Biotech Daily

Monday April 12, 2010

Daily news on ASX-listed biotechnology companies

*** ASX UP, BIOTECH EVEN: PRANA UP 8%; COMPUMEDICS DOWN 14%**

*** FDA CRITICAL OF CHEMGENEX, ODAC LESS SO**

*** BIOGUIDE BRIEF: CHEMGENEX - NO NEWS IS NOT GOOD NEWS**

*** JOURNAL ARTICLE BACKS CELLMID'S MIDKINE FOR CARDIAC ARREST**

*** BENITEC OPENS ddRNAi HIV TRIAL RECRUITMENT**

*** NOMINATIONS OPEN FOR 2010 PRIME MINISTER'S SCIENCE PRIZES**

*** WEHI: BREAST STEM CELL HORMONE SENSITIVITY AND CANCER**

*** ELLEX SUB-LICENCE OVERCOMES US PATENT PROBLEM**

*** BENITEC TAKES $6.4m LA JOLLA COVE CONVERTIBLE NOTE**

*** GOODBYE INCITIVE**

*** JM INCREASES 1.5% IN GENERA**

*** WILSON HTM REDUCES 1% IN CATHRX**

MARKET REPORT

The Australian stock market was up 0.73 percent on Monday April 12, 2010 with the S&P ASX 200 up 36.2 points to 4984.3 points. Thirteen of the Biotech Daily Top 40 stocks were up, 13 fell, 13 traded unchanged and one was untraded.

Prana was best, up one cent or 7.7 percent to 14 cents with 40,000 shares traded, followed by Cellmid up 6.9 percent to 3.1 cents with 10.1 million shares traded. Chemgenex and Patrys climbed four percent or more; Cathrx was up 3.1 percent; Genetic Technologies and Psivida rose two percent or more; with Clinuvel, Cochlear and Pharmaxis up more than one percent.

Compumedics led the falls, down 2.5 cents or 14.3 percent to 15 cents with 4,000 shares traded, followed by Phosphagenics down eight percent to 11.5 cents with 1.8 million shares traded. Antisense lost 5.6 percent; Prima was down 3.3 percent; Alchemia and Benitec shed more than two percent; with Circadian, Optiscan, Universal Biosensors and Viralytics down more than one percent.

CHEMGENEX PHARMACEUTICALS

The US Food and Drug Administration's office of oncology drug products has issued a critical "complete response letter" for Chemgenex's Omapro new drug application.

Omapro or omacetaxine mepesuccinate is being developed for chronic myeloid leukemia patients who have failed therapy with imatinib and have the Bcr-Abl T315I mutation.

Last month, the FDA's Oncologic Drugs Advisory Committee (ODAC) required the company to conduct a diagnostic test prior to approval of Omapro (BD: Mar 23, 2010).

Today, Chemgenex said the complete response letter did not contain a request for a new study, nor was there a request for enrolment of additional patients into the pivotal study.

But the FDA was critical of the numbers in the trial, the presentation of data, as well as safety concerns regarding an "overfilled vial" of the drug.

The FDA cited the trial's primary endpoints of major cytogenic responses and that 15 percent of chronic phase patients and six percent of accelerated phase patients had a major cytogenic response.

But Chemgenex chief executive officer Dr Greg Collier told Biotech Daily that the FDA had not specified how many patients reaching those endpoints were required to say the trials had reached the endpoints.

The FDA said the toxicity profile was similar to that of a conventional chemotherapeutic agent, with haematologic toxicities and "additionally 20 percent of patients had cardiac-related adverse events", mainly arrhythmias. Laboratory abnormalities included 49 percent with hyperglycemia and 36 percent with hyperbilirubinemia, the regulator said.

The FDA said the study was "single, small and incomplete" with data from 66 of an expected 100 patients, but said a further 31 patients had been enrolled.

"Thus, data from approximately one-third of the patients enrolled … are missing from the current submission. FDA believes that any efficacy claims for the accelerated and blast phase cohorts are insufficiently demonstrated due to small sample sizes," the FDA said.

The FDA said 35 percent of patients did not have a confirmation of their Bcr-Abl T315I mutation status by the central laboratories at enrolment, a required study entry criterion.

The FDA said two different assays were used to confirm T315I mutation status prior to enrollment, but there were no bridging studies to support assumptions about the similarity of the enrolled patient population at each site.

The FDA said the absence of a uniform diagnostic created uncertainty about patient selection and if a patient did not have the T315I mutation but was falsely identified as having it, the patient might not receive more effective, less toxic therapy, such as dasatinib or nilotinib; and patients with a false negative result would receive an ineffective therapy.

"Due to the single-arm trial design and lack of historical control to compare the efficacy results, the clinical meaningfulness of the observed low response rates is unclear," the FDA said.

The regulator said the applicant "presented an overfilled vial size that contains more than twice the average dose of omacetaxine used in the efficacy and safety studies".

Dr Collier told Biotech Daily the company provided 5mg of the drug which required reconstitution and the correct dose-for-weight to be drawn. He said the FDA did not like drug waste and had concerns relating to overdose and environmental toxicity, which he believed would be overcome.

Dr Collier said the 81 patient data presented at the American Society of Hematology late last year showed stronger efficacy data than the 66 patient data (BD: Dec 7, 2010).

The FDA said Chemgenex should be commended for developing of omacetaxine; ODAC members agreed the population studied needed treatments available; most had issues with the non-standardized assay; but one said the results could be interpreted accurately.

ODAC members said omacetaxine had biologic activity and the 'expanded access' route might be a possibility for this product, in those who might benefit from treatment.
Dr Collier said the two leukemia experts on the panel supported approval for the drug.
Dr Collier said he would request a meeting with the FDA, expected in May 2010.
"This is a clear process and we are working with the FDA and they have given us a path forward," Dr Collier said. "There are still major issues outstanding such as patient numbers, vial contents and a diagnostic."
In a media release Chemgenex said it had met with the FDA on April 9, 2010 to discuss the development of a well-defined diagnostic for the T315I mutation.
Chemgenex was up two cents or 4.4 percent to 47 cents with 3.5 million shares traded.

MARC SINATRA'S BIOGUIDE BRIEF: CHEMGENEX

Those of us Chemgenex shareholders who caught a fever on March 23, 2010 when the US Food and Drug Administration's Oncologic Drugs Advisory Committee (ODAC) voted that the company needed a new diagnostic to identify patients with the T315I mutation, have been sweating on the outcome of an April 9 between Chemgenex and the FDA to review the diagnostic strategy to satisfy the ODAC request.

Unfortunately, Chemgenex did not release anything from the April 9 meeting in announcing the FDA's complete response letter on the Omapro application, today. So investors know little more now than they did on March 23.

The FDA issues a complete response letter when they have determined that they will not approve a new drug application in its current form. Importantly, Chemgenex does say that neither a new study nor further enrolment in the current study is required to grant approval

My take is that Chemgenex and the FDA must decide which is the best test for T315I, then Chemgenex will need to find a reference pool of T315I patient samples and test the samples from its trial to show it recruited appropriate patients.

It is clear from the ODAC minutes that the committee believes that the T315I chronic myeloid leukaemia population needs new treatments and Omapro has biologic activity.

The committee also agreed that Omapro could be eligible to enter the market under FDA's expanded access program, which would allow Omapro to be sold before FDA approval under fairly stringent guidelines. But the amount Chemgenex could charge for Omapro is limited to direct costs and administration costs.

Omapro would be a certainty to be approved under the expanded access program and it would at least allow Chemgenex to inform the market of its existence and keep the sales force busy while the drug awaited full approval.

Gaining the FDA's approval of Omapro should have been a slam dunk. Instead the ball is hanging on the rim of the regulatory basket. It should fall in, but let's hope it doesn't hang there too long.

Marc Sinatra
Analyst

* Both Marc Sinatra and Biotech Daily editor David Langsam own Chemgenex stock.

CELLMID

Cellmid says a study published in 'Cardiovascular Research' confirms that midkine treatment ameliorates left ventricular dysfunction following cardiac arrest in a rat model

Cellmid said it was conducting trials using midkine for the treatment of acute myocardial infarction (AMI or heart attack) in collaboration with Pharmahungary.

The company said its trials were designed to advance midkine into the clinic for acute myocardial infarction.

The company said the study in Cardiovascular Research entitled 'Midkine gene transfer after myocardial infarction in rats prevents remodelling and ameliorates cardiac dysfunction' added validation to its trials confirming that in the rat model of AMI midkine treatment ameliorated left ventricular dysfunction and improving cardiac outputs.

The abstract is at: http://cardiovascres.oxfordjournals.org/content/86/1/113.abstract.

The publication concluded that overexpression of midkine prevented left ventricular remodelling and ameliorated left ventricular dysfunction by anti-apoptotic and pro-angiogenic effects.

"[Midkine] gene transfer may provide a new therapeutic modality in ischemic cardiomyopathy and ischemic heart failure," the article said.

Cellmid said the study was conducted by using gene transfer technology to confirm previous positive results using midkine in pig and mouse models of cardiac arrest.

Cellmid said the study added "important validation to results published by Cellmid's researchers demonstrating that midkine can prevent apoptosis, reduce remodeling of the cardiac tissue and increase revascularization following heart attack".

The company said the studies showed that both short and long term survival rates were improved as a consequence of midkine treatment.

Cellmid chief executive officer Maria Halasz said the study reinforced the science behind the program for using midkine therapy for cardiac arrest.

"We now have extensive in-vivo data that demonstrates midkine as a potent protector of the cardiac muscle acting simultaneously via several mechanisms of action," Ms Halasz said.

"These mechanisms act to save the heart from both the immediate and the long term effects of AMI," Ms Halasz said. "Furthermore, these studies show that midkine can be effectively delivered either as the protein or by gene therapy."

Cellmid said it held "the world's largest and most comprehensive patent portfolio concerning midkine, an embryonic cytokine implicated in a range of human diseases".

The portfolio includes a patent for midkine manufacture and 11 patents worldwide for midkine therapy for heart attack.

Cellmid said acute myocardial infarction was surgically induced in rats and 30 minutes later the heart muscle was directly injected with a genetic vector encoding the midkine gene.

The company said midkine protein expression, cardiac function, formation of new blood vessels and apoptotic cell death were assessed for up to 10 weeks following the AMI.

Cellmid said midkine gene therapy successfully induced midkine protein expression in the heart muscle for up to eight weeks.

The company said midkine-treated animals showed increased new blood vessel growth and midkine-treated animals showed reduced fibrosis of the heart tissue.

Cellmid said treatment enhanced anti-apoptotic pathways and that echocardiograms showed that heart function of midkine-treated rats was far superior to that of control animals for at least six weeks after AMI.

Cellmid was up 0.2 cents or 6.9 percent to 3.1 cents with 10.1 million shares traded.

BENITEC

Benitec says its second phase I HIV clinical trial is open for recruitment following approval by the US Food and Drug Administration and California's City of Hope medical centre.
Benitec said the "pilot study of the safety and feasibility of a therapy for AIDS lymphoma using T-cells treated with a lentiviral vector encoding multiple anti-HIV RNAs" was a phase I study using a triple vector, in which one component involved its DNA-directed RNA interference (ddRNAi) technology, along with two other proprietary RNA technologies which it had an option to licence.
The earlier phase I study was for the safety and feasibility of stem cell therapy for AIDS lymphoma using stem cells treated with a lentivirus vector encoding multiple anti-HIV RNAs (BD: Feb 9, 2009).
The company said the study expected that the HIV would be unable to replicate in T cells as the triple vector targeted three separate stages in the HIV replication cycle.
Benitec said that a triple vector was expected to reduce the chance that HIV could develop resistance to the therapy.
The company said the study expected to enroll five HIV positive patients aged between 18 and 60 years of age who have been on highly active anti-retroviral therapy for at least one year and have evidence of treatment failure.
Benitec said the study would be conducted at the City of Hope with Dr John Zaia as the principal investigator.
Dr Zaia said that Benitec's technology "coupled with two other proprietary anti-HIV RNA constructs, has the potential to provide a novel therapy for HIV".
"This trial will ensure that the use of the therapy is safe and feasible for this purpose, and we are excited to be able to deliver it to the clinic," Dr Zaia said.
Patients' own T cells will be transfected or delivered to the cell with the triple vector and then re-infused into their bloodstream and repeated for a total of three times per patient.
Benitec said the primary endpoints were patient safety and study feasibility.
The company said safety would be determined by clinical and laboratory observation and grading of adverse events, analysis of T cell repertoire clonality and the evaluation of HIV isolates for evidence of vector recombination.
Benitec said feasibility would be determined by the ability to obtain suitable numbers of expanded T cells and expression of the RNA transgenes in the cells.
The secondary endpoints are the duration of T cell circulation in blood post-infusion and the effect of the T cell infusion on CD4 count and on HIV load.
Benitec said it expected recruitment would take up to 18 months.
Benitec executive director Mel Bridges said patient recruitment for the HIV T cell study was "a significant milestone delivered by Benitec".
Benitec fell 0.1 cents or 2.2 percent to 4.5 cents with 1.2 million shares traded.

PRIME MINISTER'S SCIENCE PRIZES

The Federal Government's chief scientist Prof Penny Sackett has called for nominations for the annual Prime Minister's prizes for science.
The Prime Minister's prize for science worth $300,000 is awarded to an individual or up to four individuals jointly along with four prizes each worth $50,000 for the physical scientist of the year; the life scientist of the year; excellence in science teaching in secondary schools; and excellence in science teaching in primary schools.
Nominations close on May 21, 2010.
To nominate or for more information about the science prize program go to: https://grants.innovation.gov.au/SciencePrize/Pages/Home.aspx.

WALTER AND ELIZA HALL INSTITUTE

Walter and Eliza Hall Institute researchers have shown that breast stem cells are sensitive to oestrogen and progesterone, with implications for breast cancer.

The Institute said the discovery, by scientists in its stem cells and cancer and bioinformatics divisions, led by Dr Jane Visvader and Dr Geoff Lindeman explained "decades of evidence linking breast cancer risk to exposure to female hormones".

WEHI said the article, entitled 'Control of mammary stem cell function by steroid hormone signalling', was published online in 'Nature' today and an abstract is available at: http://www.nature.com/nature/journal/vaop/ncurrent/abs/nature09027.html.

WEHI said that sustained exposure to oestrogen and progesterone was an established risk factor for breast cancer.

"There is a clear evidence that the more menstrual cycles a woman has the greater her breast cancer risk," Dr Visvader said. "There is even an increase in breast cancer risk in the short-term following pregnancy."

"However the cellular basis for these observations has been poorly understood," she said.

The Institute said that on the mid-2000s, Dr Visvader and Dr Lindeman discovered breast stem cells in both mice and humans.

Unexpectedly they also found that breast stem cells lacked receptors that would allow them to be directly controlled by the female hormones oestrogen and progesterone.

WEHI said that further research had shown that despite lacking receptors for oestrogen and progesterone, breast stem cells were "remarkably sensitive to female hormones".

Using mouse models, they showed that when the ovaries were removed or the animals were treated with hormone inhibitors, which were in clinical use as anti-breast cancer agents, breast stem cell numbers dropped and the cells appeared to become dormant.

Dr Lindeman said the finding helped explain why the effects of chemoprevention for breast cancer continued long after anti-estrogen tablets had been stopped.

"Our discovery suggests that inhibitors of RANK or other stem cell pathways represent possible therapeutic strategies that could also be investigated as breast cancer prevention agents," Dr Lindeman said.

ELLEX MEDICAL LASERS

Ellex says it has sub-licenced a patent enabling the company to bring its 2RT technology to the US market.

Ellex says it has granted non-exclusive rights to the retinal aspects of its 'Selective Laser Targeting of Pigmented Ocular Cells' patent to an unnamed "leading medical laser research institute in the US".

Ellex said it had been prevented from entering the US market with Ellex 2RT due to the patent, but no one from Ellex was available to explain why the company had been prevented from entering the US in relation to the patent.

Ellex said in its media release that the 2RT was a non-damaging laser treatment that stimulated regeneration of the retinal pigment epithelium to preserve vision and aimed to treat the retinal pigment epithelium before vision loss occurred, which the company said was "a breakthrough treatment option for a range of degenerative diseases that ultimately result in blindness".

The company said that with the sub-licence in place Ellex customers in the US would be able to use Ellex 2RT for retinal disease and the intellectual property pathway was unencumbered outside the US.

Ellex said it had filed for four international patents related to the Ellex 2RT program.

Ellex was up half a cent or 3.2 percent to 16 cents.

BENITEC

California's La Jolla Cove Investors has agreed to provide Benitec with a convertible note facility for up to $US6 million ($A6.4 million).
La Jolla Cove provided a similar facility to Viralytics last year when $US6 million was worth $A7.4 million (BD: Jun 12, 2009).
Benitec said today that La Jolla Cove was a private investment company that invests in small to mid-sized publicly traded companies.
Benitec executive director Mel Bridges said the company was "very pleased with the commitment La Jolla Cove Investors was demonstrating via their investment".
Benitec said the facility provided up to $US6 million in four $US1.5 million convertible notes, each with a duration of two years from the first drawdown.
Funds may be drawdown by Benitec at $US250,000 per month and the notes bear interest payable to the holder at 4.75 percent a year, payable monthly on the outstanding funded and non-converted principal amount; and the notes must be repaid on maturity unless converted to shares within the terms of the notes.
Benitec said the notes could be converted at the election of the holder (or upon default triggers) at the lesser of 15 cents a share or a 20 percent discount to the value weighted average price calculated at conversion, with a floor price of four cents a share and La Jolla would not hold more than 9.99 percent of outstanding shares.
A shareholders meeting will be held to approve the facility and acquisition.

INCITIVE

All resolutions to the Incitive extraordinary general meeting to become an oil and gas explorer have been passed overwhelmingly (BD: Mar 12, 2010)
The company is in a trading suspension.

GENERA BIOSYSTEMS

JM Financial Services has increased its substantial shareholding in Genera from 4,368,570 shares (7.89%) to 5,212,190 shares (9.41%)
Last week Australian Ethical Trusts exited from its Genera holding (BD: Apr 6, 2010)
Genera was unchanged at 70 cents.

CATHRX

Wilson HTM Investment Group has reduced its substantial holding in Cathrx from 3,847,766 shares (9.03%) to 5,521,136 shares (7.86%).
Cathrx was up half a cent or 3.1 percent to 16.5 cents.