



Biotech Daily

Tuesday April 7, 2015

Daily news on ASX-listed biotechnology companies

- * **ASX UP, BIOTECH DOWN: PHARMAXIS UP 12%, GENETIC TECHNO DOWN 12%**
- * **WEHI: 'LOW MCL-1 LEVELS COMPROMISE BLOOD PRODUCTION'**
- * **PHARMAXIS PXS4728A 'SAFE, ORALLY BIO-AVAILABLE'**
- * **SOUTH AUSTRALIA UNI: 'EDARAVONE AIDS ALZHEIMER'S IN MICE'**
- * **BENITEC TT-034 'EXPRESSING shRNA IN DOSED PATIENTS LIVERS'**
- * **ADMEDUS EXPANDS ADAPT TISSUE TO BRAIN, SPINE DURA MATER**
- * **REGENEUS SCALES-UP PROGENZA FOR OSTEOARTHRITIS TRIAL**
- * **PHYLOGICA TAKES 7.5% OF UK PHOREMOST IN PHYLOMER DEAL**
- * **GOLDMAN SACHS BELOW 5% OF NANOSONICS, AGAIN**
- * **TISSUE THERAPIES LOSES CEO DR STEVEN MERCER, CHAIRMAN GOES**
- * **PHYTOTECH REQUESTS 'MMJ MERGER UPDATE' TRADING HALT**
- * **APPLICATIONS CLOSING FOR STC \$140k MEDTECH ENTREPRENEURS**

MARKET REPORT

The Australian stock market was up 0.46 percent on Tuesday April 7, 2015 with the S&P ASX 200 up 27.4 points to 5,926.0 points. Eleven of the Biotech Daily Top 40 stocks were up, 19 fell, eight traded unchanged and two were untraded.

Pharmaxis was the best, up 1.5 cents or 11.5 percent to 14.5 cents with 5.8 million shares traded, followed by Patrys up 10 percent to 1.1 cents with three million shares traded. Antisense climbed 4.4 percent; Biotron was up 3.45 percent; Atcor, Optiscan and Starpharma rose more than two percent; Admedus, Neuren, Psivida and Resmed were up one percent or more; with CSL and Sirtex up by less than one percent.

Genetic Technologies led the falls, down 0.5 cents or 11.6 percent to 3.8 cents with 9.2 million shares traded. Both Compumedics and Uscom lost 9.1 percent; Actinogen, Bionomics, IDT and Mesoblast shed six percent or more; Analytica, Medical Developments and Tissue Therapies fell more than four percent; Anteo and Impedimed were down three percent or more; Acrux, Benitec, Clinuvel, Osprey and Universal Biosensors shed more than two percent; Avita was down 1.6 percent; with Reva and Cochlear down by less than one percent.

THE WALTER AND ELIZA HALL INSTITUTE FOR MEDICAL RESEARCH

The Walter and Eliza Hall Institute says that depleted levels of cell survival protein MCL-1 fatally compromises blood cell production following massive blood cell depletion.

The Institute said that the research team led by Dr Alex Delbridge, Dr Stephanie Grabow and Prof Andreas Strasser found that reducing MCL-1 levels hindered recovery of the blood cell system after extensive destruction of mature blood cells, which was a common side-effect of chemotherapy and radiotherapy.

WEHI said that reducing MCL-1 impaired reconstitution of the bone marrow after blood stem cell transplants, a vital curative treatment for some cancers.

The article, 'Antagonism between MCL-1 and PUMA governs stem/progenitor cell survival during hematopoietic recovery from stress' was published in the journal Blood with an abstract at: <http://www.bloodjournal.org/content/early/2015/04/06/blood-2015-01-621250>.

Dr Delbridge said MCL-1 was critical for the survival of many cancer cells, including leukaemias and lymphomas, and played a role in normal blood cell production.

"Our previous research has shown that targeting MCL-1 could be used with great success for treating certain blood cancers," Dr Delbridge said.

"However we have now shown that MCL-1 is also critical for emergency recovery of the blood cell system after cancer therapy-induced blood cell loss," Dr Delbridge said. The Institute said that the overproduction of cell survival proteins, such as MCL-1, allowed emerging cancer cells to escape from death-inducing signals, enabling the accumulation of further genetic mutations that promote cancer development.

WEHI said that drugs that reduced the activity of pro-survival proteins could kill cancer cells and were a promising therapeutic strategy.

Dr Delbridge said the research team used a genetic trick to mimic the effect of reducing MCL-1 activity to examine the impact it had on the blood cell system after conventional cancer treatments such as chemotherapy.

"Removing one copy of the gene encoding MCL-1 reduced its concentration, replicating the effects of a partial inhibition by a drug," Dr Delbridge said.

"We found that reducing MCL-1 protein levels severely impaired recovery of the blood cell system following chemotherapy," Dr Delbridge said.

"This exquisite dependency on MCL-1 for emergency blood cell production has important implications for potential cancer treatments involving MCL-1 inhibitors," Dr Delbridge said.

Dr Grabow said that many current treatments for blood cancers involved patients being treated with chemotherapy or radiotherapy, sometimes followed by stem cell transplantation to repopulate the bone marrow.

"What we have shown is that, if MCL-1 activity is compromised, a patient would face a significant hurdle in producing new blood cells," Dr Grabow said.

"If MCL-1 inhibitors are to be used in combination with other cancer therapies, careful monitoring of the blood cell system will be needed," Dr Grabow said.

"The research findings would aid the design of future clinical studies trialling MCL-1 inhibitors, Dr Grabow said. "Our institute colleagues are working to evaluate a potential new drug to treat blood cancers by targeting MCL-1."

"Our findings suggest that MCL-1 inhibitors and chemotherapeutic drugs should not be used simultaneously," Dr Grabow said.

Dr Delbridge said the discovery also offered insights for improving stem cell transplantation, because until the blood cell system was functionally restored, patients were vulnerable to infection.

"Our research suggests that increasing levels of MCL-1 or decreasing the activity of opposing proteins could be a viable strategy for speeding up the regeneration process and reducing the risk of infection after stem cell transplantation," Dr Delbridge said.

PHARMAXIS

Pharmaxis says its 48-patient single ascending dose phase I trial of PXS4728A has shown no safety issues and will proceed to multiple ascending doses.

Pharmaxis said that the single ascending dose was conducted in healthy subjects divided into groups with each taking a single dose ranging from 1mg to 20mg or placebo.

In March, Pharmaxis said the Ingelheim, Germany-based Boehringer Ingelheim International GmbH had an option on PXS4728A and related semicarbazide-sensitive amine oxidase and vascular adhesion protein-1 (SSAO/VAP-1) inhibitor molecules for non-alcoholic steato-hepatitis until May 15, 2015 (BD: Mar 12, 2015).

Today, Pharmaxis reported "no safety concerns" and 24 subjects in the multiple ascending dose stage would be split into three groups and receive a dose of either active or placebo daily for 14 days, with three different doses of PXS4728A to be trialled.

The company said the trial confirmed that PXS4728A was orally bio-available and a single dose produced long lasting inhibition of the SSAO/VAP-1 enzyme.

Pharmaxis said the phase I first stage results would be presented at the International Liver Congress in Vienna from April 22 to 26, 2015.

Pharmaxis was up 1.5 cents or 11.5 percent to 14.5 cents with 5.8 million shares traded.

THE UNIVERSITY OF SOUTH AUSTRALIA

The University of South Australia says that edaravone, or Radicut, can alleviate the progressive cognitive deficits of Alzheimer's disease.

The University said that its scientists, working with colleagues from the Chongqing, China-based Third Military Medical University, found that edaravone, a free radical scavenger prescribed for ischemic stroke, could alleviate Alzheimer's disease pathologies and improve functions of learning and memory, in a mouse model, and by multiple mechanisms.

The research, entitled 'Edaravone alleviates Alzheimer's disease-type pathologies and cognitive deficits' was published in the Proceedings of the National Academy of Sciences and is available at: <http://www.pnas.org/content/early/2015/04/01/1422998112.full.pdf>.

The University said that edaravone was available in some Asian countries for the treatment of ischemic stroke, the most common type of stroke caused by blood clots.

The University's neurosciences research chair and the study's lead researcher Prof Xin-Fu Zhou said that edaravone could alleviate Alzheimer's disease pathologies and improve functions of learning and memory in a mouse model of the disease by multiple mechanisms.

"Edaravone can bind the toxic amyloid peptide which is a major factor leading to degeneration of nerve cells," Prof Zhou said.

Prof Zhou said that lessons from failures of current clinical trials suggested that targeting multiple key pathways of the Alzheimer's disease pathogenesis was necessary to halt the disease progression.

"Edaravone can suppress the toxic functions of amyloid beta to nerve cells," Prof Zhou said. "It is a free radical scavenger which suppresses oxidative stress that is a main cause of brain degeneration."

"The drug can suppress the production of amyloid beta by inhibiting the amyloid beta production enzyme," Prof Zhou said. "It also inhibits the tau hyper-phosphorylation which can generate tangles accumulated in the brain cells and disrupt brain functions."

The University said that edaravone should not be used for Alzheimer's patients before appropriate clinical trials were undertaken and Prof Zhou was seeking investment and partnership opportunities to further the research.

BENITEC BIOPHARMA

Benitec says that liver biopsies show that TT-034 for hepatitis C has expressed three short hairpin RNAs, each targeting a different part of the hepatitis C virus genome. Benitec said that biopsies from the three patients dosed in its phase I/IIa trial confirmed it was "proceeding according to expectations".

The company said that TT-034 produced three silencing short hairpin RNAs (shRNAs) in the liver and the expression of the three shRNAs in patients' liver cells was an essential requirement for TT-034 to exert a clinical reduction of hepatitis C viral load and the biopsies confirmed the expression occurred in all three patients.

Benitec said that the second patient in cohort 2 had not been biopsied yet, and the third patient in cohort 2 was yet to be dosed due to a personal issue.

The company said that the dose in cohorts 1 and 2 was sub-therapeutic and the amount of shRNA produced would not result in a reduction of hepatitis C viral load.

Benitec said that there had been no treatment-related serious adverse effects in any of the four patients dosed.

Benitec fell 1.5 cents or two percent to 73 cents.

ADMEDUS

Admedus says that a pre-clinical study of Adapt treated tissue to repair dura mater, the outer sheath of the brain and spinal cord.

Admedus said that the sheep dura mater study, undertaken in conjunction with Charles Sturt University in Wagga Wagga and a neurosurgeon from Melbourne University, demonstrated "excellent post-operative responses with no longer term negative outcomes, no fluid leakage or post-operative infections, while proving to be an excellent replacement for surgical procedures".

Admedus chief executive officer Lee Rodne said that expansion of the company's regenerative tissue portfolio into dura mater repair was "an exciting and important step in the development and growth of Admedus".

Admedus said that dura mater was often damaged during traumatic brain injuries and in the US alone, there were about 1.7 million traumatic brain injuries each year, with the Centre for Disease Control estimating around 275,000 hospitalizations a year.

The company said that after one month post implantation, the Adapt treated tissue repairs demonstrated no signs of post-operative infection, no leakage of cerebrospinal fluid, no signs of post-operative chemical meningitis and no signs of tissue rejection, which were all issues affecting the existing products used in the repair of dura mater.

Admedus said that the Adapt-treated tissue was ready to use off-the-shelf without the need for pre-implant preparation or rehydration.

The company said that after one month the repairs showed the initial stages of integration into and around the implanted Adapt treated tissue, a key factor in the longer term treatment of patients who have undergone dura mater repair.

Admedus said it would complete additional histology studies on the explanted tissues while progressing to the next study to support a product regulatory filing and additional data would be prepared for presentation.

"These initial results are very encouraging and show the potential for Adapt tissue engineered dura mater in this market," said Mr Rodne.

"The results are consistent with what we already know about Adapt treated tissue, with its improved bio-compatibility, strength and handling properties combining to give this product a definite edge in the dura mater repair market," Mr Rodne said.

Admedus was up 0.1 cents or 1.4 percent to 7.2 cents with 6.0 million shares traded.

REGENEUS

Regeneus says it has completed the first manufacture of Progenza at scale for its first-in-human trial for the treatment of osteoarthritis.

Regeneus said that the Progenza trial product was manufactured at Cryosite's Australian Therapeutic Goods Administration-licensed facility in Sydney, with the production team using its experience in large-scale stem cell manufacture of Cryoshot, the clinical-stage off-the-shelf allogeneic adipose stem cell product for the treatment of canine and equine musculoskeletal conditions.

The company said that the production was "a key manufacturing milestone for its ...off-the-shelf allogeneic stem cell therapy product Progenza", which had shown to be safe and prevented disease progression for osteoarthritis in rabbits (BD: Mar 9, 2015).

Regeneus said it expected to receive ethics approval and begin recruitment by July 2015. The company said that during manufacture, the fat-derived mesenchymal stem cells were expanded to a scale demonstrating the capacity to produce from a single donor millions of therapeutic doses of Progenza, based on five million to 10 million cells per dose.

Regeneus chief executive officer John Martin said that "production of commercial quantities of stem cells from a single donor is critical to maximize dose-to-dose consistency".

"This scale of production will minimize clinical trial and regulatory risks while reducing the cost of the final product," Mr Martin said.

Regeneus fell half a cent or 3.6 percent to 13.5 cents with 1.5 million shares traded.

PHYLOGICA

Phylogica says it has licensed specified Phylomer libraries to the Cambridge UK-based Phoremest for phenotypic screening to identify novel disease targets including cancer.

Phylogica said that the licence included the identification and development of small molecule drugs against these targets.

The company said that the licence included preference conditions capping the number of similar phenotypic deals Phylogica might make during an 18-month option period and it would retain all commercial rights to exploit any Phylomer peptides identified in the screens for therapeutic purposes.

Phylogica said it would obtain a 7.5 percent equity stake in Phoremest along with non-exclusive rights to commercialize any functional Phylomer peptides and associated disease targets identified by Phoremest for peptide therapeutics and an option to negotiate exclusive rights for such purpose.

Phylogica chief executive officer Dr Richard Hopkins said that the agreement formalized a "long standing collaboration with Prof Venkitaraman's team at the University of Cambridge who are co-founders of Phoremest and who are world leaders in cutting-edge phenotypic screening approaches to identify novel disease targets involved in cancer".

"This agreement provides Phylogica's shareholders with an equity stake in an innovative company with its own proprietary small molecule-based oncology programs," Dr Hopkins said.

"It also has the potential to feed Phylogica's oncology pipeline with novel cancer targets and peptides, accelerating our path to product development and adding significant value to the company," Dr Hopkins said.

Phylogica fell 0.2 cents or 5.6 percent to 3.5 cents with 19.8 million shares traded.

NANOSONICS

The Delaware-based Goldman Sachs Group says it has ceased its substantial shareholding in Nanosonics, again.

Goldman Sachs said that between March 27 and March 31, 2015 it received shares under a counterparty agreement, returned shares, lent and borrowed shares, with the sole paid transaction the sale of 23,529 shares for \$46,190 or \$1.96 a share.

On March 20, Goldman Sachs became a substantial shareholder in Nanosonics with 14,925,513 shares or 5.34 percent of the company, ceased its substantial holding on March 26 and resumed it on March 31, with 14,902,971 shares or 5.33 percent of the company (BD: Mar 20, 26, 31, 2015).

The substantial shareholder notice said the shares were held by subsidiaries, Rothesay Life, JP Morgan Chase, RBC Dexia Australian, HSBC Custody Nominees Australia and the Bank of New York Mellon, with some of the holdings relating to Goldman Sachs and JP Morgan Chase subject to an "overseas securities lender's agreement", as well as Rothesay Life and Morgan Stanley as parties to a "global master securities lending agreement".

Nanosonics was unchanged at \$1.81.

TISSUE THERAPIES

Tissue Therapies says that chief executive officer Dr Steven Mercer has effective from today and chairman Roger Clarke will stand down, continuing as a non-executive director. Tissue Therapies said that operations director Nigel Johnson had been appointed acting chief executive officer and search had begun for a new chief executive officer.

The company said that Mr Johnson had held key roles for more than 10 years and had "a thorough knowledge of the challenges facing Tissue Therapies in its planning for both European and US approval for its lead product Vitrogro ECM".

Tissue Therapies developed its Vitrogro wound treatment and demonstrated efficacy in 2008, but has faced continuous delays in the European registration process including questions over its device or drug categorization (BD: Oct 20, 2008; Feb 25, Mar 26, 2015).

The company said that Dr Cherrell Hirst had been appointed interim chairman and would lead the search for a chief executive officer and chairman.

Mr Clarke said that the changes "send a clear message that the board clearly acknowledges the need for focused leadership as the company moves forward with its goal of launching Vitrogro in multiple markets whilst building shareholder value".

"It has been a privilege to be closely involved with the evolution of Tissue Therapies from a startup company to an ASX listed therapeutic company with a strong and commercially valuable pipeline of wound care products," Mr Clarke said. "As a key shareholder I wish to reassure the market that I remain a devout believer in the company's future potential."

Tissue Therapies fell half a cent or 4.55 percent to 10.5 cents.

PHYTOTECH MEDICAL

Phytotech has requested a trading halt "pending an update on the company's proposed merger with MMJ Bioscience Inc".

In March, Phytotech said it would acquire the Vancouver, British Columbia-based MMJ Bioscience for up to \$20,685,000 through the issue of up to 68,000,000 Phytotech shares valued at 30.5 cents a share (BD: Mar 24, 2015).

Trading will resume on April 9, 2015 or on an earlier announcement.

Phytotech last traded at 31 cents.

[SMALL TECHNOLOGIES CLUSTER, VICTORIA GOVERNMENT](#)

Melbourne's Small Technologies Cluster (STC) says that applications for the 2015 round of Medtech's Got Talent closes tomorrow, April 8, 2015.

The Victoria Government-established Small Technologies Cluster said it would provide \$140,000 in service prizes to up to five medical technology concepts (BD: Mar 19, 2015). The Cluster said that the Victorian-wide challenge "focused on training and supporting emerging medical technology students, post-doctoral and recent graduate entrepreneurs". The Cluster said that applicants needed to submit an executive summary by April 8 and the top 30 applicants would be invited to pitch at the April 16 "rapid fire round" and 16 semi-finalists would advance to the finals, which would select five finalists, who would each receive \$20,000 plus valuable service prizes and enter a six week, intensive accelerated technology road-mapping program.

STC said that the grand prize winner would be selected at a closed-door investor boardroom pitch on August 7 and receive an additional \$40,000.

For details go to: <http://www.stcaustralia.org/entrepreneur-challenge/>.