



# Biotech Daily

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*Daily news on ASX-listed biotechnology companies*

## Dr Boreham's Crucible: Neuren Pharmaceuticals

By TIM BOREHAM

**ASX code:** NEU

**Market cap:** \$143 million; **Share price:** 7.9 cents; **Shares on issue:** 1.84 billion

**Executive chairman:** Dr Richard Treagus

**Board:** Dr Richard Treagus, Dr Trevor Scott, Bruce Hancox, Larry Glass

**Financials (2016 calendar year):** operating revenue \$1.49 million (previously \$3.1 million), loss of \$12.01 million (previously \$3.34 million); and cash burn \$12.37 million (\$12.73 million). Cash on hand \$5.05 million (\$16.64 million)

**Shareholders\*:** Lang Walker 19%, Cameron Richard Pty Ltd 4%, Essex Castle 2.6%, Larry Glass 1.13%, Trevor Scott 1.13%.

\*As of April 2016 annual report.

In the tortuous path to drug development it helps to have a plan B under your tiffers and possibly a plan C, D and E.

Just like the Cat in the Hat, the New Zealand-originated, Melbourne-based, developer of remedies for hard-to-treat neurological disorders has more than one trick under its headwear - and that's just as well.

A year ago, investors were focused on a program called Intrepid to treat traumatic brain injury (TBI), which was heavily backed by the US Department of Defense (a leading causative agent of such afflictions).

However a 260-patient clinical trial of Neuren's anti-inflammatory compound trofinetide failed to demonstrate a difference between the drug and placebo on three core efficacy measures.

While it's not necessarily curtains for Intrepid - more on that below - Neuren and the military top brass have agreed to put the program on hold for the time being.

Since then the market's attention has turned to using Neuren's lead compound trofinetide (formerly NNZ-2566) to treat Rett syndrome and the rare Fragile X syndrome in paediatric and adult patients.

A form of autism, Rett syndrome affects one in 10,000 females and is characterized by intellectual disability, loss of motor control and muscle rigidity.

A 56-patient phase II study (ranging from 16 to 45 years of age) cited "clinical improvement" as well as passing the usual safety measures.

Investors now await the top-line results from a 62-patient, US-based study of girls aged five years to 15 years. The idea here is to assess longer-term treatment in a younger cohort, based on similar endpoints to the 56-patient study.

Neuren says: "The primary endpoint for the trial in this younger population is the safety and tolerability of trofinetide compared with placebo."

"In addition, a number of outcome measures have been included in the study design in order to provide meaningful insights into the efficacy of trofinetide in younger subjects."

Results are only a few sleeps away (that is, scheduled for some time in March).

In the case of Fragile X, a phase II study involving 70 patients aged between 12 and 45 years pointed to similar clinical improvement.

A follow-up trial is slated next year, for kids between three years and 12 years of age.

Fragile X is an inherited chromosome mutation known as a cause of autism. It affects one in 4,000 males and one in 6,000 females.

As for traumatic brain injury, Intrepid failed its primary endpoints.

But the results were deemed to be "clinically significant" when it came to patients with severe TBI who completed the RBANS test.

The globally-accepted Repeatable Battery for the Assessment of Neuropsychological Studies (RBANS) tests for cognitive impairment on five scores and is especially relevant for dementia patients.

The trial design may also have played a part in the disappointing results.

Neuren argues the under the random allocation between the drug and placebo groups, harder to treat patients were assigned to the former. Discussions continue on a more targeted population, using the RBANS test as a key endpoint.

Why didn't they do that in the first place?

By the way, the peptide trofinetide is a synthetic derivative of glypromate (not to be consumed with the weed-killer glyphosate).

Trofinetide helps restore equilibrium in the brain and arrest neuro-inflammation.

Neuren's latest variant, NNZ-2591, is from the same class of peptides but with higher "bioavailability".

### **Prospects:**

As auditor PricewaterhouseCoopers diligently pointed out at the half year, Neuren faces "material uncertainty" if it can't find more of the folding stuff.

With a \$5.1 million end-of-year cash balance compared with \$16 million previously, nothing has changed.

But like the Fat Controller, management has a few levers to pull.

Firstly, it is "actively engaged" in discussions with potential commercial partners.

Secondly, Neuren also has a deep-pocketed shareholder in property developer Lang Walker.

Last year, the board gained shareholder assent to allot 100,000,000 shares to Walker at or above the prevailing share price, if the action is deemed "necessary and in the best interests of shareholders" and if Mr Walker agrees.

This arrangement, valid until June 30, implies a cash injection of \$8 million.

The Rett syndrome trial is helped along by a \$1.3 million grant from the support group [rettsyndrome.org](http://rettsyndrome.org)

### **Dr Boreham's diagnosis:**

Neuren is ably-led by Dr Richard Treagus, who built roll-on testosterone outfit Acrux to a \$730 million concern before an unfortunate case of share detumescence set in.

Neuren shares have seen better days, having peaked at 70 cents in early 2005 and having traded between four cents and 12 cents over the last 12 months.

At current levels, Neuren is a punt on decent results this month and/or the partnering or licencing discussions bearing fruit.

Bell Potter estimates the Rett syndrome market at \$US6.1 billion, assuming an annual per-patient reimbursement of \$US125,100 per patient.

The Fragile X market is estimated at \$US8.7 billion in the US alone.

Trofinetide has “orphan drug” status in the US and Europe, which should make for quicker approval

***Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. Such is the burden of proof in a court of law, he has never been found guilty of any indictable offences involving professional misrepresentation.***