# Biotech Daily

Friday October 11, 2024

*Daily news on ASX-listed biotechnology companies*

*** ASX, BIOTECH DOWN: PERCHERON UP 13%; PRESCIENT DOWN 8%**

*** DR BOREHAM'S CRUCIBLE: PHARMAUST (TO BE NEURIZON)**

*** DEMENTIA AUSTRALIA: 'DEMENTIA WILL BE TOP CAUSE OF DEATH'**

*** ACTINOGEN PRESENTS PHASE IIa XANAMEM DEMENTIA DATA**

*** ALTERITY PRESENTS ATH434 'NEURO-PROTECTIVE' DATA**

*** PROTEOMICS: 'PROMARKER D PREDICTS TYPE 1 DIABETES'**

*** CLARIFICATION: PHARMAUST**

*** TENMILE, TATTARANG, 'TWIGGY' FORREST TAKE 19.9% OF LUMOS**

*** RESPIRI REQUESTS 'STRATEGIC INVESTMENT' TRADING HALT**

## MARKET REPORT

The Australian stock market slipped 0.1 percent on Friday October 11, 2024, with the ASX200 down 8.5 points to 8,214.5 points.

Twelve of the Biotech Daily Top 40 companies were up, 17 fell and 11 traded unchanged. All three Big Caps were up.

Percheron was the best, up 1.5 cents or 13.0 percent to 13 cents, with 6.2 million shares traded. Atomo, Mesoblast and Opthea improved four percent or more; Alcidion and SDI climbed more than three percent; Imugene rose 2.1 percent; Clinuvel and Proteomics were up by more than one percent; with 4D Medical, Cochlear, CSL, Cyclopharm, Resmed and Telix up by less than one percent.

Prescient led the falls, down 0.4 cents or eight percent to 4.6 cents, with 774,734 shares traded. Compumedics and Universal Biosensors lost more than six percent; Cynata fell 5.9 percent; Actinogen and Amplia were down three percent or more; Clarity and Dimerix shed more than two percent; Avita, Medadvisor, Nanosonics, Neuren and Starpharma were down one percent or more; with Aroa, Impedimed, Orthocell and Pro Medicus down by less than one percent.

# DR BOREHAM'S CRUCIBLE: PHARMAUST (TO BE 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 its 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 he resigned, citing personal reasons. Chief operating officer (COO) John Clark repurposed himself as interim CEO.

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. The real clincher was a circa $900,000 grant from Fight MND, a charity funded by those Big Freeze beanies.

## 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 10 milligrams per kilogram could slow MND progression by up to 58 percent and increase life expectancy by as much as 56.5 months. 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 calendar 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.***

## DEMENTIA AUSTRALIA, AUSTRALIAN BUREAU OF STATISTICS

Dementia Australia says dementia is the leading cause of death for Australian women and "is set to become the nation's leading cause of death", according to ABS data.
Dementia Australia said the Australian Bureau of Statistics (ABS) data showed dementia was the cause of 12.2 percent of all female deaths and 6.4 percent of male deaths.
The ABS told Biotech Daily that 10.8 percent of men died from ischemic heart disease.
The Australian Bureau of Statistics said that ischemic heart disease was the top cause of death in Australia overall, but fewer than 250 deaths separated it from dementia which was the second leading cause, in 2023.
The Bureau said that ischemic heart disease accounted for 9.2 percent of all deaths and dementia 9.1 percent.
Dementia Australia said that dementia was the leading cause of death in South Australia, the Australian Capital Territory and, for the first time, New South Wales.
Dementia Australia chief executive officer Prof Tanya Buchanan said that given there was "no cure for dementia and poor community understanding of the terminal nature of the disease, the ABS data reinforces the urgent need for a public health approach to reducing, or preventing, the risk of developing dementia".
"This call is backed by the 2024 update of the Lancet Commission on the prevention, treatment, and care of dementia, which reports that almost half of dementia cases worldwide could be prevented or delayed," Prof Buchanan said.
"There are currently an estimated 421,000 Australians living with dementia and without a significant intervention, this number is expected to increase to more than 812,500 by 2054," Prof Buchanan said.
"As dementia edges closer to becoming the leading cause of death of Australians, it is crucial that we act now to focus on the brain health of the nation as well as provide more targeted, effective support to those impacted by dementia," Prof Buchanan said.
"Taking this dual approach will ensure we are working towards reducing the impact of dementia in the future," Prof Buchanan said.

## ACTINOGEN MEDICAL

Actinogen says it has presented "significant anti-depressant activity" from its phase IIa trial of Xanamem at the Dementia Trials Australia meeting in Sydney, today.
Actinogen said managing-director Dr Steven Gourlay hosted the presentation, titled 'Oral Xanamem: How Xanamem's benefit on depressive symptoms translates to possible efficacy in Alzheimer's disease'.
In 2022, the company said a six-week, phase II, proof-of-concept study of daily oral 10mg Xanamem cortisol synthesis inhibitor would be compared to placebo and anti-depressant therapy, for effects on depression and cognition (BD: Jun 14, 2022).
In August, Actinogen said the trial did not meet the primary endpoint of superiority to placebo in a cognitive 'attention composite' of three Cogstate tests due to an "unexpectedly large improvement in the placebo group" (BD: Aug 12, 2024).
Later that month, the company said further phase IIa data showed Xanamem was "clinically active in controlling brain cortisol and has clinically significant anti-depressant activity" (BD: Aug 26, 2024).
Today, Actinogen said the presentation outlined the "encouraging data showing clinically and statistically significant anti-depressant activity" and that the data validated Xanamem's mechanism-of-action to control cortisol in the brain, as well as the 10mg daily dose being used in the Alzheimer's program.
Actinogen fell 0.1 cents or 3.6 percent to 2.7 cents with 8.6 million shares traded.

## ALTERITY THERAPEUTICS

Alterity says it has presented data showing the “neuro-protective and mitochondrial protectant properties” of ATH434 at the Society for Neuroscience in Chicago.

Alterity said the data was presented in a poster, titled ‘Potent Antioxidant and Mitochondrial-protectant Effects of ATH434, a Novel Inhibitor of [alpha]-Synuclein Aggregation with Moderate Iron-binding Affinity’.

The company said the data included the reduction of lipid damage in “two distinct and disease-relevant neuronal injury models”, as well as additional studies showing the “inherent anti-oxidant properties and benefits of ATH434 in cellular energy usage”.

Alterity said the study was authored by the State University of New York, Buffalo’s Dr Danielle Bailey as well as its head of research and non-clinical development Dr Margaret Bradbury.

The company said the study “investigated the efficacy of ATH434 and comparator agents as lipid peroxidation protectants using a menadione-induced model and a hemin-induced oxidative stress model in a neuronal cell line”.

Alterity said the study showed that “in unstressed cells, ATH434 promoted energy production in mitochondria to a pathway less prone to causing oxidative stress … [and] detailed the mechanisms underlying ATH434’s direct antioxidant capacity with respect to potentially damaging charged molecules”.

The company said these combined properties of ATH434 could “serve to protect vulnerable mitochondria in neuro-degenerative diseases”.

The study presentation concluded that “anti-oxidant activity may be an important contributor to the efficacy of ATH434 in neuro-degenerative disorders characterized by oxidative stress, enhancing the efficacy of its moderate iron binding”.

Last year, Alterity said it had begun a 15-patient, open-label, phase II trial of ATH434 for multiple system atrophy, in addition to a separate 60-patient phase II trial in the same indication but in patients with more advanced disease (BD: May 30, 2023).

In July, Alterity said three of seven evaluable patients in its phase II trial of ATH434 for multiple system atrophy (MSA) showed “reduced disability on activities of daily living”, and two patients were clinical responders (BD: Jul 17, 2024).

At that time, the company said the two clinical responders “on average had reduced accumulation of iron on [magnetic resonance imaging] in the substantia nigra, putamen and globus pallidus and stable levels of [neurofilament light chain], a marker of axonal injury, when compared to participants who declined”.

Today, Alterity chief executive officer Dr David Stamler said the data furthered the company’s “understanding of ATH434’s potential as a disease modifying treatment for neurodegenerative diseases, including Parkinson’s disease and related disorders”.

“The study extended previous findings and demonstrated that ATH434 has intrinsic antioxidant activity,” Dr Stamler said.

“This is key as oxidative injury is an important contributor to the pathology of neuro-degeneration,” Dr Stamler said.

“By addressing this injury in two different ways, both directly and by redistributing excess labile iron, ATH434 has excellent potential to treat this group of diseases,” Dr Stamler said.

“The ability of ATH434 to reduce damage to lipid membranes undergoing oxidative stress may augment its ability to slow disease progression,” Dr Stamler said.

“We are grateful for the continued valuable contributions from our collaborators in Dr Daniel Kosman’s laboratory at [State University of New York] at Buffalo,” Dr Stamler said.

Alterity was unchanged at 0.3 cents with 3.3 million shares traded.

## PROTEOMICS INTERNATIONAL LABORATORIES

Proteomics says it has presented previously announced results showing its Promarker D blood test can predict chronic kidney disease in type 1 diabetes patients.

In August, Proteomics said its Promarker D blood test, originally designed for predicting renal decline in type 2 diabetes, showed 90 percent specificity and 78 percent sensitivity in a phase II trial of 92 type 1 diabetes patients (BD: Aug 23, 2024).

At the time, the company said the test had a 47 percent positive predictive value, a 97 percent negative predictive value, and 97 percent for predicting renal decline in type 1 diabetes, meaning it was “at least as good a prognostic test for renal decline in type 1 as type 2 diabetes”.

Today, Proteomics said that the trial results, titled ‘Application of a validated prognostic plasma protein biomarker test for renal decline in type 2 diabetes to type 1 diabetes: The Fremantle Diabetes Study Phase II’, were published in the Clinical Diabetes and Endocrinology journal and were available at: https://bit.ly/3TZC0ib.

The company said that it was focusing on commercializing its Promarker D in the US by July 2025 and in Australia by April 2025 through licencing and direct-to-patient approaches.

Proteomics was up one cent or 1.3 percent to 80 cents.

## CLARIFICATION: PHARMAUST (TO BECOME NEURIZON THERAPEUTICS)

Last night’s edition carried a headline that said there was up to 42 percent dissent at the Pharmaust annual general meeting.

The article reported that the name change resolution to Neurizon was carried with more than 99 percent of votes in favor and the greatest opposition was to the issue of shares and options to former director Dr Thomas Duthy.

Pharmaust said that up to 16.56 percent of the meeting opposed resolutions relating to the increase in the directors’ fee pool and the issue of shares and options to directors.

The mistake was made by the Thursday sub-editor and while the usual practice is to terminate sub-editors, given that is Erev Yom Kippur (the evening of the Jewish Day of Atonement) we have decided the sub-editor will be “rewarded” with a night tonight and a full day in synagogue tomorrow to atone for his sins.

Pharmaust was up one cent or 4.9 percent to 21.5 cents with 1.4 million shares traded.

## LUMOS DIAGNOSTICS HOLDINGS

Perth’s Tenmile and the Forrest family say they have increased their substantial holding in Lumos from 69,725,275 shares (12.39%) to 148,672,643 shares (19.93%).

Tenmile Ventures Pty Ltd, Tattarang Pty Ltd, Nicola and Dr Andrew Forrest said that on October 9, 2024 they bought 78,947,368 shares as sub-underwriter of a rights issue for $3,000,000, or 3.8 cents a share.

On Tuesday, Lumos said that it had raised $6.9 million at 3.8 cents a share in its retail rights offer, taking the total raised to $10 million (BD: Oct 8, 2024).

At that time, the company said that $300,000 of the retail offer was raised from investors, with the remaining $6.1 million raised from underwriter Bell Potter, as well as sub-underwriters Ryder Capital and Tenmile Ventures, a company controlled by Dr Forrest.

Lumos was up 0.1 cents or 2.2 percent to 4.6 cents with 4.2 million shares traded.

RESPIRI

Respiri has requested a trading halt pending an announcement “regarding finalization of a strategic fund investment into the company”.

Trading will resume on October 15, 2024, or on an earlier announcement.

Respiri last traded at 5.6 cents.