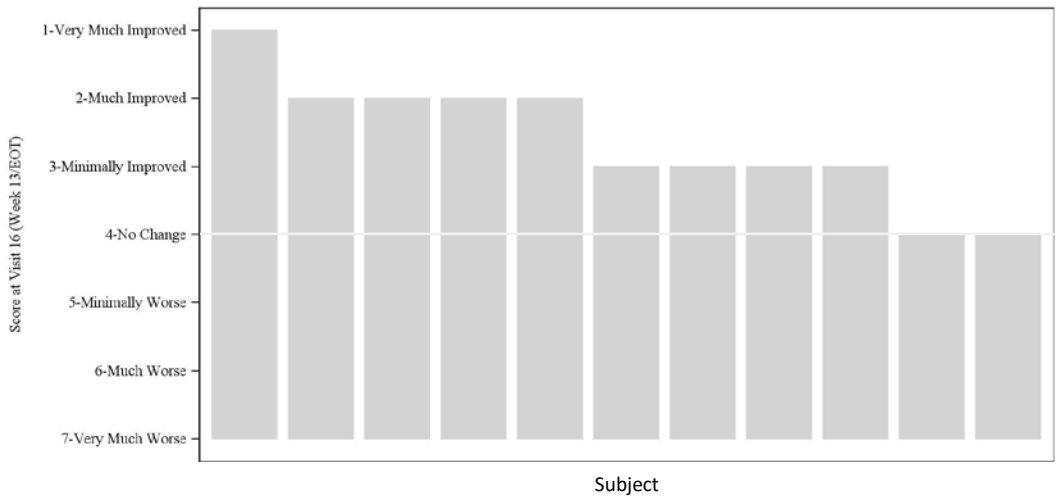
neuren pharmaceuticals

PTHS CGI-I (clinician) results by subject and by domain

Mean CGI-I score of 2.6 with 9 out of 11 children showing improvement

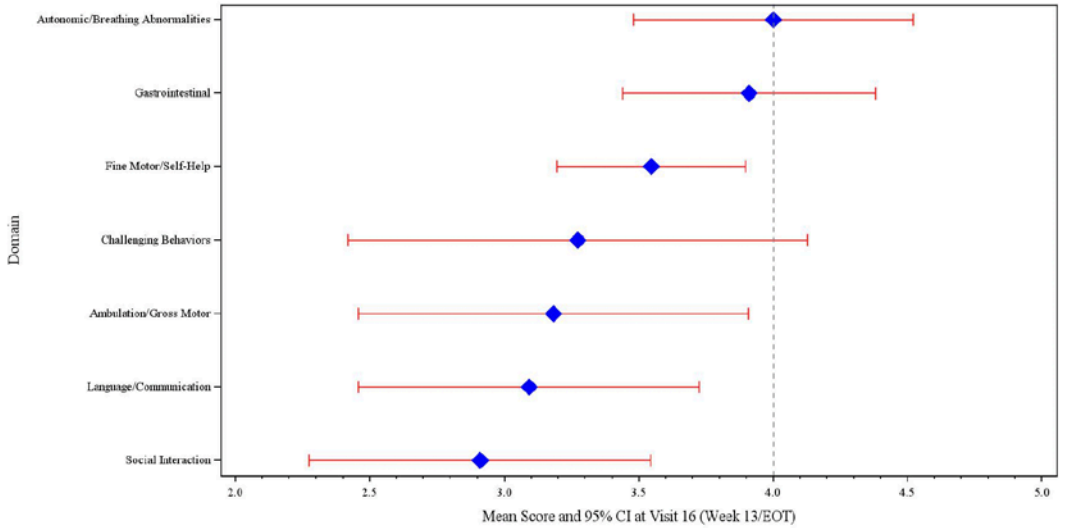
CGI-I Overall Score by subject

MITT Population



Forest Plot of mean CGI-I Domain Scores

MITT Population



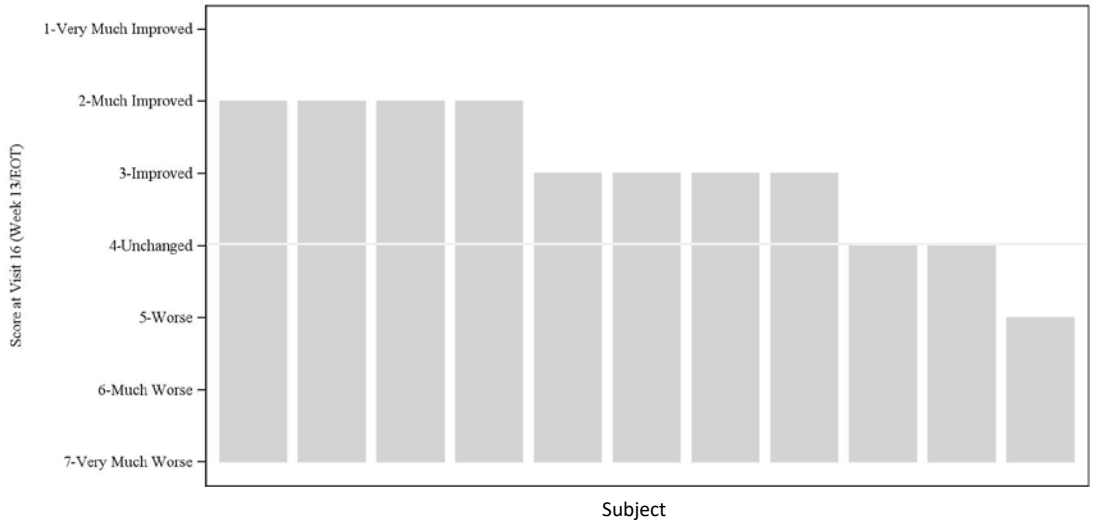
Improvement

PTHS CIC (caregiver) results by subject and by domain

Mean CIC score of 3.0 with 8 out of 11 children showing improvement

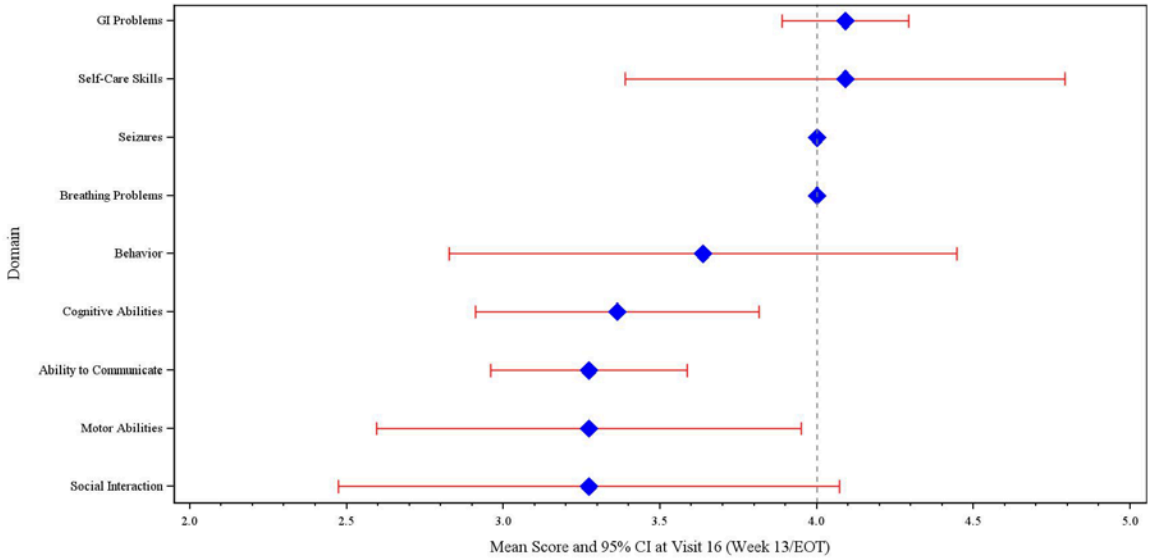
CIC Overall Score by subject

MITT Population



Forest Plot of mean CIC Domain Scores

MITT Population



Improvement

Clinician and caregiver testimonials

Clinicians

"Increased babbling and jargoning….More inflections with eye contact and consonant sounds rather than just noises."

"Decreased frequency and intensity of smacking and hairpulling."

"Supported stepping increased over last few months…Now taking steps without trainer with parent support."

"Improved expressive communication: 2 additional words, uses AAC device to ask for food. Increase vocalization."

"Less breath holding. More opinionated. More social interest."

"Able to match items/pictures…moved from 4 pictures to 6 pictures."

"Improved motor skills. Better motor coordination getting in car."

Caregivers

"Is now able to explore environment… can move towards people to initiate contact and… can seek out whatever … wants to play with."

"Can seem to hold on to things for longer periods without letting go."

"Stability when walking improved."

"Listen to conversation + follow some discussions, able to understand when we're talking about…"

"Far less hyper and easily able to concentrate better… is able to concentrate and master tasks that … has been working on for years (getting in and out of car independently, catching a ball)."

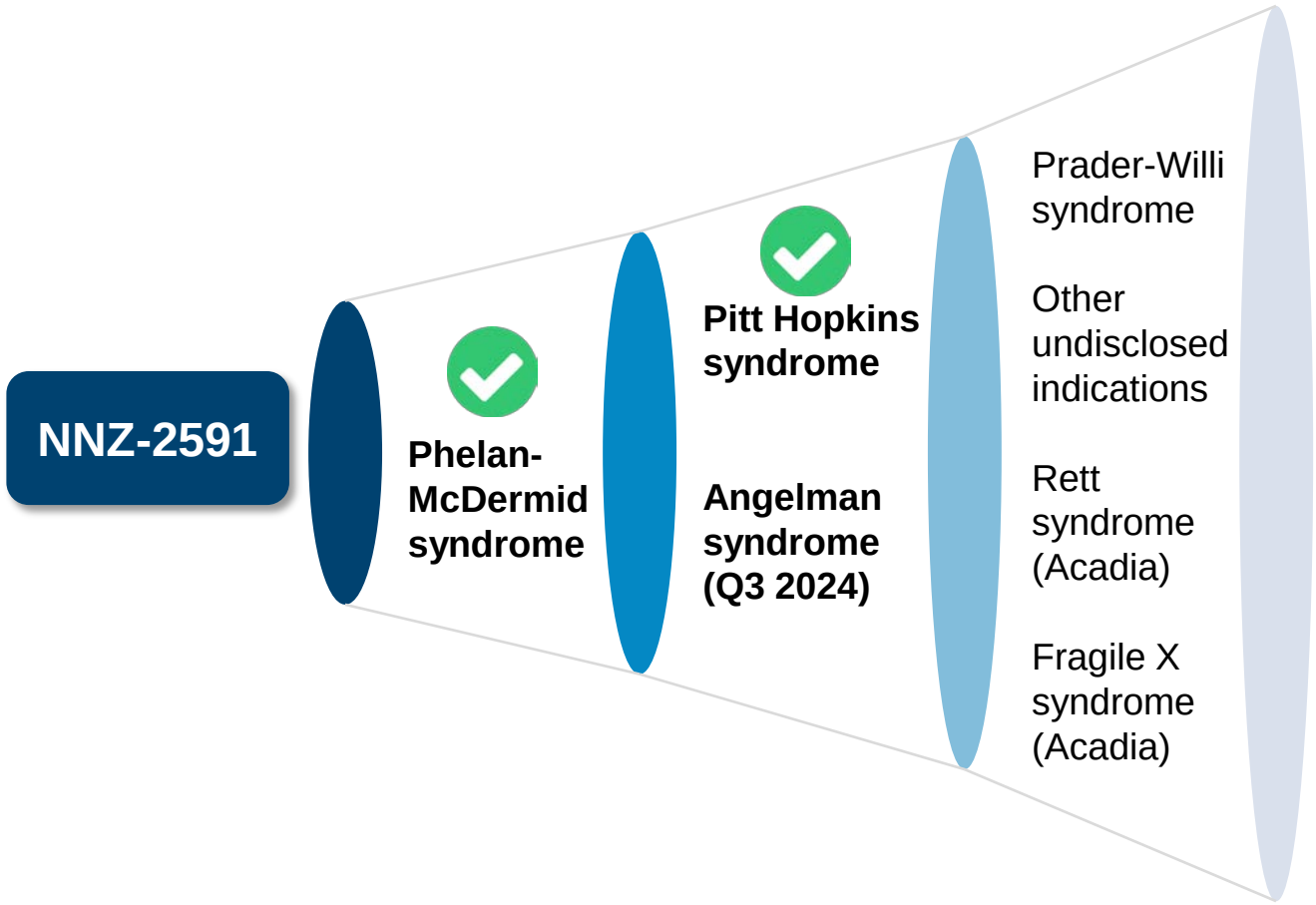
"More intentional movements… been more gentle with almost all interactions."

"Almost constant babbling and even has said "hi" and "more.""

"More calm and attentive, especially looking at faces and eyes."

neuren pharmaceuticals

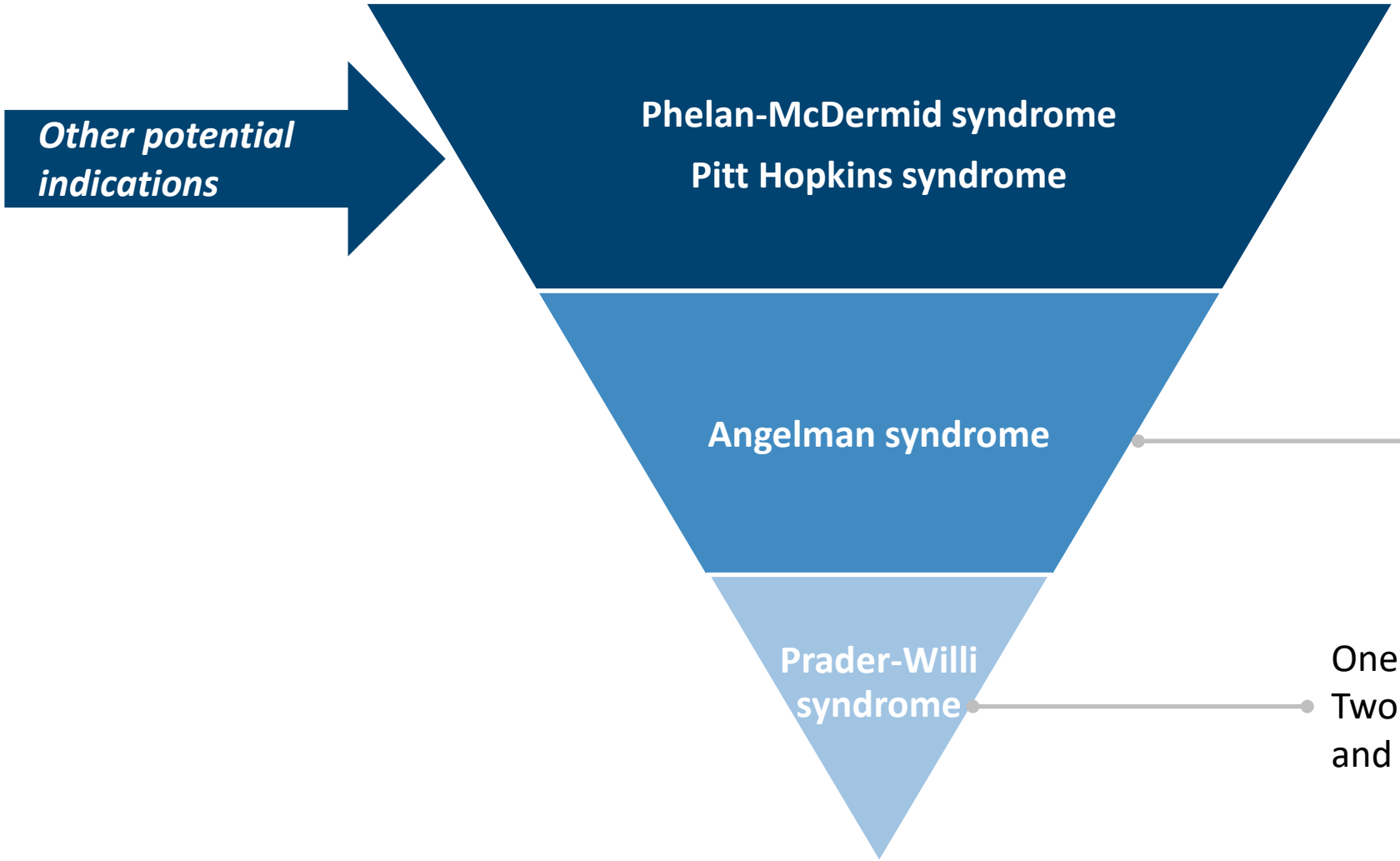
Multiple indications opportunity for NNZ-2591



- **Positive results from Phelan McDermid syndrome and Pitt Hopkins syndrome Phase 2 trials**
- **Top-line results from Angelman syndrome Phase 2 trial expected in Q3 2024**
- **End of Phase 2 meeting with FDA for Phelan McDermid syndrome planned Q3 2024**
- The mechanism of action of NNZ-2591 is relevant for many other neurodevelopmental synaptopathies
- Rett and Fragile X syndromes are licensed to Acadia, with same economics to Neuren as trofinetide; Neuren retains worldwide rights to all other indications

neuren pharmaceuticals

Competitive landscape overview



RNA therapy has goal of initiating Phase 3 by end 2024

One product NDA filed (hyperphagia)
Two products in Phase 3 (hyperphagia and excessive daytime sleepiness)

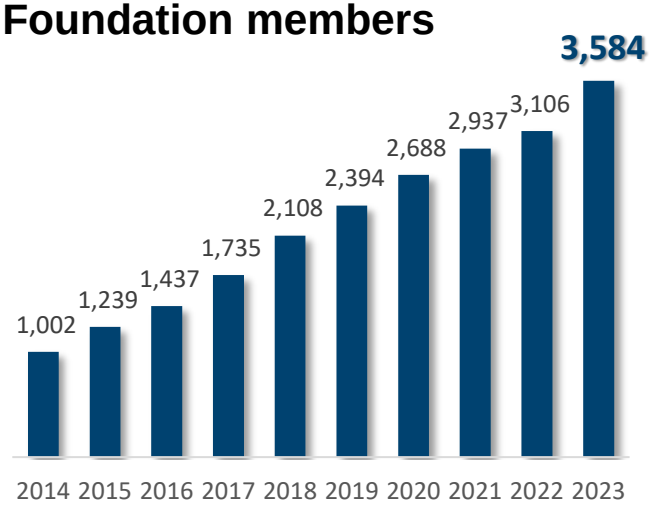
neuren pharmaceuticals

PMS is 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)

neuren pharmaceuticals

Neuren is leading development of a first approved treatment for PMS

Phase 2 Program Status

- Phase 2 clinical development in the US under an IND
- End of Phase 2 Meeting with FDA planned Q3 2024
- Orphan Drug designation in US and EU
- Eligible for Rare Pediatric Disease Designation Priority Review Voucher program

Limited products in development

Company	Product Development Stage
neuren pharmaceuticals	**Positive Phase 2 trial**
#2	Phase 2 trial closed Jan 2021
#3	Phase 1
#4	Phase 1
#5	Pre-clinical

Neuren engaging with all stakeholders

pmsf

cureSHANK

Leading clinicians

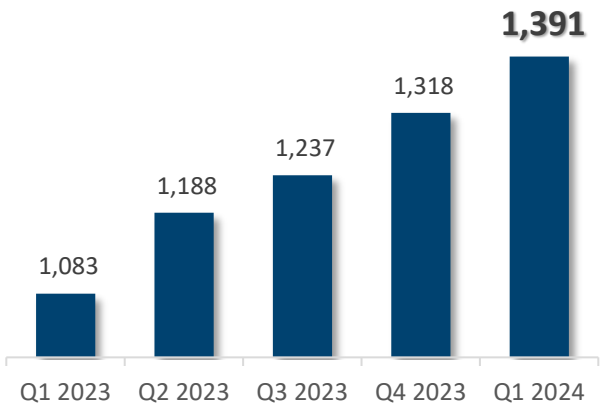
FDA

PTHS is historically under-diagnosed, but this is changing

Estimated prevalence is 1/34,000 to 1/41,000 males and females[1]

	US	Europe	Japan	China	Other[2]
Potential PTHS patients	6,000 – 7,000[3]	8,000 – 9,000[3]	1,000 - 2,000[3]	18,000 – 22,000[3]	6,000 - 7,000[3]

Pitt Hopkins Syndrome Census – initiated Q1 2023[1]



Currently 497 in US & Canada, 329 in EMA & UK, 248 in China, 60 in ANZ

Clinical similarities between PTHS, Rett and Angelman syndromes calling for TCF4 screening in suspected Rett or Angelman patients[4]

Opportunity to accelerate diagnosis

Autism

US ADDM tracks 440k children with autism spectrum disorder

- Rising awareness
- ICD code assigned in 2020
- Enhanced genetic testing technologies
- Expanding ADDM network sites

[1] Pitt Hopkins Research Foundation (PHRF) (pitthopkins.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)
[4] Takano et al, "Two percent of patients suspected of having Angelman syndrome have TCF4 mutations" Clin Genet. 2010 Sep;78(3):282-8; Armani et al, "Transcription factor 4 and myocyte enhancer factor 2C mutations are not common causes of Rett syndrome" Am J Med Genet A. 2012;158A(4):713–9

neuren pharmaceuticals

Neuren is leading development of a first approved treatment for PTHS

Neuren Program Status

- Positive Phase 2 trial
- Clinical development in the US under an IND
- Orphan Drug designation in US and EU
- Eligible for Rare Pediatric Disease Designation Priority Review Voucher program

Limited products in development

Company	Product Development Stage
neuren pharmaceuticals	**Successful Phase 2**
#2	Phase 2 *(research institute sponsored, focusing on GI symptoms)*
#3	Phase 1/2a trial *(not yet recruiting)*
#4	*Preclinical*

Neuren engaging with all stakeholders

PITT HOPKINS RESEARCH FOUNDATION

Leading clinicians

FDA

Rett syndrome program provides some precedent for Phase 3

Overview of Phase 3 conducted for trofinetide in Rett syndrome:

Placebo-controlled efficacy and safety study → **Open-label extension safety study** → **Continued use until approval**

- 12 weeks treatment
- 187 subjects
- 50/50 randomisation
- Co-primary efficacy endpoints
- 90% power
- 21 sites in US
- ~2 years from start to results

- 40 weeks treatment
- Continued efficacy assessment

neuren pharmaceuticals

Partnering food for thought

Neuren/Acadia deal comparisons:

2018
North America only
End of Phase 2

- US$10m up-front
- Up to US$455m milestones
- 10 -15% royalties

2023
Ex-North America only
Approved and launched in US

- US$100m up-front
- Up to US$427m milestones
- Mid-teens to low 20s % royalties

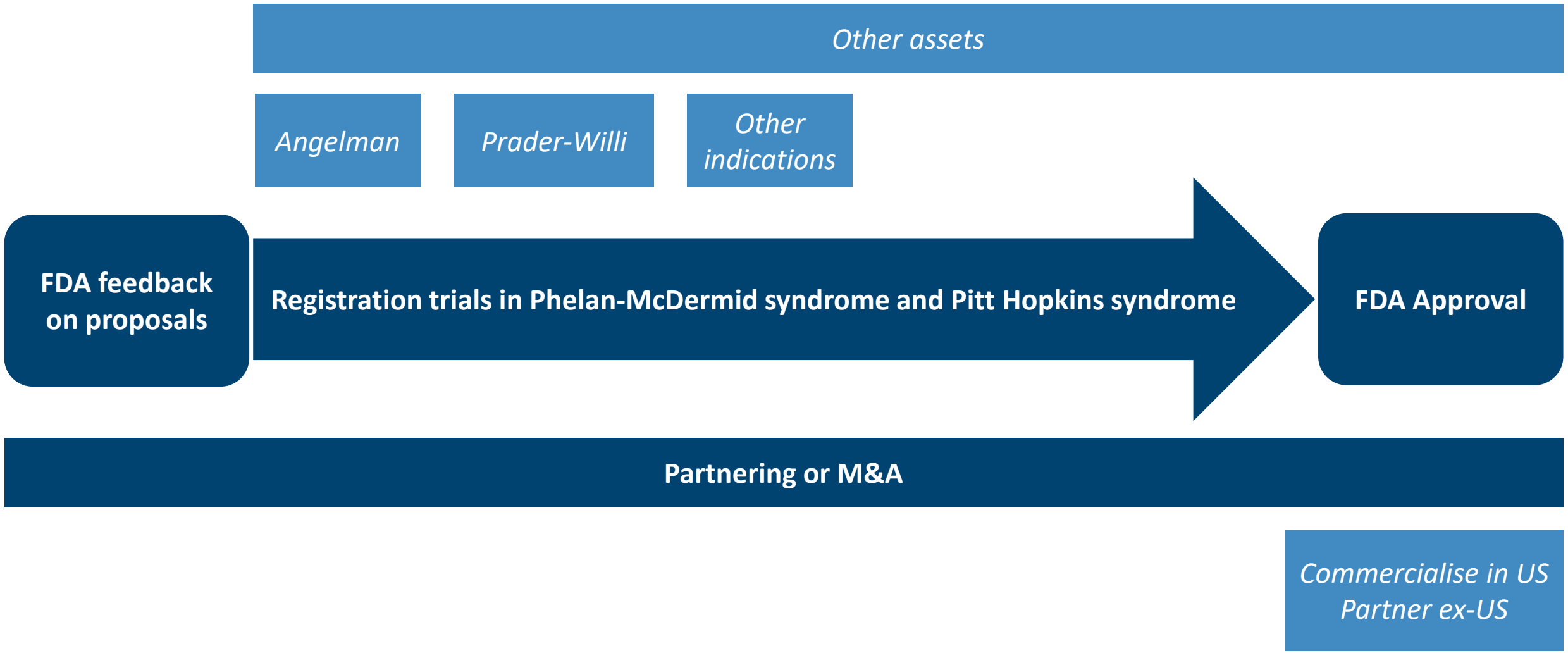
Post-FDA approval acquisition example:

2023
Reata acquired by Biogen for US$7bn+

- One product approved in US and filed in EU for one orphan neurology indication
- Global rights available
- SKYCLARIS™ is the only approved treatment
- Similar patient numbers to Rett
- Similar price to DAYBUE™

neuren pharmaceuticals

Executing “Plan A” and retaining maximum optionality



neuren pharmaceuticals

CONTACT

Jon Pilcher, CEO
jpilcher@neurenpharma.com
+61 438 422 271

neuren pharmaceuticals