Biotech Daily

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Daily news on ASX-listed biotechnology companies

Dr Boreham's Crucible: Actinogen Medical

By TIM BOREHAM

ASX code: ACW

Share price: 1.2 cents; **Shares on issue:** 3,869,768,325; **Market cap:** $46.4 million

Chief executive officer: Dr Steven Gourlay

Board: Dr Geoff Brooke (chair), Dr Gourlay, Dr George Morstyn, Malcolm McComas, Dr Nicki Vasquez

Financials (September quarter 2026): revenue nil, cash outflows $6.2 million, cash balance $15.9 million (ahead of net $6 million Federal Research and Development Tax Incentive)

Identifiable major holders: Dr Gourlay 5.5%, Ardroy Pty Ltd 1.73%, Guillermo Cesar Orselli and David Matthew Krelle 2.15%

In TV land, there's scripted content and the predictably unpredictable fare served up by myriad reality (or should that be unreality?) shows.

This year, late-stage clinical trials have produced all the spontaneous drama - and like the bitchy 'chefs' on My Kitchen Rules it hasn't been nice to watch.

Following this year's wipeouts from Paradigm Biopharmaceuticals, Cynata Therapeutics and Immutep, investors desperately needed a clinical drug trial win from Alzheimer's disease drug developer Actinogen.

Instead, investors last week booted the company from the Big Brother household after its phase III Xanamia study failed its primary endpoints. Viewers – er - investors trashed the stock by 88 percent.

In the world of reality TV, heroes and villains are black and white. Just ask The Bachelor's alleged 'love rat' Blake Garvey, who proposed to Sam Frost in the finale before pivoting to runner-up Louise Pillidge.

In 'real' reality, things are rarely so clear-cut.

Actinogen is prosecuting its view that the data was excellent – in the cohort of older patients accounting for half the study enrolment.

"Basically, we're seeing clinically and commercially relevant benefits in slowing progression and in complete stabilization rates in those older patients," said Actinogen CEO Dr Steven Gourlay.

He admits the company would have preferred a "clear win" across the overall patient population. "But there have been very few of those ever in Alzheimer's disease."

All about Xanamem

The fastest growing chronic ailment of the current century, Alzheimer's disease was discovered by German neurologist Dr Alois Alzheimer in 1906. The condition hitherto had been classed as dementia, but Dr Alzheimer isolated a protein called amyloid in some dementia patients. That was good enough to bag the naming rights.

Actinogen's Xanamem (emestedastat) inhibits production of cortisol, a naturally occurring stress hormone. Elevated cortisol levels are thought to be a cause of both Alzheimer's and mild cognitive impairment (which can often lead to the former).

Xanamem targets 11beta-hydroxy-steroid dehydrogenase type 1 (11beta-HSD1) - a cortisol-producing enzyme expressed in parts of the brain governing memory and mood. Actinogen claims Xanamem to be the "first and only potent oral inhibitor" of 11beta-HSD1.

Xanamem crosses the blood-brain-barrier: a hurdle that has proved too much for other cortisol-targeting candidates.

"Our trial is so important because the cortisol hypothesis has been around for decades, but no one ever has been able to test it," Dr Gourlay said earlier this year.

Approved Alzheimer's drugs have focused on reducing amyloid plaque in the brain.

Actinogen listed in October 2007 at 50 cents apiece, with an initial focus on soil-derived antibiotic-like compounds called actinomycetes (hence the Actinogen name).

The company decided not to stay down and dirty, instead acquiring the Xanamem (then known as UE2343) program from Edinburgh University in 2014.

Xanamia – can we go again?

The Xanamia trial enrolled 247 patients in Australia and the US. The patients were treated with 10 milligrams of Xanamem daily, over 36 weeks. Half the patients were on placebo.

The primary endpoint – slowing progression of the disease – was measured by the internationally recognized clinical dementia rating, the sum of boxes (CDR-SB) scale.

The study missed its primary endpoint of being 'statistically superior' to the placebo group; and also missed the secondary endpoints of improved cognition and daily living activities.

The company said Xanamem was "numerically but not statistically" superior to placebo for the primary endpoint.

On the 18-point CDR-SB scale, the mean benefit was 0.10 points relative to placebo, at 36 weeks. This equated to a 'p' – probability - value of 0.65, which meant there was a 65% chance the benefit was a fluke.

Xanamia's trial design was informed by an earlier phase II effort, Xanadu.

This study showed Xanamem to be "safe and well tolerated, with promising disease-modifying activity in Alzheimer's and improvement in depressive symptoms".

But in 2019, the trial failed to hit its primary endpoint of cognitive improvement.

Management ascertained that the study design was faulty because it was too short – and that up to 40 percent of enrollees actually didn't have the disease.

As a result, the phase IIb/III effort enrolled only patients with confirmed Alzheimer's disease, as measured by elevated blood levels of a protein biomarker called pTau18.

Can golden oldies carry the day?

This is where things get interesting.

Xanamem showed a much better effect in the older cohort, which had a median age of 75 years (We'll call them the Over 75s).

These patients comprised half the trial candidates.

The grouping was "predefined", which meant the company didn't go 'data mining' after the fact to prove its thesis.

The Over 75s showed a zero-disease progression rate of 40 percent, compared with 22 percent for placebo (a 'p' value of 0.02). They also exhibited a 30 percent rate of disease slowing.

“For context, this rate of disease slowing is similar to that claimed by Eli Lilly and Eisai for their approved anti-amyloid drugs,” the company said.

Dr Gourlay said it wasn't surprising the older cohort reacted better. That’s because 11-beta HSD1 “is well-known to increase in its expression in the brain with age”. As measured by two bio-markers, neuro-inflammation also is more common in older people.

“Basically, we're seeing clinically and commercially relevant benefits in slowing progression and in complete stabilization rates in those older patients,” he said.

‘Non futility’ ruling gives misleading signals

As well as the eternal question of why vapid reality shows exist, the biggest point of intrigue is why Xanamia missed its primary endpoint, when January’s interim futility analysis was so positive.

To recap, a monitoring committee recommended the study continue, based on its analysis of 88 patients. At the time, the data was blinded. Last week, the company said the interim results showed a convincing treatment benefit of 0.58 CDR-SB points (a ‘p’ value of 0.03). Of course, this effect was “not fully-sustained” in the final readout.

Dr Gourlay said the drug looked a “complete winner” on the interim score. But these efforts “analyze a small subset of the data that may or may not be truly indicative of what's going on.”

Dr Gourlay says more Americans were recruited in the later stages of the trial. For unknown reasons, their condition declined more slowly than Australian patients.

(We’re struggling for a Donald Trump/Joe Biden analogy, but in our own ‘senior moment’ we draw a blank.)

The apparent cognitive superiority of the US cohort almost certainly doesn’t explain the interim-versus-final discrepancy.

“The honest answer is we just don't know,” Dr Gourlay says. “It will probably go down in history as one of the classic trials where an interim analysis said one thing and the final result looked different.”

Open label: all on the table

Early results from an ongoing open label extension (OLE) study also showed disease stabilization over 24 weeks. This read-out covered the first 29 of 169 OLE patients.

In the short term, investor attention turns to the OLE readout of the first 100 patients, at 24 weeks. This is due by April 2027. An OLE means all patients are on the active drug, with no placebo comparator.

The company plans a larger trial, enrolling – unsurprisingly – only the Over 75s. These account for around 70 percent of Alzheimer's patients, generally.

"We need to fully explore exactly where the age cut-off might be, to optimize the inclusion criteria for that trial," Dr Gourlay says.

"For example, is 75 the right age cut-off or do people between 70 and 75 also benefit?

"We don't have enough people to analyze by age, yet, but we will have that in the relatively near future."

"In the meantime, we will get good additional data from the open-label study."

Finances and performance

The Actinogen story now becomes one of careful cash preservation - and a single-minded pursuit of a deep-pocketed partner to fund the next trial.

"We have a good balance sheet with a cash balance currently of $18.9 million and no debt," Dr Gourlay says.

"This provides us with a window of time and optionality to fully explore the trial data with potential partners and decide exactly what the optimal development path for Xanamia is."

In the three months to September 30, 2026, Actinogen reported cash outflows of $6.2 million. Closing the Xanamia study should reduce these outflows, while the company will target other cost savings.

In October, the company received a Federal Research and Development Tax Incentive of $10.8 million, or $6 million net after payment of an R&D advance to a third party. Investors exercised $5.3 million of unlisted options with underwriters picking up a shortfall.

After late January's positive futility results the company launched a $12 million placement, followed by a share placement plan (SPP) to raise up to $5 million. As you do!

Over the last 12 months, Actinogen shares have danced between 7.0 cents on January 7 this year and the November 19 post results low of 0.5 cents. Historically, the shares peaked shortly after listing in October 2007, at 55 cents.

Dr Boreham's diagnosis:

Valuation wise, Actinogen looks like another biotech equivalent of a Bachelor/Love Island/Married at First Sight pantomime villain.

But the company still hopes to be the endearing equivalent of Sara-Marie Fedele of Big Brother 'bum-dancing', bunny ears fame.

Dr Gourlay says the study set-back doesn't change the company's phase III plans, "other than having a slightly older" patient group.

"Given the attractive clinical and commercial opportunity that older patients with Alzheimer's represent, we have a reasonable and strong belief that a number of potential parties will be interested in partnering with us to take Xanamia forward for patients with mild to moderate Alzheimer's disease."

Broker Canaccord says: "while Xanamia failed, the Over 75 signal is sufficiently substantial and prospectively defined that it deserves to be interrogated in phase III rather than be discarded as data mining".

"[The] partnering picture for Xanamem remains alive in our view".

Dr Gourlay said the causal factors of Alzheimer's remained poorly understood.

"Trials like this add information to the field. Lots and lots of trials have been plain negative."

Of course, investors expect more than a trial that adds some heft to academic tomes.

In our view, Actinogen still has a decent shot in an Alzheimer's treatment market worth $US380 billion, with only sub-standard offerings.

As always with drug development, it's a case of 'time is money'.

If Xanamia had held up, the company was eyeing a potential FDA approval entreaty, with only a post-marketing confirmatory study required.

Now, any such shortcut has been abruptly curtailed.

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. The only reality shows your columnist watches are earnest stuff such as the ABC's Four Corners and SBS Insight – promise