



# Biotech Daily

Friday October 23, 2015

*Daily news on ASX-listed biotechnology companies*

- \* ASX UP, BIOTECH DOWN: ACRUX UP 16%; BENITEC DOWN 14%
- \* WEHI, BAKER, GARVAN FIND OBESITY SENSOR PROTEIN
- \* ANU, GARVAN, GENENTECH FIND GENE TO FIGHT SEPSIS
- \* ELI LILLY RETURNS VEGFR-3 TO CIRCADIAN
- \* ACRUX LILLY Q3 AXIRON SALES UP 14% TO \$57m
- \* MMJ RAISES \$2m, PIPER ALDERMAN FOR AUSTRALIAN REGULATION
- \* 3D, HEPHAESTUS DENTAL PROSTHETIC DESIGN COLLABORATION
- \* MAYNE AGM FOR \$3m CEO LOAN SHARES, PAY POOL RISE 71% TO \$1.2m
- \* ANALYTICA AGM FOR 14m DIRECTOR OPTIONS
- \* CVC, STINOC DOWN TO 14.5% IN CYCLOPHARM, UNNAMED INSTITUTION
- \* AMP BELOW 5% OF MEDICAL DEVELOPMENTS
- \* HUNTER HALL TAKES 16% OF GI DYNAMICS
- \* ASIA UNION REDUCES to 7% IN COGSTATE
- \* GOLDMAN SACHS ABOVE 5% OF NANOSONICS, YET AGAIN
- \* STIRLING LOSES M-D PETER BOONEN, GAINS CO SEC ELIZABETH HUNT
- \* GENERA HPV ADVISORY BOARD APPOINTMENTS

## MARKET REPORT

The Australian stock market was up 1.67 percent on Friday October 23, 2015, with the ASX200 up 87.8 points to 5,351.6 points. Sixteen of the Biotech Daily Top 40 stocks were up, 20 fell, three traded unchanged and one was untraded. All three Big Caps were up.

Acrux was the best, up 11 cents or 16.3 percent to 78.5 cents with 2.3 million shares traded, followed by Osprey, recovering 15.5 percent 33.5 cents with 831,223 shares traded. Uscom climbed 9.4 percent; Living Cell was up 7.7 percent; Bionomics rose 5.8 percent; Ellex was up 4.2 percent; Mesoblast, Orthocell, Pharmaxis and Sirtex were up more than two percent; with Admedus and Nanosonics up more than one percent.

Benitec led the falls, down eight cents or 14.3 percent to 48 cents with 775,387 shares traded. Antisense lost 9.3 percent; Compumedics was down 7.1 percent; Genetic Technologies, Reva, Tissue Therapies and Universal Biosensors fell five percent or more; Avita fell 4.55 percent; Actinogen, Atcor, Cellmid, Circadian, Oncosil, Polynovo and Prima lost more than three percent; with Anteo and Clinuvel down two percent or more.

## THE WALTER AND ELIZA HALL INSTITUTE OF MEDICAL RESEARCH BAKER IDI HEART AND DIABETES INSTITUTE

The Walter and Eliza Hall Institute says its researchers have identified an internal sensor that helps fight obesity by instructing cells to burn their fat stores.

The Institute said the finding could play a major role in the fight against obesity and metabolic diseases, including type 2 diabetes.

WEHI said that the researchers showed that the NLRP1 protein switched-on when increased dietary energy, or food, intake triggered the cell to become unstable, setting-off a chain of events that instructed cells to use up their energy or fat stores to prevent excess fat accumulating.

The Institute said that the research, entitled 'IL-18 Production from the NLRP1 Inflammasome Prevents Obesity and Metabolic Syndrome', was led by WEHI's Dr Seth Masters, the Baker IDI Heart and Diabetes Institute's Dr Andrew Murphy and Dr Michael Kraakman, with Garvan Institute obesity expert Mark Febbraio.

WEHI said the research was published in the journal Cell Metabolism and an abstract is at: [http://www.cell.com/cell-metabolism/abstract/S1550-4131\(15\)00481-7](http://www.cell.com/cell-metabolism/abstract/S1550-4131(15)00481-7).

Dr Masters said that NLRP1 was a biological sensor that "could hold the key to developing new ways of treating obesity and type 2 diabetes".

"The sensor is activated if it detects that the body's energy intake is too high," Dr Masters said. "When the sensor is activated, it tells cells to burn fat stores to prevent excess build-up of fat."

"We showed that without NLRP1, fat stores continue to build up, especially with a high-energy diet, leading to obesity," Dr Masters said.

Dr Masters said NLRP1 was more commonly known for its role in the immune system, but it was "becoming increasingly clear that immune signalling proteins also have an important role in regulating metabolism".

Dr Murphy said the collaboration between two of Australia's leading institutes in immunology and metabolism research provided new insights into obesity.

"This study provides compelling evidence that the immune system is activated not only during infection, but also in response to the loss of metabolic equilibrium associated with a high-energy diet," Dr Murphy said.

"In order to combat the world-wide obesity epidemic it is essential to understand the immune mechanisms the body uses to prevent obesity, insulin resistance and development of type 2 diabetes," Dr Murphy said.

"The key to NLRP1 and its anti-obesity effects is how it controls an important lipid-regulating hormone called interleukin-18," Dr Murphy said.

"We showed for the first time that NLRP1 is the key to IL-18 production, explaining how it acts to reduce obesity," Dr Murphy said.

"Our long-term goal would be to develop a small molecule that activates the pathway to produce IL-18," Dr Murphy said.

In people who are obese, this would help the body to switch on this system and burn existing fat stores," Dr Murphy said.

Dr Masters said that treatment would have to be tightly controlled to avoid potential side-effects and the research "showed that activation of NLRP1 could be exacerbated by some diets, and identified that there is a fine balance between increasing the cell's fat burning abilities and causing harm".

"This shows us just how active the pathway is, which is important if you are looking at it in a therapeutic sense," Dr Masters said.

"It suggests that treatment would be most safe if given in small doses over a long period of time, which is less likely to have potentially negative consequences."

### AUSTRALIAN NATIONAL UNIVERSITY, GARVAN INSTITUTE

The Australian National University says its researchers have identified a gene that triggers the inflammatory condition that can lead to sepsis.

The University said that, with the Garvan Institute and the San Francisco-based Roche subsidiary Genentech, its researchers found the protein gasdermin-D played a critical role in the pathway to sepsis.

The University said the research, entitled 'Caspase-11 cleaves gasdermin D for non-canonical inflammasome signaling', was published in Nature, and an abstract was available at: <http://www.nature.com/nature/journal/vnfv/ncurrent/full/nature15541.html>.

The ANU said scientists at Genentech showed that gasdermin-D usually existed in cells in an inactive form, but when lipopolysaccharides (LPS) on the surface of some bacteria infiltrated cells they triggered the caspase-11 enzyme "a kind of chemical hatchet, to lop the protective chemical cap off gasdermin-D, which in turn leads the cells to self-destruct". The University said that how the self-destruct mechanism was initiated remained a mystery until the Australian Phenomics Facility screened thousands of genes and isolated the gene that produced gasdermin-D.

The University's John Curtin School of Medical Research director Prof Simon Foote said that "isolating the gene so quickly was a triumph for the team".

Genentech senior scientist Dr Nobuhiko Kayagaki said the work would help researchers understand and treat other diseases as well as sepsis.

"The identification of gasdermin-D can give us a better understanding not only of lethal sepsis, but also of multiple other inflammatory diseases," Dr Kayagaki said.

The University said that sepsis was a severe whole-body infection that killed an estimated one million people in the US alone each year, occurred as a complication to an existing infection and if not treated quickly can lead to septic shock and multiple organ failure, with death rates as high as 50 percent.

### CIRCADIAN TECHNOLOGIES

Circadian says Eli Lilly will terminate its licence to therapeutic uses of antibodies to vascular endothelial growth factor receptor 3 (VEGFR-3).

Circadian said the Eli Lilly would discontinue development of its VEGFR-3 antibody IMC-3C5 (LY3022856) and termination of the licence would be effective within 60 days, at which time the rights would revert to Circadian.

The company said that the VEGFR-3 agreement was signed in 2004 by the Ludwig Institute for Cancer Research and transferred to Circadian following its acquisition of the VEGF assets from the Ludwig Institute in 2006, in return for an annual licence fee payable to Circadian (BD: May 1, 2006; Jun 11, 2008; Apr 6, 2011).

Circadian said that termination of the licence would "not have any material impact ...as the company's forecasts do not include annual licence income from Eli Lilly".

The company said that termination of the agreement did "not have any impact on Circadian's program to develop OPT-302 for the treatment of wet age-related macular degeneration", other than providing more comprehensive intellectual property cover for agents targeting the VEGFR- 3 pathway, including ophthalmology applications.

Circadian chief executive officer Dr Megan Baldwin said that the return of rights covering the use of VEGFR-3 antibodies for all fields, including ophthalmology, "strengthens Circadian's intellectual property position, particularly in relation to our OPT-302 program for the treatment of wet [age-related macular degeneration]".

Dr Baldwin said Eli Lilly completed a phase I trial of IMC-3C5 (BD: Jun 2, 2015).

Circadian fell one cent or 3.7 percent to 26 cents.

### ACRUX

Acrux says Eli Lilly's Axiron revenue rose 14.0 percent to \$US41.4 million (\$A57.4 million) for the three months to September 30, 2015, compared to September 30, 2014.

Acrux said that the three month revenue was up 27.8 percent compared to the \$US32.4 million for the three months to June 30, 2015.

It is the first quarter-on-quarter rise since December 31, 2014, following the February 2014 news that the US Food and Drug Administration was investigating cardio-vascular risks in men taking approved testosterone products (BD: Feb 4, 2014; Feb 2, 2015).

Today, Acrux said that the total Axiron revenue for the nine months to September 30, 2015 was \$US112.9 million compared to \$US122.9 for the nine months to September 2014 and \$US124.8 million for the nine months to September 2013 (BD: Oct 24, 2014).

Acrux climbed 11 cents or 16.3 percent to 78.5 cents with 2.3 million shares traded.

### MMJ PHYTOTECH

MMJ says it has raised \$2 million through the issue of 6,557,377 shares at 30.5 cents a share with 1,311,475 attaching options.

MMJ said the placement was to an unnamed European institutional investor and the options were exercisable at 45 cents each by September 8, 2018.

The company said that the funds would accelerate "its entry into the Australian medicinal cannabis market as a result of the indicated regulatory reform by the Federal Government" and it had engaged the Adelaide-based law firm Piper Alderman to advise on Australian regulatory and licencing approvals.

MMJ fell one cent or 2.7 percent to 36.5 cents with 4.3 million shares traded.

### 3D MEDICAL

3D says it will collaborate with dental research and prosthetic design company Hephaestus CAD CAM for the commercial production of dental prosthetics.

3D said that the collaboration agreement with the Adelaide-based Hephaestus allowed the two companies to undertake joint testing and evaluation of three-dimensional printing and workflow processes for patient-specific dental prosthetics such as crowns, partial dentures, maxillofacial and craniofacial prostheses and implant-bridges.

The company said that if successful, the collaboration would provide Hephaestus with scalable production allowing the construction of personalized prosthetics reducing the time to deliver tooth-supported and dental implant-supported prostheses.

3D was up 0.2 cents or 2.6 percent to 7.8 cents.

### MAYNE PHARMA

Mayne will vote to issue chief executive officer Scott Richards \$3,140,800 for loan shares and increase directors' remuneration 71.4 percent from \$700,000 to \$1,200,000.

Mayne said that the ESLS provided "a non-recourse loan for the sole purpose of acquiring shares in the company" and that since the 2014 annual general meeting Mr Richards received 3,823,529 shares at an issue price of 68.15 cents.

The company said that shareholders would vote to re-elect directors Phillip Hodges and Ian Scholes and adopt the remuneration report.

The meeting will be held at Minter Ellison, Level 23, 525 Collins Street, Melbourne, on November 26, 2015 at 11am (AEST).

Mayne was unchanged at \$1.03 with 1.5 million shares traded.

### ANALYTICA

Analytica's annual general meeting will vote to grant chief executive officer Dr Thomas Lönngren 10,000,000 options and director Carl Stubbing 4,000,000 options.

Analytica said that the options would vest in three tranches and be exercisable at 1.62 cents each within five years of the grant date.

The company said shareholders would vote on the remuneration report, elect directors Dr Michael Monsour and Dr Lönngren, ratify the top-up placement and the previous issue of options, approve the 10 percent placement capacity and adopt a new constitution.

The meeting will be held at the Flinders Room, Level 1, Christie Conference Centre, 320 Adelaide Street, Brisbane, on November 24, 2015 at 10am (AEST).

Analytica was unchanged at 0.5 cents with 1.9 million shares traded.

### CYCLOPHARM

CVC says that it has reduced its substantial shareholding in Cyclopharm from 10,636,242 shares (17.85%) to 8,636,242 shares (14.49%).

The Sydney-based CVC said that shares, held by Stinoc Pty Ltd, were sold on-market for \$1,017,900 or 50.9 cents a share.

Biotech Daily believes the 2,000,000 shares (3.36%) were acquired by an unnamed Australian institution with other biotechnology investments.

Cyclopharm was unchanged at 50 cents.

### MEDICAL DEVELOPMENTS INTERNATIONAL

The Sydney-based AMP says it has ceased its substantial shareholding in Medical Developments.

In May, AMP became substantial with the acquisition of 3,000,000 shares (5.20%), following Medical Developments chairman David Williams statement that he had sold 7,000,000 shares at \$2.40 a share to increase liquidity (BD: May 12, 13, 2015).

Today, AMP said that it bought and sold shares between July 21 and October 22, 2015 with the single largest sale 138,858 shares for \$454,066 or \$3.27 a share.

The substantial shareholder notice said that the holders of the relevant interest in the shares included AMP Life and AMP Capital Investors, with registered holders including AMP Life, Citicorp Nominees, HSBC Custody Nominees, JP Morgan Nominees and National Nominees.

Medical Developments was up three cents or 0.9 percent to \$3.25.

### GI DYNAMICS

Hunter Hall Investment Management says it has increased its substantial shareholding in GI Dynamics from 69,779,090 shares (14.71%) to 75,779,090 shares (15.98%).

The Sydney-based Hunter Hall said that on October 20, 2015 it acquired 1,300,000 shares for \$33,885 or 2.61 cents a share, but did not disclose the cost of the other 4,700,000 shares.

On July 30, GI Dynamics told the market that it had closed its pivotal US trial of the Endobarrier due to serious adverse events (BD: Jul 30, 2015).

Following a teleconference on July 31, GI Dynamics fell as much as 9.4 cents or 69.6 percent to 4.1 cents, before closing down 9.3 cents or 68.9 percent at 4.2 cents with 5.6 million shares traded, falling to 3.7 cents on August 4 and 5 (BD: Jul 31, 2015).

GI Dynamics was up 0.1 cents or 3.7 percent to 2.8 cents with 2.1 million shares traded.

### COGSTATE

Asia Union Investment says it has reduced its holding in Cogstate from 7,472,928 shares (8.5%) to 6,600,000 shares (6.66%).

The Sydney-based Asia Union said it received \$600,000 for the sale of the 872,928 shares or 68.7 cents a share, a price that Cogstate has not reached.

Cogstate was up four cents or 12.9 percent to 35 cents.

### NANOSONICS

The Delaware-based Goldman Sachs Group says that, yet again, it has become substantial in Nanosonics with 14,728,433 shares or 5.20 percent.

Goldman Sachs said that between June 22 and October 21, 2015 it acquired between one single share and 1,344,230 shares for no cost, with the single largest purchase 194,961 shares for \$258,323 or \$1.325 a share, which the company has previously reported.

Throughout October, Goldman Sachs has repeatedly increased above or reduced below the five percent substantial threshold in Nanosonics, primarily borrowing or returning shares "to the counterparty under a repurchase agreement" for no applicable consideration (BD: Oct 2, 5, 15, 16, 20, 2015).

Nanosonics was up 2.5 cents or 1.75 percent to \$1.455.

### STIRLING PRODUCTS

Stirling says that Peter Boonen is no longer a director of the company and Elizabeth Hunt has been appointed company secretary.

Last month, Stirling completed a deed of company arrangement with Peter James Dykes, Peter Alan Torney and Timothy Shaw directors (BD: Sep 18, 2015).

Biotech Daily understands that the company is likely to depart the biotechnology sector. In 2011, with former Victoria Police officer Mr Boonen as managing director, Stirling was placed in administration having failed to commercialize the Kiev, Ukraine- acquired Immunoxel for AIDS, tuberculosis, kidney disease, H1N1 influenza, or 'swine' influenza (BD: Jul 26, 2011; Aug 6, 2015).

In 2009, Stirling claimed 100 percent efficacy for drug-resistant tuberculosis with the Immunoxel natural product citing a 12-patient Kiev, Ukraine trial (BD: Apr 16, 2009).

Mr Boonen told Biotech Daily his company was involved in the commercialization of Immunoxel and the intellectual property was owned by the Kiev-based Ekomed.

Stirling was suspended at 0.2 cents, or \$4.00 following the 2,000-to-one consolidation.

### GENERA BIOSYSTEMS

Genera says it has Prof Jack Cuzick, Prof Cosette Wheeler, Prof Susan Garland and Prof Sepehr Tabrizi to its scientific advisory board.

Genera said the appointments had a "strong focus on human papilloma virus screening".

The company said that Prof Jack Cuzick was the head of London's Centre for Cancer Prevention, Prof Cosette Wheeler was a professor at the University of New Mexico's departments of pathology and the obstetrics and gynaecology and Prof Garland was at the University of Melbourne's department of obstetrics and gynaecology.

Genera was unchanged at 28 cents.

**Biotech Daily can be contacted at: PO Box 5000, Carlton, Victoria, Australia, 3053  
email: [editor@biotechdaily.com.au](mailto:editor@biotechdaily.com.au); [www.biotechdaily.com.au](http://www.biotechdaily.com.au); twitter: @biotech\_daily**