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Daily news on ASX-listed biotechnology companies

Dr Boreham's Crucible: Neuren Pharmaceuticals

By TIM BOREHAM

ASX Code: NEU

Share price: $19.95; **Shares on issue:** 127,345,676; **Market cap:** $2.54 billion

Chief executive officer: Jon Pilcher

Board: Patrick Davies (chair), Mr Pilcher, Dr Trevor Scott, Dianne Angus, Dr Jenny Harry, Joe Basile

Financials (year to December 31, 2023): revenue $231.9 million (previously $14.5 million), net profit $157.1 million (previously $184,000), earnings per share $1.2016 (previously 0.1 cents), cash balance $228.1 million (previously $40.2 million)

December quarter 2023: receipts $10.11 million, net cash inflows $4.776 million, cash on hand $228.54 million, quarters of available funding: lots

A year since Neuren and its US partner Acadia Pharmaceuticals gained US Food and Drug Administration (FDA) approval for their rare genetic neuro-degenerative disease drug Daybue (trofinetide), the companies have been reaping the financial rewards in dramatic style.

Last week, Neuren reported a $157 million profit for calendar 2023, compared with a $183,000 surplus previously. Corporate accounts usually describe such increments as 'large', but the company calls it out as an 85,270 percent increase - to be precise.

The profit derives from milestone and royalty payments from Acadia, which is selling the drug in North America and has the rights to distribute elsewhere. Daybue treats the paediatric ailment Rett syndrome, for which there is no other treatment.

Given the company is also swimming in cash, one would think that management would be afforded a ticker-tape parade.

Instead, Neuren shares had their worst fall in 12 months, partly the result of a research report from activist New York short-seller Culper Research, alleging Daybue had been a “complete flop”.

Neuren chief Jon Pilcher declined to comment on the report, which is aimed at Acadia and does not mention Neuren. But he couldn’t resist describing the missive as having “zero credibility”.

He adds: “there’s an atmosphere of people looking for negatives rather than taking a great story at face value.”

An overnight 20-year success story

A rare story of an Australian company getting a drug to market, Neuren (and Acadia) worked on Daybue for more than two decades, at a cost of at least $US250 million.

Trofinetide was invented 20 years ago at Auckland University, in a program spearheaded by eminent chemist Prof Margaret Brimble.

A Nasdaq-listed neurological diseases specialist, Acadia acquired the North American rights in August 2018 as well as the responsibility for a phase III trial and securing FDA approval.

In March 2023, the FDA approved Daybue (trofinetide) for the treatment of Rett syndrome in adults and children aged two or more. In April, Acadia started selling the drug.

Acadia assumed the global rights in mid-July 2023, triggering a $US100 million upfront payment, as well as potential milestones of up to $US427 million plus royalties.

Neuren’s chief financial officer since 2003, Mr Pilcher succeeded Dr Richard Treagus who stepped down in 2020 after seven years in the top job.

About Daybue

Affecting only girls - not the sort of affirmative action we want - Rett syndrome is caused by a genetic mutation that results in inadequate signalling between brain cells.

Rett syndrome is marked by problems including difficulties in talking, breathing, eating and sleeping. Often the girls appear to be normal until about 18 months, but then they stop meeting developmental milestones.

There are about 15,000 sufferers in Europe and 28,000 in China. In the US there are approximately 5,000 diagnosed patients, out of an estimated 6,000 to 9,000 in toto.

Based on naturally-occurring molecules in the brain, Daybue reduces inflammation associated with excessive inflammatory cytokines and normalizes abnormally low levels of the insulin-like growth factor hormone 1 (IGF-1).

Because Daybue targets the underlying problems but does not fix them, patients need to continue taking the drug over their lives.

Acadia's FDA application was supported by the results from a 187-patient phase III trial, called Lavender. Lavender replicated the results of an earlier phase II trial called Lilac and came up roses; and to date, 860 patients have been treated in the US.

Mr Pilcher says 80 percent of the patient population is covered by Medicaid or private reimbursement.

Finances and performance

Given Acadia bears the cost of selling Daybue, Neuren's accounts are a simple case of the revenue from Acadia going straight to the bottom line.

Neuren reported revenue of $232 million, 1,500 percent higher than previously, generating the $157 million net profit after the taxman took a $48.1 million cut.

The revenue consisted of $27 million of royalties, $59.4 million of sales milestone payments and a $146 million upfront payment for the global rights.

The royalties reflected Acadia's fourth quarter Daybue revenue of $US87.1 million, more than the top end of the guided $US80 million to $US85.7 million.

Neuren's cash balance ballooned to $247 million, from $43.2 million previously.

Did someone mention dividends? Mr Pilcher says there's no point paying them until the company pays more tax and accrues franking credits.

Neuren shares fell 14 percent in reaction to the Culper report, but they are now only eight percent lower.

The shares have tripled over the last year but are adrift of their record high of $25.11 struck on December 28, 2023. They are a very long way from the three cents a share from 2009 to 2013 - or 60 cents if you include the 20-to-one consolidation in 2017.

A stunning Dayb-ut

Meanwhile, Acadia reported full-year Daybue sales of $US177 million and guided to calendar 2024 turnover of $US370 to $US420 million. This is despite January sales being softer than expected because of the holiday period, with most Rett clinics closed.

Neuren expects $61 million to $70 million in royalties this year, and should pocket a $US50 million ($A77 million) milestone when Acadia achieves $US250 million of sales.

All up, Neuren stands to collect milestone payments of up to US$350 million based on four sales thresholds, capping out at $US1 billion in sales.

Neuren is also entitled to one-third of the value of a Rare Paediatric Disease Priority Review Voucher (PRV), awarded to by the FDA to Acadia when it approved Daybue.

These fungible vouchers are normally sold to other pharma companies seeking fast-track FDA review of a potentially lucrative drug.

With the vouchers changing hands for around $US100 million, Neuren factors in a $US33m benefit although Acadia appears in no hurry to sell the valuable paper.

The long and the short of discontinuances

Thanks - or no thanks - to the Culper report, investor interest centred on what Acadia had to say about patient discontinuances.

Acadia reported an 80 percent 'real world' persistency rate after four months, a substantial increase from 66 percent for the tightly-controlled Lilac trial. The difference is partly explained by the ability to modify dosages in real-world use, according the level of patient discomfort.

Seven months in, the persistency stands at 63 percent.

"Adoption of Daybue in the diagnosed Rett syndrome population has been faster than expected and caregivers and physicians have continued to report meaningful improvements in patients," Neuren says.

In short - excuse the pun - Culper claimed that Daybue discontinuances were much higher than Acadia said, because of adverse events such as diarrhoea and seizures and a high hospitalisation rate.

Culper models a 72 percent discontinuation rate in 2025, abating to 46 percent after 2026. The report claims that while Acadia estimates Daybue sales at $US650 to $US880 million, sales will peak at only $US316 million in 2024.

Culper disclosed a 'short' position in Acadia, but not Neuren. Short sellers 'borrow' stock from institutional holders for a fee, in the hope of purchasing the shares at a lower price and returning the stock to the 'long' owner.

Neuren supporters, unite

As well as being dismissed by Acadia and Neuren, the report drew a crucial response from several brokers and fund managers.

In its own report, Phoenix Growth Fund (PGF) said: "Our findings support an estimated 35 to 25 percent discontinuance rate from October 2023 - a period [for which] Acadia has not disclosed sales numbers."

As with Culper, PGF based its claims partly on analysis of Facebook posts from the Rett community.

“Whilst our study isn’t scientific in nature, it offers a more comprehensive approach than choosing to report just the negative comments and being heavily subject to selection bias.”

Broker Wilsons says the Culper report “misconstrues available data to over-extrapolate dramatic conclusions that simply are not rooted in fact.”

The firms concur that Daybue’s adverse event profile is “not great” - but that is not news.

Phelan’ good about the pipeline

Acadia expects a European filing for Daybue for Rett syndrome in the first half of 2025, a Japanese filing this year and potential Canadian approval this year.

Acadia also expects a European launch of Daybue in 2026.

But Neuren’s greater fortunes could lie with a second compound to treat four other related severe genetic disorders with the exotic monikers of Phelan-McDermid, Angelman, Pitt Hopkins and Prader-Willi syndromes, all of which have ‘orphan’ drug designation.

The compound, NNZ-2591, is thought to be more effective and less toxic than Daybue.

In December last year, Neuren released the top-line results of a Phelan McDermid phase II children’s trial, showing the drug results in a statistically significant improvement on several measures (based on caregivers’ and clinicians’ observations).

Pitt-Hopkins and Angelman trials are ongoing, with top-line result expected in the June 2024 and September 2024 quarters respectively.

Across the four diseases, the addressable market is five times bigger than the Rett catchment: 56,000 sufferers in the US, 71,000 in Europe and 205,000 in Asia.

Dr Boreham’s diagnosis:

Neuren’s experience with Culper once again highlights the controversial practice of activist ‘short’ funds taking a negative view of a company out of self-interest.

Your columnist believes such research is not intrinsically illegitimate, as it can counter over-optimistic research from ‘long’ investors with a similar vested interest in making money from the share price.

But if the shorters’ claims are a beat-up - as looks to be the case here - facts will prevail. The shares will rise and the shorters will fall - well - short of their objectives.

As Phoenix Growth Fund cheekily asserted, the Culper report was “refreshing” as it tested the fund’s thesis about whether it should be long in Acadia - and the answer is “yes”.

Meanwhile, Mr Pilcher says Neuren’s key challenge is to realise its broader opportunities, notably around NNZ-2591. He’s also on a tiring investor briefing circuit that would leave even the most sober pollie [tr: politician] supine on a Canberra street.

“We have never been in such a strong position and we have never had such good opportunities ahead of us,” he says.

Wilsons brokers exclaims that Neuren has “oodles of cash to fund their [research and development] pipeline, strong phase II data likely supporting registrational trial progression in the near term and - even better - an asset that is going to keep on giving in NNZ-2591 with two more key clinical trial catalysts within the next nine months.”

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. He likes to think his musings do not “misconstrue available data to over-extrapolate dramatic conclusions that simply are not rooted in fact.”