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Daily news on ASX-listed biotechnology companies

Dr Boreham's Crucible: Pharmaust

(To become Neurizon Therapeutics)

By TIM BOREHAM

ASX code: PAA (to be NUZ)

Share price: 21.5 cents; **Shares on issue:** 486,634,555; **Market cap:** $104.6 million

CEO: Dr Michael Thurn

Board: Sergio Duchini (chair), Dr Thurn, Dr Katie MacFarlane, Marcus Hughes

Financials: (year to June 30 2024): revenue nil, loss of $7.7 million (previous deficit $6.2 million), cash of $9.7 million (up 259%)

Identifiable major holders: Hybrid Holdings (Darcy family superannuation trust) 4.57%, Dr Roger Aston 3.09%, Gerard and Gillian Van Blommestein 3.8%, Chek Loon Tan 1.8%

True to its history of reinvention and repurposing, Pharmaust will be renamed Neurizon Therapeutics after shareholders approved the moniker change at Wednesday's AGM.

The new name "combines our focus on neuro-degenerative diseases with the promising horizon of patients," chair Sergio Duchini helpfully explained. The change is expected to be completed by next Monday, October 14, 2024.

Pharmaust – er, Neurizon - is based on repurposing an old animal drug - a parasitic sheep drench called monepantel – initially as a human and animal cancer drug.

Marketed by Eli Lilly's animal health arm Elanco as Zolvix, the treatment had been long approved in Europe and the UK so has an established safety profile.

Now, under ‘repurposed’ management, the company has changed its focus to amyotrophic lateral sclerosis (ALS), better known as motor neuron disease (MND).

“The company was a bit of a hotch-potch,” CEO Dr Michael Thurn says.

Profile-wise MND used to play second fiddle to multiple sclerosis – remember the Readathons? - but the efforts of ex-AFL footballer Neale Daniher and the Big Freeze fundraising campaign changed all of that.

Affecting about 350,000 people globally, MND weakens muscles and impacts physical function. While invariably fatal, progression can be slow or fast but the average life expectancy is only about 27 months.

Having released the results of a phase I study, Neurizon was preparing for a pivotal phase II/III trial - and fast-track approval. The company still is girding for the trial, but in reinvented form (see below).

Going back in time

Pharmaust listed on the ASX in October 2001 as Echo Technologies, which had a travel business called Tardis Travel.

Going forward into the time-space continuum to 2005, the company turned to developing mimotopes, which are research-grade peptides for the drug discovery.

In 2011, Pharmaust acquired Pela Resources for scrip and was going to go mining but changed its mind and in 2012 decided to focus on its Epichem subsidiary (see below).

Monepantel was ‘discovered’ by a clinical oncologist and part-time sheep farmer named Prof David Morris, who chanced on the anti-cancer properties of the sheep dip.

A spin-off from St George’s Hospital in Sydney, Pitney Pharmaceuticals negotiated an option for the animal cancer rights with Novartis (now Elanco) in 2012.

Pharmaust acquired Pitney in 2013 in a $6 million scrip deal, effectively a back-door listing. The deal introduced Pitney’s chief, the well-known Dr Roger Aston, to Pharmaust.

Pharmaust also had a subsidiary called Epichem, providing synthetic and medicinal chemistry services (contract research work) to drug researchers and pharma companies.

In its day, Epichem was a nice little earner, but times change. In August last year, Pharmaust put Epichem into voluntary liquidation - another form of reinvention, we guess - after a long-standing research contract was not renewed.

With the company’s formerly Perth-based share register becoming more eastern seaboard oriented, Neurizon has repurposed – er, relocated - its headquarters from Perth to Melbourne.

Er, welcome back

Dr Thurn became CEO in September last year but on April 23 this year he resigned, citing personal reasons. Chief operating officer (COO) John Clark repurposed himself as interim CEO.

But on May 9 the company announced that Dr Aston, Pitney co-founder Rob Bishop and Dr Thomas Duthy had resigned from the board. Dr Duthy - who was only appointed in February - now runs Neurotech International.

Another director (and company secretary), Sam Wright resigned on May 16 and on May 31 the company declared Dr Thurn to be back in the building. Mr Clark resumed COO duties and the last of the old guard directors, Neville Bassett, resigned on June 13.

“I had a different outlook on the company to the board. There was a disconnect,” Dr Thurn says.

“I have been given a second opportunity, largely because of the major shareholders wanting me to come back and lead the company after cleaning out the old board.”

In his first stint as CEO, Dr Thurn oversaw the completion of the phase I study, called Mend and engaged with the US Food and Drug Administration (FDA) to win orphan drug status.

Prior to that, he co-founded private anti-viral drug house MARP Therapeutics and had roles with Novogen and the ASX-listed Botanix Pharmaceuticals and Cytopia.

mTORing along

Monepantel works by inhibiting the mTOR signaling pathway, which plays a central role in the growth of cancer cells and the degeneration of neurons.

mTOR stands for the ‘mechanistic Target of Rapamycin’, a reference not to a Tolkien novel but a well-known oncology target (rapamycin).

“Our mechanism of action is universal, in that it stimulates a cleaning mechanism in all cells - a process called autophagy,” Dr Thurn says.

“There’s a reasonable expectation we will be able to treat well over 90 percent of MND patients.”

Monepantel is also potentially relevant for Alzheimer’s disease, Huntington’s disease, multiple sclerosis and Parkinsons disease.

The company was mulling a Parkinsons-focused trial, but opted for MND because of the huge unmet need. But the real clincher was a circa $900,000 grant from Fight MND, a charity funded by those Big Freeze beanies.

“It was the path of least resistance because funding was available,” Dr Thurn says.

Tastes like … yuk

Armed with the rights for monepantel from Elanco, the company has developed a manufacturing process for the drug and filed a provisional patent.

Dr Thurn says monepantel's animal use means there's a huge dossier of positive safety data - bearing in mind the drug enters the human food chain when used a sheep drench.

Monepantel is notoriously foul tasting and deliberately so. Rather like the additives in methylated spirits to prevent folk from drinking it, substances are added to prevent human use.

Naturally, these additives won't go into the human pills.

On the Mend

The 12-patient, 'Mend', phase I study showed the drug crosses the blood-brain barrier and is safe to use at "therapeutically meaningful" doses.

Preliminary efficacy data showed administering monepantel at a dose of 10 milligrams per kilogram could slow MND progression by up to 58 percent and increase life expectancy by as much as 56.5 months.

Current approved treatments extend life expectancy by two to six months.

An adaptive phase II/III clinical trial, dubbed Strike, was expected to begin this year.

But in mid-July the company said Monepantel has been selected for Healey ALS, a collaborative MND trial across 70-plus sites in the US.

The platform will test several drugs simultaneously, thus increasing patient access and reducing study costs and completion and enrolment times.

Healy is being run at Boston's Massachusetts General Hospital, the "pre-eminent brains" behind ALS.

"We know our arm of the platform will be designed to the best of their capability, with no stone left unturned," Dr Thurn says.

"They have skeletons in the closet from other arms that have failed and are building on that information."

Saving time and money

The company envisaged enrolling around 200 patients for its own trial, but under the Healey banner the number is likely to reduce to around 160 (120 of them on active treatment). The trials can share placebo groups.

Dr Thurn expects a 30 percent saving compared to a stand-alone study, which was costed at $25 million to $30 million. “It’s a very convenient set up, especially for an Australian biotech. We can just hand over the drug and let the experts run it,” he says.

The company expects to have 24-week data – enough to approach the FDA about an accelerated approval process – by the end of 2025. Accelerated approval could mean the company only has to carry out a confirmatory study rather than a full phase III effort.

In May, the FDA granted orphan drug designation status. Applicable for rare disease affecting fewer than 200,000 people in the US, orphan status allows for tax credits, potential grants, waived clinical fees and - crucially - seven years’ exclusivity from generic and branded competition.

Finances and performance

Neurizon raised $10.66 million in June and then $7.8 million by way of a follow-up share purchase plan.

The raisings were done at 19 cents a share, a 15.6 percent discount.

“I would like to think there’s a high prospect of our partnering early, perhaps during that first phase of the phase II,” Dr Thurn says.

He says the current funding is “close” to what would be needed to complete the Healey trial, but a “top up’ capital raising of $5 million to $8 million is likely.

Neurizon’s MND pivot has spurred strong investor interest, with the shares climbing from 7.0 cents in mid-August last year to 43 cents on April 2, 2024. The stock peaked at over $6.00 in early 2001, but it was a very different company then.

Going to the dogs

Neurizon was progressing a canine cancer trial - for B-cell lymphoma - in the hope of commercializing a drug less toxic than the current treatments. One in four dogs die of cancer, including half of dogs over 10 years old.

Despite claiming “encouraging” results, the company has shelved the program. (Pharmaust also tried monepantel on humans for cancer and as a treatment for Sars-Cov-2 (Covid-19), all without success.)

“The trouble is that the vet drugs might be worth $2,000 to $3,000 per year, compared with $150,000-plus for an orphan MND drug,” Dr Thurn says.

This meant human patients could be tempted to buy the doggy drug cheaply and use it off-label.

“The MND community is very tight knit, so if there’s news of a drug being used for a veterinary application then everyone would know about it.”

Dr Boreham's diagnosis:

Dr Thurn believes Neurizon is at the forefront of MND drug development, even though it is only a small Australian company.

But being on top of the science and commercialization are different disciplines and Dr Thurn says furthering the drug will require a partnering deal, or an outright acquisition of Neurizon.

Of course, the drug has to work and the company needs enough patent strength to protect itself from rip-offs. And there's no Plan B.

The size of the prize is an MND treatment market worth more than $US9 billion in 2022 and forecast to reach $US23 billion by 2035.

The FDA has approved only four MND drugs, the oldest of which was approved in 1995 and is now generic. While they all improve life expectancy only by months, one of them is effective for only for two percent of patients (with a certain mutation).

One of them - Relyvrio - was withdrawn from last year because of sub-standard trial results.

"We are in phase I now but we could be selling the drug within two and a half years," Dr Thurn says.

"The bottom line is that MND is an indication with a high unmet need."

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. These are not his only unmet needs.