



# Biotech Daily

Monday September 29, 2014

*Daily news on ASX-listed biotechnology companies*

- \* ASX, BIOTECH DOWN: CLINUVEL UP 20%, TISSUE THERAPIES DOWN 13%
- \* FDA PSIVIDA ILUVIEN APPROVAL TRIGGERS \$29m PAYMENT
- \* BIONOMICS BNC105 COMBINATION CANCER BIOMARKERS
- \* VIRALYTICS CLAIMS CAVATAK PHASE II MELANOMA EFFICACY
- \* ADVANCED SURGICAL 23-FOR-50 RIGHTS ISSUE FOR \$1m
- \* DIMERIX READY FOR PHASE II DMX200 KIDNEY DISEASE TRIAL
- \* LIVING CELL, AUCKLAND UNI NEURO-DEGENERATION COLLABORATION
- \* BLUECHIIP PLAN RAISES \$763k, TAKES TOTAL TO \$1.863m
- \* MR MARKETING OPTISCAN-BASED CELL-LIVE IMAGING
- \* CALZADA, TGA RULE CHANGE IMPACT ON AOD9604
- \* IM MEDICAL DELAY IN BECOMING DATA CENTRE
- \* BIOTA'S PATTI, PLUM, FOX SHUFFLE JOBS, RICHARD HILL RETIRES
- \* BONE'S ORAL PARATHYROID HORMONE NOT FOUND IN BLOOD TESTS
- \* ANALYTICA REQUESTS CAPITAL RAISING TRADING HALT
- \* OBJ REQUESTS 'PRODUCT LAUNCH' TRADING HALT

## MARKET REPORT

The Australian stock market fell 0.93 percent on Monday September 29, 2014 with the S&P ASX 200 down 49.2 points to 5,264.2 points. Fourteen of the Biotech Daily Top 40 stocks were up, 17 fell, five traded unchanged and four were untraded.

Clinuvel was the best, up 51 cents or 19.6 percent to \$3.11 with 212,076 shares traded. Optiscan climbed 10.8 percent; Psivida was up 8.45 percent; Bionomics and GI Dynamics were up more than six percent; Alchemia was up 5.6 percent; Anteo, Compumedics and Genetic Technologies rose four percent or more; Impedimed was up 3.5 percent; Avita rose 2.1 percent; with Acrux, Neuren and Viralytics up more than one percent.

Tissue Therapies led the falls, down 4.5 cents or 12.9 percent to 30.5 cents with 514,935 shares traded, followed by Oncosil down 12.5 percent to 10.5 cents. Universal Biosensors lost 6.25 percent; Patrys fell 5.3 percent; Admedus was down 3.45 percent; Atcor, Ellex, Mesoblast, Phosphagenics and Prana shed more than two percent; with Living Cell, Nanosonics, Osprey, Pharmaxis, Sirtex and Starpharma down more than one percent.

## PSIVIDA

The US Food and Drug Administration has approved Psivida's fourth new drug application for Iluvien for diabetic macular oedema, triggering a \$US25 million milestone payment. The FDA rejected applications by Psivida licensee Alimera Sciences in 2010, 2011 and 2013, requesting more data from existing trials, a new trial and finally suggesting labelling changes (BD: Jan 19, Nov 14, 2011; Oct 21, 2013).

Today, Psivida said that the FDA had approved Iluvien for the treatment of diabetic macular oedema in patients previously treated with a course of corticosteroids who did not have a clinically significant rise in intraocular pressure.

The company said that a single injection of the 0.19mg fluocinolone acetonide intravitreal implant Iluvien micro-insert provided sustained treatment of diabetic macular oedema for 36 months.

Psivida said that about 560,000 people in the US had clinically significant diabetic macular oedema, the most frequent cause of vision loss in individuals with diabetes and the leading cause of blindness in young and middle-aged adults in developed countries. The company said it expected Iluvien to be commercially available in the US in early 2015.

The company said that the FDA approval entitled it to a \$US25 million (\$A28.7 million) milestone from Alimera, as well as 20 percent of the net profits from US sales of Iluvien. Psivida chief executive officer Dr Paul Ashton said the approval was the company's third FDA-approved product for retinal disease and provided an important treatment option for diabetic macular oedema (DME) patients in the US.

Dr Ashton said that despite anti-vascular endothelial growth factor (VEGF) intra-ocular injections as frequently as monthly the majority of patients' diabetic macular oedema was "not optimally managed".

"Iluvien's clinical trials showed that Iluvien can actually reverse vision loss in many DME patients," Dr Ashton said.

"Another advantage of Iluvien over existing therapies is that a single injection provides sustained therapy for three years," Dr Ashton said.

"The \$US25 million milestone will help finance our ongoing product development program, including Medidur for posterior uveitis and Tethadur for the sustained delivery of biologics," Dr Ashton said.

Psivida said it was developing Medidur, an injectable, sustained release micro-insert of the same design and delivering the same drug as Iluvien, for the treatment of chronic posterior uveitis, the third largest cause of blindness in the US.

The company said it planned to seek FDA approval for Medidur on the basis of its ongoing single phase III clinical trial, with enrollment expected to be completed by April 2015.

Psivida said that Iluvien was commercially available in the UK and Germany, and has received or was pending marketing approval in 17 other European Union countries, for the treatment of patients with the chronic diabetic macular oedema insufficiently responsive to available therapies.

"We are very pleased that the FDA's approval of Iluvien is not limited, as in the EU, to the subset of patients with chronic DME, patients who have failed other therapies, or patients who have had cataract surgery," Dr Ashton said.

Psivida first applied to the FDA for approval in 2010, receiving priority review status, and at that time hoping for approval that year (BD: Sep 1, 2010).

The company listed on the ASX to develop its bio-silicon drug delivery technology, which was subsequently sold to Oncosil, following the company's merger with the US-based Control Delivery Systems in 2008 (BD: Jun 10, 2008; Feb 7, 2013).

Psivida was up 41 cents or 8.45 percent to \$5.26.

## BIONOMICS

Bionomics says that four biomarkers are associated with patient response to BNC105 in combination with everolimus (Afinitor)

Bionomics said it analyzed a panel of blood biomarkers to detect changes resulting from the administration of BNC105 and to determine whether any changes indicated benefit and found that four biomarkers could be used to significantly enrich treatment success for the patient group treated with BNC105 with everolimus.

The company said that 57 percent of patients were positive for the four biomarker signature, with 60 percent of these disease-free at six months, with only five percent of the patients that were negative for the four-biomarker signature disease-free at six months. Bionomics said it was "noteworthy that for this sizeable patient group the 60 percent six month [progression-free survival] primary endpoint target was achieved".

Bionomics said that the data was presented by the Duarte, California-based City of Hope Comprehensive Cancer Center's Dr Sumanta Pal at the European Society for Medical Oncology congress in Madrid, Spain.

The presentation concluded that "exploratory biomarker analyses identified associations between clinical outcome with combination therapy and [the four biomarkers]".

The presentation said that the four markers were matrix metalloproteinase-9 (MMP9), stem cell factor (SCF,) sex hormone binding globulin (SHGB) and serum amyloid-P component (SAP) and "a biomarker profile comprised of these four markers consistently identified patients who were progression free at six months".

The company said that blood samples were obtained from 44 patients before and after treatment with BNC105 in the BNC105 with Afinitor arm, enabling statistical correlation of blood biomarker changes with disease status at six months of treatment.

In March, Bionomics said its 136-patient phase II 'Disruptor-1' trial of BNC105P for renal cell carcinoma failed to meet its primary endpoint with no significant difference in six-month progression-free survival with the addition of BNC105P to everolimus (Afinitor) as compared to everolimus alone (BD: Mar 19, 2014).

Bionomics chief executive officer Dr Deborah Rathjen told Biotech Daily at that time that the results were "just the beginning of the data from the trial" which would inform future trials.

Bionomics said in March that biomarker changes correlated with progression-free survival or lack thereof at six months, in a statistically significant manner ( $p = 0.0136-0.0348$ ) consistent with previous BNC105 studies and the first time biomarkers that correlated with progression-free survival reported for a vascular disrupting agents in renal cancer.

Today Dr Pal said it was "the first time a biomarker signature associated with clinical outcomes for a [vascular disrupting agent, BNC105] plus Afinitor has been reported for renal cancer patients".

"These biomarkers should be further evaluated in future studies, within the frame of personalized medicine, to guide drug administration in those patients with the highest chances of benefiting from a significant clinical outcome," Dr Pal said.

Bionomics said the finding suggested that future studies might select renal cancer patients using the four-biomarker signature to demonstrate a much higher probability of benefiting from BNC105 with everolimus.

The company said that future studies might also evaluate overall survival after five years and overall response rate of the combination of BNC105 monotherapy following everolimus treatment.

Bionomics said that data collection and analysis on these parameters was continuing and would be reported as it became available.

Bionomics was up 3.5 cents or 6.0 percent to 61.5 cents.

## VIRALYTICS

Viralytics says that to date, 22 of 57 late-stage melanoma patients in its phase II Cavatak trial have achieved the six-month immune-related progression-free survival endpoint. Viralytics said that the rate of immune-related progression-free survival “significantly [exceeded] the initial target of 18.5 percent, or 10 of 54 evaluable patients ... at six months after the first dose of Cavatak”.

The company said that the results were presented in a poster entitled ‘CALM study: Secondary endpoints of a Phase II study of a novel oncolytic immunotherapeutic agent, Cocksackievirus A21, delivered intratumorally in patients with advanced malignant melanoma’ at the European Society of Medical Oncology congress in Madrid, Spain. Viralytics said that Cavatak was a novel cancer immunotherapy based on the Cocksackievirus A21 cold virus that had been shown to preferentially infect and attack cancer cells.

The company said that investigators reported an overall response rate in 16 of 57 (28%) patients, with an additional three patients remaining in the extension phase of the study and being monitored for the development of an overall response.

Viralytics said that Cavatak demonstrated activity in both injected tumors and non-injected tumors, including local and distant lymph nodes, lungs and other distant sites, suggesting an anti-tumor immune response.

The company said that an interim one-year survival rate of 73 percent or 33 of 45 patients was achieved in the population with advanced, difficult-to-treat disease.

Viralytics said that Cavatak treatment was well-tolerated, with no reports of drug-related serious adverse events or grade 3 or 4 adverse events, with the majority of side effects reported as grade 1.

Viralytics chief executive officer Dr Malcolm McColl said the results “further demonstrate Cavatak’s oncolytic immunotherapeutic activity”.

“Based on Cavatak’s outstanding performance in this trial, and with strong support from leading oncologists, we plan to aggressively pursue our clinical development program,” Dr McColl said. “The commercial opportunity for Cavatak, either as a monotherapy or in combination with other new agents, is reinforced by these very promising outcomes.”

The Salt Lake City, Utah-based Huntsman Cancer Institute lead study investigator Dr Robert Andtbacka said that Cavatak’s activity and tolerability in late-stage melanoma patients was “impressive”.

“Given this growing body of clinical and pre-clinical data, Cavatak appears to be an excellent candidate for use, either as a single agent in earlier disease, or in combination with other new therapies,” Dr Andtbacka said.

Viralytics was up half a cent or 1.75 percent to 29 cents.

## ADVANCED SURGICAL DESIGN AND MANUFACTURING

Advanced Surgical says it hopes to raise \$1,006,279 through an underwritten, non-renounceable 23-for-50 rights issue at five cents a share.

Advanced Surgical said that Kaz Capital had underwritten the issue to \$1 million.

The company said that Kaz Capital was a director related company.

Advanced Surgical chairman Peter Kazacos was the founder of Kaz Capital.

The company said the funds would be used to accelerate research and development and sales projects as well as corporate rebranding.

Advanced Surgical company said the record date was October 7, the offer would open on October 13 and close on October 21, 2014.

Advanced Surgical was untraded at 5.5 cents.

### DIMERIX BIOSCIENCE

Dimerix says it has Australian Therapeutic Goods Administration clinical trial notification ethics approval for its phase II trial of DMX200 for chronic kidney disease.

The Melbourne-based Dimerix said that recruitment of patients at Melbourne's Austin Hospital was expected to commence shortly and the study would investigate the effect of DMX200 on proteinuria in patients with pre-existing chronic kidney disease.

The company said that the DMX200 treatment involved patients who were currently treated with irbesartan, an angiotensin receptor blocker, also taking propagermanium, an anti-inflammatory molecule which acted through the chemokine 2 receptor.

Dimerix said that the therapeutic rationale for DMX200 was developed from its core technology, known as receptor-heteromer identification technology which could be used to elucidate receptor, or drug target, interactions.

The company said that applying this technology to receptors such as G-protein coupled receptors it was able to identify differences in signalling behavior when receptors interacted as heteromers, as expected in-vivo, compared with the traditional analysis of single target receptors in isolation.

Dimerix executive chairman Dr James Williams said the start of the trial was "an exciting step for Dimerix as we focus on establishing clinical proof of concept for the DMX200 therapy in an area of unmet clinical need".

Dimerix said the study's principal investigator was the Austin Hospital's director of nephrology Prof David Power.

Dimerix is public unlisted company.

### LIVING CELL TECHNOLOGIES

Living Cell says it will collaborate with the Centre for Brain Research to identify additional neurodegenerative disease targets for studies of its NTCell product.

Living Cell said that the University of Auckland's Centre for Brain Research director Prof Richard Faull had a specialized interest in neurodegenerative diseases such as Parkinson's, Huntington's, motor neurone and Alzheimer's diseases.

The company said it had the expertise to identify and commercialize treatments and products from the Centre's research.

Living Cell said that the NTCell, encapsulated, porcine brain choroid cells treatment, was in a phase I/IIa study targeting Parkinson's patients who had failed symptomatic therapy.

Prof Faull said that the results of Living Cell's research studies were "impressive and provide strong evidence that NTCell has the potential to provide significant improvement in patients with Parkinson's disease".

Living Cell chief executive Dr Ken Taylor said that the collaboration was "in line with our focus to develop and market NTCell therapy for Parkinson's patients failing current therapy while also investigating the potential of our patented cell therapy for other neurodegenerative disorders".

Living Cell fell 0.1 cents or 1.4 percent to 6.9 cents.

### BLUECHIIP

Bluechiip says it has raised \$763,000 in a share plan at 10 cents a share and with its earlier placement of \$1.1 million has raised \$1,863,000 (BD: Sep 8, 2014).

Bluechiip previously said that each new share came with an attaching option exercisable at 13 cents by March 31, 2015 and the proceeds were for working capital.

Bluechiip was up half a cent or five percent to 10.5 cents.



### OPTISCAN

Optiscan says that magnetic resonance imaging company MR Solutions is marketing Cell-Live, an imaging system based on its second generation endomicroscopy platform.

Optiscan said that the Guildford UK-based MR Solutions had begun the marketing campaign for the pre-clinical research imaging system with a live demonstration at the World Molecular Imaging Conference in Seoul, Korea.

The company said it had worked closely with MR since February 2014 to develop a system dedicated to a targeted scientific market and the second generation Optiscan platform had features including full 3-D imaging capabilities and seamless integration of advance analysis software.

MR chairman David Taylor said his company had been “excited about this market introduction for some time but still have been pleasantly surprised with the interest and market reaction to the Cell-Live system”.

Optiscan said that product release and sales was expected within six months subject to completion of key tasks and required regulatory clearances.

The company said that Cell-Live was a research platform and not a medical device, so no clinical trials or medical device approval submissions were required.

Optiscan was up 0.4 cents or 10.8 percent to 4.1 cents.

### CALZADA

Calzada says that the Australian Therapeutic Goods Administration intends to schedule its controversial human growth fragment AOD9604 in Schedule 4 and Appendix D.

Calzada said that the TGA had issued a notice that proposed amendments to the Poisons Standard would be referred to relevant expert advisory committees in November 2014.

The company said that the change to its wholly-owned subsidiary Metabolic Pharmaceuticals AOD9604 would “mandate certain controls around the possession and supply of AOD9604 in Australia”.

Calzada said that while the controls might more definitely prescribe the legitimate supply of AOD9604, it would seek advice on the proposed scheduling and if necessary make a submission to the TGA.

The company said that income from the supply of AOD9604 was “not material at present”.

In 2007, a phase II trial of AOD9604 for obesity did not meet its primary endpoint and subsequently the drug has been at the centre of a doping inquiry involving the Essendon Football Club (BD: Feb 21, 2007; Jun 29, 2013).

Calzada fell 0.2 cents or 2.2 percent to nine cents.

### IM MEDICAL

IM Medical says its proposed acquisition of ADX Management to manage the Australian Data Exchange Property Trust has been delayed further.

IM Medical said that earlier this month there was an extension to the exclusivity agreement for the acquisition by the Trust of a property at Tullamarine, Victoria for conversion into a major data centre, but the Trust had clerical delays in the transfer of a separate 3.4 hectare Brisbane data centre development site into the Trust, which was linked to the payment of a deposit for the Tullamarine property by the Trust.

IM Medical said that the Trust expected to complete the transfer of the Brisbane site within two weeks.

IM Medical was untraded at 0.2 cents.

## BIOTA PHARMACEUTICALS

Biota says it effective from October 1, 2014 Dr Joseph Patti will replace Russell Plumb as president and chief executive officer and Dr Jim Fox has resigned as chairman.

Biota said that Mr Plumb would assume the role of executive chairman and "continue to have certain other ongoing responsibilities with the company".

The company said that Dr Fox would continue as "lead independent director" and director Richard Hill would retire at the annual general meeting.

Biota said that Dr Patti joined the company on November 12, 2012 as its executive vice-president of corporate development and strategy.

The company said that previously Dr Patti was a co-founder of Inhibitex and served as its chief scientific officer and head of research and development from 2007 until it was acquired by Bristol Myers Squibb in February 2012 and was a director of Inhibitex from 1998 to 2005.

Biota said that before co-founding Inhibitex in 1998, Dr Patti was a professor at Texas A&M's Institute of Biosciences and Technology, held a Bachelor of Science from the University of Pittsburgh and a Doctorate of Philosophy from the University of Alabama at Birmingham.

Mr Plumb said the changes were due to "personal reasons of mine, and with Jim's desire to reduce his board commitments, this is an opportune time to implement these changes".

In August, Biota said that top-line data from its phase II 'Igloo' trial comparing 40mg and 80mg laninamivir octanoate to placebo showed no significant benefit (BD: Aug 4, 2014).

Biota said at that time that the 639-patient, randomized, double-blind, placebo-controlled, parallel-arm trial found that the primary endpoint, median time to alleviation of influenza symptoms, was 102.3 hours for the 40mg cohort, 103.2 hours for the 80mg cohort and 104.1 hours for the placebo cohort.

The company said that patients in both the 40mg ( $p < 0.001$ ) and 80mg ( $p = 0.070$ ) cohorts demonstrated a statistically significant reduction in viral shedding on day-3 of the study compared to placebo and a statistically significant proportion of patients in both the 40mg ( $p = 0.002$ ) and 80mg ( $p = 0.020$ ) cohorts were culture negative on day-3 of the study as compared to placebo.

Biota said that influenza-infected patients in the 40mg cohort had a statistically significant reduction in the incidence of secondary bacterial infections compared to placebo ( $p = 0.013$ ) and the nature and extent of adverse events were similar in the three cohorts, with the incidence of serious adverse events low and balanced across the three cohorts.

Biota said it intended to provide a detailed update on the efficacy and safety results of the trial, the status of the program and its corporate strategy in September 2014.

In June, following the termination of its \$US231 million 2011 Biomedical Advanced Research and Development Authority (BARDA) contract, Biota said it would close its Australian operations and sack more staff (BD: Jun 3, 2014).

Biota was developing its long-acting neuraminidase inhibitor laninamivir octanoate, when it merged with Nabi Pharmaceuticals to access its \$US54 million in cash, eventually settling for \$US27 million in cash (BD: Apr 1, 2011; Apr 23, Oct 30, 2012).

In April 2014, BARDA halted work on the contract and terminated it in May, refuting the company's claims that it had not been given reasons either for the stop-work order or the termination (BD: Apr 30, May 1, 9, 2014).

Last year, Biota sacked 30 percent of its workforce and closed its pre-clinical antibiotic programs (BD: Apr 17, Nov 22, 2014).

On the Nasdaq on Friday, August 26, Biota was up 13.5 US cents or 5.81 percent to \$US2.46 (\$A2.81 - equivalent to 35.1 cents prior to the Nabi merger, when it was trading around \$A1.00), with 227,963 shares traded.

## BONE MEDICAL

Bone Medical says its eight-patient study comparing its oral Caphymone to injected Forteo for osteoporosis has not shown meaningful blood levels of parathyroid hormone. Bone said the trial was intended to assess and compare parathyroid hormone blood levels based on administering different strengths of Caphymone compared to Forteo, with each patient receiving three Caphymone dose strengths, Forteo, or placebo (BD: Jul 2, 2014). Today the company said that intact parathyroid hormone peptides in the blood would permit a faster, simplified development plan for Caphymone but the two different laboratory assays measuring parathyroid hormone levels showed "that the oral doses did not generate meaningful [parathyroid hormone] blood levels as measured by either of the two different assay methods".

Bone said that a similar study in 2013 with a different oral parathyroid hormone formulation gave positive indications of biological activity, but did not generate significant parathyroid hormone blood levels as measured by the enzyme-linked immunosorbent assay (Elisa) method used in the present study, but the second assay, which had shown positive parathyroid hormone levels in previous studies, was not completed.

The company said it was evaluating whether testing stored clinical samples from the 2013 study using the second assay would provide an effective avenue for further development of its oral parathyroid hormone program and it was working to complete the final analysis of the data from the current study.

Bone fell four cents or 22.2 percent to 1.4 cents with 25.2 million shares traded.

## OBJ

OBJ has requested a trading halt "pending an announcement in relation to a product launch".

Trading will resume on October 1, 2014 or on an earlier announcement.

OBJ last traded at nine cents.

## ANALYTICA

Analytica has requested a trading halt pending "an announcement to the market in relation to the capital raising".

Trading will resume on October 1, 2014 or on an earlier announcement.

Analytica last traded at 3.9 cents.