Biotech Daily

Tuesday October 7, 2014

Daily news on ASX-listed biotechnology companies

*** ASX, BIOTECH DOWN: LIVING CELL UP 4.5%, GI DYNAMICS DOWN 20%**

*** WEHI MOLECULE PREVENTS INFLAMMATORY CELL DEATH**

*** PHOSPHAGENICS: 'PHASE II ACNE TRIAL ENDPOINT NOT SIGNIFICANT'**

*** REGENEUS FALLS 57%, REQUESTS ABC-TV 7.30 REPORT TRADING HALT**

*** GI DYNAMICS EU ENDOBARRIER SHIPMENTS HALTED, SYSTEMS REVIEW**

*** ATCOR SPHYGMOCOR FOR US OBESITY CHOLESTEROL TRIAL**

*** UNILIFE SIGNS SANOFI 15-YEAR WEARABLE INJECTOR DEAL**

*** ANTEO AGM FOR 17m DIRECTOR OPTIONS**

*** TISSUE THERAPIES 9% OPPOSE PLACEMENT**

*** PROGEN 2nd STRIKE BOARD SPILL AGM**

MARKET REPORT

The Australian stock market fell 0.16 percent on Tuesday October 7, 2014 with the S&P ASX 200 down 8.7 points to 5,284.2 points. Seven of the Biotech Daily Top 40 stocks were up, 24 fell, seven traded unchanged and two were untraded.

Living Cell was the best, up 0.3 cents or 4.5 percent to seven cents with 300,000 shares traded. Universal Biosensors climbed 3.45 percent; Atcor rose 2.2 percent; Starpharma and Tissue Therapies were up more than one percent; with Acrux, Bionomics and Cochlear up by less than one percent.

GI Dynamics led the falls, down as much as 23 cents or 50 percent to 23 cents, closing down nine cents or 19.6 percent to 37 cents with 2.5 million shares traded, followed by Genetic Technologies down 16 percent to 2.1 cents with 304,103 shares traded and Patrys down 10 percent to 1.8 cents with 220,000 shares traded.

Analytica, Anteo and Cellmid lost more than six percent; Optiscan fell 5.7 percent; Benitec, Clinuvel and Viralytics fell more than four percent; Admedus was down 3.3 percent; Alchemia, Avita, Circadian, Ellex, Mesoblast, Neuren, Prana and Prima shed more than two percent; CSL, Nanosonics, Pharmaxis and Phosphagenics were down one percent or more; with Psivida, Resmed and Sirtex down by less than one percent.

THE WALTER AND ELIZA HALL INSTITUTE FOR MEDICAL RESEARCH

WEHI says a small molecule that blocks a form of cell death that triggers inflammation, could herald new treatments for rheumatoid arthritis, Crohn's disease and psoriasis.

The Institute said that its researchers made the discovery while investigating how the mixed lineage kinase domain-like (MLKL) protein kills cells in necroptosis.

WEHI said the study, entitled 'Activation of the pseudokinase MLKL unleashes the four-helix bundle domain to induce membrane localization and necroptotic cell death' was published in the journal Proceedings of the National Academy of Sciences, with an abstract at: http://www.pnas.org/content/early/2014/10/02/1408987111.abstract.

The abstract said that the researchers "identified a small molecule [called compound 1 in the article] that binds the nucleotide binding site within the MLKL pseudokinase domain and retards MLKL translocation to membranes, thereby preventing necroptosis".

"This inhibitor provides a novel tool to investigate necroptosis and demonstrates the feasibility of using small molecules to target the nucleotide binding site of pseudokinases to modulate signal transduction," the abstract said.

WEHI said that necroptosis was a recently-discovered cell death pathway linked to immune disorders and was a vital process in which cells underwent programmed death while warning the immune system that something was wrong, such as during viral infection, but when necroptosis was inappropriately activated, it could promote inflammation and the development of inflammatory disease.

The Institute said that Dr Joanne Hildebrand, Maria Tanzer, Dr James Murphy, Prof John Silke and colleagues studied how MLKL changed shape to trigger cell death.

"MLKL is the final protein in the cell death pathway but it needs to be activated before it can kill the cell," Dr Hildebrand said.

"Understanding how it becomes active can help uncover new ways to treat disease," Dr Hildebrand said.

Dr Hildebrand said that the team found that a particular part of the protein became unlatched when activated, allowing it to attach to the cell membrane and trigger cell death.

"It's like flicking a molecular switch," Dr Hildebrand said.

"We showed that when the switch can't be turned on, MLKL doesn't become active and necroptosis is prevented," Dr Hildebrand said.

Ms Tanzer said the team tested a range of small molecules to see if any could stop the switching on of MLKL and had identified one that prevented MLKL from becoming active.

"This small molecule binds to MLKL in such a way that it jams the switch that makes it active," Ms Tanzer said.

"We are really excited by this discovery because not only have we shown this particular part of the protein is essential for necroptosis, we also have a starting point in a drug discovery program," Ms Tanzer said.

Dr Murphy said that Institute scientists would begin a collaborative project with the Melbourne-based Catalyst Therapeutics a joint venture between WEHI and Synthesis Med Chem to develop a new drug based on the small molecule identified in the study.

"MLKL is an appealing target because research suggests it does only one thing, which is kill the cell," Dr Murphy said.

"Blocking this protein doesn't impact other functions of the cell, reducing the chance of unwanted side-effects," Dr Murphy said.

"If we can create a compound that better targets this particular part of MLKL, we can prevent necroptosis and improve treatments for inflammatory disease," Dr Murphy said.

WEHI said that the research was funded by the Australian National Health and Medical Research Council, the University of Melbourne, the Australian Research Council, the Australian Cancer Research Foundation and the Victorian Government.

PHOSPHAGENICS

Phosphagenics says its 53-patient phase II trial showed no significant difference on the primary endpoint between tretinoin and TPM-tretinoin gel for acne vulgaris.

Phosphagenics said the study showed that the tocopheryl phosphate mixture or TPM topical tretinoin formulation had several advantages over acne market-leaded Retin-A.

The company said the randomized, active and vehicle controlled study evaluated the efficacy, safety and tolerability of TPM-tretinoin, compared with Retin-A and TPM vehicle.

Phosphagenics said the trial examined the reduction in acne lesions from baseline and the percentage of subjects with a successful outcome on the investigator's global assessment (IGA) score after 12 weeks of treatment.

The company said that the IGA was a five-point scale that differentiated acne by its severity, with success defined as a reduction by two points.

Phosphagenics said that all three formulations displayed a mean reduction in IGA scores over 12-weeks corresponding to an improvement in acne, but there was no significant difference between treatment groups in the number of patients that had an IGA two-point reduction.

The company did not provide the numbers of patients in each of the three groups achieving a two-point reduction.

Phosphagenics said 70 percent of patients treated with TPM-tretinoin showed a reduction of one or two points in IGA scores, compared with 42 percent of patients treated with Retin-A alone and 46 percent treated with the TPM vehicle gel alone.

Phosphagenics said that the mean percentage reduction in IGA scores was 28.2 percent for TPM-tretinoin, 15.3 percent for Retin-A and 17.9 percent for TPM vehicle gel.

The company said that after two weeks of treatment with Retin-A, the number of patients suffering erythema and dryness was increased ($p < 0.05$) and remained above baseline measures for eight to 12 weeks of treatment while TPM-tretinoin produced only a minor increase in the number of patients with erythema and no increase in the number of patients reporting dryness.

In 2009, Phosphagenics said a phase I trial showed its TPM technology increased retinoic acid delivery with less irritation than a commercial acne treatment (BD: Apr 30, 2009).

Today, Phosphagenics said that while the trial was not powered for significance, all three formulations demonstrated a statistically significant ($p < 0.05$) mean reduction in total lesion counts over the 12-week treatment period, with the TPM-tretinoin formulation producing the highest mean reduction in number of acne lesions (-76.6 lesions), followed by Retin-A (-68.9 lesions) and the TPM vehicle (-51.6 lesions).

The company said that the percentage reduction in total lesions comparing the TPM-tretinoin gel to TPM-vehicle gel was statistically significant ($p < 0.05$), but the difference between Retin-A and TPM vehicle was not statistically significant.

Phosphagenics said the performance of the TPM vehicle was "extremely interesting", the reduction was greater than typical vehicle effects and might be attributed to the vitamin E properties of TPM.

Phosphagenics director and former Johnson & Johnson head of skin care and dermatology research and development Dr Geert Cauwenbergh said the results were "very encouraging considering the relatively small number of patients, and confirm that tretinoin when combined with our TPM formulation produced directional trends indicative of better performance than Retin-A against inflammatory lesions in particular".

"The company will continue development of TPM-tretinoin for the prescription market in addition to assessment of a topical formulation containing TPM as an over-the-counter product," Dr Cauwenbergh said.

Phosphagenics fell 0.1 cents or 1.2 percent to 8.4 cents.

REGENEUS

Regeneus has requested a trading halt pending “to consider and respond to recent media commentary in relation to Regeneus’ stem cell therapy, Hiqcell”

Regeneus said it was responding to the ABC 7.30 Report which aired last night, October 6, 2014 and cited a written complaint to the ASX.

The program included comment from Stem Cells Australia program leader Prof Martin Pera and reflected on announcements to the ASX by Regeneus referring to approvals by the Australian Football League.

In August, Regeneus said that the Australian Football League had granted limited approval for the use of its Hiqcell fat-derived stem cell treatment for joint injuries on a case-by-case basis for injured, typically including impact related osteoarthritis and tendonitis (BD: Aug 27, 2014).

Regeneus said in August, that Hiqcell had been approved under the AFL Prohibited Treatments List, initially released in March 2014, but formally approved in August and said at that time that Hiqcell also had clearance as an approved therapy from the Australian Sports Anti-Doping Authority for use with athletes who participate in sporting competitions subject to the World Anti-Doping agency anti-doping code, including the AFL.

Regeneus said at that time that Hiqcell was the only stem cell treatment for osteoarthritis that had undergone the highest level of clinical scrutiny, a double-blind, placebo-controlled safety trial which demonstrated that Hiqcell was safe and treatment reduced pain and halted cartilage degradation in arthritic joints.

Last year, Regeneus said its 40-patient, double-blind, placebo-controlled clinical study of Hiqcell for knee osteoarthritis showed that Hiqcell was safe and clinically feasible but did not publish directly comparable pain and cartilage degradation results, concentrating on Hiqcell’s ability to stabilize levels of the cartilage break-down marker CTX-II and reduce macrophage migration inhibitory factor in osteoarthritis patients (BD: Oct 8, 2013).

The company said last year that 20 patients received the fat-derived Hiqcell, injected into an arthritic knee, while the 20 patients in the surgical placebo group underwent the liposuction but received an intra-articular injection of saline rather than their stem cells.

Regeneus said assessment of cartilage degradation by magnetic resonance imaging mapping was performed at baseline and 24 weeks post-treatment.

The 7.30 Report said that it had a complaint letter to the Australian Stock Exchange about a Regeneus announcement in August 2013, which 7.30 said was “written by a group of Australia's leading stem cell scientists” alleging that Regeneus “misled the market”.

On page 25 of the 118 page prospectus lodged in August 2013, Regeneus said: “Both the treatment and placebo groups experienced significant decrease in total pain scores from baseline.”

“Due to a large placebo effect, there was no significant difference between the Hiqcell treatment and placebo on total pain scores,” the prospectus said.

The 7.30 Report cited the letter saying the announcement was “misleading because the control (placebo) group in that trial also achieved the same reduction in pain and slowing of cartilage degeneration”.

“A reasonable person ‘.... would draw the conclusion that the company's product had been shown to be clinically efficacious when rigorously tested. ... there are no data we are aware of that support that conclusion’," the 7.30 Report said, quoting the complaint.

Regeneus raised $10.5 million in an initial public offer last year and listed on the ASX in September 2013 to commercialize Hiqcell (BD: Sep 19, 2013).

Trading will resume on October 9, 2014 or on an earlier announcement.

Regeneus fell as much as 13 cents or 56.5 percent to 10 cents before the trading halt and last traded down nine cents or 39.1 percent at 14 cents with 766,682 shares traded.

GI DYNAMICS

GI Dynamics says its method and timelines in reporting adverse events in clinical use caused the European Union suspension of commercial shipments of Endobarrier.
In a teleconference, chief executive officer Michael Dale said the halt to shipments of the Endobarrier duodenal insert for obesity and type 2 diabetes was effectively a global stop as nearly all sales were to countries recognizing the Conformité Européenne (CE) mark.
Mr Dale said “we own the problem ... we know what needs to be rectified”.
Mr Dale said that the specific problem was not a fault with the Endobarrier but “our methods and timelines in reporting adverse events in clinical use”.
Mr Dale said that the issue was not about the adverse events, which the company had on file, but its reporting of those events to the EU notified body, the Geneva-based SGS.
“As part of a regulatory review it was discovered that there were judgment calls on what needed to be reported,” Mr Dale said. “It developed over time.”
GI Dynamics chief medical officer Dr David Maggs said that complication rates over the past three years had not changed either qualitatively or quantitatively.
Mr Dale said that expenses associated with rectifying the issue were “not significant”.
GI Dynamics fell nine cents or 19.6 percent to 37 cents with 2.5 million shares traded.

ATCOR MEDICAL

Atcor says it will supply its Sphygmocor non-invasive measure of central aortic blood pressure and arterial stiffness for a publicly-funded US cholesterol-lowering obesity study.
Atcor said chief executive officer Duncan Ross said the company was “delighted that Sphygmocor technology has been selected to provide measures of central blood pressure and arterial stiffness in a trial with significance to public health”.
“Sphygmocor continues to be chosen as the preferred device in trials such as these due to the system’s gold standard status, supporting clinical data and excellent customer support,” Mr Ross said.
Atcor said that more than 115 million US adults and children were obese which put them at higher risk for health problems such as heart disease, stroke, high blood pressure, diabetes and more and the US spent more than $US300 billion a year in direct and indirect costs for cardiovascular disease and stroke.
Atcor was up 0.2 cents or 2.2 percent to 9.2 cents.

UNILIFE CORP

Unilife says it has an agreement with Sanofi to provide cartridge-based wearable injectors for Sanofi’s large dose volume drugs, excluding insulins, for a minimum 15 years.
Unilife said that the global agreement with Unilife as sole provider would allow Sanofi to make Unilife’s wearable injectors available to its partners for use with applicable molecules under joint collaborations.
The company said that Sanofi had the option to extend the agreement for additional periods and in addition to an upfront payment and device sales, Unilife expected to receive about $US50 million from customization programs relating to Sanofi molecules and indications.
Unilife said that additional revenue was expected from customization programs conducted under joint collaborations with Sanofi partners and the company would begin to generate revenue from Sanofi this fiscal year from an upfront payment, customization programs and initial commercial sales of the devices to Sanofi.
Unilife was up 7.5 cents or 18.1 percent to 49 cents with 2.6 million shares traded.

TISSUE THERAPIES

All resolutions at the Tissue Therapies annual general meeting were passed, but with up to 9.3 percent opposition to resolutions ratifying the company's 2013 placement.
The strongest opposition was to the ratification of the issue of 14,500,000 placement shares with 3,042,002 votes (9.3%) against and 29,718,167 votes (90.7%) supporting the issue (BD: Nov 4, 2013).
The company said 3,043,502 votes opposed the issue of 8,270,640 shares to Allan Gray Australia under the priority sub-underwriting arrangements with 53,432,873 votes in favor.
All other resolutions, including the issue of consultancy shares, 480,000 options to chief executive officer Dr Steven Mercer, and the re-election of directors Dr Cherrell Hirst and Dr Mel Bridges were passed with majorities of 96.6 percent to 3.4 percent, or more.
The company's most recent Appendix 3B said it had 263,113,571 shares on issue, meaning that the largest opposition vote amounted to 1.16 percent of the company's total shares on issue, not sufficient to requisition extraordinary general meetings.
Tissue Therapies was up 0.5 cents or 1.6 percent to 31.5 cents.

PROGEN

Progen's annual general meeting will vote on the remuneration report, a potential second strike board spill and the re-election of directors.
Last year, Progen's remuneration report was opposed by 22,376,117 votes or 71.4 percent, providing the first trigger for a potential board spill at this year's annual general meeting (BD: Nov 28, 2013).
Under the Corporations Amendment (Improving Accountability on Director and Executive Remuneration) Act 2011 any company sustaining a vote of 25 percent or more against the remuneration report in two successive annual meetings is required to vote on a board spill and at the later meeting and if passed by more than 50 percent of votes the directors must stand for reelection at a subsequent meeting within 90 days.
If the spill vote fails, the trigger is reset to no opposition.
Progen shareholders will also vote on the re-election of directors Heng Hsin Tang and Dr Hongjen Chang, along with grant of 690,000 options to directors and contractors.
The meeting will be held at Level 27, 101 Collins Street, Melbourne on November 7, 2014 at 11am (AEDT).
Progen fell one cent or five percent to 19 cents.

ANTEO DIAGNOSTICS

Anteo will vote to grant four directors 17,000,000 options, re-elect director Richard Martin, approve the 10 percent placement capacity and the executive and employee share plan.
Anteo said it proposed to grant 6,000,000 options to director Mr Martin, 5,000,000 options to chairman Mark Bouris, with 3,000,000 options each to directors Dr John Hurrell and Sandra Anderson.
The company said that the options would be exercisable at 40 percent above the 30-day volume weighted average price to the date of the resolution and within four years of issue.
The meeting will be held at Level 51, MLC Centre, 19-29 Martin Place, Sydney, on November 10, 2014 at 2.30am (AEDT).
Anteo fell one cent or 6.45 percent to 14.5 cents with 3.7 million shares traded.