Biotech Daily

Friday November 25, 2022

Daily news on ASX-listed biotechnology companies

*** ASX UP, BIOTECH EVEN: NANOSONICS UP 11%;**
- GENETIC SIGNATURES DOWN 10%

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

*** FEDERAL $50m FOR 10 MEDICAL RESEARCH PROJECTS**

*** QUEENSLAND BACKS AEGROS HQ MOVE TO BRISBANE**

*** ANATARA RIGHTS RAISE $525k; TOTAL $1.4m; $308k SHORTFALL**

*** MACH7 $1.52m FOR HONG KONG ST PAUL'S IMAGE SYSTEMS**

*** INOVIQ 1st US EXO-NET SALES CAMPAIGN, HTERT DIRECT SALES**

*** ARGENICA STARTS 3rd ARG-007 COHORT**

*** NEW ZEALAND APPROVES INVEX PRESENDIN IIH TRIAL**

*** MEDLAB UK MARIJUANA NANABIS 'COMPASSIONATE' APPROVAL**

*** INCANNEX: EUROFINS TO MANUFACTURE CANNQUIT FOR ADDICTION**

*** EXOPHARM TAKES $961k RADIUM RDTI LOAN**

*** ARGENICA AGM 13% OPPOSE CHAIR GEOFF POCOCK**

*** NANOSONICS LOSES FOUNDER, FORMER CHAIR MAURIE STANG**

MARKET REPORT

The Australian stock market was up 0.24 percent on Friday November 25, with the ASX200 up 17.7 points to 7,259.5 points. Thirteen of the Biotech Daily Top 40 stocks were up, 14 fell, 10 traded unchanged and three were untraded.

Nanosonics was the best, up 46 cents or 11.1 percent to $4.62, with 952,962 shares traded. Compumedics climbed 6.8 percent; Cyclopharm was up five percent; Actinogen improved 4.35 percent; Emvision, Immutep, Micro-X, Prescient and Proteomics were up more than three percent; Paradigm and Polynovo rose more than two percent; Atomo was up 1.75 percent; with CSL, Pro Medicus and Resmed up by less than one percent.

Genetic Signatures led the falls, down nine cents or 9.8 percent to 82.5 cents, with 15,160 shares traded. Avita, Patrys, Universal Biosensors and Volpara fell more than four percent; Dimerix, Next Science and Nova Eye were down more than three percent; Kazia and Neuren shed more than two percent; Opthea and Telix were down one percent or more; with Clinuvel, Cochlear and Medical Developments down by less than one percent.

DR BOREHAM'S CRUCIBLE: ACTINOGEN MEDICAL

By TIM BOREHAM

ASX code: ACW

Share price: 12 cents; **Shares on issue:** 1,797,393,817; **Market cap:** $215.7 million

Chief executive officer: Dr Steven Gourlay

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

Financials (September quarter 2022): revenue nil, cash outflows $3.38 million, cash balance $17.2 million, quarters of available funding: five

Identifiable major holders: Biotech Venture Fund 13.77%, Dr Steve Gourlay 3.7%, Edinburgh University Technology Fund 2.68%, Tisia Nominees (Henderson family) 1.86%, JSC Wealth Management 2.49%.

Actinogen chief Dr Steve Gourlay does not demur on his assessment of the company's lead drug Xanamem, to treat the notoriously difficult Alzheimer's disease.

"This is probably going to be the most successful drug in the world's history because nothing else really works in Alzheimer's and this appears to do the trick," he says.

Dr Gourlay's confidence stems from the drug's success to date in improving the cognition of patients with Alzheimer's disease, which is forecast to be the world's number two killer behind heart disease.

The company is about to launch its biggest clinical effort to date: a phase IIb study enrolling 330 patients with mild to moderate cognitive impairment.

Dr Gourlay rates the trial as having a 70 to 80 percent chance of success, because it uses the same patients and endpoints as a recently-completed smaller study. But just to hedge its bets, the company is launching a smaller trial to treat cognitive impairment in major depression sufferers.

From actinomycetes to Alzheimer's

Actinogen listed in October 2007 at 50 cents apiece and initially was focused on soil-derived antibiotic-like compounds called actinomycetes (hence the Actinogen name).

Xanamem hails from Edinburgh University, which completed an early-stage trial of a predecessor drug with the $25 million backing of the Wellcome Trust charity. Clinical development of Xanamem started in 2013.

Actinogen acquired Xanamem by purchasing Corticrine Limited, an arm of Edinburgh University, in August 2014.

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 chairman) at GBS Venture Partners.

Dr Gourlay returned to the US and with some "Genentech mates" and took on novel small molecule development at Principia Biopharma in San Francisco. They progressed two small molecules from pre-clinical to phase III and floated the company on the Nasdaq in 2018, before selling out to Sanofi for $US3.7 billion ($A5.5 million) in 2020.

All about Xanamem

Xanamem 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).

The drug acts by inhibiting the 11 beta HSD1 enzyme. To achieve this, any drug first must negotiate the blood-brain barrier, the organ's natural defence against foreign agents. Dr Gourlay stresses the drug is not based on amyloid mechanisms, on which most of the other Alzheimer's drug developers have focused.

"The drug has the potential to be rapidly cognitive enhancing, improving memory in a few weeks," Dr Gourlay says. "It is potentially disease modifying and may well be an anti-depressant as well."

More than 300 people have been treated for up to 12 weeks without any safety concerns.

"We have seen a positive effect on attention and working memory and cognition in two independent, placebo-controlled trials in healthy, older volunteers," he says.

Actinogen also has a quiescent secondary program underway to treat Fragile X syndrome, a genetic condition resulting from the mutation of the X chromosome in new-borns.

Out of the poo after Xanadu

Actinogen's prospects looked far from upbeat in May 2019, when the results of its then key trial, Xanadu, proved a 'box office' flop in the same way as the 1980 musical of the same name (and vale Olivia Newton-John).

The company's shares lost four-fifths of their value after the results showed Xanamem worked no better than placebo, on a 185-patient sample of mild Alzheimer's sufferers.

The Xanadu data was re-examined using a blood test to choose the patients with amyloid-based, 'real' Alzheimer's disease. Strong signals of protection against cognitive decline were evidenced in these 34 patients, who had elevated levels of the biomarker phosphorylated tau, or p-Tau, a protein blood biomarker indicative of Alzheimer's.

The prophylactic effect was measured by a US Food and Drug Administration-approved endpoint called the Clinical Dementia Rating Scale-Sum of Boxes (CDR-SB). A so-called functional endpoint, CDR-SB assesses patients on six criteria and rates them on a scale of 0.5 to 3.0 ranging from questionable impairment to severe dementia.

Twice as many Xanamem-treated patients had stable or improved disease relative to placebo, meaning there was a 60 to 80 percent reduction in disease progression over 12 weeks. Put in context, the injectable drug called Lecanemab had a 27 percent reduction in disease over 18 months. Pundits expect the FDA to approve the drug.

Alzheimer's v dementia

"There are 500,000 people in Australia with dementia," Dr Gourlay says. "Two thirds of people with dementia have Alzheimer's, which means they have amyloid in the brain.

"But others might have Lewy body dementia, strokes, fronto-temporal dementia or strokes."

Given that, the original Xanadu trial certainly had at least one-third of patients with non-Alzheimer's dementia - and maybe even more. Those patients typically do not progress over a short period such as 12 weeks, whereas Alzheimer's sufferers do.

Dr Gourlay says the company's approach is "not data dredging, but the real deal" using a rigorous new protocol.

"One of the reasons I took the job is that I looked at the clinical results from that study in detail," he says. "I knew the 10-milligram dose had been proved to be active and there were some sub-groups where patients really benefited. We have now proved that very clearly".

More trials, more validation

In April this year, the company reported the top-line results from a phase Ib dose ranging component of a study, called Xanamia.

There's a lot of science-y stuff in the presentation, but the digestible bottom line is that Xanamem was safe and effective for dosages at or below 10 milligrams.

The results confirmed the findings of an earlier, smaller trial called Xanahes.

Mamma mia! It's Xanamia

The next whopper stage is the Xanamia phase IIb trial to study improvements in cognitive ability for patients with biomarker-confirmed early Alzheimer's.

The placebo-controlled study aims to sign up 330 patients over multiple countries, including Australia, with enrolment starting in early 2023.

“We are quite optimistic about enrolment because it is a simple oral drug taken once a day, not a complicated antibody infusion,” Dr Gourlay says.

Describing Xanamia as a quasi-phase III trial, Dr Gourlay hopes the US Food and Drug Administration (FDA) will view it as a pivotal trial for registration purposes, although a second phase III effort would be required.

Results are expected towards the end of 2024.

Tackling the black dog

The company expects to start enrolling a 160-patient proof-of-concept depression trial within the next month or so, with results in late 2023 or early 2024.

“We didn’t want to put all the eggs in one basket and having a second indication makes the story just that much bigger,” Dr Gourlay says.

He says that while anti-depressants might improve mood, they do nothing for the “foggy thinking” of Alzheimer’s patients.

“The hope is that Xanamem might have a dual action in improving depression and cognitive impairment,” he says.

Proving efficacy with depression could pave the way for Xanamem to be used in other psychiatric conditions, such as schizophrenia.

Aduhelm underwhelms

Controversially, the FDA last year approved Biogen’s Alzheimer’s drug Aduhelm (aducanumab), which had only just entered phase I trials.

In doing so, the agency snubbed the view of its own 10-member expert committee, with three quitting and one dubbing the decision “the worst drug approval in recent history”.

Aduhelm targets the build-up of amyloid plaque in the brain after its formation.

Dr Gourlay opines that Biogen was overly ambitious charging $US56,000 for a drug with accelerated - rather than full - FDA approval.

Biogen is trying again with the aforementioned Lecanemab, which has been subject to an 1,800-patient study. The FDA is expected to approve the fortnightly antibody infusion.

Finances and performance

Actinogen had $13 million of cash at the end of September quarter, with research and development tax incentive received in October taking the tally to around $17 million.

Cash burn will step up as the trials progress (September quarter outflows were $3.38 million).

US research house Edison estimates Actinogen will burn $39 million in 2023-'24 and will need $390 million to fund both clinical programs to global marketing approvals.

The company last raised equity ($12.4 million) in December last year.

Over the last year Actinogen shares have traded between four cents (mid-June this year) and 19 cents (early November last year).

Historically the shares peaked shortly after listing in October 2007, at 55 cents and plumbed to a nadir of one cent in September 2019.

Dr Boreham's diagnosis:

Despite drug companies throwing not just the kitchen sink but the bath as well at the problem, Alzheimer's is as intractable problem as ever.

What drugs are approved for Alzheimer's disease?

Aducanumab (as it's generically known) is the only disease-modifying medication currently approved to treat Alzheimer's.

"Whichever way you look at it, it is a gazillion dollar opportunity," Dr Gourlay says.

He notes that three independent trials have shown that Xanamem works.

If the FDA agrees and eventually approves the drug, Actinogen will be worth many billions of dollars - even "gazillions" - rather than the current $220 million.

While Dr Gourlay rates Xanamia as a 70 to 80 percent chance of success, he's a realist who believes there's a 50 percent chance of the drug actually getting to market.

"Some US [Alzheimer's drug developers] are worth $US2.5 billion and they don't have anywhere near the amount of data that we have," Dr Gourlay says.

Meanwhile, Edison ascribes only a 10 percent chance of marketing success, while Bell Potter concurs that it's more a 50-50 bet.

Nonetheless, Edison values Actinogen shares at 36 cents - thrice the level they're at now - while Bells plumps for a more conservative 15 cent valuation.

So, take your pick.

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort – as far as he can remember.

FEDERAL GOVERNMENT

The Federal Government says the National Health and Medical Research Council 'synergy grant scheme' has provided $50 million for 10 medical research projects.
In a media release, the Minister for Health and Aged Care Mark Butler said an RMIT University research program, led by Prof Ricky O'Brien, would receive $5 million to develop integrated technology "to understand the heart's response to radiation".
The Federal Government said that other synergy grants would support research into childhood cancers, malaria, the link between body clock dysfunction and mood disorders, and understand and reduce the impact of sleep disturbance on the development of dementia.
The Government said it would prove $23.1 million for research infrastructure costs for 23 medical research institutes and $5.7 million for 44 grants for equipment for health and medical research.

QUEENSLAND GOVERNMENT, AEGROS

The Queensland Government says it has invested in Aegros' $352 million manufacturing facility in Brisbane for blood fractionation and plasma therapeutic use.
Aegros founder and chair Prof Hari Nair told Biotech Daily that with co-founder and managing-director John Manusu the company expected to have the same blood fractionation output in Australia as CSL.
Prof Nair and Mr Manusu were formerly the managing-director and chair of Nusep, which later became Memphasys (BD: Nov 30, 2012; Dec 2, 2013).
Today, Prof Nair said the Queensland Government investment was confidential but the $350 million facility would increase in value to be worth up to $500 million.
Prof Nair said his company was moving its headquarters from Sydney to Brisbane but that the existing fractionation facility would continue in Sydney.
The media release from Queensland Treasurer and Minister for Trade and Investment Cameron Dick said that Aegros was a plasma therapeutics company focused on the development of its 'Haemafrac' process to fractionate hyper-immunes from plasma.
The Government said that Aegros, would move its headquarters from Sydney to the "advanced production facility at Biopark Australia" in Brisbane.
The media release said that "through the process of fractionation, plasma proteins are separated, purified, and concentrated for different therapeutic uses".
Mr Dick said he congratulated Aegros on their move, which would "bring more good, highly-skilled jobs for Queenslanders".
"Once Aegros has secured all necessary approvals and finance, the two-year construction will support an estimated 230 jobs," Mr Dick said.
"Aegros estimates that its facility will create 348 long-term jobs across its first four years of operation… [and] the company aims to use its unique advanced technology to develop and manufacture lifesaving therapeutic blood products," Mr Dick said.
"Therapies produced from the plasma in blood can help fight infection or diseases such as Lupus and type 1 diabetes, can promote blood clotting, prevent shock and assist with post-surgical recovery," Mr Dick said.
"The Springfield, [Brisbane] facility will have the capacity to process one million litres of human plasma per year," Mr Dick said.
"Australia imports almost half of the essential plasma and blood products used to develop biopharmaceuticals, so this new facility will position Aegros to meet the needs of the domestic market," Mr Dick said.
Aegros is a public unlisted company.

ANATARA LIFESCIENCES

Anatara says it raised $524,691 of a hoped for $832,482 in its one-for-three, rights offer at 3.5 cents a share, taking the total to $1,389,691, and will place the shortfall.
In October, Anatara said had commitments to raise $865,000 in a placement and would offer a non-renounceable rights offer to raise a further $832,000 (BD: Oct 21, 2022)
At that time, the company said that participants in the raising would receive one attaching option for two new shares, exercisable at seven cents by December 11, 2025.
Today, Anatara said it would seek to place the $307,791 shortfall within three months.
Anatara was untraded at four cents.

MACH7 TECHNOLOGIES

Mach7 says it has a $1.52 million agreement with Hong Kong's St Paul's Hospital to replace its picture archiving and communications systems (PACS).
The company said the agreement included its entire imaging platform, with a one-year contract value of $1 million and a total contract value of $1.52 million.
Mach7 managing-director Mike Lampron said St Paul's Hospital was "a prestigious institution in Hong Kong and this agreement allows us to extend our footprint in the area as well as solidify our offerings throughout the Asia Pacific Region".
Mach7 was up three cents or 4.6 percent to 68 cents.

INOVIQ (FORMERLY BARD1 LIFE SCIENCE)

Inoviq says it has begun its first US Exo-Net sales campaign and will revert to direct sales for its hTERT adjunct diagnostic for bladder cancer.
In July, Inoviq said the Plymouth Meeting, Pennsylvania-based Percorso Life Sciences would provide sales and logistics for a rollout of Exo-Net in the US (BD: Jul 21, 2022).
In 2021, the then Bard1 said Exo-Net was designed to capture exosomes from body fluids and cell culture for diagnostic and therapeutic purposes (BD: Jan 28, 2021).
Today, Inoviq said Percorso had begun the first sales campaign for Exo-Net targeting more than 1,000 researchers involved in extracellular vesicle research and expected to deliver US-based Exo-Net revenue by July 2023.
Inoviq said that from early January 2023, it would sell its human telomerase reverse transcriptase (hTERT) directly to laboratory customers in the US, for which Percorso would provide warehousing and logistic services.
Inoviq was up 3.5 cents or 6.5 percent to 57.5 cents.

ARGENICA THERAPEUTICS

Argenica says it has dosed the third cohort of its 32-subject, phase I trial of ARG-007, with no serious safety issues 24 hours after dosing.
Earlier this month, Argenica said it would progress to the second cohort following independent review of first cohort safety data (BD: Nov 2, 2022).
Last month, the company said the first cohort of eight healthy subjects had been dosed, indicating "good safety and tolerability" (BD: Oct 26, 2022).
Today, Argenica the phase I trial was "designed to assess the safety and tolerability of ARG-007 across four cohorts of healthy adult volunteers, with each cohort receiving an ascending dose of ARG-007".
Argenica was up four cents or 7.4 percent to 58 cents.

INVEX THERAPEUTICS

Invex says it has New Zealand Medicines approval for its 240-patient 'Evolve' phase III trial of Presendin for idiopathic intracranial hypertension (IIH).
In October, Invex said it "activated" its first Australia and UK sites after it won ethics approval for three additional sites of its up-to 40 sites trial (BD: Sep 30, Oct 24, 2022).
In July, the company said the randomized, placebo-controlled, double-blind trial would test the safety and efficacy of Presendin, or sustained release Exenatide, once weekly over 24 weeks (BD: Jul 4, 2022).
Invex fell 5.5 cents or 9.2 percent to 54 cents.

MEDLAB CLINICAL

Medlab says it has UK Medicines and Healthcare Product Regulatory Agency approval for its one-to-one tetrahydrocannabinol and cannabidiol Nanabis oral spray.
Medlab said the marijuana derived Nanabis would have the UK alternative name of Nanadol and was approved for use in the UK Named Patient Program and compassionate areas as an unapproved medicine, with the London-based WEP Clinical as its distribution partner.
The company said the Nanabis would be provided to UK patients for pain, including bone cancer pain, and patients would be charged a "compassionate price for access to the medicine".
Medlab said the product was already manufactured and was clearing importation approval with the UK Home Office, for potential shipment in January 2023.
Medlab was up one cent or 0.1 percent to $8.01.

INCANNEX HEALTHCARE

Incannex says it has an agreement with Eurofins Scientific to manufacture its marijuana-based chewable products for nicotine and opioid addition.
Incannex said the two combination drug assets, Cannquit Nicotine and Cannquit Opioid, were transferred to it as a result of its acquisition of the Apirx, marijuana and psychedelics company, for about $125 million (BD: Aug 5, 2022).
The company said Cannquit Nicotine combined nicotine and cannabidiol within a controlled-released medicated chewing gum, and that Cannquit Opioid combined cannabidiol and an "off-patent prescription opioid antagonist, and/or partial agonist-antagonist within the formulation".
Incannex did not disclose the commercial terms but said that the Luxembourg-based Eurofins would develop and manufacture the products to be used in clinical trials to assess the safety and efficacy of the drugs.
Incannex chief scientific officer Dr Mark Bleackley said "opioid and nicotine addiction are significant health problems and a major burden on health systems throughout the world".
"Cannquit products are designed to improve established therapies for the treatment of addiction…. they do this by adding [cannabidiol], which is known to reduce cravings and anxiety which is critical for breaking the addiction cycle," Dr Bleackley said.
"Both [cannabidiol] and the act of chewing, are conducive to stress and anxiety reduction," Dr Bleackley said.
Incannex fell one cent or 3.9 percent to 24.5 cents with 2.7 million shares traded.

EXOPHARM

Exopharm says it has borrowed $961,000 from Radium Capital, up to 80 percent of its rebate under the Federal Government Research and Development Tax Incentive program.
Exopharm said the advance from the Melbourne-based Radium was “expected in the next week,” and was at a compounding interest rate of 1.17 percent a month, with repayment timed to coincide with the receipt of its tax incentive, expected by November 30, 2023.
Exopharm fell 0.1 cents or 1.1 percent to nine cents.

ARGENICA THERAPEUTICS

Argenica says its annual general meeting saw up to 12.79 percent dissent against the re-election as a director of non-executive chair Geoff Pocock.
Argenica said that all other resolutions passed easily but the re-election of Mr Pocock had 4,742,986 votes (12.79%) against and 32,327,254 votes (87.21%) in favor.
According to its most recent filing, Argenica had a total of 86,922,250 shares, meaning the votes against Mr Pocock amounted to 5.45 percent of the company, sufficient to requisition extraordinary general meetings.

NANOSONICS

In an Appendix 3Z Final Director’s Interest notice Nanosonics founder Maurie Stang says he retired from the company, effective from November 18, 2022.
In May, Nanosonics said Steve Sargent would replace Maurie Stang as chair, effective from July 1, 2022, with Mr Stang continuing as deputy chair until he retired in November (BD: May 31, 2022).
The company said Mr Stang was a founder of the company, joining the board in 2000 and chair since 2007.
In his address to the annual general meeting Mr Sargent said that Mr Stang had “made an enormous contribution to Nanosonics and the broader infection control community over the last two decades”.
“In addition to listing Nanosonics on the stock exchange and guiding its growth into a successful international business, Maurie has created a number of other very successful businesses in the healthcare sector,” Mr Sargent said.
“He is one of Australia’s leading authorities in medical technologies, infection control and biosciences,” Mr Sargent said.
Mr Sargent said that Mr Stang would chair the informal Innovation and Infection Control Advisory Committee to advise the company.
“I am personally very thankful and appreciative of Maurie’s guidance and advice over the last six years I have been on the board,” Mr Sargent said.
Nanosonics was up 46 cents or 11.1 percent to $4.62 with 952,962 shares traded.