



# Biotech Daily

Friday December 5, 2014

*Daily news on ASX-listed biotechnology companies*

- \* **ASX, BIOTECH DOWN: IMPEDIMED UP 6.5%, ANTISENSE DOWN 10%**
- \* **MONASH-LED STUDY SHOWS OBESITY-LEPTIN-HYPERTENSION LINK**
- \* **STARPHARMA CONDOM DELAYED UP TO 6 MONTHS IN JAPAN**
- \* **CORRECTION: LIVING CELL**
- \* **PRIMA UPGRADES PATIENT CELL COLLECTION SYSTEMS**
- \* **MESOBLAST TO RELEASE 2.9m ESCROW SHARES**
- \* **RETROPHIN REDUCES TO 7% OF (FORMER) TARGET CLINUVEL**
- \* **BANK OF AMERICA, MERRILL LYNCH 'BORROW' UP TO 8% OF SUDA**
- \* **CHAIRMAN MARTIN ROGERS TAKES 8% OF ACTINOGEN**

## MARKET REPORT

The Australian stock market fell 0.62 percent on Friday December 5, 2014 with the S&P ASX 200 down 33.5 points to 5,335.3 points.

Eight of the Biotech Daily Top 40 stocks were up, 14 fell, 14 traded unchanged and four were untraded.

Impedimed was the best, up 4.5 cents or 6.5 percent to 74 cents with 857,433 shares traded, followed by Phosphagenics up 6.15 percent to 6.9 cents with 186,491 shares traded.

Admedus climbed 4.55 percent; Cellmid was up 3.6 percent; Acrux and Prana rose more than two percent; GI Dynamics was up 1.8 percent; with Resmed and Sirtex up by less than one percent.

Antisense led the falls, down 0.9 cents or 9.6 percent to 8.5 cents with 400,000 shares traded.

Benitec and Optiscan lost six percent or more; Bionomics and Patrys were down more than five percent; Uscom fell 4.55 percent; Biotron, IDT, Nanosonics and Pharmaxis shed two percent or more; CSL, Living Cell, Mesoblast, Psivida and Viralytics were down more than one percent; with Cochlear down 0.9 percent.

## MONASH UNIVERSITY

Monash University Obesity and Diabetes Institute director Prof Michael Cowley says the mechanism of action between obesity and high blood pressure has been found.

Prof Cowley said that a research collaboration led by his Institute investigated the link between obesity and elevated blood pressure and discovered that the hormone leptin which was secreted by fat cells was significantly elevated following weight gain and in obesity, acted in the brain to elevate blood pressure.

The research was undertaken at Monash as well as Warwick and Cambridge Universities in the UK, along with several American universities.

The article, entitled 'Leptin Mediates the Increase in Blood Pressure Associated with Obesity' was published in the journal Cell and the full article is available at:

<http://www.cell.com/cell/abstract/S0092-8674%2814%2901430-5>.

A summary of the article said that leptin was the link between obesity and increased blood pressure, acting through the dorsomedial hypothalamus to increase blood pressure, and that the blockade of leptin signalling reduced blood pressure in obese mice, and humans with defects in leptin signalling were protected from obesity hypertension.

Prof Cowley said that the studies involved both animal and human experiments, including a unique cohort of patients lacking the hormone leptin or lacking the leptin receptor.

The study found that both blocking leptin from producing its actions in the brain and removal of the leptin receptors from the brain reduced obesity-induced hypertension.

Prof Cowley said that as much as 80 percent of common hypertension was caused by excess body fat and the study, for the first time, described the mechanism by which obesity elevates blood pressure and opening new approaches to treat obesity-induced high blood pressure.

Prof Cowley said that the study used a number of new and unique technologies to link leptin in obesity-induced hypertension.

He said that in genetically engineered mice, only those with normal leptin signalling showed an increase in blood pressure when they became obese.

Prof Cowley said that the rodent data was confirmed in human studies, in which obese leptin-deficient and leptin receptor deficient patients had lower systolic blood pressure compared to aged and BMI matched controls.

Prof Cowley said that restoring leptin receptors to the brain of obese leptin receptor deficient mice increased their blood pressure and multiple blockage methods of the leptin receptor in the brain reduced the hypertension of obese mice.

He said that acute blockage of the electrical activity of the leptin receptor expressing cells in the brain of obese hypertensive mice immediately reduced their blood pressure, confirming the role of these neurons in elevating blood pressure in obesity.

"This study shows that a hormone secreted by fat, leptin, increases blood pressure and explains the mechanism of the known link between obesity and high blood pressure," Prof Cowley said.

"Our data suggest that pharmacological approaches based on altering the effect of leptin in the dorsomedial hypothalamic region of the brain could potentially represent a therapeutic target for the treatment of obesity-induced hypertension and potentially could be exploited to alleviate the incidence of obesity induced cardiovascular diseases," Prof Cowley said.

Prof Cowley said that the researchers were investigating whether blocking the leptin receptor might be a way to reduce the incidence of hypertension and cardiovascular diseases in obesity.

He said that the anti-hypertensive drug market was expected to exceed \$40 billion a year by 2018.

## STARPHARMA HOLDINGS

Starpharma says the launch of its Okamoto Industries-partnered Vivagel condom in Japan will be delayed by up to six months following a review of the medical device classification. Starpharma said since receiving Japanese regulatory certification earlier this year, Okamoto had been undertaking launch preparations “with a view to launching the product shortly” (BD: Mar 14, 2014).

The company said that “in the context of pre-launch labelling discussions and against a background of recent changes to medical device regulations in Japan, the parties have been informed by the Japanese regulatory authorities that they are reviewing the specific device classification of the Vivagel condom”.

Starpharma said that the Vivagel anti-microbial-coated condom could not be sold in Japan until the review process was complete.

The company said it and Okamoto were working closely with Japan’s Ministry of Health, Labour and Welfare to confirm the classification as soon as possible.

“At this time, Starpharma cannot be certain about the precise extent of the delay in the Japanese market launch but estimate it to be at least three to six months,” the company said.

Starpharma said that the regulatory status of the Vivagel condom in other regions where the product was approved for sale, in Australia and New Zealand, or was undergoing regulatory review was not affected and did not rely on the Japanese classification or approval process.

Starpharma chief executive officer Dr Jackie Fairley said that the company was “disappointed and surprised with the need to review the classification of our Vivagel condom in the Japanese market [but] we are working closely with Okamoto and the authorities to expedite this process”.

“This is a matter of regulatory classification in one market and there is no indication of concern with the product itself,” Dr Fairley said.

“Last week the [Ministry of Health, Labour and Welfare] introduced significant changes to medical device regulations in Japan,” Dr Fairley said.

“These include changes to the regulatory bodies that approve certain categories of medical devices and the associated regulatory processes in Japan and it appears that these changes may have influenced this situation,” Dr Fairley said.

Starpharma said that Vivagel condoms were on sale in Australia as Ansell Lifestyles Dual Protect and approved for sale in New Zealand (BD: Jul 21, Oct 2, 29, 2014)

The company said that regulatory processes were underway in other markets and were not impacted in any way by the review of the classification status in Japan.

Starpharma was untraded at 52 cents.

## LIVING CELL TECHNOLOGIES

Last night’s edition reported Living Cell raising \$1.08 million in its share purchase plan at 6.08 cents a share.

The \$3 million placement was at 6.08 cents a share, a 10 percent discount to the five-day volume weighted average price to October 3, 2014 but the share plan was at 6.16 cents a share, a 10 percent discount to the five-day volume weighted average price to October 8, when the plan was announced.

We apologize for the misreporting. The Thursday sub-editor has been sent to purchase fine-print reading glasses and will be seconded to Optical Prescription Spectacle Makers Monthly for the rest of this year.

Living Cell fell 0.1 cent or 1.4 percent to 7.0 cents.

### PRIMA BIOMED

Prima says it has made several enhancements to its CVac manufacturing and logistics infrastructure.

Prima said it would adopt a new apheresis, or separation, system for collection of patient mononuclear cell products, the Spectra Optia Apheresis System, manufactured by Terumo BCT.

The company said that the Spectra system was simpler and more robust for the collection of mononuclear cells collected from each patient.

Prima said that the more automated system would make the initiation process for new clinical centres, especially for the CVac CAN-004B ovarian cancer trial, more efficient. The company said that Terumo had an established technical support network and the Spectra Optia had the necessary regulatory approvals for collections in the US, Australia and Europe.

Prima said it was at an advanced stage of introducing new equipment which will allow patients' blood to be transported at 20C to 80C for 48 hours without altering its mononuclear cell quality.

The company said that previously, the maximum allowable transport time for blood collected from patients was up to 24 hours and the longer duration supported the ability to centralize manufacturing.

Prima chief executive officer Marc Voigt said the initiatives were part of the ongoing effort to optimize manufacturing and supply chain capabilities and would have no significant cost implications.

Prima was unchanged at 3.6 cents with 2.5 million shares traded.

### MESOBLAST

Mesoblast says that 2,948,729 shares will be released from voluntary escrow on December 18, 2014.

Mesoblast's most recent Appendix 3B New Share Issue notice said it had 324,176,029 shares on issue.

Mesoblast fell five cents or 1.1 percent to \$4.33 with 338,351 shares traded.

### CLINUVEL PHARMACEUTICALS

The New York-based Retrophin says it has reduced its substantial holding in former takeover target Clinuvel from 3,311,908 shares (7.8%) to 2,856,031 (6.73%).

Retrophin said it bought shares between September 15 and October 14, 2014 at prices ranging from \$2.74 to \$4.44 and sold shares between October 14 and November 24, 2014 at prices ranging from \$1.84 to \$4.15.

In September Retrophin has increased its substantial holding in potential takeover target Clinuvel to 3,309,356 shares (7.79%) in an extraordinary large number of very small trades, some as small as single shares, with prices escalating from \$2.10 on August 1 to \$3.10 on September 10, 2014 (BD: Sep 12, 2014).

In August, Clinuvel rejected Retrophin's bid of about \$95 million to buy the company saying the proposal "materially undervalues" the company (BD: Jul 28, Aug 8, 2014).

In late October, the European Medicines Agency Committee for Medicinal Products for Human Use voted to approve Clinuvel's Scenesse skin darkening treatment for erythropoietic protoporphyria (BD: Oct 27, 2014).

Clinuvel was unchanged at \$4.15.

### SUDA

The Bank of America Corp and related bodies say they have increased their substantial shareholding in Suda from 50,859,856 shares (5.17%) to 77,146,856 shares (7.84%). The Bank of America said it had “borrowed” the shares under a prime brokerage agreement.

In November, the Bank of America reduced the holding from 77,806,856 shares (7.95%) to 50,859,856 shares (5.17%), saying it had “returned” the shares (BD: Nov 24, 2014). In July, the Charlotte, North Carolina-based Bank of America substantial shareholder notice said that the Sydney-based Merrill Lynch (Australia) Futures and London-based Merrill Lynch International were the holders of the shares as beneficial owner and as the borrower of securities in a prime brokerage agreement, respectively (BD: Jul 22, 2014). Suda fell 0.1 cents or 1.8 percent to 5.4 cents with 1.7 million shares traded.

### ACTINOGEN

Actinogen non-executive chairman Martin Rogers has become a substantial shareholder with 36,250,000 shares or 7.55 percent of the company.

Mr Rogers said that he acquired 11,250,000 shares on December 12, 2013 and December 1, 2014 for \$212,500 or 1.9 cents a share and was granted 25,000,000 loan shares under the employee share plan on December 3, 2014 (BD: Oct 17, 2014). Actinogen fell 0.4 cents or 9.3 percent to 3.9 cents with 1.4 million shares traded.