



# Biotech Daily

Tuesday October 16, 2012

*Daily news on ASX-listed biotechnology companies*

- \* **ASX, BIOTECH FLAT: CIRCADIAN UP 8%, GENERA DOWN 13%**
- \* **CALZADA, POLYNOVO NOVOSORB HUMAN PROOF-OF-CONCEPT**
- \* **COCHLEAR REMUNERATION 1<sup>st</sup> STRIKE WITH 31% AGAINST**
- \* **TWO STRIKES POLICY – BIOTECH DAILY EDITORIAL**
- \* **PSIVIDA DEVELOPING TETHADUR BIOSILICON PROTEIN EYE TREATMENT**
- \* **BIOTRON CLAIMS ‘100% BIT225 48-WEEK EFFICACY’**
- \* **BIONOMICS DETAILS ALPHA-7 COMPOUNDS FOR ALZHEIMER’S DISEASE**
- \* **COGSTATE TEST ‘USEFUL IN DETECTING ALZHEIMER’S’**
- \* **PHASE IIa OBSERVATIONS BACK CLINUVEL SCENESSE FOR VITILIGO**
- \* **PHYLOGICA NOTES TO RAISE \$1.6m**
- \* **AVITA PLAN RAISES \$4.2m, TOTAL \$10.5m**
- \* **NABIL LUYER TAKES 10.5% OF HEALTHLINX**
- \* **PRIMA AGM FOR 1.2m NEW DIRECTORS’ OPTIONS, RIGHTS**

## MARKET REPORT

The Australian stock market was up 0.18 percent on Tuesday October 16, 2012 with the S&P ASX 200 up 8.1 points to 4,491.5 points. Twelve of the Biotech Daily Top 40 stocks were up, 12 fell, nine traded unchanged and seven were untraded. All Big Caps were up.

Circadian was the best, was up three cents or 7.7 percent to 42 cents with 7,350 shares traded, followed by Cellmid up 7.1 percent to 1.5 cents with 805,000 shares traded. Prana climbed 6.5 percent; Sunshine Heart was up 5.4 percent; Living Cell was up four percent; Avita, Neuren and Phylogica were up more than three percent; Alchemia, Bionomics and Cochlear were up more than one percent.

Genera led the falls, down two cents or 13.3 percent to 13 cents with 34,600 shares traded, followed by Patrys down 12.5 percent to 2.8 cents, with 50,000 shares traded and Prima down 10.3 percent to 13 cents with 13.7 million shares traded. Anteo and Phosphagenics fell more than four percent; Pharmaxis and Psivida were down more than three percent; Starpharma shed 2.7 percent; with Heartware, Tissue Therapies and Universal Biosensors down more than one percent.

## CALZADA

Calzada says that wholly-owned subsidiary Polynovo's human flap trial shows that Novosorb is effective in treating full thickness wounds.

Calzada said that the Novosorb biodegradable temporizing matrix (BTM) wound repair material was performing in humans as intended, consistent with the results obtained in earlier pre-clinical studies in pigs.

The company said that the Novosorb BTM had been implanted, successfully integrated into a wound and closed with skin grafts in two patients.

Calzada said the achievement was "an important milestone" and demonstrates Novosorb BTM integrated into the wound bed of burns patients, resisted contraction, repaired the dermal layer of the skin without scarring, resisted infection, inhibited wound water loss, limited reliance on immediate skin grafting and stayed intact, temporizing and protecting the wound until definitive closure was available.

The company provided photographs with its announcement demonstrating Novosorb BTM implanted into a full-thickness, free-flap donor site wound immediately after surgery of an adult thigh with an initial wound size of 132 cm<sup>2</sup>.

Calzada said the Novosorb Novoskin project was a joint venture with Adelaide burn surgeon Dr John Greenwood.

Dr Greenwood said the early findings "demonstrate that the BTM is well tolerated by human tissues, provides a scaffold into which host tissue can grow and inhibits wound contraction".

"Once fully integrated, it provides a bed suitable for graft take," Dr Greenwood said.

Dr Greenwood said he was confident that Novosorb BTM would provide a bed for the Novoskin composite cultured skin.

"We are very close to a real paradigm change in burn management," Dr Greenwood said. Calzada said Novoskin was in the process of completing the current clinical trial work with further recruitment and treatment of patients underway and that the positive early observations should enable the clinical team to broaden patient recruitment into other free flap donor sites or different wound applications, including burns.

Calzada said Novoskin was invited to submit a proposal for a \$US16.9 million US Biomedical Advanced Research and Development Authority (BARDA) contract to develop its Novosorb products as a medical countermeasure for mass burn casualties.

The company said that if successful, the funds would be used to develop for Novosorb BTM go to US regulatory approval of in the US and expected to be advised of the outcome within six months.

Calzada was unchanged at 4.8 cents.

## COCHLEAR

Cochlear's remuneration report was opposed by 10,355,483 votes or 31.0 percent, providing the first trigger for a potential board spill at the next annual general meeting.

Cochlear said that 24,112,162 votes (69%) supported the remuneration report.

There was a similar level of dissent against the issue of 231,161 options valued at \$4.44 each or a total of \$1,026,353 and exercisable at \$62.78 each, vesting in three years pending performance hurdles.

The Corporations Act (Section 250U) provides for a 'two strikes and re-election' process (see below).

Director Prof Edward Byrne and Andrew Denver were re-elected overwhelmingly with more than 35 million votes in favor and fewer than 361,000 votes against.

Cochlear was up \$1.05 or 1.5 percent \$71.92 with 217,634 shares traded.

## BIOTECH DAILY EDITORIAL

Until the Cochlear shareholder's vote today, the recently enacted 'Two Strikes Policy' had received three biotechnology strikes.

Intended to give shareholders a greater degree of power over the companies in which they invest, the Corporations Amendment (Improving Accountability on Director and Executive Remuneration) Act 2011, took effect on July 1, 2011, amending Section 250 of the Corporations Act so that if a company receives 25 percent or more votes against the remuneration report at two successive annual general meetings, the company must propose a 'spill' resolution requiring a 50 percent majority to re-elect directors, except for the managing director, with 90 days.

But under the Law of Unintended Consequences, the biotechnology industry has seen three successive examples where a single shareholder can provide either all or most of the votes to lead to the spill resolution.

Biotech Daily strongly supports openness, transparency and shareholder activism, but the potential for disruption by a single disenfranchised investor is high among small and medium capitalization companies, and in any industry.

At last year's Sirtex meeting, 9.7 million of about 10 million votes against resolutions came from founder and former chairman Dr Bruce Gray, providing 33.24 percent of the votes against the remuneration report (BD: Sep 21, 2012).

Cryosite included a spill resolution in its notice of meeting following last year's 'first strike', believed to be primarily the shareholding of Cell Care Australia which holds about 21 percent of the company (BD: Sep 27, 2012).

Calzada has also included a spill resolution following a first strike in 2011 with 32,441,152 proxy votes (25.46%) against the remuneration report, believed to be primarily the 29,158,903 shares held by Fleming SG Capital Special Opportunities, which has since sold all of its holding (BD: Oct 12, 2012).

While Cochlear shareholders may have vindicated the amendments with a depth and breadth of votes against the remuneration report, it is clear the policy is open to abuse.

Biotech Daily believes that apart from the 25 percent of votes cast, a minimum number of individual shareholders, possibly as few as 10 or 20, should be required in order for the dissent to count towards a 'strike'.

While this could lead to a form of branch-stacking, a single dissenting shareholder would at least need to convince others of the merits of his or her case.

**David Langsam**  
**Editor**

## PSIVIDA

Psivida says it is developing a sustained release protein delivery system called Tethadur, based on its Biosilicon technology, for use in ophthalmology.

Psivida said chief executive officer Dr Paul Ashton would discuss the technology in a talk entitled 'Cross Fertilization: Sustained Delivery and Nanotechnology in Ophthalmology' at a formulation and drug delivery committee meeting of the Massachusetts Biotechnology Council on, October 17, 2012.

The company said that Dr Ashton would focus on delivery of peptides and proteins in ophthalmology.

Psivida said the ophthalmology space was dominated by two anti-vascular endothelial growth factor (VEGF) proteins, Roche-Genentech's Lucentis and Regeneron's Eylea, both of which needed to be repeatedly injected into the eye, every one to two months.

"The development of a sustained release protein delivery system would offer a significant advantage in ophthalmology," Dr Ashton said.

Psivida fell five cents or 3.2 percent to \$1.50.

## BIOTRON

Biotron says 48-week phase IIa data shows that 400mg BIT225 with interferon and ribavirin reduced all patients' hepatitis C virus levels below the limit of detection.

Biotron did not disclose how many patients were in the 400mg BIT225 group, but has previously said the Thailand trial had 24 patients in total.

Last year, Biotron said that final data from the phase IIa trial of hepatitis C drug candidate BIT225 showed evidence of improved benefit at three months and published interim data of "good antiviral activity" in hepatitis C virus patients and that the orally administered, small molecule BIT225 in combination with the current standard of care for treating hepatitis C interferon and ribavirin had greater reductions in viral levels than patients receiving interferon and ribavirin alone (BD: Oct 10, Dec 7, 2011).

Today, Biotron said the data would be detailed in a presentation entitled 'High sustained viral response with a HCV p7 inhibitor, BIT225: Antiviral activity and tolerability of BIT225 plus pegylated interferon alfa 2b and weight-based ribavirin for 28 days in HCV treatment-naïve patients' at the American Association for the Study of Liver Diseases conference in Boston, Massachusetts November 9-13, 2012.

Biotron said that at three-months 87 percent of patients who received BIT225 in addition to standard of care, interferon and ribavirin, were clear of the virus, compared to 63 percent of those receiving interferon and ribavirin alone.

The company said that the latest results "demonstrate that 100 percent of patients who received 400mg dose of BIT225 in addition to [interferon and ribavirin] maintained a sustained virological response, with virus levels below the limit of detection".

Biotron said that patients who received 200mg of BIT225 in addition to interferon and ribavirin had 87.5 percent sustained virological response, while patients who only received treatment with interferon and ribavirin had 75 percent sustained virological response.

Biotron was up 5.4 cents or 59.3 percent to 14.5 cents with 6.8 million shares traded.

## BIONOMICS

Bionomics says it has developed compounds which act as positive allosteric modulators of the alpha-7 nicotinic acetylcholine receptor and restore memory in animals.

Bionomics said the alpha-7 compounds outperformed benchmark compounds including Pfizer's donepezil, marketed as Aricept, that reported \$US2.5 billion in sales in 2011.

The company said it would present two poster presentations entitled 'Three novel Type II positive allosteric modulators of the alpha-7 nicotinic acetylcholine receptor demonstrate safe, effective cognitive enhancement' and 'Characterization of novel type I positive allosteric modulators of the alpha-7 nicotinic acetylcholine receptor' at the Neuroscience meeting in New Orleans, October 13-17, 2012.

Bionomics said positive allosteric modulators had competitive advantages including: greater potency combined with selectivity, rapid onset of action, and allowed greater efficacy without increasing side-effects or causing receptor desensitization.

The company said the positive allosteric modulators preserved the normal signaling patterns of the receptor and no potential for development of tolerance.

Bionomics said that the alpha-7 program was expected to reach drug candidate selection soon, leading to pre-clinical and clinical trials.

Bionomics chief executive officer Dr Deborah Rathjen said "the alpha-7 nicotinic acetylcholine receptor is a highly promising target for treatment of memory impairment associated with Alzheimer's disease, which contrasts with the historical focus on beta-amyloid in the search for new therapies".

Bionomics was up half a cent or 1.6 percent to 32.5 cents.

## COGSTATE

Cogstate says a study using its cognition test along with brain imaging for beta amyloid plaques is useful in detecting the early onset of Alzheimer's disease.

Cogstate said the study, entitled 'Stronger effect of amyloid load than APOE genotype on cognitive decline in healthy older adults' was co-authored by its chief scientific officer Prof Paul Maruff and was published today in the journal *Neurology*.

The company said the research confirmed that elevated brain levels of beta amyloid could be used as a marker for very early-stage Alzheimer's disease.

"Up to now, we've known there are some healthy older people who have elevated amyloid in their brain but the meaning of this was unknown," says Prof Maruff said.

"We found that despite people with high amyloid having no symptoms or problems with thinking, careful measurement over time revealed clear evidence of a subtle but progressive decline in their memory," Prof Maruff said.

"The data suggest that high amyloid does indicate early disease and the combination of this biomarker and the cognitive test is really useful," Prof Maruff said.

Cogstate said the Australian Imaging, Biomarker and Lifestyle Flagship Study of Ageing (AIBL) study was a collaboration between universities, the Commonwealth Scientific and Industrial Research Organisation and the biotechnology and pharmaceutical industries.

The company said that 141 healthy and cognitively normal older people with a mean age of 76 years enrolled in the control arm of the study.

Cogstate said the participants underwent positron emission tomography (PET) brain scans, were tested for the APOE gene and had their memory function tested using its computer-based tests at the start of the study and 18 months later.

The company said that none in the group showed clinical signs of Alzheimer's disease either before, or at the end of, the 18 month study, but those known to have higher brain levels of beta amyloid showed up to a 20 percent greater decline in memory performance over the period when compared to people with normal levels of amyloid.

"The research validates the use of tests within the Cogstate battery, showing that they are highly sensitive and able to detect even subtle changes in memory performance in otherwise healthy elderly people," Professor Maruff said. "These tests could play an important role in the early detection of Alzheimer's disease in patients who would not be diagnosed using conventional clinical assessment."

Prof Maruff said the discovery could assist efforts to develop a treatment that could intervene in the earliest phase of Alzheimer's disease and curb, or stop, its progression.

Cogstate said that beta amyloid was a component of the plaques in the brains of people with Alzheimer's disease and about 95 percent of people diagnosed with Alzheimer's had elevated levels when checked with a PET scan, but elevated levels were seen in about 25 percent of elderly people who appeared healthy and so the link had been unclear.

The director of Victoria's Mental Health Research Institute and study co-author Prof Colin Masters said the research suggested "Alzheimer's disease processes have begun" in these people.

"The combination of a decline in memory, along with amyloid imaging, may be useful for the identifying Alzheimer's disease in people who don't meet any clinical criteria for cognitive impairment," Prof Masters said.

"Furthermore, it is possible to detect this decline in memory using a brief but repeatable assessment," Prof Masters said.

Cogstate said that the study found that beta amyloid levels had a stronger effect on memory performance than those carrying the APOE gene, which was associated with a more rapid decline in memory in healthy older people.

Cogstate was up 3.5 cents or 9.6 percent to 40 cents.



### CLINUVEL

Clinuvel says observations on four of 56 patients in its phase IIa US trial of afamelanotide (Scenesse) for vitiligo have been published in the journal Archives of Dermatology. Clinuvel said that the article entitled 'The Efficacy of Afamelanotide and Narrowband UV-B Phototherapy for Repigmentation of Vitiligo' described four patients with Fitzpatrick skin types III-VI, who received four doses of Scenesse alongside narrowband ultra-violet B therapy over six months.

An abstract is at: <http://archderm.jamanetwork.com/article.aspx?articleid=1377949>.

The company said that in all cases, patients' lesions repigmented within the six month treatment period, with 50-90 percent overall repigmentation reported.

Clinuvel said that the three patients with darker skin types (Fitzpatrick V-VI) saw no relapse of their repigmentation at their three month follow up, whereas the lighter skinned patient (Fitzpatrick III) had a 10 percent relapse.

The company said that fatigue, nausea, headaches and dizziness were reported as adverse events.

The Archives of Dermatology abstract said that patients were treated three times per week with narrowband ultra-violet-B and starting in the second month received a series of four monthly implants containing 16mg of afamelanotide.

The abstract said that afamelanotide induced faster and deeper repigmentation in each case and all patients experienced follicular and confluent areas of repigmentation within two days to four weeks after the initial implant, which progressed throughout treatment.

The abstract said that all patients experienced diffuse hyperpigmentation.

The abstract concluded that afamelanotide was "a novel and potentially effective treatment for vitiligo" and combined with narrowband ultra-violet B appeared to promote melanoblast differentiation, proliferation, and eumelanogenesis, with further studies necessary to confirm the observations.

Clinuvel said trial results were expected by the end of 2012.

Clinuvel was unchanged at \$1.61.

### PHYLOGICA

Phylogica says it hopes to raise \$1.6 million through a placement of 16,000 unlisted converting notes each with an issue price of \$100.

Phylogica said the funds would go to finalize expected research and development collaborations.

The company said that the new shares would be issued at up to 5.3 cents a share subject to shareholder approval at the annual general meeting on November 22, 2012.

Phylogica said that each converting note would convert into a variable number of shares and potentially PYCOA options.

Phylogica was up 0.1 cents or 3.85 percent to 2.7 cents.

### AVITA MEDICAL

Avita says its share plan raised \$2,996,621 through the issue of 24,721,847 shares at 12 cents each along with a further placement of 9,908,334 shares raising \$1,189,000.

Avita said that along with the placement raising \$6.3 million last month the raising should fund the company to its US Food and Drug Administration submission (BD: Sep 5, 2012).

The company said the placement was managed by Octa Phillip Securities, with the second tranche subject to shareholder approval on October 19, 2012.

Avita was up half a cent or 3.7 percent to 14 cents.

### HEALTHLINX

Nabil Luyer has become a substantial shareholder in Healthlinx with the acquisition of 41,000,000 shares or 10.5 percent.

The initial substantial shareholder notice said that the North Perth, Western Australia-based Mr Luyer was a private investor who acquired the shares for \$141,012 or 0.34 cents a share.

Healthlinx fell 0.1 cents or 20 percent to 0.4 cents with 30.5 million shares traded.

### PRIMA BIOMED

Prima shareholders will vote to issue 1,200,000 options, to chief executive officer Matthew Lehman, exercisable at 18.51 cents, by August 1, 2015.

Prima said shareholders would vote on the issue of performance rights and or options under an 'umbrella' executive incentive plan, but did not provide specific details.

The company said shareholders would also vote on the remuneration report and the re-election of director Albert Yue-Ling Wong.

The meeting will be held at the Radisson Blu Plaza Hotel, 27 O'Connell Street, Sydney, on November 16, 2012 at 10.30am (AEDT).

Prima fell 1.5 cents or 10.3 percent to 13 cents with 13.7 million shares traded.