Biotech Daily

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Daily news on ASX-listed biotechnology companies

Dr Boreham's Crucible: Neurotech International

By TIM BOREHAM

ASX code: NTI

Share price: 6.7 cents; **Shares on issue:** 1,017,388,587; **Market cap:** $68.2 million

Executive director: Dr Thomas Duthy

Board: Mark Davies (chair), Dr Duthy, Gerald Quigley, Max Johnston

Financials (March quarter 2024): receipts nil, cash outflows $1.74 million, cash balance $4.236 million, 2.4 quarters of funding - ahead of a placement that raised $10 million

Identifiable major shareholders: Merchant Funds 7.12%

Is Neurotech the next Neuren Pharmaceuticals, or has the boat sailed in terms of treating children with a suite of rare neurological disorders?

For those living under a rock – or perhaps an internet blind spot – Neuren was last year's superhero stock after gaining US Food and Drug Administration (FDA) approval for its Rett syndrome treatment, Daybue (previously trofinetide).

Firming its status as the 'next most likely', in early May, Neurotech announced highly encouraging phase results for a small study to treat the quixotic disorder, which causes behavioral developmental difficulties in girls.

The results pertained to the company's cannabinoid-based candidate, NTI-164, which has also produced good clinical results for childhood autism and the rare neurological disorder Pandas-Pans.

Neurotech executive director Dr Tom Duthy says the results vindicated the company's September 2022 strategy shift, to focus on paediatric neurological disorders for which NTI-164 has been shown to have an anti-neuroinflammatory effect.

"We have been scouring for paediatric indications where there is a correlation between persistent and progressive neuro-inflammation in children," Dr Duthy says.

"We now have a bona fide clinical development pipeline."

A brief history of Neurotech

Neurotech was incorporated in 2016 to house the acquired Malta-based AAT Research, which developed a home-based device called Mente Autism to relax kids' minds.

AAT Research was founded by neuroscientist Dr Adrian Attard Trevisan.

Neurotech then listed on November 3, 2016, having raised $7 million at 20 cents a pop.

A Neurotech director and the company's chief scientific officer, Dr Trevisan ceased to be a company employee in April 2016 and resigned as a director in June 2018.

In March 2019, the "disappointed" company confirmed a report in the Times of Malta that Dr Trevisan did not hold a Doctorate of Philosophy in Neuroscience from University College London, as claimed.

His role as an adviser was terminated. Dr Trevisan sold his major holding of 19 million shares in June 2019.

In January 2020, the local Therapeutic Goods Administration (TGA) cancelled Mente Autism registration, citing a lack of clinical evidence to "substantiate compliance with the regulations".

In July 2020, the company turned to pot - so to speak - having acquired the rights to a unique cannabis strain from Dolce Cann Global Pty Ltd.

NTI-164 is a proprietary drug formulation derived from a cannabis strain with low levels of the psychoactive component tetra-hydro-cannabinoid (THC).

To cut a long story short, trials in autism ensued, while a Pandas/Pans study also bought home the bamboo (see below).

Rett syndrome appeared on the company's radar in mid-2023.

Dr Duthy joined as a director and adviser in August 2022.

Dr Duthy has a decades-long involvement in the sector, including as investor relations adviser to Nova Eye, head of corporate development and investor relations at Sirtex Medical and as a director of the ASX-listed Invex Therapeutics.

Rett on trial

Rett syndrome is a rare genetic neurological and developmental disorder that affects the way the brain develops in girls and young women.

Rett symptoms include delayed development milestones, lack of motor skills, seizures, intellectual disabilities, behavioral problems and sleep disturbance.

Conducted locally, an open-label, phase I/II Rett trial enrolled 14 girls aged 8.8 years, on average.

The study compared the endpoints against a baseline score at 12 weeks, with the dose increased in the first week to the maximum tolerance.

The girls showed no serious adverse effects, with some vomiting and no weight loss - although one of them broke out in hives.

The kids were measured by two standard Rett tests, the Clinical Global Impression-Improvement (CGI-I) score and the Rett Syndrome Behavior Questionnaire RSBQ score.

On the CGI measure, the subjects at 12 weeks had improved an average 10 percent from a baseline score.

The trial covered nine “exploratory anchors” but the company focused on the four that rated best: communication skills, mental alertness, social interactions and anxiety levels.

With these, the improvement was 23 percent from baseline at 12 weeks.

One patient had “very much’ improved behavior, four were much improved, eight were minimally improved and one had no change.

“In essence, 93 percent of patients improved on the CGI-I score,” Dr Duthy says.

Dr Duthy says typically registrational Rett trials focus on two to three anchors and it would have been an “own goal” for the company to focus on weaker ones such as seizures and sleep patterns.

RSBQ is completed by the care giver who - let’s face it - is best place to discern any improvement.

Used as a secondary endpoint, RSBQ scoring showed an average improvement was minus 13.4 points on the baseline mean of 44.6 points - a 30 percent betterment.

Measurements included mood, facial expressions, body rocking and fear/anxiety.

The trials were overseen by lead investigator, Westmead Children’s Hospital’s Prof Carolyn Ellaway.

Compare the pair

Dr Duthy says: “I’m unashamedly a fan of Neuren and the work they have done to develop their asset.”

That said, Neurotech is not afraid to highlight a few flattering differences between the NTI-164 and Daybue results. Neuren’s registration trial, dubbed Lavender, showed an improvement of 4.9 points on the RSBQ score compared with baseline, equating to an 11 percent improvement versus Neurotech’s 30 percent. (Unlike Neurotech, Lavender had a placebo arm, which showed a four percent improvement).

Crucially, NTI-164’s safety profile was superior to Daybue, which has had a high discontinuance rate because of side effects.

“It’s clearly an apples-and-oranges comparison, but from a safety perspective [NTI-164] is incredibly clean,” Dr Duthy says.

He adds that it’s positive for NTI-164’s prospects that Daybue is the standard-of-care for Rett syndrome in the US, even with that safety profile.

“They [Neuren and Acadia] have broken the soil for us and there is nothing wrong in being a fast follower. They set the endpoints which the FDA will accept and how the agency thinks about safety.”

Tackling autism

In April this year, the company announced final results from its 54-patient phase II/III autism trial, which showed a statistically significant improvement at eight weeks compared with placebo.

The enrollees were classed as either level two (requiring substantial support) or level three (very substantial support).

The children were enrolled at the Monash Medical Centre’s paediatric neurology unit, overseen by principal investigator Prof Michael Fahey. The trial kicked off in December 2022.

After eight weeks’ treatment, children in the NTI-164 group were reclassified from markedly or severely ill at baseline, to mild-to-moderately ill. This was measured on the CGI-S scale (severity of illness).

“Currently there are no FDA or TGA-approved treatments that show clinically significant improvements in one or more of autism’s three core symptom domains: communication, impaired social interaction and restricted behaviors,” Prof Fahey says.

The trial followed a phase I/II, non-placebo-controlled effort showing efficacy up to 52 weeks and safety beyond 90 weeks. The patients have now crossed the two-year milestone without any adverse events.

As rare as … pandas

Largely untreatable, paediatric auto-immune neuropsychiatric disorders associated with streptococcal infections (Pandas) and paediatric acute-onset neuropsychiatric syndrome (Pans) affect about one in 11,000 children in the US and 300 to 500 kids here.

The children go to bed perfectly normal but wake up with uncontrollable tic movements in their hands and legs and become severely obsessive compulsive, with heightened anxiety and depression. The disorder manifests from streptococcus, or other unknown pathogens which cause an auto-immune response resulting in brain inflammation.

This month, the company said its 15-patient phase I/II trial reached its primary endpoint of a 30 percent reduction in anxiety and depression at 12 weeks, with follow-up results at 52 weeks showing a “highly significant and clinically meaningful” 45 percent improvement.

“It’s a rainbow of colors as to what can happen,” Dr Duthy says. “But we have shown NTI-164 blunts that total misalignment of the inflammatory processes.”

Australia first

The company is channeling the Prime Minister’s ‘Made in Australia’ mantra with an ‘act local, think global’ strategy of approaching the TGA first.

The local autism market is especially attractive given the National Disability Insurance Scheme, which covers 235,000 kids at a cost of $7 billion a year.

As for Rett syndrome, Daybue is not approved here and at a cost of $US1,000 a day per patient it probably would be too expensive to be approved under the Pharmaceutical Benefits Scheme.

“We are taking a bit of time to look at our regulatory strategy and what we can achieve in Australia in terms of smart clinical design for all three of our indications,” Dr Duthy says.

Accelerated approval is possible under the TGA’s provisional registration route, by which the agency will approve a drug for sale but require more safety data later on.

Finances and performance

After the positive autism results, Neurotech raised $10 million in a placement, at 10 cents apiece (a 4.6 percent discount to the prevailing price). The company now has proforma cash now of around $13.6 million.

“We are well funded to prepare the work for what looks like the next trial, in Pandas-Pans, Rett syndrome and autism,” Dr Duthy says.

Commercialization options include licencing or a Neuren-style partnering.

The company could also be in line for a valuable paediatric review voucher, which the FDA awards to a company with an approved childhood indication.

“We also have provision for one new paediatric study … for a Rett-like disorder with a small number of patients,” Dr Duthy says.

Over their listed life Neurotech shares have traded between 41 cents (late November 2016) and one cent (early April 2020). Over the last 12 months the shares have ranged between three cents (late June 2023) and 12 cents (late February 2024).

The company’s circa $60 million market cap compares with Neuren’s $2.5 billion valuation.

Dr Boreham’s diagnosis:

For investors, a key focus will be the advice the TGA proffers on a follow-up Rett trial. There’s also potential news on orphan drug designation for Rett and Pandas in the US and Europe.

Autism approval would require two full-blown trials in the US and Europe - well beyond the company’s resources. But for Rett and Pandas/Pans, one well-designed trial could make the drug “registration worthy”.

NTI-164 potentially could emerge as a combination treatment with Daybue, or a second-line therapy for girls who have gone off the drug because of the side effects.

“While there is a standard of care, we believe there is room in the market for more than one,” Dr Duthy says.

Much more needs to be done before Neurotech becomes the next Neuren, but it’s kicking more goals than your standard ‘pot stock’.

“The company has delivered in spades,” Dr Duthy says. “It’s been a good journey but it’s only just begun.”

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. He is approaching 60 but life has only just begun.