# Biotech Daily

Thursday October 24, 2013

*Daily news on ASX-listed biotechnology companies*

*** ASX UP, BIOTECH DOWN: PHOSPHAGENICS UP 19%, ACRUX DOWN 22.5%**

*** MESOBLAST, INTREXON, ZIOPHARM UNITE FOR NEW CANCER DRUGS**

*** STARPHARMA: 'DENDRIMER-DOCETAXEL STOPS NEUTROPENIA IN RATS'**

*** PHOSPHAGENICS: 'OPIOID PATCH BEATS HIGH DOSE TABLET'**

*** FEDERAL GOVERNMENT RECOMMITS TO RESEARCH FUNDING**

*** ACRUX AXIRON SALES DOWN, $26m MILESTONE**

*** SCHRODER, ASSOCIATES TAKE 7% OF COCHLEAR**

*** INVERAREY TAKES 7% OF IMMURON**

*** OBJ PLEADS SCHULTZ TO ASX 23.5% QUERY**

*** WEHI 'IT'S A HIT - DECADE OF DRUG DISCOVERY' SYMPOSIUM**

*** BIO-MELBOURNE, INFECTION NETWORK BREAKFAST ON SUPERBUGS**

## MARKET REPORT

The Australian stock market was up 0.31 percent on Thursday October 24, 2013 with the S&P ASX 200 up 16.8 points to 5,372.9 points. Twelve Biotech Daily Top 40 stocks were up, 20 fell, four traded unchanged and four were untraded. All three Big Caps were up.

Phosphagenics was the best, up five cents or 47.6 percent to 15.5 cents with 29.6 million shares traded. QRX climbed 5.6 percent; Clinuvel and Living Cell were up more than three percent; IDT and Osprey rose more than two percent; Alchemia, Anteo, Benitec, Cochlear, Genetic Technologies, GI Dynamics, Mesoblast and Resmed were up one percent or more; with CSL up 0.7 percent.

Acrux led the falls, down 37 cents or 11.8 percent to $2.76 with four million shares traded. Cellmid and Phylogica lost more than nine percent; Allied Health fell eight percent; Antisense, Patrys and Prima were down more than seven percent; Atcor and Optiscan were down five percent or more; Avita, Psivida and Universal Biosensors fell four percent or more; Prana was down 3.85 percent; Bionomics, Impedimed, Medical Developments and Nanosonics shed more than two percent; with Sirtex, Starpharma and Viralytics down more than one percent.

MESOBLAST

Mesoblast says it will collaborate with Intrexon Corp and Ziopharm Oncology to develop a new class of cancer therapeutics.

Mesoblast said the collaboration would combine its mesenchymal lineage cells with the Blacksburg Virginia-based Intrexon's synthetic biology Rheoswitch platform to co-develop complex transgene-enabled, cell-based treatments for oncology applications.

The company said the goal was to develop therapeutic candidates for cancer which both had specific tumor-targeting characteristics and controlled gene expression.

Mesoblast said the partnership was a 50-50 collaboration between Mesoblast and the Boston, Massachusetts-based Ziopharm cancer therapeutics company, with Intrexon participating through its collaboration with Ziopharm.

Mesoblast said that if successful in feasibility studies targeting lung cancer, the companies expected to form a joint venture to advance development of candidates.

Intrexon chairman Randal Kirk said the combination of expertise, technologies and production capabilities in Mesoblast, Ziopharm, and Intrexon was "an excellent example of how collaborations will be expanded into new areas of therapeutic research and development".

Mesoblast chief executive officer Prof Silviu Itescu said that mesenchymal lineage cells (MLCs) modified with Rheoswitch technology "could be ideal vehicles to deliver therapeutic transgenes to targeted tumors at specific sites in the body".

"Additionally, our cells can be commercially manufactured to industrial scale for clinical use as they are readily expanded to large numbers in culture, can be used in allogeneic recipients without the need for matching or immuno-suppression and are available cryopreserved for off-the-shelf use," Prof Itescu said.

"By seeking to develop anti-cancer effectors using our proprietary MLCs, we are now expanding the focus of our oncology therapeutic area beyond the field of bone marrow transplants and the treatment of its major complication, acute graft-versus-host disease," Prof Itescu said.

"If this complex cell plus transgene approach is successful for lung cancers, the technology will be explored for the treatment of other cancers," Prof Itescu said.

Mesoblast said that in initial studies, Ziopharm would leverage Intrexon's Ultravector platform to design and optimize therapeutic gene expression in MLCs to mediate an anti-cancer effect against lung cancer.

The company said that Intrexon's Rheoswitch platform would be used for inducible control over the amount and timing of therapeutic gene expression providing precise regulation for MLC-delivered therapies.

Ziopharm chief executive officer Dr Jonathan Lewis said that the ability of Intrexon's Rheoswitch platform to induce and regulate expression of anti-cancer effectors through dosing with an activator had been demonstrated in phase II studies for advanced melanoma and breast cancer.

"By integrating Mesoblast's MLC platform into our therapeutic complex transgene research and development program, we hope to target advanced non-small-cell lung cancer and advance a new field of cell-based therapies," Dr Lewis said.

Intrexon's head of health and former National Cancer Institute director Dr Samuel Broder said the co-development of Rheoswitch-regulated transgenes and cell-based therapy meant lung cancer cells could be attacked simultaneously in two dimensions, delivering modified MLCs to the lung tissue and through Intrexon's Rheoswitch technologies, in which therapeutic transgenes were expressed under the control of a small molecule activator, permitting MLCs to deliver anti-tumor proteins to sites where they are needed.

Mesoblast was up seven cents or 1.2 percent to $5.96 with 243,965 shares traded.

STARPHARMA HOLDINGS

Starpharma says that rats treated with its dendrimer-docetaxel exhibited a lack of neutropenia a sign of bone marrow toxicity compared to Taxotere (docetaxel) alone.

Starpharma said that rats treated with Taxotere exhibited severe neutropenia which was the most important dose-limiting side effect of Taxotere.

The company said that severe neutropenia, or abnormally low circulating neutrophil numbers, was a life-threatening toxicity that occurred in more than 75 percent of patients treated with docetaxel.

Starpharma said that neutrophils were a type of white blood cell and severe neutropenia exposed the patient to a high risk of serious infection and required modification to dosing schedules, rescue therapy with expensive drugs and additional clinical management. The company said that Taxotere had an US Food and Drug Administration warning in its product information regarding neutropenia including contraindications and management.

Starpharma chief executive officer Dr Jackie Fairley said the results were “really very positive for our dendrimer-docetaxel formulation in the lead up to its move into the clinic”.

“We have now shown that Starpharma’s dendrimer technology can prevent neutropenia as observed in independent studies of two leading cancer drugs, docetaxel and oxaliplatin,” Dr Fairley said.

“These findings suggest that the ability to avoid these important toxicities is likely to be a feature of the dendrimer platform and therefore, could also be anticipated with other cancer drugs,” Dr Fairley said.

Starpharma said that its dendrimer-docetaxel had been shown to be water soluble, removing the need for Polysorbate 80, a detergent which is present in Taxotere and most other formulations of docetaxel and which caused anaphylaxis; had excellent drug targeting to tumor tissue, more than 40-times greater levels than Taxotere; had a 60-fold increase in plasma half-life; and had significantly enhanced anti-cancer effect when compared to Taxotere.

“When all these advantages and clinically significant benefits of the Starpharma dendrimer-docetaxel formulation are placed alongside the latest findings of a lack of neutropenia, it places the dendrimer formulation in a very compelling competitive position,” Dr Fairley said.

“It is particularly pleasing to have these latest findings ahead of taking the product into the clinic later this year,” Dr Fairley said.

Starpharma said that the neutrophil counts of the dendrimer-docetaxel formulation treated rats remained normal throughout the study, but rats treated with Taxotere exhibited a significant neutropenia resembling the neutropenia that was commonly seen in humans.

The company said that the results indicated that dendrimer-docetaxel did not cause neutropenia.

Starpharma said that dendrimer-docetaxel treated rats were also free from other bone marrow toxicities such as thrombocytopenia, or low platelets, which were observed in Taxotere treated animals.

“The potential to be able to use docetaxel with reduced need for expensive rescue therapies or additional hospital stays represents an important advance for patient care,” Dr Fairley said.

“Apart from better patient outcomes, the potential savings for constrained health-care budgets are also very attractive,” Dr Fairley added.

Starpharma said the dendrimer technology could be applied to a wide variety of drugs including proteins, antibodies, hormones in addition to being valuable in cancer treatments.

Starpharma fell one cent or 1.1 percent to 89 cents.

PHOSPHAGENICS

Phosphagenics says its tocopheryl phosphate mixture-oxymorphone patch delivered therapeutic plasma concentrations to all 12 subjects in its multi-dose phase I trial.

Phosphagenics said the trial, at Linear Clinical Research in Perth, Western Australia, was designed to characterize the oxymorphone delivery profile from repeated applications of a three-day patch that mimicked a pain medication regime.

The company said that all 12 subjects demonstrated oxymorphone plasma concentrations well above the threshold therapeutic concentrations produced by the oral long-acting or extended release dosage form (Opana ER) within the first application period of three days.

Phosphagenics said that oxymorphone plasma concentrations increased with repeated patch application, while maintaining the profile desirable for transdermal products.

The company said that the results demonstrated that the maximum plasma concentration in subjects could be as high as that produced by a single oral dose of the highest strength 40mg Opana ER tablet.

Phosphagenics said the relationship between oxymorphone plasma concentration and analgesic effect was well established and exceeding the defined target plasma concentrations ensured the product would be therapeutic.

The company said the tocopheryl phosphate mixture or TPM-oxymorphone pharmacokinetic profile resulting from the multiple-dosing regime “exceeded expectations and showed plasma concentrations equivalent to those attained by oral dosages used to treat moderate-to-severe chronic pain”.

Phosphagenics chief scientific officer Dr Paul Gavin said: “The importance of the success of this trial cannot be overstated”.

“While we were confident going into the trial, the magnitude of the oxymorphone concentration in plasma surpassed our expectations,” Dr Gavin said. ”The result is also significant with respect to abuse potential, a major concern of the (US Food and Drug Administration) and a significant hurdle for product registration of any opioids.”

Last month, the FDA issued class-wide safety labeling changes and new post-market study requirements for all extended-release and long-acting opioid analgesics for pain.

http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm367726.htm

The FDA announcement has been seen as the FDA raising the bar for opioid approvals, but Phosphagenics said the rules were an advantage for its patch which it said contained about 25 percent of the amount of the drug normally used in high dosage strengths of Opana ER over the same 72-hour dosage period, “thereby significantly reducing the amount of dispensed opioid that could be the target of abuse”.

“Not only can the patch deliver therapeutic amounts of oxymorphone, the results suggest that the patch can compete with the therapeutic value of the higher dosage strengths of the oral product and surpass them with respect to bioavailability,” Dr Gavin said.

Phosphagenics said it would proceed to a phase II trial, in mid-2014, but instead proving that the product was capable of providing analgesia for patients with chronic pain conditions, which was answered in the phase I trial the phase II trial would shift to defining the dosage regimes to be used and enhancing its commercial value.

Phosphagenics’ US commercialization partner Neura Therapeutik chief executive officer John LaLota said that “if approved, this product has the potential to capture significant market share in the extended release opioid market”.

Phosphagenics chief executive officer Harry Rosen said the study was “the biggest milestone in the company’s history”.

Phosphagenics said it had been allowed a very broad US patent for its patch.

Phosphagenics climbed five cents or 47.6 percent to 15.5 cents with 29.6 million shares traded.

## FEDERAL GOVERNMENT, NATIONAL HEALTH AND MEDICAL RESEARCH COUNCIL

The Member of the House of Representatives for Higgins Kelly O'Dwyer says the Coalition Government is committed to maintaining research funding levels.

Yesterday, the Federal Government said it will provide $559 million for 963 National Health and Medical Research Council grants, down 14.3 percent on the previous year.

In the lead up to the Federal Election Ms O'Dwyer said the Coalition was committed to maintaining NHMRC and Australian Research Council funding (BD: Mar 5, 2013).

Today, Ms O'Dwyer told Biotech Daily that the Coalition Government "recommits to medical health and research and identifies it as one of the key pillars to Australia building a diverse and robust five-pillar economy".

"Yesterday's announcement of $559 million of National Health and Medical Research Council grants provides certainty to a number of research facilities who were eagerly awaiting the announcement," Ms O'Dwyer said.

"Despite the report yesterday that the total was less than that of a similar announcement made 12 months prior, the Coalition is committed to honoring the total funding commitments to the NHMRC over the forward estimates; a year-on-year increase," Ms O'Dwyer said.

"In addition, the Coalition Government has also dedicated $200 million over five years to accelerate the work of Australian scientists and medical researchers working on a cure for dementia," Ms O'Dwyer said. "This round of NHMRC funding announcements is the first of a number for the new Government.".

"The Coalition Government is committed to fully funding the NHMRC as promised at the 2013 Federal Election, who will in turn, fund specific research projects," Ms O'Dwyer said.

## ACRUX

Acrux says Eli Lilly reports Axiron testosterone replacement sales of $US40.6 million for the three months to September 30, 2013, triggering a $US25 million payment.

Acrux share price fell as much as 40 cents or 12.8 percent to $2.73 on the news that the global net sales were down from $US47.1 million in the three months to June 30, 2013.

Last year, Acrux's share price fell on news that US sales of Axiron had fallen from $US17.7 million in the three months to June 30 to $US16.0 million in the three months to September 30, 2012 (BD: Nov 9, 2013).

Acrux said that sales for the nine months to September 30, 2013 totalled $US124.8 million and the company would receive a $US25 million ($A25.9 million) milestone payment in March 2014 as worldwide sales for the 2013 calendar year exceeded $US100 million, unless there was a material event resulting in a product recall.

Acrux said that the market continued to slow and Axiron's share had flattened at the same time that Eli Lilly had undertaken a sales force restructuring.

The company said that the sales for the three months to September 30 had improved its position, with the average royalty percentage of net sales increasing.

Acrux closed down 37 cents or 11.8 percent to $2.76 with four million shares traded.

## OBJ

OBJ has told the ASX that it is not aware of any information it has not announced which, if known, could explain recent trading in its securities.

The ASX said the company's share price rose 23.5 percent from 17 cents on October 23 to 2.1 cents today, October 24, 2013 and noted an increase in trading volume.

OBJ was up 0.2 cents or 11.8 percent to 1.9 cents with 20.4 million shares traded.

## COCHLEAR

Schroder Investment Management has increased its substantial shareholding in Cochlear from 3,039,486 shares (5.33%) to 3,949,650 shares (6.92%).
In September, the Pitt Street, Sydney and Gresham Street, London-based Shroder said it acquired shares and the then registered shareholders included BNP Paribas, Citicorp Nominees, HSBC Custody Nominees, JP Morgan Custodial Services, National Nominees, State Street Australia, Brown Brothers Harriman, Sommerzank, JP Morgan Chase Bournemouth and NT London (BD: Sep 20, 2013).
Today, Shroder said that between September 20 and October 23, 2013 it acquired 929,172 shares for $54,919,120 or an average price of $59.105 a share and sold 19,008 shares for $1,127,991 or an average price of $59.34 a share.
Cochlear was up 61 cents or 1.05 percent to $58.87 with 291,596 shares traded.

## IMMURON

The Melbourne-based Inverarey as trustee for Kilchurn Trust says it has become a substantial shareholder in Immuron with the acquisition of 71,250,000 shares (6.88%).
The Inverary announcement substantial shareholder notice said that Inverarety Pty Ltd (sic) held 70,000,000 shares and Ian Pattison and Kathherine Forrest held 1,250,000 shares with Chimaera Capital as registered holder.
The Inverarey notice said it acquired the 70,000,000 shares for $210,000 or 0.3 cents a share on May 13, 2013.
Immuron raised $284,000 in a rights issue at 0.3 cents a share (BD: May 1, 2013).
Immuron was unchanged at 0.8 cents with seven million shares traded.

## THE WALTER AND ELIZA HALL INSTITUTE FOR MEDICAL RESEARCH (WEHI)

The Walter and Eliza Hall Institute will hold a one-day symposium on the past 10 years of drug discovery research and the future for drug discovery.
The symposium, entitled ‘It’s a hit - Celebrating a decade of drug discovery’ will be held at the Institute on November 19, 2013.
The Institute said that the one day symposium would highlight the successes and the future of drug discovery at the Walter and Eliza Hall Institute
WEHI chemical biology division laboratory head and head of medicinal chemistry Dr Chris Burns told Biotech Daily the “aim of the day is to celebrate 10 years of drug discovery at WEHI, as well as present some of what the future might hold in this space”.
“The symposium is being sponsored by the State Government through the Department of State Development Business and Innovation and will provide ample opportunity to network with like-minded individuals from both the academic and commercial sectors,” Dr Burns said.
The Institute said that speakers included the University of Edinburgh’s Prof Manfred Auer, Griffith University’s Prof Vicky Avery, Monash Institute of Pharmaceutical Sciences’ Prof Jonathan Baell, Alfred Health’s Prof Stephen Jane, WEHI’s Prof Ben Kile and Dr Guillaume Lessene.
The Symposium will be held at the Walter and Eliza Hall Institute, 1G Royal Parade, Parkville, Victoria on November 19, 2013, from 9am to 5pm (AEDT).
The Institute said that registration for the free event was “essential” and should be emailed to registration@wehi.edu.au by November 8, 2013
For more information go to: www.wehi.edu.au/decadeofdrugdiscovery or contact Dr Kurt Lackovic on +613 9345 2542 or email lackovic@wehi.edu.au.

## BIO-MELBOURNE NETWORK

The Bio-Melbourne Network says that with the Victorian Infection and Immunity Network Industry Alliance it will explore the growing threat of antibiotic resistance bacteria.

The Network said that the November 12, 2013 Bio-Breakfast would outline the challenge facing the world from “the rapidly growing threat of superbugs or antibiotic resistance bacteria”.

The Bio-Melbourne Network said the meeting would discuss research, new product development, Government policy and incentives for pharmaceutical companies to invest in antibiotic discovery and development pipelines.

The Network said that speakers included University of Melbourne head of the Department of Microbiology and Immunology and Victorian Infection and Immunity Network co-convenor Prof Elizabeth Hartland, Austin Health director of infectious diseases Prof Lindsay Grayson, Biodiem projects manager Cathy Cropp and University of South Australia researcher Suzanne Schultz.

The Bio-Breakfast will be held on November 12 at Alfred Medical Research and Education Precinct Education Centre, 89 Commercial Road, Melbourne.

Registration is from 7:15am with presentations from 8am to 9am.

For more information and to register go to http://www.biomelbourne.org/events/view/300.