Biotech Daily

Friday June 18, 2021

Daily news on ASX-listed biotechnology companies

*** ASX, BIOTECH UP: PRESCIENT UP 35%; OPTISCAN DOWN 16%**

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

*** SUDA TO RAISE $3m FOR IMPERIAL COLLEGE T-CELL CANCER THERAPY**

*** STARPHARMA: 'SPL7013 KILLS SARS-COV-2 VARIANTS, IN-VITRO'**

*** BRAZIL OKAYS PARADIGM PPS FOR MPS VI TRIAL**

*** ZELIRA, CURTIN UNI IMPROVE MARIJUANA BRAIN DELIVERY, IN MICE**

*** CLIME TAKES 9% OF MACH7**

*** NICHOLAS MARSHALL REPLACES CARDIEX CO-SEC PHILIP LEIGHFIELD**

MARKET REPORT

The Australian stock market was up 0.13 percent on Friday June 18, 2021, with the ASX200 up 9.9 points to 7,368.9 points.

Twenty-five of the Biotech Daily Top 40 stocks were up, 10 fell, three traded unchanged and two were untraded. All three Big Caps were up.

Prescient was the best on no news, up five cents or 34.5 percent to 19.5 cents, with 11.5 million shares traded.

Patrys climbed 22.5 percent; Imugene and Proteomics improved more than 14 percent; Telix was up 11.7 percent; Paradigm and Starpharma climbed more than nine percent; Clinuvel, Mesoblast and Orthocell were up more than seven percent; Avita and Impedimed improved more than four percent; Nanosonics and Pro Medicus were up three percent or more; Antisense, Cyclopharm, Medical Developments and Resmed rose more than two percent; Cochlear, CSL, Cynata, Kazia, Neuren, Oncosil and Pharmaxis were up more than one percent; with Polynovo, Universal Biosensors and Volpara up by less than one percent.

Optiscan led the falls for the second day in a row, down four cents or 16 percent to 21 cents, with 2.1 million shares traded. Opthea lost 13.5 percent; Resonance retreated 5.9 percent; Actinogen and Alterity were down three percent or more; Dimerix and LBT shed more than two percent; Compumedics, Genetic Signatures and Next Science were down one percent or more.

DR BOREHAM'S CRUCIBLE: ACTINOGEN MEDICAL

By TIM BOREHAM

ASX code: ACW

Market cap: $215.9 million; **Share price:** 13 cents; **Shares on issue:** 1,660,558,547

Chief executive officer: Dr Stephen Gourlay

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

Financials (March quarter 2021): revenue nil, cash outflows $1.04 million, end of quarter cash balance $15.2 million, quarters of available funding 14.6

Identifiable major holders: Biotech Venture Fund 14.5%, Dr Steve Gourlay 3.9% Edinburgh University Technology Fund 2.9%, Tisia Nominees (Henderson family) 2.8%, JSC Wealth Management 2.7%.

Whether it's ultimately justified or not, the US Food and Drug Administration's approval of an apparently less-than-effective drug for Alzheimer's disease has created a ripple of excitement around the sector.

This is evidenced by a mob called Acumen Pharmaceuticals filing for a $US100 million ($A130 million) public offering on the Nasdaq exchange, a mere two days after the FDA last week green-lighted Biogen's Alzheimer's drug Aduhelm (aducanumab).

While the Virginia-based Biogen had slaved away on its drug candidate since 1996, Acumen only entered phase I studies this year for its monoclonal antibody.

The Biogen approval and the big-ticket Acumen raising are music to the ears of Actinogen, which in early June said a much-anticipated trial of its lead candidate Xanamem would progress after receiving ethics approval.

"This molecule is looking pretty good to me. We look forward to progressing it to approval as fast we can," says CEO Dr Stephen Gourlay, who recently replaced Dr Bill Ketelbey.

The 'dirt' on Actinogen

Actinogen listed in October 2007 at 50 cents apiece, just before the onset of the global financial crisis. At the time the company 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 backing of the Wellcome Trust charity.

Actinogen acquired Xanamem by purchasing Corticrine Limited, an arm of Edinburgh University, in August 2014. The scrip deal introduced the Caledonian learning institution as a major Actinogen holder.

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 25 years ago. On February 8, Dr Ketelbey stepped down, effective immediately.

Dr Gourlay previously worked in senior roles at Genentech and then with Dr Geoff Brooke (now Actinogen chairman) at GBS Venture Partners. There, they designed clinical trials for portfolio companies.

Dr Gourlay returned to the US and with some "Genentech mates" started Principia Biopharma. They took two small molecules from pre-clinical to phase III stage, before selling out to Sanofi for $US3.7 billion.

While skeptical of Principia, at first, Dr Gourlay was "blown away by the quality of the science and the opportunity" his colleagues demonstrated.

"Actinogen is a similar story. It has really interesting clinical data, including cognition in humans and a good safety profile."

What Xanamem does

Xanamem inhibits production of cortisol, a naturally occurring stress hormone. Elevated cortical 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 an enzyme called the 11 beta HSD1 (for 1980s nostalgia freaks, not a Peter Brock Holden Special Vehicle). To achieve this, any drug first has to negotiate the blood-brain barrier, the organ's natural defence against foreign agents.

The unsuccessful trial was called Xanadu, which was not a reference to the eponymous 1980s film flop, but could have been.

The follow up study was called Xanahes, as in 'Xanamem in Healthy Elderly Subjects'.

Enrolling 30 elderly but hearty patients and primarily a safety study, the trial showed a "robust and statistically significant" improvement in cognition.

A key difference was that Xanadu involved a 10mg daily dose while Xanahes amped it up to 20mg.

Dr Gourlay believes the failed study was well-designed, but the 12-week outcome was too soon to demonstrate the chosen endpoints that typically required six months.

While the 20mg dose showed "excellent clinical efficacy", initially it was thought the 10mg dose was too low.

“We now have direct evidence that 10mg fully suppresses the enzyme function in the brain itself,” Dr Gourlay says.

Another possible reason for the Xanadu floperoo was that the cohort was “heterogeneous”. For example, it could have included patients who had had strokes.

Xanamia: here we go again

Called Xanamia, the latest Xanamem trial is designed to study improvements in cognitive ability in older volunteers, as well as patients with mild cognitive impairment in the first clinical stage of Alzheimer’s disease.

The study will be conducted at four clinics in Australia, and enrol about 100 healthy volunteers aged 50 years and over.

Xanamia has also been re-tweaked to a dose-ranging effort, Part A, testing 5mg and 10mg administrations against placebo. Part B will measure the presence or otherwise of blood bio-markers for beta amyloids, an abnormal protein.

“These biomarkers could not have been measured before,” Dr Gourlay says. “We now have better endpoints and understand the stages of the disease and can measure things in blood.”

Participants are assessed by the computerized Cogstate cognitive function tests (as used to gauge concussion in groggy footballers).

Results from Part A are expected in the first half of 2022, with the Part B (biomarker) read-out expected in 2023.

What the Biogen approval means

Biogen’s Aduhelm has a different mechanism of action to Xanamem, targeting the build-up of amyloid plaque in the brain that’s a suspected - and disputed - cause of Alzheimer’s disease.

There have been screeds of scholarly material on what the Aduhelm means in terms of the FDA’s stance on other drug approval applications where the evidence is also underwhelming.

In potted terms, two earlier trials of Aduhelm were discontinued on ‘futility’ grounds, but on further parsing of the data, the drug was deemed beneficial to a highly-dosed cohort.

More precisely, they slowed the progression of the amyloid plaques by 22 percent. The FDA itself admitted the evidence was imperfect, but with no other effective treatment available it snubbed its own expert committee and approved the $US56,000 ($A72,000) a year drug.

Three of the 10 members of the committee that recommended rejecting Aduhelm have quit in disgust, with one dubbing the agency's subsequent approval decision as "probably the worst drug approval decision in recent history".

We're not sure about that: wasn't there Thalidomide?

Dr Gourlay believes the approval 'bar' has been enshrined rather than lowered - as it was quite low in the first place.

"I have studied the FDA information carefully and believe they made a reasonable, balanced decision to approve the drug conditionally in this difficult disease," he says.

The "accelerated approval" means marketing approval depends on the results of at least one new, major trial confirming efficacy and safety.

He notes the agency's observation that the negative trial might have been influenced by a small number of "rapid progressors".

"All of that said, the efficacy levels in the approval are relatively modest and there are some safety issues associated with the drug."

Whatever the merits of Aduhelm or otherwise, the FDA approval sends a message that it is amenable to approving novel therapies for difficult to treat indications such as Alzheimer's.

Tackling Fragile X

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

Also pertaining to elevated cortisol levels, Fragile X affects about one in 2,400 to 4,000 males and one in 7,000 to 8,000 females. This discrepancy results from females having two X chromosomes, while males have the X-Y combo which increases the risk.

Fragile X normally is identified between the ages of three to five, when development problems (such as lack of language skills) become apparent.

In early February, Actinogen won rare paediatric disease designation (RPDD) status from the US Food and Drug Administration.

Benefits include lower approval hurdles, tax credits and – potentially - a valuable paediatric review voucher (PVR).

Called Xanafx, the study aims to recruit up to 40 adolescents and will be run under the auspices of Melbourne's Murdoch Children's Research Institute, a world leader in Fragile X research.

The company expects to start enrolling patients shortly with the first data read-out expected in 12 months, from what in essence is a proof-of-concept study.

Finances and performance

In October last year Actinogen launched a $10.9 million capital raising, by way of a $5 million placement and $4.9 million one-for-five rights issue. Both were struck at 2.2 cents apiece.

The rights issue fell short but was eventually filled by investors including Dr Gourlay, who chipped in $300,000 of his own dosh.

Dr Gourlay says the company is funded for both trials and possibly a third one pertaining to a mystery indication that he can't talk about.

The Murdoch Institute is stumping up for most of the Fragile X trial costs.

Battered Actinogen shares spent much of 2019 trading at one cent and lingered at two cents for much of 2020, before taking off in mid-March this year to hit their current ten year high of 18 cents on June 1. The shares peaked at 55 cents shortly after the October 2007 listing.

Dr Boreham's diagnosis:

Dr Brooke notes that Actinogen's current $260 million-ish market valuation compares with recent Alzheimer's related corporate transactions valued at $160 million to $2.4 billion.

"If we were on the Nasdaq with this story our market cap would be three to five times higher at least," Dr Brooke says.

Lest we forget, Alzheimer's disease is becoming a leading cause of death, especially in women.

Dr Gourlay cites estimates of $US13.7 billion in peak sales by 2036, but that's likely to be an underestimate if drugs with different mechanisms of action are available.

"No one has the magic bullet," he cautions. "We hope the biology of our molecule might contribute to delay or prevent disease progression but we have to wait to do longer trials."

While Actinogen's path to a receptive FDA remains littered with hazards, let's not forget that 1980 flop Xanadu - dubbed "stupendously bad" by one critic - cost $US23 million to make and reaped only $US20 million at the box office.

The more recent film version of Cats - which won a rare 'no star' raspberry from some critics - cost $US95 million and clawed back only $US30 million.

Our point? Drug development might not always hit the right note, but at least it's still a less risky proposition than investing in musicals.

Disclosure: Dr Boreham is not a qualified medical practitioner. He does not possess a doctorate of any sort, forged or otherwise. He wishes to stress that Xanadu flopped despite - not because of - 'our' Olivia Newton-John's sparkling leading role.

SUDA PHARMACEUTICALS

Suda says it hopes to raise $3 million for a “no-dilutive” licence with Imperial College London for an “invariant natural killer T-cell therapy” platform for blood cancers.
Suda said it hoped to raise a minimum of $3 million through an institutional placement to support development of the T-cell platform, which included hiring personnel and manufacturing critical components of the product.
The company said the invariant natural killer T-cell (Inkt) therapy platform would be used with its chimeric antigen receptors to develop Car-Inkt-cells to have two ways to recognize, attach to, and destroy cancer cells making them dual targeting.
Suda said the Inkt technology was developed at Imperial College by Prof Anastasios Karadimitris and showed it was protective against graft-versus-host disease.
The company said the Inkt platform might be used off-the-shelf, with cells isolated from a donor, modified to enhance activity against cancer and stored frozen, ready for use.
Suda provided a link to a 2018 article from Imperial College, titled ‘Supercharged natural killer cells may hold promise for cancer’ and available at:
https://www.sciencedaily.com/releases/2018/10/181009102535.htm.
Suda said the platform had a patent life until 2038 and had national phase applications in Europe, China, Canada, Australia and the US.
The company said the licencing agreement was non-dilutive for Suda shareholders and the licencing payments included an upfront fee, annual maintenance fees and development milestones for the clinical trials, receipt of regulatory approval, sales target-based commercial milestones, single digit royalty on future sales and sublicencing fees.
Suda managing-director Dr Michael Baker said “cell therapies have transformed the way we think about cancer treatment.”
“The Inkt-cell therapy platform provides an opportunity to target several cancers using a product that we expect to have superior activity and to be more cost-effective, which should allow the therapy to reach more individuals,” Dr Baker said.
Suda said that it expected to enter into a collaboration with Imperial College London to further research and develop additional intellectual property.
Suda was in a trading halt and last traded at 3.6 cents.

STARPHARMA HOLDINGS

Starpharma says SPL7013 reduces more than 99.9 percent of severe acute respiratory syndrome coronavirus-2 (Sars-Cov-2) variants, in-vitro.
Earlier this month, Starpharma said the SPL7013-based Viraleze nasal spray had shown “potent” anti-viral activity against the UK strain of Sars-Cov-2 (BD: Jun 1, 2021).
Today, the company said that within one minute of exposure to SPL7013 there was a more than 99.0 percent reduction of the South African beta and Japan and Brazil gamma strains, with a more than 99.9 percent reduction in five minutes, and a more than 99.9 percent reduction of the UK alpha strain within one minute.
Starpharma chief executive office Dr Jackie Fairley said the company was “very pleased to see such potent and rapid virucidal activity of Viraleze against multiple Sars-Cov-2 variants of concern, alpha, beta, and gamma”.
“These variants continue to spread across the globe and challenge efforts to control the Covid-19 pandemic,” Dr Fairley said. “Viraleze could prove to be particularly beneficial as an additional protective measure against these variants.”
The company previously said its anti-microbial SPL7013 was the active ingredient in its Vivagel BV for bacterial vaginosis and its Vivagel condom coatings.
Starpharma was up 14.5 cents or 9.3 percent to $1.70 with 1.1 million shares traded.

PARADIGM BIOPHARMACEUTICALS

Paradigm says Brazil has approved a 12-patient, phase II trial of injectable pentosan polysulfate sodium (PPS) for muco-poly-saccharidosis type VI (MPS VI).
Paradigm said the randomized, double-blind, placebo-controlled trial would evaluate the safety and tolerability of PPS for people with muco-poly-saccharidosis type VI who had pain and functional deficiency due to disease-related musculo-skeletal symptoms.
The company said that eight patients would receive PPS while four would receive placebo and all subjects would be provided enzyme replacement therapy throughout the trial.
Paradigm said subjects would have weekly sub-cutaneous PPS at 1.5mg/kg for nine years or above or 1.0mg/kg for subjects below the age of nine years, or placebo, for 24 weeks.
The company said the muco-poly-saccharidosis type VI was an orphan disease and classified as a rare autosomal recessive, inherited lysosomal storage disorder caused by a deficiency of N-acetyl galactosamine 4–sulfatase.
Paradigm said the Porto Alegre-based Federal University of Rio Grande do Sul's professor Dr Roberto Giugliani would be the principal investigator of the study.
Paradigm was up 19 cents or 9.55 percent to $2.18 with 1.8 million shares traded.

ZELIRA THERAPEUTICS

Zelira says that with Perth's Curtin University it has improved the delivery of marijuana-based drugs to the brains of mice by up to 40 times.
Zelira said the Curtin University researchers developed small cannabidiol (CBD) capsules, when taken orally "were absorbed by the body faster and penetrated the brain quicker in mice models with neurological diseases, than when delivered in liquid form".
The company said the research, titled 'Sodium alginate microencapsulation improves the short-term oral bioavailability of cannabidiol when administered with deoxycholic acid' was published in the journal Plos One, with an abstract available at: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0243858.
Zelira said the technology had the potential to treat neurological disorders such as Alzheimer's disease, multiple sclerosis and traumatic brain injury.
Zelira fell 0.1 cents or 2.1 percent to 4.6 cents with 4.4 million shares traded.

MACH7 TECHNOLOGIES

Clime Investment Management says it has increased its substantial shareholding in Mach7 from 19,047,502 shares (8.08%) to 21,791,222 shares (9.22%).
The Sydney-based Clime and its subsidiaries said that between May 6 and June 16, 2021 it bought and sold shares at prices ranging from $1.00 to $1.15 a share.
Mach7 fell half a cent or 0.5 percent to $1.035.

CARDIEX

Cardiex says Nicholas Marshall will replace Philip Leighfield as joint company secretary, effective from June 17, 2021.
Cardiex fell 0.1 cents or 1.2 percent to eight cents with 1.3 million shares traded.