Biotech Daily

Friday August 2, 2024

Daily news on ASX-listed biotechnology companies

*** ASX, BIOTECH DOWN: RESONANCE UP 7%;**
- MEDICAL DEVELOPMENTS DOWN 8%

*** DR BOREHAM'S CRUCIBLE: ACTINOGEN MEDICAL**

*** RESMED REVENUE UP 11% TO $7.2b; PROFIT UP 21% TO $2.3b**

*** UNIVERSAL BIO H1 REVENUE UP 19% TO $3m; LOSS DOWN 4% TO $7m**

*** CURVEBEAM PLACEMENT, RIGHTS FOR $13.6m**

*** VICTORIA UP-TO $1m FOR RESEARCH FELLOWS**

*** REDHILL JUMPS 98% ON 6-YEAR-OLD DATA**

*** PYC BUYS-BACK $29k UNMARKETABLE PARCEL SHARES**

*** L1 CAPITAL TAKES 17.5% OF ANTERIS**

*** AVITA APPOINTS ROBIN VANDENBURGH US SALES HEAD**

MARKET REPORT

The Australian stock market was down 2.11 percent on Friday August 2, 2024, with the ASX200 down 171.5 points to 7,943.2 points.

Seven of the Biotech Daily Top 40 companies were up, 26 were down, six traded unchanged and one was untraded. All three Big Caps were down.

Resonance was the best, up 0.4 cents or 6.7 percent to 6.4 cents, with 745,280 shares traded. Opthea improved 5.6 percent; Actinogen climbed 4.4 percent; Cynata, Micro-X and Prescient rose two percent or more; with Immutep up by 1.5 percent.

Medical Developments led the falls, down 3.5 cents or 7.6 percent to 42.5 cents, with 72,287 shares traded.

Avita, Cyclopharm and Polynovo lost more than six percent; Amplia and Dimerix fell five percent or more; Clarity was down 4.5 percent; Compumedics and Universal Biosensors were down more than three percent; Emvision, Mesoblast, Neuren, Paradigm, Pro Medicus, Proteomics, Starpharma, Syntara and Telix shed two percent or more; with Aroa, Clinuvel, Cochlear, CSL, Impedimed, Imugene, Nanosonics, Orthocell, Percheron, Resmed and SDI down by more than one percent.

DR BOREHAM'S CRUCIBLE: ACTINOGEN MEDICAL

By TIM BOREHAM

ASX code: ACW

Share price: 7.1 cents; **Shares on issue:** 2,711,639,883; **Market cap:** $192.5 million

Chief executive officer: Dr Steven Gourlay

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

Financials (June quarter 2024): revenue $100,000, cash outflows $5.1 million, cash balance $9.5 million, quarters of funding: 1.9, but says it has resources to late 2025.

Identifiable major holders: Biotech Venture Fund 9.2%, Dr Steven Gourlay 3.6%

An imminent trial result may validate whether Actinogen's Xanamem is 'the next Ozempic'.

Originally developed for diabetes and embraced as a weight loss drug by the beautiful people, Ozempic is also showing promise in the $US4.8 billion-a-year Alzheimer's disease treatment market.

Actinogen chief Dr Steve Gourlay says type 2 diabetes is a known risk factor for Alzheimer's and GLP-1 drugs have been shown to reduce the chance of developing the disease in diabetics.

Not surprisingly, drug companies are on the GLP-1 case, with Novo Nordisk and Eli Lilly both carrying out large phase III oral formulation trials, with an approval as early as 2027.

Xanamem shares some similar traits to the mechanisms of GLP-1 drugs, in that it improves insulin sensitivity and may share some of the same metabolic benefits in the brain. But it has been developed by Actinogen to target the toxic effects of the "stress hormone" cortisol in the brain - something that GLP-1 drugs don't do.

Xanamem also has a different safety profile.

"GLP-1 drugs work by in part by preventing your stomach emptying, which makes you feel full, with nausea as a main side effect," Dr Gourlay says. "This is not a good profile for many Alzheimer's patients who forget to eat and are already losing weight."

A bit of history

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).

In a radical course correction, Actinogen acquired Xanamem as UE2343 in 2014 from Edinburgh University, which had completed a phase I trial. Australian clinical development started in 2015.

Dr Bill Ketelbey joined the company as CEO in December 2014. Dr Ketelbey was involved in developing Aricept, which remains the leading Alzheimer's treatment despite being developed almost 30 years ago.

Dr Gourlay succeeded Dr Ketelbey in early 2021. Dr Gourlay previously worked in senior roles at Genentech and then with Dr Geoff Brooke (now Actinogen chair) at GBS Venture Partners.

As founding chief medical officer of the San Francisco-based Principia Biopharma, he helped to take two immunology programs to advanced trials, at which point Sanofi acquired the company for $US3.7 billion ($A5.5 billion).

About Xanamem

Xananem is a brain tissue cortisol synthesis inhibitor, potentially with applications for psychiatric and neuro-degenerative diseases beyond Alzheimer's and depression (such as Fragile X syndrome and cognitive impairment in schizophrenia).

Other Alzheimer's drugs work by inhibiting the formation of amyloid proteins, which form as plaques and are thought to be a key contributor to the disease. Xanamem takes a different tack by inhibiting production of cortisol, which is synthesized by an enzyme called 11 beta HSD1.

Cortisol is a naturally occurring stress hormone and essential for the body, but elevated levels over a long period are thought to contribute to both Alzheimer's and mild cognitive impairment (which can often lead to the former).

Xanamem is expected not to interact with other drugs so could be used in older patients taking medications for conditions such as cholesterol and blood pressure.

To date, Actinogen has studied 11 beta HSD1 inhibition in more than 350 patients and volunteers.

Learning from past mistakes

Actinogen has staged a remarkable recovery from the dark days of mid-2019, when its key trial - Xanadu - failed.

The study of 185-patients with clinical mild Alzheimer's disease showed Xanamem over 12 weeks worked no better than placebo. But the company cut the data another way - as you do - by examining the stored blood samples of 72 of the enrollees to see if they had 'confirmed' Alzheimer's. This was measured by elevated blood levels of a protein biomarker called pTau181 or phosphorylated tau.

The results showed half the patients had a low level of the biomarker and showed no progression at all - and thus possibly didn't have Alzheimer's disease in the first place.

In patients with a high level of the biomarker, indicating 'real' Alzheimer's, twice as many Xanamem-treated patients had stable or improved disease relative to placebo, with a 60 to 80 percent reduction in disease progression over 12 weeks.

On trial (1)

The company is running two phase II trials, the first of which is about to report results.

The phase IIa trial, Xanacidd, is studying the ability of Xanamem to improve cognitive dysfunction (difficulty thinking, remembering and solving problems) associated with major depression.

The trial has completed visits with 167 patients enrolled and will report top-line data on the primary endpoint of cognition, with secondary endpoints including reducing depression.

Over six weeks, the patients receive 10 milligrams of either Xanamem or a placebo daily (in some cases in addition to their existing anti-depressant drugs).

The primary endpoint is a composite of three computerized Cogstate tests for working memory and attention. A key secondary endpoint is the commonly used Montgomery-Asberg Depression Rating Scale.

Dr Gourlay says that while anti-depressants might improve mood, they do little for the cognitive impairment or foggy thinking of patients with depression.

"Demonstrating improved cognition in patients with depression could pave the way for Xanamem to be used in other psychiatric conditions such as schizophrenia, where cognitive impairment is profound."

On trial (2)

A second phase IIb trial, Xanamia, is recruiting patients with biomarker-positive mild to moderate Alzheimer's disease. The 220 patients are dosed over 36 weeks - also with 10mg - and are included if they have elevated p-Tau blood levels.

The patients are assessed on both cognition and Alzheimer's progression.

"We believe we have already validated the target by showing improved cognition in healthy older volunteers and a potentially a big clinical benefit in biomarker-positive patients with Alzheimer's," Dr Gourlay says.

Interim results - covering the first 100 patients at the 24-week mark - are expected in mid-2025. Final results are expected in mid-2026.

What next?

Dr Gourlay says getting a depression drug to market would require at least two more pivotal trials, about twice the size of the current trial.

He expects the depression drug to be progressed with a partner, while the company would like to expand the current Alzheimer's study to more sites, off its own bat.

"This potentially could form one of the pivotal studies," he says. "We would start the second phase III pivotal study as soon as we could and hopefully that would bring forward approval by a year or so."

The company expects FDA breakthrough designation for Alzheimer's and potentially for cognitive impairment in depression.

Eyeing the competitive landscape

Plenty of Alzheimer's drug development is taking place but so far there is no magic bullet.

In July, the FDA approved Eli Lilly's Kisunla (donanemab), a monoclonal antibody infusion for mild cognitive impairment or early Alzheimer's that targets the amyloid protein.

In February, sales of Biogen's first amyloid antibody, Aduhelm (aducanumab), were discontinued, reportedly because of poor sales and/or side effects.

Biotech scholars will recall that the FDA in 2021 approved Aduhelm on the basis of only one positive phase III trial, snubbing the advice of its own 10-member expert committee. (Three of them quit, with one describing the decision as the worst drug approval in history).

Dr Gourlay says such drugs have set a low bar for approval because of their modest benefits and need for intensive safety monitoring and side effects.

"The amyloid drugs have probably shown the best data they can, so we are unlikely to see a better story emerge with amyloid as the target."

Finances and performance

Actinogen has completed a placement and rights offer that raised $8.9 million, at 2.5 cents apiece. Holders received one share for every 15 held, plus one option for every two shares subscribed for.

The options are exercisable at five cents within three years. The company also has unlisted options exercisable at 3.75 cents, expiring in 2026 and if fully exercised all of these options would raise up to $16 million.

Actinogen's new CFO Will Souter says that with around $9.5 million in the bank and an expected $8 million Federal Research and Development Tax Incentive, the company is funded to late 2025.

Current cash burn is "elevated" but is expected to subside in the December quarter with the completion of the cognition/ depression trial.

Unlike many other drug developers, Actinogen carries out most of the clinical work in house, rather than cede it to a contract research organization (CRO).

"It is significantly cheaper than using a CRO and trial staff at sites love the direct relationship," Dr Gourlay says.

Over the last year Actinogen shares have traded between two cents (in a prolonged period between August 2023 and January 2024) and the current zenith. Historically the shares peaked shortly after listing in October 2007, at 55 cents and hit a nadir of one cent in September 2019.

Dr Boreham's diagnosis:

Globally, 55 million people have Alzheimer's disease - 500,000 in Australia - and at 2020 the World Health Organisation rated the disease as the seventh-biggest cause of death.

If Xanamem succeeds, Edison Research estimates peak sales of $US5 billion in the early 2030s, while depression is a $US2 billion market.

Naturally, Actinogen has a long way to go, but Dr Gourlay is heartened by some big-ticket transactions in the neurology sector at pre-approval or even early stage.

Last December, Bristol Myers Squibb acquired the Nasdaq-listed Karuna Therapeutics for $US14 billion. Karuna is developing its Karxt agent for schizophrenia and Alzheimer's, having lodged an FDA submission for the former. Karxt works by reducing dopamine levels in the brain, so we there's more than one way to skin this rabbit.

As for the Ozempic-style drugs, do they pose a competitive threat to Actinogen in the same manner as Resmed (sleep apnoea) and CSL's Vifor arm (kidney dialysis)?

Dr Gourlay's premise is there will be a place for the 'Ozempics' in the Alzheimer's space: "they probably will be better than the anti-amyloids but they won't be the safe and effective oral treatment, such as the one we are developing".

So, the short answer is "no".

Ozempics or not, the Alzheimer's treatment Olympics is still an open race to the winner's podium.

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort – or a gold medal.

RESMED INC

Resmed says revenue for the year to June 30, 2024 was up 10.95 percent to $US4,685,297,000 ($A7,192,000,000), with net profit after tax up 20.7 percent to $1,478,350,000 ($A2,269,000,000).

Resmed said the increase in revenue was driven by ongoing patient and customer demand for its sleep health and breathing disorder devices and software.

The company said it provided both US generally accepted accounting principles (GAAP) and non-GAAP data.

Resmed said it "uses non-GAAP information internally in planning, forecasting, and evaluating the results of operations in the current period and in comparing it to past periods ... [and] believes this information provides investors better insights".

Biotech Daily quotes the non-GAAP data.

Resmed said it would pay an unfranked dividend up 10.4 percent to 5.3 US cents per Chess depository interest (CDI), with 10 CDIs equal to one US share, for the three months to June 30, for a record date of August 15, to be paid on September 19, 2024.

Resmed chief executive officer Mick Farrell said the company's results showed "strong performance across all sectors of our business".

"Ongoing patient and customer demand for our best-in-class products and software solutions is incredibly strong, driving solid growth across our devices, masks, and software businesses," Mr Farrell said.

"Nearly 2.5 billion suffer from major sleep health and breathing disorders," Mr Farrell said.

"As the market leader in these significantly under-penetrated markets, we're well-positioned as the clear leader to drive increased market penetration, demand generation, and accelerate growth for our businesses," Mr Farrell said.

"We're laser-focused on increasing awareness with the fast-growth population of sleep-health-interested consumers, creating virtual pathways that expand access to therapies, while offering a broad portfolio of medical device products, software solutions, and beyond, as we deliver value for all Resmed stakeholders," Mr Farrell said.

The company said non-GAAP diluted earnings per share was up 19.9 percent to $US7.72 and it had cash and equivalents of $US238,361,000 at June 30, 2024, compared to $US227,891,000 at June 30, 2023.

Resmed fell 59 cents or 1.8 percent to $31.80 with 6.3 million shares traded.

UNIVERSAL BIOSENSORS

Universal Biosensors says revenue for the six months to June 30, 2024 was up 19.1 percent to $3,095,076, with net loss after tax up 202.6 percent to $7,232,875.

Universal Biosensors said sales of its biosensors for oncology, coagulation, women's health and fertility, water testing, the wine industry and veterinary diabetes, for the three months to June 30, 2024 was up 24.7 percent to $1,625,566.

The company said underlying net loss after tax was determined by adjusting statutory net loss after tax for certain non-operational items, and that its underlying net loss after tax for the six months to June 30, 2023 was adjusted for one-off income of $5,110,786.

A Universal Biosensors spokesperson told Biotech Daily that the unrecognized $5,110,786 was made up of $2,896,764 in accrued marketing support costs and $2,214,022 in accrued licence fees payable to Siemens which were no longer payable.

The company said diluted loss per share tripled from one cent to three cents, with net tangible assets per security unchanged at 11 cents and cash and cash equivalents of $16,675,984 at June 30, 2024 compared to $16,323,900 at June 30, 2023.

Universal Biosensors fell half a cent or 3.6 percent to 13.5 cents.

CURVEBEAM AI

Curvebeam says it hopes to raise up-to $13.6 million at 18.0 cents a share in a $4.0 million placement and $9.6 million, non-underwritten, one-for-six entitlement offer.
Curvebeam said the issue price was a 25.9 percent discount to the 10-day volume weighted average price of 24.3 cents.
The company said the two-tranche placement's second tranche was subject to shareholder approval of an entity associated with director Hashan De Silva.
Curvebeam said the funds were for research and development, intellectual property, inventory and supply costs, sales, marketing, general administration and working capital.
The company said it would offer institutional and retail rights offers, with the retail record date of August 6, opening on August 8 and closing on August 22, 2024.
Curvebeam said E&P Capital and Canaccord Genuity (Australia) were joint lead managers to the placement.
Curvebeam was in a trading halt and last traded at 23.5 cents.

VICTORIA GOVERNMENT

The Victoria Government says applications are open for its $1 million Fostering Achievement in Research Fellowships (FAIR).
A media release from Victoria's Minister for Medical Research Ben Carroll said the fellowships were open for "early-to-mid-career researchers" who were unsuccessful in the Federal Government's National Health and Medical Research Council funding.
The Government said the program would use existing grant review processes and co-funding from organizations to help researchers continue their work and apply for future national grants.
The Victoria Government said that there was only a 10 to 15 percent success rate in applications for research grants in Australia.
The Government said the fellowships would "strengthen diversity and inclusion in Victoria's medical research sector by supporting outstanding emerging and future leaders who face challenges to success including women, Aboriginal and Torres Strait Islander peoples, people with disability, and the LGBTQIA+ community".
For more information and applications, go to: www.veski.org.au/fair-fellowships/.

REDHILL BIOPHARMA

Redhill climbed 97.9 percent on the Nasdaq to 76 US cents ($A1.17) on the journal publication of phase III RHB-104 for Crohn's disease data, first released in 2018.
In 2010, Israel's Redhill bought Myoconda (RHB-104), Heliconda (RHB-105) and Picoconda (RHB-106) from the Sydney-based Giaconda (BD: Aug 17, 2010) and according to its website, Giaconda founder Prof Tom Borody was an advisor.
In 2018, Redhill said its 331-patient, phase III trial of RHB-104 for Crohn's disease was superior for remission at week-26 compared to placebo (p = 0.013) (BD: Jul 31, 2018).
Redhill said the study of RHB-104 in the indication was based on the hypothesis that Crohn's disease was caused by Mycobacterium avium subspecies paratuberculosis (MAP) infection in susceptible patients.
Today, the company said the article, titled 'Randomized, Double-Blind, Placebo-Controlled Study of Anti-Mycobacterial Therapy (RHB-104) in Active Crohn's Disease' was published in Antibiotics with the article available at: https://www.mdpi.com/2079-6382/13/8/694.
On the Nasdaq, Redhill was up 37.59 US cents or 97.87 percent to 76.0 US cents ($A1.17) with 6.1 million shares traded.

PYC THERAPEUTICS

PYC says it has bought back 278,542 shares at an average price of 10.5 cents a share in unmarketable parcels worth $500 or less, held by 206 shareholders.
Earlier this year, PYC said it had established an unmarketable parcels facility for holders at the record date of May 22, 2024 (BD: May 24, 2024).
Today, the company said the shares were sold on market by Euroz Hartleys and the payment was dispatched to shareholders on August 1, 2024.
PYC was up 0.1 cents or one percent to 9.7 cents with 5.3 million shares traded.

ANTERIS TECHNOLOGIES

L1 Capital Pty Ltd says it has increased its substantial shareholding in Anteris from 2,843,398 shares (15.96%) to 3,693,941 shares (17.48%).
The Melbourne-based L1 Capital said that on April 12, 2024 it bought 413,043 shares on-market for $9,499,989, or $23.00 a share, and on July 30, 2024 it purchased 437,500 shares in a placement for $7,000,000, or $16.00 a share.
Last week, Anteris said that it had raised $30.0 million in an institutional placement at $16.00 a share for its Duravr transcatheter heart valve (BD: Jul 24, 2024).
Anteris fell 15 cents or one percent to $15.00 with 9,067 shares traded.

AVITA MEDICAL INC

Avita says it has appointed Robin Vandenburgh as its head of US sales, effective from August 6, 2024.
Avita said Ms Vandenburgh would “spearhead Avita Medical’s efforts to expand its market presence and drive sales growth in the US”.
The company said Ms Vandenburgh had more than 25 years of experience in healthcare sales, having worked for Smith & Nephew, Aureon Biosciences, St Jude Medical and Johnson & Johnson.
Avita fell 20 cents or 6.8 percent to $2.73 with 581,827 shares traded.