

Biotech Daily

Monday May 12, 2014

Daily news on ASX-listed biotechnology companies

- * ASX, BIOTECH DOWN: CIRCADIAN UP 41%, UNIVERSAL BIO DOWN 39%
- * WEHI: 'RIPK1 LINKS CELL DEATH, INFLAMMATORY DISEASE'
- * CIRCADIAN'S OPTHEA, FDA MEET ON OPT-302 FOR WET AMD, 2015 TRIAL
- * ADMEDUS RAISES \$8m, SHARE PLAN FOR MORE
- * XERAYA, JP ASIA INVEST \$14m IN NUSEP'S PRIME BIOLOGICS
- * BONE CEO PETER YOUNG GOES, OSTEOPOROSIS TRIAL APPROVED
- * LBT PRESENTS APAS AUTO-PLATE ASSESSMENT
- * VIRAX FALLS ON 1-FOR-5 SHARE NEWS
- * UNIVERSAL BIOSENSORS SLIDES 39% ON SLIDE
- * CLINUVEL REQUESTS CAPITAL RAISING TRADING HALT
- * M&G BUYS 8m GI DYNAMICS SHARES, DILUTED TO 13%; CORRECTION

MARKET REPORT

The Australian stock market fell 0.23 percent on Monday May 12, 2014 with the S&P ASX 200 down 12.4 points to 5,448.4 points. Twelve of the Biotech Daily Top 40 stocks were up, 16 fell, nine traded unchanged and three were untraded.

Circadian was the best, up seven cents or 41.2 percent to 24 cents with 231,500 shares traded, followed by Biotron up 11.1 percent to 10 cents with 777,169 shares traded and Oncosil up 10 percent to 11 cents with 4.1 million shares traded. Atcor climbed 4.2 percent; Acrux, Analytica, Prana and Sirtex were up more than three percent; Osprey and Starpharma rose more than two percent; Benitec and Tissue Therapies were up more than one percent; with Resmed up 0.9 percent.

Universal Biosensors led the falls, down 14 cents or 39.4 percent to 21.5 cents with 1.2 million shares traded (see below) followed by Prima down 12.5 percent to 4.2 cents with 19.2 million shares traded and Admedus down 12 percent to 11 cents with 11.7 million shares traded. Living Cell and Medical Developments lost eight percent or more; Optiscan fell 4.3 percent; Bionomics was down 3.3 percent; Anteo, Impedimed and Patrys shed more than two percent; GI Dynamics, Nanosonics and Neuren were down more than one percent; with Alchemia, Cochlear, CSL and Mesoblast down by less than one percent.

THE WALTER AND ELIZA HALL INSTITUTE FOR MEDICAL RESEARCH

The Walter and Eliza Hall Institute says its staff have shown that a type of cell death called necroptosis could be the underlying cause of inflammatory disease.

WEHI said the research team discovered that a previously identified molecule involved in necroptosis, receptor-interacting protein kinase 1 (RIPK1), was essential for survival by preventing uncontrolled inflammation.

The Institute said that the finding could lead to future treatments for inflammatory diseases including Crohn's disease, rheumatoid arthritis and psoriasis.

WEHI said its researchers also discovered that the survival molecule RIPK1 acted as the gatekeeper between cell life and death.

The research paper, entitled 'RIPK1 Regulates RIPK3-MLKL-Driven Systemic Inflammation and Emergency Hematopoiesis' was published in the journal Cell and an abstract is at: <u>http://www.cell.com/cell/abstract/S0092-8674%2814%2900537-6</u>.

WEHI said the research, by Prof John Silke, Dr Motti Gerlic and Dr Ben Croker, working with Doctorate of Philosophy students James Rickard, Joanne O'Donnell and Joseph Evans, showed RIPK1 was essential for a cell's decision to live or die, and how to die. Prof Silke said the team had shown for the first time that RIPK1 was a master controller of cell life and death and played a role in programmed cell death, or apoptosis.

"We showed that, in the body, RIPK1 is not only essential for initiating necroptosis, but also for inhibiting necroptosis and the runaway inflammation that can cause severe tissue damage," Prof Silke said.

WEHI said that necroptosis was a type of controlled death that instructed a cell to die while stimulating an inflammatory reaction to let the immune system know something had gone wrong.

The Institute said that when the cell death pathway began to spiral out of control, it could lead to inflammatory disease.

WEHI said that necroptosis had been implicated in neurodegenerative disease, brain injuries caused by blood loss and some viral infections.

Dr Gerlic said the study provided the first evidence that RIPK1 was essential for inhibiting necroptosis.

"This research puts a new dogma on the table about RIPK1 and its role in controlling or inhibiting necroptosis," Dr Gerlic said.

"It is also the first time that we have shown necroptosis and the molecules involved actually induce inflammatory disease, suggesting that targeting this pathway could be useful for treating human conditions such as psoriasis, rheumatoid arthritis and Crohn's disease," Dr Gerlic said.

Prof Silke said necroptosis was a newly discovered type of cell death that had been studied in the past five years.

"When our time comes to die, we don't have a choice," Prof Silke said. "However cells make this choice all the time, not only whether they die, but also how they die."

"They can choose to die quietly, or they can make a fuss," Prof Silke said.

Necroptosis is their way of letting everyone else know that they are dying and help is needed usually when something has gone wrong such as a viral infection," Prof Silke said. Dr Gerlic said the research team had shown RIPK1 played other important roles in the body and was essential for keeping blood stem cells alive after bone marrow transplant. "This finding is particularly important when considering treatments that target RIPK1, as it

could have unwanted side-effects for other cells in the body," Dr Gerlic said.

Prof Silke said the Institute was capitalizing on its expertise in necroptotic cell death with a program to identify small molecules that could target molecules downstream of RIPK1 in the necroptotic pathway, such as mixed lineage kinase domain-like.

CIRCADIAN TECHNOLOGIES

Circadian says it has completed a type B pre-investigational new drug meeting with the US Food and Drug Administration for OPT-302 for wet age-related macular degeneration. Circadian said that wholly-owned subsidiary Opthea Pty Ltd requested the meeting on May 9, 2014 with the FDA division of Transplant and Ophthalmology Products, Centre for Drug Evaluation and Research (CDER).

The company said the purpose of the meeting was to obtain guidance for the regulatory and clinical path for OPT-302 and clarity on the steps required for an investigational new drug (IND) application submission.

Circadian said that the discussions included manufacturing criteria, scope and design of IND-enabling preclinical studies and the scope and design of phase I/IIa clinical trials. The company said that the FDA agreed to Opthea's proposed indication for OPT-302 as a drug for the treatment of wet age-related macular degeneration (AMD), which was an important unmet medical need.

Circadian said that Wet AMD was the leading cause of blindness for people over the age of 50 years in the US and Europe and was estimated to affect more than 1.5 million people worldwide.

The company said that the prevalence of wet AMD was increasing annually as the population aged and was forecast to rise to three million people globally by 2020 and that wet AMD had an estimated \$5 billion a year market in the US alone.

Circadian said that OPT-302 was a soluble receptor that blocked vascular endothelial growth factor C and D and inhibited the hallmarks of wet AMD in preclinical models, including blood vessel growth and vessel leakage.

Circadian chief executive officer Dr Megan Baldwin said the meeting with the FDA was "successful and productive".

"We are pleased to complete this key milestone which is a major step forward towards filing the IND for OPT-302," Dr Baldwin said.

"Clarity has been provided on our strategy to bring this novel therapy to patients suffering from wet AMD and we aim to submit an IND and initiate a phase I/IIa clinical study in the first half of 2015," Dr Baldwin said.

Circadian climbed seven cents or 41.2 percent to 24 cents.

ADMEDUS

Admedus says it has raised \$8 million through "an oversubscribed placement to sophisticated and professional investors" at 10 cents a share.

Admedus said that existing shareholders at the record date of May 9, 2014 could participate in a share plan at the same price.

The company said the funds would be used to support programs including the expansion of sales teams in Europe and the US to market Cardiocel treated bovine cardiac repair tissue; post-market studies and further product development to expand the use of Cardiocel in cardiovascular surgical applications and fund the herpes simplex virus-2 therapeutic vaccine phase II study to begin by the end of 2014.

Admedus said the share plan would open on May 19 and close on June 3, 2014. The company said that Morgans was the lead manager to the placement, supported by WG Partners, with Baillieu Holst acting as co-manager.

Admedus fell 1.5 cents or 12 percent to 11 cents with 11.7 million shares traded.

NUSEP HOLDINGS

Nusep says that Malaysia's Xeraya Capital Labuan and Singapore's JP Asia Prime Capital have invested \$S16 million (\$A13.7 million in its Prime Biologics subsidiary. Nusep said that both entities had agreed to make an aggregate investment through the acquisition of series A preference shares in Prime Biologics.

Nusep executive chairman Alison Coutts told Biotech Daily that her company's holding in Prime would be reduced from 97 percent to about 60 percent with the investment. The company said that holders of series A preference shares would receive a fixed cumulative preferential dividend at the rate of 10 percent a year of its issue price and a preference to any distribution in a liquidation event.

Nusep said that its shareholding would be converted to series B preference shares, which would not have the right to vote at any general meeting of the company except in certain circumstances.

The company said that the investment would be through four tranches with the first tranche of \$S6.4 million to be received on the completion of the first milestone. Nusep said the funds would enable Prime to commercialize its human blood plasma fractionation business at its Singapore facility and develop its business throughout Asia and the Indian sub-continent.

The company said that the investment provided JP Asia Prime with an option to invest a further amount of up to \$S4 million but only within a timeframe of no more than three months from the date of signing the investment transaction documents.

Nusep said that following the investment, Xeraya and JP Asia Prime would collectively hold a 37.21 percent interest in the company with Nusep retaining 60.22 percent and the balance of 2.57 percent being held by independent third party contributors to the transaction.

The company said that Ms Coutts had been appointed as a non-executive director of Prime replacing Andrew Goodall, who remains a non-executive director of Nusep, with Thee Woon Goh retiring as a non-executive director of Prime.

Nusep said that Xeraya's investment was conditional on, among other things, the appointment of two directors to the Prime board, joining executive directors, Dr Hari Nair and John Manusu and Ms Coutts.

The company said that following the investment it would be free to pursue all applications of the core technology apart from applications to do with human blood plasma, which would be carried out by Prime from its Singapore base.

Nusep said it would continue to supply the membranes and cartridges to Prime under a new supply agreement on a commercial basis.

The company said monies flowing into Prime, subject to appropriate budgets and board approvals, would be used to repay loans made over time by Nusep to Prime.

Nusep said that once received, it would use some of these funds to repay monies owing by it as well as to assist in the development of other applications from the core technology such as Spermsep and also to expand and develop further capabilities around membrane technologies for biological separations.

The company said that it was investigating its rights in respect of taking enforcement action against Mr Goh and it had agreed debt arrangement in place with Mr Goh in relation to an outstanding sum of \$1.3 million in relation to his investment in Nusep. Today, Nusep said that Ti Rakau Developments, a company related to director Mr Goodall, had bought 3,000,000 shares over which Nusep had an interest, at 10.5 cents a share, the sale reduced the debt owed by Mr Goh and the \$315,000 raised would reduce a loan owed by Nusep to Ti Rakau Developments (BD: Sep 27, Oct 3, 2012).. Nusep was untraded at 8.3 cents.

BONE MEDICAL

Bone says chief executive officer Peter Young has resigned, as its clinical trial comparing oral Capthymone for osteoporosis with an available injectable treatment is approved. Bone said that the study was approved by the Queensland Institute of Medical Research human research ethical committee.

The company said that the study would conducted at the Institute's Berghofer Medical Research Institute in Brisbane and was expected to begin before the end of May and conclude within three months.

Bone chairman Rob Towner said that "one of our goals when recapitalizing the company in January 2014 was to advance the company's technology and so we are very pleased that it has taken only four months to recommence the clinical studies of Bone's orally delivered [parathyroid hormone]".

The company said that Mr Young had resigned as chief executive officer and as a director and would be a "senior consultant and advisor" providing operational support and advice. Bone fell 0.1 cents or 4.8 percent to two cents with 7.55 million shares traded.

LBT INNOVATION

LBT says scientific director John Glasson has presented the Automated Plate Assessment System to microbiologists and diagnostic companies at a European conference. LBT said the Automated Plate Assessment System (APAS) was "a cutting-edge cultureplate interpretation and reporting system, developed in a joint venture with Swiss instrumentation company Hettich AG.

The company said that the first results from studies using the APAS diagnostic technology were presented to the European Congress of Clinical Microbiology and Infectious Diseases and showed the initial evaluation of an image analysis device for the screening of cultures from clinical specimens and provided the first published clinical review of LBT's intelligent imaging platform for automating the analysis of biomedical imagery, based on a series of algorithms and medical reporting systems.

LBT said that Mr Glasson's presentation reported the results of a trial last year, in which cultures from a number of clinical sample types were screened by APAS and the results compared with those of a team of experienced microbiologists.

The company said that the results showed that the automated system agreed with the microbiologists' findings, without missing a single potential pathogen.

LBT said that global business development vice-president Peter Bradley, who was also the general manager of the LBT and Hettich joint venture company Clever Culture Systems AG established to drive the marketing and sales of APAS laboratory instruments, presented on the practical benefits of APAS to attendees at the conference.

LBT said the APAS technology was due to undergo clinical trials in Australia and the US ahead of regulatory submissions this year and Hettich was in the process of integrating APAS with auto-incubators and automated plate readers ahead of a global launch in 2015. LBT fell one cent or 7.7 percent to 12 cents.

VIRAX HOLDINGS

After the market closed on Friday, Virax said that it would issue one free share for every five shares acquired in the \$3,000,000 placement at 1.2 cents a share.

Earlier in the day, Virax posted meeting results showing overwhelming shareholder approval for the Pathway Oncology acquisition and the placement.

Virax fell 0.2 cents or 18.2 percent to 0.9 cents with 18.8 million shares traded.

UNIVERSAL BIOSENSORS

One slide in Universal Biosensors 18-page 'Value Drivers Presentation' is believed to have triggered selling that led to a 39.4 percent share price fall today.

Biotech Daily was contacted by a specialist finance group asking whether it was publicly known that Johnson & Johnson had a lump sum service fee option to acquire all the rights to the Universal Biosensors produced blood glucose test strips after Lifescan had reached a threshold of \$US45 million in cumulative quarterly service fees.

Universal Biosensors said the lump sum payment would be double the total for the 12 months following the threshold limit request.

Johnson & Johnson recently announced it would produce test strips in competition to Universal Biosensors and with the Australian company having recorded its first quarter of service fees above \$1 million, it could be five to 10 years to reach the \$US45 million threshold (BD: Nov 7, 2013).

Universal Biosensors has been paid one US cent per strip under the quarterly service fee agreement with Lifescan, which continues irrespective of the manufacturer of the strips. For the year to December 31, 2012, Universal Biosensors received service fees of \$2.2 million implying as the sole manufacturer it made about 220 million strips

A slide in a quarterly presentation also released today said that total quarterly service fees received since January 2010 totalled \$7,417,000.

Universal Biosensors fell 14 cents or 39.4 percent to 21.5 cents with 1.2 million shares traded.

CLINUVEL PHARMACEUTICALS

Clinuvel has requested a trading halt pending "an announcement to the market regarding a capital raising".

Trading will resume on May 14, 2014 or on an earlier announcement. Clinuvel last traded at \$1.50.

<u>GI DYNAMICS</u>

M&G Investment Funds says it has increased its substantial holding in GI Dynamics from 55,265,110 Chess depositary interests to 63,190,038 CDIs but has been diluted from 15.38 percent to 13.34 percent.

The London-based M&G group said it acquired 2,000,000 shares on May 8, 2014 in the placement at 52 cents as well as 7,411,464 shares for \$4,019,926 or an average of 54.2 cents a share between August 8 2013 and April 8, 2014 (BD: May 2, 2014).

On Friday, GI Dynamics filed a substantial shareholder notice naming both Polaris Venture Partners and Domain Ventures (BD: May 9, 2014).

Today the company said that the notice related to Domain Partners.

No sub-editors were hurt in making this correction.

GI Dynamics fell one cent or 1.9 percent to 51.5 cents.