Biotech Daily

Wednesday November 12, 2014

Daily news on ASX-listed biotechnology companies

*** ASX, BIOTECH DOWN: NEUREN UP 54%, ANTISENSE DOWN 12%**

*** NEUREN: 'NNZ-2566 PHASE II SAFETY, EFFICACY FOR RETT SYNDROME'**

*** WEHI, PETER MAC, GARVAN BLOCK NEOCHROMOSOMES**

*** MELBOURNE UNI SHOWS GENETIC RESISTANCE TO TYPHOID**

*** ADMEDUS REGEN INVESTORS LEGAL ACTION**

*** NOVOGEN RAISES $1.8m OF HOPED FOR $3m-$20m; NASDAQ LETTER**

*** BIONOMICS SURVIVES 21.5% REMUNERATION DISSENT**

*** UP TO 45% OF PATRYS OPPOSE CHAIRMAN JOHN READ**

*** PATRYS APPOINTS DR JAMES CAMPBELL DIRECTOR**

*** SIENNA APPOINTS TONY DI PIETRO CFO**

*** AGENIX LOSES DIRECTOR ANTHONY LEE**

MARKET REPORT

The Australian stock market fell 0.98 percent on Wednesday November 12, 2014 with the S&P ASX 200 down 54.0 points to 5,463.1 points. Nine of the Biotech Daily Top 40 stocks were up, 12 fell, 12 traded unchanged and seven were untraded. All three Big Caps fell.

Neuren was the best, up as much as 6.7 cents or 85.9 percent to 14.5 cents before closing up 4.2 cents or 53.85 percent at 12 cents with 50.6 million shares traded, followed by Prana up 10 percent to 22 cents with 301,770 shares traded.

Biotron climbed 6.5 percent; GI Dynamics rose five percent; Cellmid was up four percent; Mesoblast, Tissue Therapies and Viralytics were up more than one percent; with Acrux up 0.95 percent.

Antisense led the falls, down 1.3 cents or 11.8 percent to 9.7 cents with 623,555 shares traded. Admedus, Anteo and Oncosil fell more than eight percent; Alchemia and Genetic Technologies lost more than seven percent; Circadian was down three percent; Starpharma shed 2.5 percent; Clinuvel and Phosphagenics were down more than one percent; with Benitec, Cochlear, CSL, Resmed and Sirtex down less than one percent.

NEUREN PHARMACEUTICALS

Neuren says its phase II trial of NNZ-2566 for Rett syndrome “exceeded ... expectations”, and would lead to applications for orphan drug and breakthrough therapy designation.

Neuren published detailed results showing that the two trial doses of 35mg/kg and 70mg/kg twice daily were safe and well-tolerated, with no drug related serious adverse events and that the higher dose met several of the efficacy secondary endpoints.

The company said the next step would be to submit applications to the US Food and Drug Administration for both orphan drug and breakthrough therapy designation.

Neuren said it expected to meet with the FDA by April 2015 to discuss the trial results and the requirements for the further development of NNZ-2566 in Rett syndrome.

The company said that there were no approved medicines for the treatment of Rett syndrome, which was a severe genetic neurological disorder.

Neuren said its trial was the first multi-site, sponsor-led clinical trial in Rett syndrome and the first trial in an adolescent and adult population.

Harvard Medical School professor of neurology and Boston Children’s Hospital Rett syndrome program director Prof Walter Kaufmann, who was not involved in the trial, said that the outcome was “very promising in terms of both safety and clinical improvement”.

“It opens not only the possibility of successful treatment of adults with Rett syndrome, but also of early interventions modifying the course of the disease,” Prof Kaufmann said.

Neuren said that 53 subjects aged 16 to 45 years completed the double-blind placebo-controlled trial.

The company said that efficacy was measured across six core measures in four efficacy domains, the analysis plan was pre-specified and submitted to the FDA before the data was unblinded and compared clinical responses in the core measures for each subject individually, as well as the mean clinical responses for each treatment group.

Neuren said that evidence of clinical benefit in the group-level analysis required improvement in at least two core outcome measures from two different efficacy domains, with no clinically significant worsening in all other core endpoints and this was exceeded at day 26 in the higher dose group, with three measures from three different efficacy domains achieving the target, the motor-behavior assessment change index, the clinical global impression of improvement and the caregiver top three concerns.

The company said that the 70mg/kg dose group achieved a benefit in the subject-level efficacy analysis.

Neuren said the probability of the results being chance rather than a drug effect was determined as 2.3 percent ($p = 0.023$) by permutation testing, which the FDA had accepted in previous trials in other therapeutic areas, including for the development of a product recently granted breakthrough therapy designation.

Neuren executive chairman Dr Richard Treagus said the trial results “exceeded our expectations and we look forward to discussing with the FDA the remaining requirements to develop NNZ-2566 for the treatment of Rett syndrome”.

In a teleconference Dr Treagus said that given the safety profile the company had “the ability to contemplate going to a higher level dose” possible for a longer treatment period.

Dr Treagus said that the data showed “a clear separation between drug and placebo”.

University of Alabama professor of paediatric neurology, trial investigator Prof Alan Percy said that the results “suggest a very promising proof of concept as we continue on the pathway to develop a disease-altering treatment for girls and women with Rett syndrome”.

“Not only was this short-term trial managed successfully, but also the data analyses were conducted in a very robust fashion,” Prof Percy said.

Neuren climbed as much as 6.7 cents or 85.9 percent to 14.5 cents before closing up 4.2 cents or 53.85 percent at 12 cents with 50.6 million shares traded.

THE WALTER AND ELIZA HALL INSTITUTE FOR MEDICAL RESEARCH

The Walter and Eliza Hall Institute says a collaboration has uncovered how DNA molecules in some tumors are formed, explaining how the tumors ensure their survival.

WEHI said that the collaboration with Melbourne's Peter MacCallum Cancer Centre and Sydney's Garvan Institute had solved "a decades-old mystery" of tumor survival and discovered that the tumors were "like Frankenstein's monster, stitched together from other parts of the genome".

The research, entitled 'The Architecture and Evolution of Cancer Neochromosomes', was published in the Elsevier journal Cancer Cell and an abstract is available at: http://www.cell.com/cancer-cell/abstract/S1535-6108%2814%2900373-0.

WEHI said that the discovery also identified a potential drug target for treating cancers that were well-known to harbor the neochromosome molecules.

The Institute said that neochromosomes were giant extra chromosomes found in up to three percent of all cancers, most commonly in liposarcomas, or fat tissue tumors, sarcomas, or soft tissue tumors and some brain and blood cancers.

WEHI said that the research showed that spontaneous and catastrophic chromosomal explosions triggered the formation of neochromosomes and the shattered relics reassembled haphazardly, followed by a genetic frenzy of amplification and deletion.

WEHI said that genes known to be important for cancer development were massively amplified, assuring the cancer's survival.

The Institute said that each normal cell had 23 pairs of chromosomes, the packages of genetic information found in all cells of the body and neochromosomes were first identified in the 1950s, but their development was a mystery until now.

WEHI said that neochromosomes were large, often many times the size of the largest normal chromosome, and harbored many extra copies of oncogenes, or altered genes known to drive cancer development.

WEHI said that the researchers, led by Prof David Thomas and Prof Tony Papenfuss, mapped the neochromosomes from liposarcomas, using DNA sequencing.

The Institute said the team used mathematical modelling to reconstruct the events causing the neochromosome to form, deducing that chromosomal shattering was to blame.

Prof Papenfuss said the research was like archaeology.

"We showed that chromosome 12 shatters and its remnants form a ring of DNA in a haphazard fashion," Prof Papenfuss said. "As cells divide, and the circular chromosomes get copied and pulled into different cells, a constant abnormal morphing takes place."

He said that small circles gradually became giant circles, progressively amplifying certain genes in what appeared to be a selective process and the growing giant sucked in DNA from all parts of the genome, until the circle stopped growing and became linear.

"By the time we look at tumor cells through the microscope, we see giant linear chromosomes," Prof Papenfuss said.

Prof Thomas said that the extent of the genetic rearrangement was "truly astonishing".

"These cancers manipulate the normal replication process in an ingenious way, creating a monster that can selectively steal and amplify the genes it needs to grow and survive," Prof Thomas said.

"In some liposarcoma cell lines, DNA from every chromosome in the cell was found in the neochromosome, with between 60 and 100 copies of key oncogenes," Prof Thomas said.

"Patient tumors also exhibited similar gene rearrangement," Prof Thomas said.

"The study also identified a potential therapeutic target to explore for treating liposarcomas," Prof Thomas said.

"When the key oncogenes that were massively amplified in the cancer cells were blocked, the cancer cells died," Prof Thomas said.

THE UNIVERSITY OF MELBOURNE

The University of Melbourne says that people with a variation in the HLA-DRB1 gene have natural resistance against typhoid fever.

The University's said that the lead researcher, the Nossal Institute of Global Health's Dr Sarah Dunstan described the study as "the first large-scale, unbiased search for human genes that affect a person's risk of typhoid".

The University said that the research, entitled 'Variation at HLA-DRB1 is associated with resistance to enteric fever' was published in Nature Genetics and an abstract was at: http://www.nature.com/ng/journal/vaop/ncurrent/full/ng.3143.html.

The University said that enteric fever, or typhoid fever as it was commonly known, was a considerable health burden to lower-income countries and the finding was important because the natural resistance was one of the largest human gene effects on an infectious disease.

"We screened the human genome to look for genes associated with susceptibility to, or resistance from typhoid," Dr Dunstan said. "We found that carrying a particular form of the HLA-DRB1 gene provided natural resistance against typhoid fever."

"This gene codes for a receptor that is important in the immune response, by recognizing proteins from invading bacteria," Dr Dunstan said.

Dr Dunstan said that typhoid was contracted by consuming food or water contaminated with the bacteria Salmonella typhi or Salmonella paratyphi and caused 200,000 deaths a year infecting 26.9 million people per year.

Dr Dunstan said that understanding the natural mechanism of disease resistance could assist develop improved vaccines for typhoid fever and other invasive bacterial disease.

The University said better treatments and vaccines were needed for typhoid as the bacteria were increasingly antibiotic resistant, the current vaccine was moderately effective and did not protect against paratyphoid fever, which was increasing in Asia.

ADMEDUS

Admedus says that co-investors in its Cardiocel subsidiary Admedus Regen have issued legal proceedings against it, Admedus Australia and Admedus Regen.

Admedus said the proceedings would have "no material impact on ... ongoing activities".

The company said the legal action had been taken by Dr Geoffrey Lane, Dr Keith Woollard and associated entities, Palkingston Pty Ltd and K V Woollard Pty Ltd under sections 232 and 233 of the Commonwealth Corporations Act 2001, which relate to the conduct of a company's affairs, an actual or proposed act or omission by or on behalf of a company, or a resolution, or proposed resolution, of members or a class of members of a company, that is either contrary to the interests of the members as a whole or oppressive to, unfairly prejudicial to, or unfairly discriminatory against, a member or members.

Admedus said that Dr Lane, Dr Woollard, Palkingston and K V Woollard collectively owned about 20 percent of Admedus Regen, with Admedus holding about 80 percent.

Section 232 and 233 of the Corporations Act The company said that the plaintiffs alleged that the affairs of Admedus Regen were "being conducted in a manner that is contrary to the interests of the members of Admedus Regen as a whole and oppressive of the interests of Dr Geoffrey Lane, Dr Keith Woollard, Palkingston Pty Ltd and K V Woollard Pty Ltd".

Admedus said it and Admedus Australia "strenuously deny the allegations made by Dr Geoffrey Lane, Dr Keith Woollard, Palkingston Pty Ltd and K V Woollard Pty Ltd and will vigorously defend the proceedings".

Admedus fell one cent or 8.3 percent to 11 cents with 6.2 million shares traded.

NOVOGEN

Novogen says it has raised $1,795,000 with acceptances for 16,318,184 shares at 11 cents a share with attaching one year unlisted options exercisable at 12.5 cents each.
Novogen is believed to be the first biotechnology company to use the Bookbuild facility.
The company said that on August 13, 2014, shareholders approved the issue of 80 million shares and 80 million options at a general meeting.
In July, the company said it hoped to raise $20 million through the issue of 80 million shares and options, but last month Novogen said it hoped to raise up to $10 million through the ASX Bookbuild facility (BD: Jul 10; Oct 16, 2014).
Last week, Novogen said it hoped to raise $3,000,000 through the facility, reducing that to $1,000,000 yesterday (BD: Nov 3, 2014).
Novogen executive chairman Dr Graham Kelly said the raising was part of a broader funding strategy to see the company progress through to clinical trials.
“We had hoped for more, and we are disappointed, because we wanted to give more Australian investors the opportunity to be part of this company,” Dr Kelly said.
Dr Kelly said that with the Federal research and development tax incentive the company would have sufficient capital to progress programs and consider other funding.
Novogen said that deputy chairman John O’Connor would lead funding initiatives and US investment banker Robert Kennedy had been appointed and secure medium-term funding, while director Iain Ross would work with Dr Kelly to ensure continued funding of the Cantx joint venture with Yale University.
Novogen said it had “as [a] matter of urgency initiated a number of discussions to secure non-dilutive funding for its discovery projects”.
Separately, Novogen said it was on a 45-day Nasdaq notice to comply with maintaining a minimum of $US2.5 million ($A2.9 million) in stockholder equity.
The company said that the Nasdaq letter said it had 45 days, from November 7, 2014 to submit a plan to regain compliance and if the plan was accepted, it could be granted an extension of up to 180 days to evidence compliance.
Novogen said the deficiency notice did not immediately affect its Nasdaq listing.
Novogen fell 0.5 cents or 4.2 percent to 11.5 cents.

BIONOMICS

Bionomics has survived a first strike on its remuneration report with 21.5 percent opposed, but all resolutions at the annual general meeting were carried.
Bionomics said that the vote went to a poll which showed that 44,587,345 proxy votes (21.5%) opposed the company’s remuneration report and 162,801,068 proxy votes (78.5%) were in favor.
The Corporations Act (Section 250U) provides for a ‘two strikes and re-election’ process if a company’s remuneration report is opposed by more than 25 percent of votes on two consecutive occasions, taking the company to a vote on a board spill motion.
A similar percentage opposed the issue of options to chief executive officer Dr Deborah Rathjen, the approval of the employee share plan and the employee option plan, with the re-election of director Trevor Tappenden passed overwhelmingly.
Bionomics most recent Appendix 3B share issue announcement said there were 417,266,565 shares on issue, meaning that the strongest opposition vote of 50,972,305 votes against the employee option scheme represented 12.2 percent of all shares on issue, sufficient to requisition extraordinary general meetings.
Bionomics was unchanged at 55.5 cents.

PATRYS

Patrys annual general meeting almost spilled chairman John Read in his bid for re-election as a director.
The re-election vote went to a poll and was opposed by 146,611,097 votes (44.9%), with 179,813,797 votes (55.1%) in favor.
The company's most recent Appendix 3B new issue announcement said that Patrys had 697,060,986 shares on issue, meaning that the votes against Mr Read amounted to 21.0 percent of the company, sufficient to requisition extraordinary general meetings.
The remuneration report was approved overwhelmingly as was the ratification of a prior share issue.
The 10 percent placement capacity required a 75 percent majority to pass and was opposed by 36.3 million votes (15.5%) with 198.4 million votes in favor (84.5%).
Patrys was unchanged at 1.8 cents with 1.9 million shares traded.

PATRYS

Patrys says it has appointed Dr James Campbell as a non-executive director, effective from the close of today's annual general meeting.
Patrys said that the appointment "strengthens the board ... as it progresses the clinical development and partnering efforts for its pipeline of clinical and pre-clinical assets".
The company said that Dr Campbell was formerly the Chemgenex chief financial officer and chief operating officer and had more than 20 years of biotechnology research, management and leadership experience and had been involved in the creation and/or transformation of several biotechnology companies.
Patrys said the Dr Campbell guided the creation of Invion as an executive director and remained a non-executive director and had recently joined Bioprospect as a non-executive director.
Patrys chairman John Read said that Dr Campbell brought "substantial and complementary experience to the ... board, including [intellectual property] management, partnering with global pharmaceutical companies, financial management and strategic transformation within a range of biotech companies".

SIENNA CANCER DIAGNOSTICS

Sienna says that it has appointed Tony Di Pietro as its chief financial officer.
Sienna said that Mr Di Pietro was formerly the chief financial officer and company secretary at Acrux, where he had been employed for more than 10 years.
The company said that Mr Di Pietro held senior roles at Acrux through the transition from a small loss-making company to an ASX listed company generating significant profits.
Sienna said that Mr Di Pietro was an accountant with more than 15 years of corporate accounting experience in Australia and the United Kingdom.
The company said that Mr Di Pietro held a Bachelor of Business from Melbourne's Swinburne University and Graduate Diploma of Applied Corporate Governance from the Governance Institute of Australia.
Sienna managing-director Dr Kerry Hegarty said that with her company expecting its first reagent sales shortly, "resourcing with talent at management level becomes a priority".
"Tony obviously has a very distinguished career in a listed environment and is well-known and respected in the biotech community," Dr Hegarty said.
Sienna is a public unlisted company.

AGENIX

In an Appendix 3Z Final Director's Interest Notice to the ASX, Agenix said that Anthony Lee was no longer a director.

No other information was given by the company.

Mr Lee was appointed to the board in 2007 after the company's failed venture to China under then chief executive officer Neil Leggett, who was later gaoled for his theft of $4 million from the company (BD: Aug 27, 2007; Feb 18, May 18, 2010).

Agenix was up 0.1 cents or 6.7 percent to 1.6 cents.