Biotech Daily

Friday March 17, 2023

Daily news on ASX-listed biotechnology companies

*** ASX, BIOTECH UP: PROTEOMICS UP 9%; ONCOSIL DOWN 55%**

*** DR BOREHAM'S CRUCIBLE: NEUREN PHARMACEUTICALS**

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*** MEDIBIO LOSES DIRECTOR DR MATT MESNIK**

MARKET REPORT

The Australian stock market was up 0.42 percent on Friday March 17, 2023, with the ASX200 up 29.3 points to 6,994.8 points. Twenty-two of the Biotech Daily Top 40 stocks were up, 11 fell and seven traded unchanged. All three Big Caps fell.

Proteomics was the best, up 6.5 cents or nine percent to 78.5 cents, with 537,274 shares traded.

Medical Developments and Volpara climbed seven percent or more; Actinogen and Neuren were up six percent or more; Cynata, Emvision, Starpharma and Telix were up five percent or more; Alcidion, Antisense, Clinuvel and Dimerix improved more than four percent; Avita, Cyclopharm and Kazia were up more than three percent; Genetic Signatures, Mesoblast and Pro Medicus rose more than two percent; Immutep and Next Science were up more than one percent; with Paradigm up by 0.75 percent.

Oncosil led the falls, down 1.7 cents or 54.8 percent to 1.4 cents with 83.2 million shares traded. Pharmaxis lost 11.8 percent; Compumedics was down 6.25 percent; Opthea shed 5.2 percent; Amplia and Prescient fell four percent or more; Resonance and Uscom shed more than two percent; Orthocell and Polynovo were down one percent or more; with Cochlear, CSL, Nanosonics and Resmed down by less than one percent.

DR BOREHAM'S CRUCIBLE: NEUREN PHARMACEUTICALS

By TIM BOREHAM

ASX Code: NEU

Share price: $13.23; **Shares on issue:** 126,265,676; **Market cap:** $1.67 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, 2022): revenue $14.55 million***** (previously nil, mostly Acadia payment), net profit $184,000 (from $7.8 million loss), cash $40.1 million up 9%

Major shareholders: Milford Asset Management 5.08%, Cameron Richard Pty Ltd 3.4%, Stuart Andrew Pty Ltd 1.95%, Linwierik Super 1.5%, Essex Castle 1.88%, Smithley Super Pty Ltd 1.6%.

Last Saturday, was a typical balmy autumnal afternoon in Melbourne, but Neuren chief Jon Pilcher was despondent as he awaited news from the company's US partner Acadia on whether the US Food and Drug Administration (FDA) had approved Neuren's neurological drug trofinetide.

As 5.30 pm Friday ticked by in the US, he assumed the FDA's bureaucrats had stowed their HB pencils for the weekend.

He sought solace by repairing to one of his favorite beaches, the wild and woolly surfie hangout of Cape Paterson.

"I went to the ocean to clear my head by diving into the waves, then got out and saw the email," he says. "I didn't plan to be on the beach but it was a nice place to find out."

The email from Acadia confirmed that the FDA had approved trofinetide for the treatment of the rare disorder Rett syndrome in adults and children aged two or more.

Now dubbed Daybue - and thanks for that one, Acadia - trofinetide is one of only a handful of drugs developed from scratch in Australia (with help from the Kiwis) in this case) and approved by the FDA. It's the first since the agency green-lighted Telix Pharmaceuticals' Illucix prostate cancer diagnostic in December 2021.

Earlier ones were Pharmaxis's Bronchitol for cystic fibrosis in 2020 and Clinuvel's Scenesse to treat the rare skin diseases erythropoietic protoporphyria (in 2019).

And let's not forget Hatchtech, which won FDA approval for its head lice treatment Xeglyze in 2020 or Medicines Development for Global Health's moxidectin for river blindness in 2018.

The FDA approval is great news for sufferers of the hitherto untreatable genetic disorder Rett syndrome, which affects only girls.

The news also vindicates the faith of investors who have piled into the stock over the last 12 months, in anticipation of approval. Neuren is now poised to receive hundreds of millions of dollars of sales milestones and royalties (see below).

And there's more: the approval crystallizes receipt of a Rare Paediatric Disease Priority Review Voucher (PRV), a Willy Wonka-style ticket that enables fast-track FDA approval of a second drug. Neuren receives one-third of the value of these fungible devices, estimated at $US33 million.

Neuren's long journey

The FDA approval is the culmination of an estimated $US250 million expended by Neuren and Acadia on developing the drug.

Strictly speaking, Acadia won the approval. The neurology specialist is listed on the Nasdaq and has an $US8 billion market cap. The approval was not exactly unexpected, given Daybue (trophinetide) had orphan and rare paediatric diseases status.

Neuren started working on the drug almost a decade ago, when it started its first Rett syndrome trial. Trofinetide was invented 20 years ago at Auckland University, in a program spearheaded by eminent chemist Prof Margaret Brimble.

Neuren's therapies are based on naturally-occurring molecules in the brain, targeting the underlying problem of deficient signaling between brain cells caused by genetic mutations. Symptoms include behavioral and cognitive problems, deficient motor skills and breathing and cardiovascular issues.

Both Daybue and Neuren's second candidate NNZ-2591 seek to reduce inflammation associated with excessive inflammatory cytokines and normalize abnormally low levels of the insulin growth factor hormone 1, IGF-1. Mr Pilcher describes Daybue as a copy of the molecules already in the IGF-1 pathway, but makes more of it available in the brain.

"It's not a symptomatic treatment, it's trying to improve the architecture of the brain but it doesn't fix the underlying mutation," he says. "So, if you stop taking it, we think the brain will destroy itself again."

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 Rett syndrome

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. While there's a higher mortality rate, most will become adults. The disease is similar to autism, but quite different in some respects.

“They don’t suffer to the same extent, it is very variable,” Mr Pilcher says, adding that the disease is no more prevalent in one geography over another. Environmental factors also appear not to be relevant. There are about 10,000 sufferers in the US, 15,000 in Europe (including Eastern Europe) and 28,000 in China.

Lavender trial smells like roses

In 2021, Acadia released the results of a phase III trial, which led to the filing of the FDA new drug application in July 2022.

Enrolling 187 females between five and 20 years, the double-blinded trial was carried out over 12 weeks. An open-label phase involving 154 of these patients continues for 52 weeks, with the 40-week results so far read out.

Based on the primary endpoints around caregiver and physician assessment, the drug showed “sustained and continual improvement”, relative to a baseline measure. In short, Lavender needed only to replicate the results of an earlier phase II trial and it came up smelling of roses.

Only the beginning?

What happens after Daybue’s US debut?

While winning approval in the world’s most important medical market is a momentous occasion, greater joy could be in store elsewhere. That’s because Neuren retains the rights to trofinetide outside of North America.

Elsewhere, the company is “advancing discussions with a number of third parties”, with some interested in a holus-bolus ‘rest of world’ deal, while others were interested in Europe and Japan.

Australia has hundreds of Rett sufferers, but a well-established Rett Association.

“I want to make sure it gets to Australia but we need to go through the TGA [Therapeutic Goods Administration] process, which is not a slam dunk,” Mr Pilcher says.

Acadia also has purview over a separate program for Fragile X syndrome, another neurological disorder potentially treatable with Daybue. There are more Fragile X patients than Rett patients, but their conditions are more variable and they exhibit more difficult behavior. The program is shelved, but never say never.

Neuren’s second drug front

The company is also targeting four related disorders with NNZ-2591. “All are genetic conditions from the start of life, with a broad range of problems,” Mr Pilcher says.

Affecting both males and females, these conditions are the Phelan-McDermid, Angelman, Pitt Hopkins and Prader-Willi syndromes. The company has orphan indication for all of these diseases.

Perks of orphan status include seven and a half years of market exclusivity in the US and 12 years in the European Union.

Following phase I trials that established safety and tolerance, the company has started phase II trials of up to 60 patients here and in the US, across the former three indications. After gaining FDA trial approval last January, a Prader-Willi trial is also in the offing.

The results will be released sequentially starting with Phelan-McDermid by July 2023.

Mr Pilcher says that as well as mitigating the risk of pursuing a single drug, the NNZ-2591 program eventually could be more valuable than trofinetide. Patient wise, the market is five times bigger. Neuren estimates 56,000 sufferers across all four diseases in the US, 71,000 in Europe and 205,000 in Asia.

“There’s a massive unmet need with all of them,” Mr Pilcher says. “If we can be successful in all of them, it completely dwarfs Daybue from an economic point of view.”

Finances and performance

Like Mr Pilcher, Neuren will be swimming … but in cash.

Neuren’s December 31, 2022 cash balance was $40 million, partly courtesy of a $US10 million milestone from Acadia.

Under the terms of the Acadia tie-up, Neuren gets $US40 million on first commercial US sales - expected as early as next month - with royalties on net sales and potential sales milestone payments.

The milestones are valued up to $US350 million, if four tiered sales thresholds are met. Sales need to be $US250 million or more for the first $US50 million to be realized, while the benefit caps out at $US1 billion of sales.

Under the uncapped tiered royalty arrangements, the company receives 10 percent on sales under $US250 million, rising to 15 percent on any sale over $US750 million.

On Monday, Mr Pilcher cited a typical orphan drug pricing in the US of $US186,758 a year - and bear in mind patients probably will have to take the drug for the rest of their lives.

A few hours later, Acadia revealed its pricing at a staggering $US375,000 a year. According to broker Wilsons, between 60 percent and 67 percent of the addressable patients are covered by the US Medicaid program and a further 30 percent by private insurance.

Let’s hope the parents of the remaining three percent have deep pockets or a kindly maiden aunt.

Mr Pilcher notes that about half of the 10,000 US Rett suffers have been diagnosed and are thus identifiable. Covering half of this cohort - a conservative assumption - equates to almost a $US1 billion-a-year market.

If Acadia furthers a second indication or even more, the sales count towards the milestone payments, thus making Neuren's targets all the more achievable.

As for the Willy Wonka vouchers, Mr Pilcher says the last six or so have changed hands for between $US90 million and $US110 million: "The market for them has been very stable."

Investors reacted to Monday's initial news by sending the shares up $1.67, or 22 percent to $9.35. After Acadia's pricing news they piled on another 10 percent on Tuesday and were at it again on Wednesday, taking the cumulative gain to $4.22, or 55 percent.

Over the last 12 months Neuren shares have traded between $3.45 (May 2022) and Wednesday's zenith of $11.90. Two years ago, the shares were worth less than $1. This followed a 20-to-one consolidation in 2017 when shares were around 16 cents.

Dr Boreham's diagnosis:

The surf-loving Mr Pilcher dubs the FDA approval as an "historic occasion" - but is it merely a beach head for the company?

"For Neuren, this is a transforming milestone that places us in a position to make the most of opportunities ahead of us as we work … to make a difference in [the] four other neuro-development disorders," he says.

Meanwhile, Mr Pilcher says the beauty of Rett syndrome is that it's rare - but not ultra rare - which puts Neuren and Acadia in a Goldilocks position in the US.

The US reimbursement position is supported by the argument the drug will avoid multiple, expensive hospitalizations over a patient's lifetime.

"But because volumes are relatively small it is not costly in comparison to, say, a diabetes drug," Mr Pilcher says.

The market being the market, investors are already looking at what happens beyond Acadia initiating its first commercial US sales of Daybue.

European approval would almost certainly create waves, but the NNZ-2591 could cause spur a longer-term earnings tsunami.

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. He often feels he is swimming in it, but not in cash or pristine surf.

MODERNA INC

Moderna says it will provide a $500,000 a year Australian Fellowship Program to support scientists with an interest in advancing mRNA innovation.

Moderna said the program would run from 2023 to 2027 and award two fellowships a year to support Australia-based mRNA research that could “translate into clinical studies and ultimately new medicines”.

A Moderna spokesperson told Biotech Daily that the fellowships were each worth about $250,000 a year.

The company said the initiative would partner with its Global Fellowship Program, and include salary and research costs, mentorship, experience and collaboration with Moderna’s research and development teams.

Moderna Australia and New Zealand general-manager Michael Azrak said the company was committed to “advancing mRNA science in as many unsolved, untreatable diseases as possible”.

“The medical and scientific community around the world has a significant focus on the acceleration of the transformational possibilities that mRNA offers,” Mr Azrak said.

“With this program, we can help Australia’s … medical research and biotech community to be at the forefront of contributions to unlocking the potential of mRNA science,” he said.

Moderna said the program was open until June 30, 2023, for applications from researchers who live and work in Australia, with details about eligibility and application processes available at: https://www.modernatx.com/en-AU/fellowship.

MICRO-X

Micro-X says it has received $US2 million ($A2.99 million) from the Salt Lake City, Utah-based Varex Imaging in milestone payments for its Nex multi-beam x-ray tubes.

In 2022, Micro-X said it had a $15 million collaboration with Varex to licence its Nex multi-beam x-ray tubes, and take a 9.9 percent holding in Micro-X (BD: Sep 19, 2022).

At the time, the Micro-X said it would provide licence its Nex x-ray tubes to Varex exclusively for $US5 million, payable in five equal milestones over 12 months.

Today, Micro-X said the second and third milestones brought the total amount received to $US3 million.

The company said that the details of the milestones related to “ongoing technology transfer to the Varex facilities in Salt Lake City and remain commercial-in-confidence”.

Micro-X was unchanged at 11 cents.

ONCOSIL MEDICAL

Oncosil says it has a “binding commitment” for up-to $2 million in a $9.9 million rights offer at one cent a share, with one attaching option for each share purchased.

Oncosil said an unnamed investor committed to subscribe for up to $2 million of any shortfall in its non-underwritten, one for one, non-renounceable, entitlement offer, with one option for every share purchased, exercisable at three cents each by April 30, 2027.

Oncosil said the record date for the offer was March 23, it would open on March 28, and close on April 27, 2023, and the funds would be used to commercialize its radiation device in Europe and the UK, for manufacturing and supply chain optimization, clinical trial expenditure and working capital.

Oncosil said it had appointed Kidder Williams to “assess strategic options, including potential merger and acquisition opportunities”.

Oncosil fell 1.7 cents or 54.8 percent to 1.4 cents with 83.2 million shares traded.

NEUROTECH INTERNATIONAL

Neurotech says an 11-child trial shows its marijuana-based NTI164 has “statistically significant efficacy in improving the symptoms associated with autism spectrum disorder”.
In February, Neurotech said it ethics approval to extend its phase I/II trial of its marijuana-based low tetrahydrocannabinol and combination cannabidiol NTI164 for autism spectrum disorder by up to six months (BD: Feb 14, 2023).
Today, Neurotech said the final results from 11 patients in its phase I/II trial of NTI164 for children with autism spectrum disorder treated for 52 weeks with up to 20/milligram per kilogram a day of NTI164 showed a mean difference between 52 weeks of treatment and baseline for the seven-point clinical global severity (CGI-S) scale fell 1.1 units ($p = 0.032$), and that patients’ adaptive behavior as measured by Vineland-3 was “significantly improved overall” ($p = 0.028$).
Neurotech said that “individual domains of communication” improved ($p = 0.0001$), along with daily living skills ($p = 0.005$) and socialization ($p = 0.1181$).
Neurotech said that adaptive behavior was an “important factor” in predicting long-term outcomes for people with autism spectrum disorder, and that improving behavior was a goal of any treatment intervention.
The company said that patients assessed with the social responsive scale after 52 weeks of treatment scored a mean of 73.8, which was a “significant improvement” from the baseline mean score of 78.7 ($p = 0.049$).
Neurotech said that there were no serious adverse events recorded.
Neurotech was unchanged at 5.8 cents with 2.4 million shares traded.

GENETIC TECHNOLOGIES

Genetic Technologies has told an ASX aware query that it believed that its validation study was material at the time of publication.
Earlier this week, in an announcement marked “market-sensitive”, Genetic Technologies said its Genetype breast cancer risk assessment test performed better than the BCRAT “gold-standard model,” and provided a link to an article in Cancer Prevention Research by lead author Dr Erika Spaeth, who is the company’s director of clinical and medical affairs (BD: Mar 13, 2023).
Today, the ASX asked whether the company believed that the information released would have a material effect on the price or value of its securities, and when it first became aware of the information?
Genetic Technologies said that “initially at the time of announcement… [it] considered the information potentially to have a material impact on price or value of our securities, however this assessment and the marking of an announcement as price-sensitive is a subjective judgement” but that it did not note “any significant market response at all to this announcement on either share price or volume”.
The company said that it received notice of publication of the paper on March 6, 2023, but that “the process of assessment was longer than ideal” due to time zones, unavailable executives, and agreement on the final version of the announcement, which was lodged on March 13, 2023.
Genetic Technologies said that “market trading was monitored during this period by the company secretary and there were no indications that the company’s shares were being traded on the news of the publication of this paper prior to the release being lodged pre-market open on March 13, 2023”.
Genetic Technologies was unchanged at 0.3 cents with three million shares traded.

AVITA MEDICAL

Avita says it has appointed Cary Vance as a director, effective from April 1, 2023.
Avita said Mr Vance had more than 25 years of experience in the healthcare industry and was currently Titan Medical's chief executive officer.
The company said that Mr Vance had previously worked for XCath and Hansen Medical as chief executive officer and held "similar roles" at Optiscan Biomedical, Myoscience, Teleflex, Covidien and GE Healthcare.
Avita said that Mr Vance held a Bachelor of Arts and a Master of Business Administration from Marquette University in Milwaukee, Wisconsin.
Avita was up 14 cents or 3.6 percent to $4.05 with 276,486 shares traded.

MEDIBIO

Medibio says Dr Matt Mesnik has resigned as a director "as part of the ongoing restructure" and to use his skillset and industry contacts in a more meaningful way.
Medibio said that 12-month director Dr Mesnik would continue to assist the company as an adviser (BD: Mar 2, 2022).
Medibio was unchanged at 0.1 cents.