



# AusBiotech Invest and Partnering 2018

30 October 2018

# 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 investment proposition

- Two drugs (trofinetide and NNZ-2591) targeting broad impact on debilitating childhood disorders with urgent unmet need
  - Regulatory incentives – *Orphan Drug, Fast Track, Priority Review*
  - Strong support from advocacy groups and leading physicians
  - Protected by Orphan Drug exclusivity periods as well as patents to 2032/4
- Trofinetide Phase 3 program, with US commercial partner secured
  - ACADIA provides capabilities, strategic intent and funding required to bring trofinetide to market in the US
  - Rett syndrome Phase 3 trial commencing 2019, Fragile X syndrome in Phase 2
  - Significant participation for Neuren in future value of trofinetide in North America
  - Neuren retains 100% of value of trofinetide outside North America
- NNZ-2591 promising follow-on compound in pre-clinical development
  - Neuren now able to advance with \$24 million cash at 30 September



neuren

pharmaceuticals

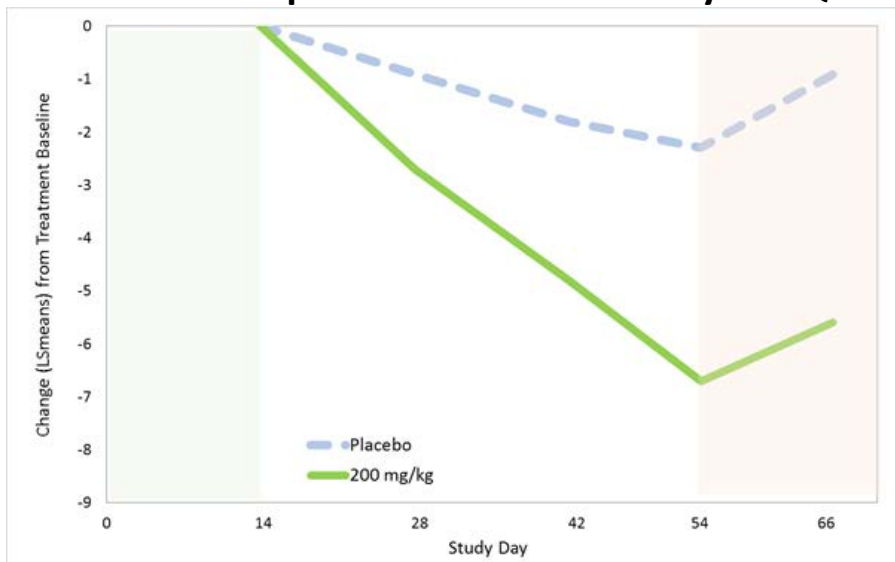
# ACADIA partnership metrics

- ACADIA funds all development costs for trofinetide in North America (including ~US\$55 million for Rett syndrome)
- Neuren retains all rights outside North America, with free use of all data generated by ACADIA in the US for registration outside North America
- Neuren receives escalating tiered double-digit percentage royalties on net sales of trofinetide
  - ACADIA's stated peak annual sales potential >US\$500m in Rett syndrome alone
- Neuren receives milestone payments of up to US\$465 million
  - US\$10 million already received
  - Up to US\$105 million on achievement of US development milestones for Rett syndrome and Fragile X syndrome
  - Up to US\$350 million on achievement of thresholds of annual net sales of trofinetide
- Neuren receives one third of the value of any Rare Pediatric Disease Priority Review Voucher awarded by the FDA
  - 5 vouchers sold for between US\$110 million and US\$150 million in 2017

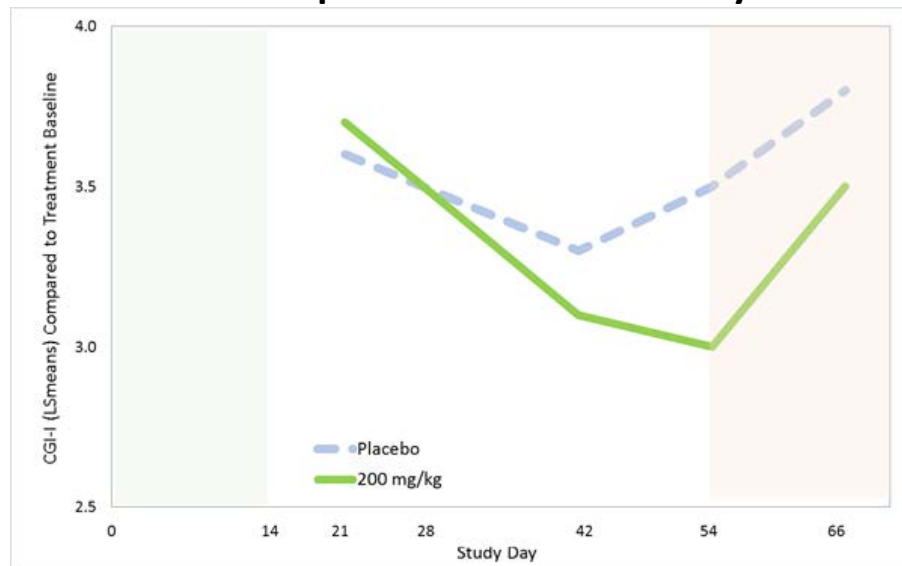


# Rett syndrome Phase 2 highlights

## Clinical improvement measured by RSBQ



## Clinical improvement measured by CGI-I



- ❑ RSBQ is a caregiver rating, reflecting the severity of the syndrome. Mean improvements for trofinetide and placebo were, respectively, 16% and 6%
- ❑ CGI-I is a clinician rating of how much the subject's overall illness has improved or worsened. 22% of subjects on trofinetide received a score of 2 ("much improved") compared with 4% of subjects on placebo
- ❑ Trofinetide was well tolerated with no safety concerns identified
- ❑ Journal publication pending

# Rett syndrome Phase 3 program

- Continuing strong support and participation from leading Rett syndrome physicians and largest advocacy group (rettsyndrome.org)
- Targeting underlying biology causing the disorder rather than treating one symptom
- US Phase 3 program with single trial agreed at End of Phase 2 Meeting with FDA Division of Neurology Products
- ACADIA to commence Phase 3 trial in H2 2019, following completion of manufacturing of all drug substance required for the trial
  - RSBQ and CGI-I as co-primary efficacy endpoints
  - One active group and placebo, ~180 subjects in total
  - Longer treatment than Phase 2 trial
  - Optimised weight-banded dosing



# Neuren's near-term priorities

- Actively support ACADIA in development of trofinetide for North America
  - Assist with preparations for Rett syndrome Phase 3 trial:
    - Manufacture of drug supplies
    - Finalise protocol, sites and logistics
    - Scientific Advisory Board
  - Optimise Fragile X syndrome development plan
- Advance Neuren's strategy to commercialise trofinetide outside North America, including Europe and Japan
  - Engage with regulators to confirm requirements for registration in Rett syndrome
  - Progress partnering discussions
- Accelerate development of NNZ-2591
  - Advance CMC and toxicology studies to enable clinical trials
  - Confirm indication strategy to maximise value worldwide



# Appendix



# About Rett syndrome

- ▣ Seriously debilitating and life-threatening neurological disorder, with no approved medicines
- ▣ Caused by non-inherited mutation on the X chromosome – estimated 1 in 10,000 to 15,000 live female births in all racial and ethnic groups
- ▣ After apparently normal development for the first six months of life, girls experience a period of rapid regression between 6 to 18 months of age
- ▣ Profoundly disabling range of symptoms:
  - Loss of speech and motor control
  - Neurobehavioral, cognitive and intellectual disability
  - Seizures
  - Autonomic dysfunction – breathing, cardiovascular and gastrointestinal abnormalities
- ▣ Most require life-long medical care and 24 hour supportive care - profound financial and emotional impact on families



# About Fragile X syndrome

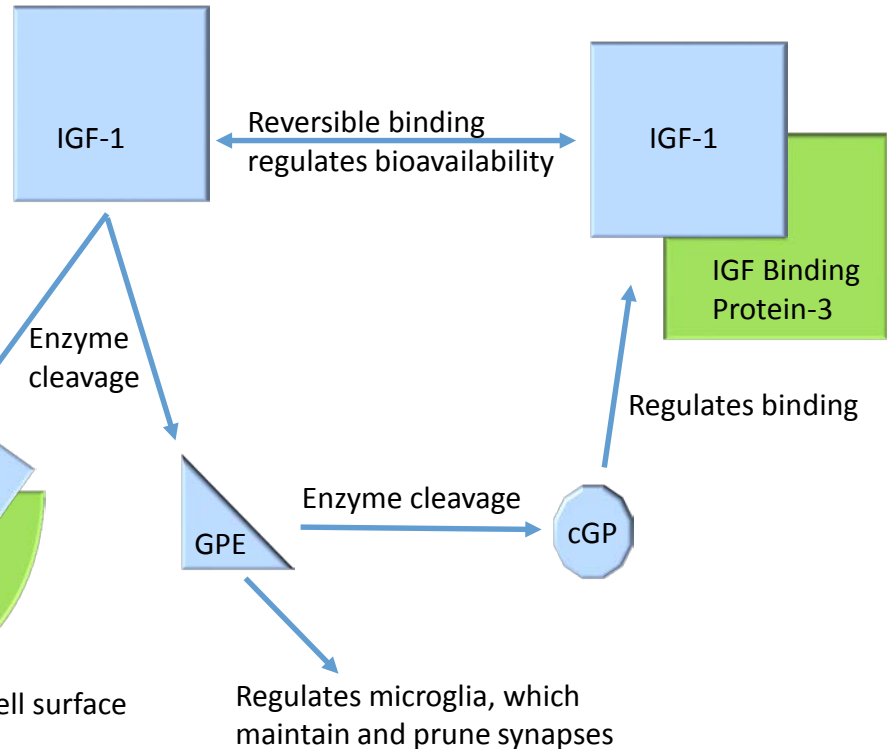
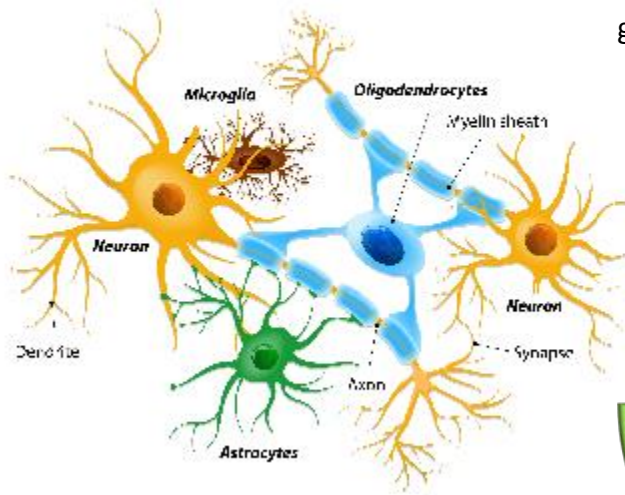
- Inherited X chromosome mutation – full mutation causes Fragile X syndrome
  - 1 / 4,000 males and 1 / 6,000 females estimated to have full mutation
  - More severe in males, ~50% of females have some features of the syndrome
- The most common inherited cause of intellectual disabilities and the most common known cause of autism - symptoms include:
  - Intellectual disabilities
  - Anxiety and unstable mood
  - Seizures (approximately 1 in 4)
  - Attention deficit, hyperactivity and autistic behavior
- Appears in people of all ethnic, racial and socio-economic backgrounds
- No approved medicines available



# Normal biology of IGF-1 in the brain

## NEURONS AND NEUROGLIAL CELLS

Produce essential growth factor



Activates PI3K-Akt-mTOR and Ras-MAPK-ERK signalling pathways in neurons, regulating formation of new synapses

IGF-1 receptor on cell surface

Regulates microglia, which maintain and prune synapses

Neuren's **trofinetide** and **NNZ-2591** are synthetic analogues of GPE and cGP:

- Replicate the activity of the natural molecules
- More stable and orally bioavailable
- Readily cross the blood-brain barrier