Biotech Daily

Friday October 4, 2019

Daily news on ASX-listed biotechnology companies

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MARKET REPORT

The Australian stock market was up 0.37 percent on Friday October 4, 2019, with the ASX200 up 24.1 points to 6,517.1 points. Twenty-two Biotech Daily Top 40 stocks were up, 12 fell, three traded unchanged and three were untraded. All three Big Caps rose.

Antisense was the best, up 0.9 cents or 10.2 percent to 9.7 cents, with 12.4 million shares traded. Paradigm climbed 10.1 percent; Impedimed improved 9.4 percent; Actinogen was up 6.4 percent; Clinuvel, Dimerix and Patrys were up five percent or more; LBT was up 4.8 percent; CSL and Proteomics were up more than three percent; Opthea, Pharmaxis and Polynovo rose more than two percent; Cynata, Ellex, Mesoblast, Next Science, Oncosil, Orthocell, Pro Medicus and Resmed were up more than one percent; with Cochlear, Nanosonics, Neuren and Telix up by less than one percent.

Optiscan led the falls, down 0.5 cents or 10.4 percent to 4.3 cents, with 203,000 shares traded. Uscom lost 8.3 percent; Prescient fell 5.2 percent; Imugene and Osprey fell more than four percent; Avita was down 3.6 percent; Universal Biosensors shed 2.6 percent; with Amplia, Kazia, Starpharma and Volpara down more than one percent.

DR BOREHAM'S CRUCIBLE: ACTINOGEN MEDICAL

By TIM BOREHAM

ASX code: ACW

Market cap: $56.0 million; **Share price:** 5.0 cents; **Shares on issue:** 1,119,231,320

Chief executive officer: Dr Bill Ketelbey

Board*: Dr Geoff Brooke (chairman), Dr Ketelbey, Dr George Morstyn, Malcolm McComas

***** Dr Jason Loveridge resigned in November last year

Financials (year to June 30, 2019): revenue $204,536 (bank interest, investments; up 123%), loss of $9.9 million (previously $6.3 million deficit), cash $7.6m (down 22%)

Identifiable major holders: Biotech Venture Fund 19.9%, Edinburgh Technology Fund 4.3%, Platinum Asset Management (sub 5%), Tisia Nominees (Henderson family) 2.67%, Sarah Cameron 2.25%, Jinark family 1.82%, Bannaby Investments 1.62%.

It may not have been quite a case of Lazarus with a triple bypass, but a recovery of miraculous proportions happened in the biotech sector this week as Actinogen jagged some remarkable efficacy results from what otherwise was a bog-standard safety trial.

But don't take our word; take the gospel of investors. Post Tuesday's clinical results revelation, Actinogen shares shot up from the 0.7 cents a share death zone to close at 5.1 cents - a 467 percent gain for anyone prescient enough to invest at those levels.

The phase I results showed that Actinogen's Alzheimer's disease candidate Xanamem improved the cognition of a cohort of 30 healthy elderly patients, compared to the 12 who received a placebo. This improvement - measured by the industry standard Cogstate Cognitive Test Battery - came after 12 weeks of dosing at 20 milligrams.

The study was called Xanahes, as in 'Xanamem in Healthy Elderly Subjects'. The "breakthrough results" reinforce the company's key hypothesis that lowering persistently-raised cortisol levels in the brain can enhance cognition.

Actinogen shares tanked in May after the company reported that its phase II Alzheimer's trial of 186 patients missed both primary and secondary endpoints, having failed to show any significant difference between Xanamem (delivered at 10mg daily over 12 weeks) and a placebo.

"We are back on track but on a different track," says Actinogen chief Dr Bill Ketelbey. "But that's the reality of biotech research."

He says Actinogen pretty much tacked on the efficacy endpoint as an afterthought. The company was inspired by a 2014 Edinburgh University study that also identified “cognitive signals” in a group of 24 elderly patients.

“We added the cognitive model to see if we could replicate it,” Dr Ketelbey says.

With a decent cash kitty, Actinogen is now mulling its next move in tackling Alzheimer’s and/or the cognitive effects of schizophrenia and bipolar disorder. The company is most interested in mild Alzheimer’s, which presents a $US7.5 billion ($11 billion) global market.

A brief history of Actinogen

Actinogen carries on the fine work of Edinburgh University, which completed a phase I study of what now is known as Xanamem or UE2343 (originally developed for type 2 diabetes) 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 learning institution as a major Actinogen holder.

Actinogen itself listed way back in October 2007 at 50 cents apiece, but at the time it was focused on soil-derived antibiotic-like compounds called actinomycetes (hence the Actinogen name).

Dr Ketelbey joined the company in December 2014. Dr Ketelbey was involved in developing Aricept at Pfizer, which remains the leading Alzheimer’s treatment despite being developed 25 years ago.

Chairman Dr Geoff Brooke is well known as founder of venture capital firms Medvest Inc and GBS Venture Partners.

Questions, questions

Xanamem seeks to inhibit production of the naturally occurring stress hormone cortisol in the brain, with research linking excessive cortisol with the development and progression of Alzheimer’s.

Xanamem aims to negotiate the blood-brain barrier and thus deliver the active ingredient more effectively.

But Dr Ketelbey says the results raise “intriguing questions” about the role of elevated cortisol levels - the condition Xanamem seeks to modulate - and cognitive decline in both Alzheimer’s patients and healthy patients with normal age-related cognitive diminution.

The patients in the second trial were aged between 50 and 75 years, with a mean age of about 65 years.

The obvious question is why the Xanahes trial succeeded while Xanadu crashed (technically, the trial showed cortical reduction, but not the cognitive improvement). One possible reason is a complex disease like Alzheimer's adds all sorts of variables, which may have contributed to the dud phase II result. Or the patient sample was too heterogeneous, or too early or too advanced in their disease.

"Alzheimer's disease is confounded by heterogeneity, meaning that all patients are different and there's a broad array of presentation of symptoms and response to therapy," Dr Ketelbey says. "Because there's not one distinct biomarker or target for treating the disease, it's a difficult disease to research and to treat."

The other possible explanation is that the Xanadu dosage was at half the level as the Xanahes dosage, so may have been insufficient. Or else the patients needed to be treated for longer than the three months.

Another possibility is that by the time a patient has been diagnosed with Alzheimer's disease it may be far too late – by 20 years - to intervene, whereas the healthy elderly patients had a positive response.

What's next?

"Clearly we are not trying to develop a drug for age-related cognitive impairment," Dr Ketelbey says. "We will go for pathologies where there are chronically raised cortisol levels."

The conditions include Alzheimer's, schizophrenia, bipolar disease, diabetes, Parkinson's disease and epilepsy (as we said, the company will focus on the former three).

"We are at the point of shaping-out the next full set of studies," Dr Ketelbey says. "We are urgently working on [the next step] as we have such compelling cognitive data."

Actinogen has also launched a phase I 'occupancy study', which tests the absorption of Xanamem into the brain, as measured by its occupancy of the target enzyme that promotes cortical production.

Finances and performance

Actinogen had $7.63 million in the bank as at the end of June, with $4.5 million of research and development rebates expected to flow in over the next month.

Dr Ketelbey says the funds are more than enough to fund current research, but monetary requirements thereafter depend on what clinical path the company decides to take.

The company last raised $5.28 million in an oversubscribed placement at 4 cents a share in December 2018, thus fully funding the Xanadu trial.

Despite its setback, Actinogen is heavily backed by the Biotech Venture Fund (BVF), which has the maximum allowable 19.9 percent stake.

Platinum owns a decent wad of scrip, while Australian Ethical sold out immediately after the May setback, taking an unconfirmed loss of about $1.6 million.

“Since the share price collapse in May the shareholdings have been pretty stable, whether retail or institutional,” Dr Ketelbey says.

Actinogen shares peaked at 15 cents in April 2015 and troughed at 0.7 cents in September this year. At its share price nadir, the company was valued at around $8 million - in effect less than cash backing - and now it’s worth $56 million.

The company also has $39 million in accumulated losses, so can ward off the taxman pretty much forever.

Dr Boreham’s diagnosis:

There’s no shortage of research dollars being spent on Alzheimer’s disease, which is expected to become the world’s biggest killer as the population ages. The www.clinicaltrials.gov site lists 536 active and recruiting Alzheimer’s trials, including 27 in Australia.

But while there are drugs to treat the symptoms, there is no effective treatment of the cause, with at least a dozen proposed drugs biting the dust.

Dr Ketelbey says: “They have mainly targeted beta amyloids [abnormal protein produced by the bone marrow] but the general view is that while amyloids are important the traditional approach to treating Alzheimer’s to prevent amyloids forming with is not the way forward.

“Now people are looking at novel approaches and that’s where we begin to stand out.”

Helpfully, Edinburgh University is interested in funding future diabetes and cognitive impairment trials - so no quips please about Scots having short arms and deep sporrans.

While Actinogen’s programs remain at an early stage, the company is a potential takeover target. Last year, Abbvie, Takeda and Eli Lilly all executed pre-clinical Alzheimer’s deals.

“Big pharma in the past has said ‘we like what you do, but bring us a signal that your hypothesis has some clinical substance’,” Dr Ketelbey says.

Xanahes trial lead investigator Prof Michael Woodward from Melbourne’s Austin Health says that given the many past failures in the development of Alzheimer’s drugs, the Xanahes results “renewed hope for a treatment breakthrough for this devastating disease”.

Let’s hope so.

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. Being on the wrong side of 50 he is eligible to participate in Actinogen’s trials, but probably would forget to turn up.

GENETIC TECHNOLOGIES

Genetic Technologies says it hopes to raise up to $4.5 million in a one-for-two non-renounceable pro-rata rights issue at 0.4 cents a share.
Genetic Technologies said the record date for the rights issue was October 9, with the offer opening on October 11 and closing on October 22, 2019.
The company said the funds would be used for general product, research and development, to expand in the People's Republic of China, to fund the development of polygenic risk tests with TGen in the US and to satisfy and remedy its Nasdaq deficiency notice (BD: Jul 30, 2019).
Genetic Technologies said shareholders who took up their full entitlement would be eligible to apply for additional new shares not taken up by other shareholders.
The company said oversubscriptions would be scaled back on a pro-rata basis based on the application amount.
Genetic Technologies fell 0.1 cents or 16.7 percent to 0.5 cents with 26.9 million shares traded.

SUDA PHARMACEUTICALS

Suda says the Australian Government refused its Artimist oral paediatric malaria spray due to "an overall negative benefit-to-risk profile" and could be misused or abused.
In 2013, Suda said a 151-subject, phase III, trial of sub-lingual Artimist (artemisinin) was superiority to intravenous quinine for severe or complicated falciparum malaria, or uncomplicated falciparum malaria with gastrointestinal complications (BD: Apr 30, 2013).
On Tuesday, the company said the Australian Therapeutic Goods Administration refused its appeal to reconsider approval of Artimist, upholding its original decision, a preliminary notice of denial for marketing approval (BD: Jul 18, Oct 1, 2019).
Today, Suda said a delegate of the Federal Minister for Health Greg Hunt "was not satisfied that the safety and efficacy of the product had been satisfactorily established for the purpose for which it is intended for use".
The company said the delegate was concerned about the use and potential misuse or abuse of an artemisinin monotherapy, resulting "in the formation of artemisinin resistance".
Suda said the delegate was concerned that the low level of adherence to treatment guidelines in malarial endemic areas, the ease of use of Artimist and the number of doses in a vial, could lead to further non-compliance to treatment guidelines and lead to further resistance.
The company said it proposed an education program for healthcare workers, but the delegate was concerned about the success of the program because of the reported lack of adherence to treatment guidelines.
Suda was up 0.05 cents or 16.7 percent to 0.35 cents with 1.05 million shares traded.

PHARMAUST

Pharmaust says Epichem has won a Western Australia industry export award with chief executive officer Dr Martine Keenan winning a women in business award.
Pharmaust said that its synthetic and medicinal chemistry subsidiary Epichem won the award for international health and Epichem chief executive officer Dr Keenan won the women in international business award.
The company said the Western Australian industry and export awards were managed by the Export Council of Australia.
Pharmaust was unchanged at 15 cents.

KOLABTREE

Kolabtree says its science freelance platform has surpassed 10,000 registered scientists and academics providing specialist skills for business projects.

In a media release from Stone Junction public relations agency, the London-based Kolabtree said its experts provided specialist skills, including data analysis, clinical trial design, regulatory approval assistance and scientific writing, to help businesses develop products, conduct research and grow their businesses.

The company said the platform was launched in 2015, more than 400 projects were posted each month and more than 2,500 businesses had successfully completed projects with Kolabtree experts.

Kolabtree said freelancer registrations increased 150 percent from 2018 to 2019.

Kolabtree chief executive officer Ashmita Das said, “access to specialist skills used to be a privilege reserved to large companies with extensive budgets”.

“All businesses deserve to access the skills they need to thrive and Kolabtree provides a mechanism of linking small and medium sized businesses with scientific experts,” Ms Das said.

“As our pool of freelancers increases, we will be able to match the skills of the freelancer even more precisely with the requirements of a project,” Ms Das said.

For more information or to register, go to https://www.kolabtree.com/.

IMUGENE

Imugene says it has a share sale facility for holders of unmarketable parcels of its shares, worth less than $500, at 2.2 cents a share.

Imugene said there were 5,365 holders of unmarketable parcels of 22,727 shares or less and the record date for the facility was October 1, 2019.

The company said the facility would allow it to reduce administrative costs and allow holders of unmarketable parcels to sell their shares without brokerage or handling costs.

Imugene said the closing data would be November 27, 2019.

Imugene fell 0.1 cents or 4.55 percent to 2.1 cents with 9.4 million shares traded.

RESAPP HEALTH

Resapp says it is joining Plug and Play’s Munich, Germany-based 12-week Start-up Creasphere digital health program.

Resapp said it would work with subject matter experts and mentors from Sanofi’s consumer healthcare business unit, starting this month, to co-develop consumer health-focused respiratory disease products.

Resapp was up four cents or 14.8 percent to 31 cents with 14.9 million shares traded.

ALTHEA GROUP HOLDINGS

Althea says it has prescribed 462 new medical marijuana patients in September, an average of 22 new patients per business day, and a total of 2,329 patients in Australia.

Althea said 319 Australian healthcare professionals had prescribed its medical marijuana products to patients.

Althea was up four cents or 6.45 percent to 66 cents with 1.3 million shares traded.

STEMCELL UNITED

Stemcell United says it has a collaboration with China Tobacco subsidiary Yunnan Hongyi Agriculture Development for dendrobium, or orchid, stem cell research centre.
Stemcell said the five-year collaboration would invest an initial RMB1.0 million ($A207,123) for a 50 percent equity to research and commercialize dendrobium, tobacco and hemp stem cells for pharmaceutical and healthcare industries.
Stemcell fell 0.1 cents or 6.25 percent to 1.5 cents.

LIVING CELL TECHNOLOGIES

Living Cell says investors will vote on proposals to replace directors Robert Willcocks, Laurie Hunter and Dr Ken Taylor with Dr Andrew Kelly and Dr Roland Toder.
In September, Living Cell said it received a board spill call from unnamed members who collectively held about 5.26 percent of the company, but gave no reasons for the proposal (BD: Sep 10, 2019).
Today, the company said the board opposed the board spill and shareholders would also vote to issue 600,000 options to Prof Carolyn Sue, elect Mr Willcocks and Prof Sue as directors and adopt the remuneration report.
The meeting will be held at the Regatta Room, Pullman Hotel, Cnr Princes Street and Waterloo Quadrant, Auckland, New Zealand on November 7, 2019 at 2pm (NZT).
Living Cell was untraded at 2.1 cents.

IMUGENE

Imugene says its annual general meeting will vote to issue 100,000,000 options to directors Dr Lesley Russell, Dr Jens Eckstein, Dr Axel Hoos and Charles Walker.
Imugene said it would vote to grant 25,000,000 options each to Dr Russel, Dr Eckstein, Dr Hoos and Mr Walker at 4.0, 4.2 and 4.5 cents per option, vesting over 24 months from the date of shareholder approval and expiring three years after approval.
The company said it would vote on the renumeration report, to elect chairman Paul Hopper and directors Dr Russell and Dr Eckstein, and the 10 percent placement capacity.
The meeting will be held at McCullough Robertson Lawyers, Level 32, 19 Martin Place, Sydney on November 8, 2019 at 11am (AEDT).

PARADIGM BIOPHARMACEUTICALS

Paradigm says it will vote to increase its non-executive director fee pool by 100 percent to $500,000 and issue staff shares worth $1,117,950.
Paradigm said the annual general meeting would vote to issue shares worth $578,250 to chief executive officer Paul Rennie and shares worth $539,700 to Claire and Nicole Kaufman, daughters of non-executive chairman Graeme Kaufman.
The company said it would vote to approve an employee share plan and on a special resolution to renew and reinstate clause 11 of its company constitution for proportional takeover requirements for a period of three years.
Paradigm said the meeting would vote to ratify the prior issue of 34,370,099 shares, to adopt the remuneration report and to re-elect director John Gaffney.
The meeting will be held at K & L Gates Lawyers, Level 25, Rialto South Tower, 525 Collins Street, Melbourne on November 7, 2019 at 11am (AEDT).
Paradigm was up 29 cents or 10.1 percent to $3.15 with 1.6 million shares traded.

IMMURON

Immuron says it will vote to issue 5,000,000 options to chief executive officer Dr Gary Jacob, issue 437,500 shares to Grandlodge Pty Ltd and re-elect directors.

Immuron said it would vote to issue 5,000,000 unlisted options to chief executive officer Dr Jacob, under its executive share option plan, with an exercise price of 50 cents a share by February 10, 2024.

The company said that at the time the options were approved by shareholders on November 13, 2017 the 50 cents exercise price was a 127 percent premium to the share price, but at June 14, 2019 the exercise price was a 335 percent premium.

Immuron said the options were proposed to be issued to Dr Jacob as renumeration for his appointment as a director.

The company said it would vote to issue 437,500 shares at 16 cents a share to Grandlodge in lieu of a $70,000 cash payment for fees payable for a service agreement for management, sales, logistics, warehouse and marketing services from January 1 to December 31, 2019.

Immuron said that directors, Stephen and Peter Anastasiou were also directors of Grandlodge.

The company said it would vote to adopt the renumeration report, re-elect directors Stephen Anastasiou and Prof Ravi Savarirayan, ratify the prior issue of 20,000,000 shares at 10 US cents a share and represented by 500,000 American depositary shares (ADSs) at $US4.00 an ADS.

Immuron said it would vote to ratify the prior issue of 13,565,200 shares at 10 US cents a share and representing 339,130 ADSs at $US4.00 an ADS, as well as renew the placement facility.

The meeting will be held at Level 2, 62 Lygon Street, Carlton, Victoria on November 6, 2019 at 3:30pm (AEDT).

Immuron fell 1.5 cents or 10.7 percent to 12.5 cents with four million shares traded.

GI DYNAMICS

GI Dynamics says it has exercised $US2 million ($A2,962,200) in Chess depositary interests (CDIs) to Crystal Amber Fund at 1.27 cents per CDI.

In August, GI Dynamics said it had $US10 million ($A14,773,150) in convertible notes and warrants with Crystal Amber to fund trial enrolments and European approval, including 229,844,650 CDIs, which would be issued at two US cents per CDI (BD: Aug 22, 2019).

Today, the company said the 157,480,314 CDIs or tranche two warrants represented 50 CDIs for each share.

GI Dynamics said the funds would be used for general working capital, to assist the initiation of patient enrolment for its Step-1 and I-Step trials in the US and India and to continue work towards Conformité Européenne (CE) Mark approval for Endobarrier.

GI Dynamics was up 0.1 cents or 2.2 percent to 4.6 cents.