Biotech Daily

Wednesday April 7, 2010

Daily news on ASX-listed biotechnology companies

US Patient Protection and Affordable Care Act Special Edition

*** ASX, BIOTECH UP: BENITEC UP 7%; IMPEDIMED DOWN 12.5%**

*** BIOGUIDE BRIEF: BIOLOGICS, BIOSIMILARS & DATA EXCLUSIVITY 101**

*** PETER MOLLOY: BIOSIMILAR PROTECTION GREAT FOR INVENTORS**

*** SPRUSON & FERGUSON: US LAW NOT A MONOPOLY LIKE A PATENT**

*** GRIFFITH HACK: PROTECTED BIOLOGICS STILL NEED PATENTS**

*** IMPEDIMED APPLIES TO FDA FOR LOWER LIMB LYMPHOEDEMA TEST**

*** LIVING CELL'S PIG CELLS 'SAFE AT 34 MONTHS', PROOF-OF-PRINCIPLE**

*** BIOMD OPTIONS RAISE $1.3m; 55% UNDERWRITTEN SHORTFALL**

*** BIOSIGNAL COMPLETES SHARE CONSOLIDATION**

MARKET REPORT

The Australian stock market climbed 0.15 percent on Wednesday April 7, 2010 with the S&P ASX 200 up 7.2 points to 4960.9 points.

Twelve of the Biotech Daily Top 40 stocks were up, 10 fell, 12 traded unchanged and six were untraded.

Benitec was best, up 0.3 cents or 6.98 percent to 4.6 cents with 70,000 shares traded, followed by Cellestis up 13 cents or 4.35 percent to $3.12 with 23,346 shares traded.

Alchemia, Cellmid and Living Cell climbed more than three percent; Novogen rose 2.35 percent; with Clinuvel, Heartware and Mesoblast up more than one percent.

Impedimed led the falls, down 9.5 cents or 12.5 percent to 66.5 cents with 180,000 shares traded, followed by Antisense down 0.2 cents or 10 percent to 1.8 cents with 13.1 million shares traded.

Sunshine Heart lost 6.1 percent; Phosphagenics fell 4.6 percent; Prima was down 3.2 percent; Circadian, Genetic Technologies and Optiscan shed more than two percent; with Pharmaxis, Resmed and Viralytics down more than one percent.

MARC SINATRA'S BIOGUIDE TO BIOLOGICS, BIOSIMILARS & EXCLUSIVITY

When the US Government passed the Obama healthcare reform package, biologics were granted 12 year data exclusivity through the Patient Protection and Affordable Care Act. But what does this all mean? It's time to go back to school.

The US Health Services Act defines a biologic as "any virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product or analogous product applicable to the prevention, treatment or cure of diseases or injuries of man". Okay, it's time to call the lawyers, but that's far too expensive, so I'll try my own definition of biologic: "Anything, at least originally, of biological origin that is relatively complex, such as a monoclonal antibody, that can be used to treat a disease or injury of humans" (removing the US government sexism) (© M Sinatra/Biotech Daily; Apr 7, 2010).

As for 'biosimilars', it turns out, the US Food and Drug Administration doesn't actually have a definition of biosimilars, as far as I know or could find.
The best definition I could find comes from Astra Zeneca: "Biosimilars [are] follow-on biopharmaceuticals that are biologically similar to an existing medicine."
Doesn't really help much, does it?
Time for another Sinatra original: "A biosimilar is essentially a generic version of a referenced biologic, but because of the complexity of biologics, making an exact generic of a biologic is pretty much impossible – it will only ever be similar" (© M Sinatra/Biotech Daily; Apr 7, 2010).
Think of all the amino acids in an antibody, how the peptides fold and are linked together. Trying to replicate that is like try to find the pot of gold at the end of the rainbow.

For data exclusivity, I am going to abandon using other people's definitions because I am running out of space.
"Data exclusivity is a period of time from marketing approval of a new medicine in which other companies are not allowed to use the data from that new medicine to support their application to market a generic medicine" (© M Sinatra/Biotech Daily; Apr 7, 2010).
If they can't use the new drug's data, the generic maker must collect their own. This is too costly and time consuming for them.
So, essentially, data exclusivity is a period time where others cannot replicate an originator's drug without going to considerable effort and expense, even if the new drug's patent has expired. In the US, data exclusivity lasts five years for your standard new drug; in the EU it is 10 years.

Finally, we come to the point of this piece: Under the new US legislation biologics have essentially been granted 12-years before a biosimilar or, if you like, a biogeneric can gain entry to the market without doing a full set of preclinical and clinical trials.
Is this a good or bad thing?
Certainly, biologics originators will say it is good, while would-be makers of biosimilars believe it to be a bad.
The US government will be hoping that they have chosen the perfect balance between incentives for biologics originators to produce new medicines, while limiting their ability to avoid competition to the benefit of the consumer.
Have they got it right? That is another article or, more likely, a PhD thesis.

Marc Sinatra
Analyst

PETER MOLLOY

The US ‘Pathway for Biosimilars’ is important, not because it provides a pathway for bio-generics primarily, but because it crystallizes a new value chain for biologics innovators that makes partnering of biologic drugs very different from small molecules.

The reality is that the biosimilars legislation in the US (and Europe) does not make life any easier or that much clearer for bio-generic drugs and it is likely bio-generics will never have the same impact or easy pathway to market as small molecule generics. One report (URCH Publishing, London) forecasts that bio-generics will acquire only 2.6 percent of the $US100 billion biologics market by 2016.

Apart from the regulatory hurdles, biologic drug markets have significant barriers to entry and rich ever-greening (product life-cycle extension) opportunities are unavailable in small molecule drug markets.

However, what’s really important about the legislation is that it establishes a 12 year in-market exclusivity period for biologic drugs (10 years in Europe) regardless of the patent expiry. This is very different to the Hatch-Waxman laws applicable to small molecules.

Add this to the barriers to entry and ever-greening defences and the value proposition for biologics innovators is dramatically enhanced. Moreover, the partnering process and the deal modeling underpinning the negotiations must take into account these factors.

Small biotechs must not be trapped into negotiating around the patent life only, with no terminal value post-patent-expiry (applicable with small molecules) because more than half of the net present value of a biologic drug could be realized after the patent expires.

Peter Molloy
Aquarius Consulting, California

* Peter Molloy was formerly Biota’s chief executive officer. A detailed presentation on this issue is at: http://www.aquarico.com/web-storage/Presentations/Biologics%20and%20HCR%20Mar%2023%202010.pdf

SPRUSON & FERGUSON LAWYERS

While it's useful for innovative biotech companies to get an extended period of regulatory exclusivity in the US market, regulatory exclusivity is not the same as, or a substitute for, patent protection.

As yesterday’s Mesoblast announcement notes, the protection under the US Patient Protection and Affordable Care Act is against “abbreviated approval” of biosimilars - not against the production or marketing of biosimilars. It doesn't create a monopoly right in the way that patent protection does (BD: Apr 6, 2010).

If a company enjoys regulatory exclusivity over a product, the exclusivity will prevent competing products from being approved by reference to approvals of the company's existing product.

But regulatory exclusivity can't stop competing products from being approved independently of the approval of the existing product. Only patent rights can do that.

Regulatory exclusivity is a speed limit on the road to competition from near-identical products, not a fence around the product preventing competition from substitutable products.

This isn't to downplay the financial impact of the new US laws, which will no doubt be material for many biotechnology companies doing business in the US.

But it's noteworthy that Mesoblast's announcement stresses the strength of the company's patent portfolio. We don't expect to see Australian biotechnology companies dropping their US patent applications any time soon.

Rob McInnes
Principal, Spruson & Ferguson Lawyers

GRIFFITH HACK
The US biosimilars legislation introduces a 12 year data exclusivity period in the US, determining how long before abbreviated regulatory approval for a biosimilar can be obtained. The alternative is for the company to do its own clinical trials.

Australia provides a five year exclusivity period and the European Union gives eight years exclusivity, a further two years marketing exclusivity and a further one year for new indications determined during the initial eight year data exclusivity period. The US provides a five year data exclusivity for new chemical entities and the new legislation distinguishes the exclusivity for new chemical entities from biologics. Australia and Europe do not distinguish.

A generic pharmaceutical is a copy of the approved drug whereas a follow-on biologic or biosimilar will not be exactly the same as the approved drug. Biologics often rely on multiple patents, including narrow product patents and process patents that are more vulnerable to design around than small molecule patents.

Without data exclusivity the biosimilar could obtain abbreviated marketing approval and avoid the patents which cover the innovator biologic, placing competing drugs on the market which rely on the same data package.

The US position is a win for biotechnology lobbyists who argued that biologic drugs take longer to get to market and are more costly to invent and produce than chemical pharmaceuticals and that patent protection for biologics is harder to obtain and easier to design around. It will be interesting to see if other countries revisit their legislation.

Patent protection is entirely separate from data exclusivity. Patents are awarded for inventions and run for 20 years, whereas data exclusivity recognizes the cost and risk of taking a drug through approval for marketing and run from the date of marketing approval.

From marketing approval, data exclusivity runs concurrently with patent protection. The data exclusivity period becomes more important the longer the drug's development time. Patents can be extended to a maximum of 25 years in specific circumstances. If it takes 15 years to get regulatory approval for a biologic, in Australia the patent and data exclusivity period will expire together but the patent may be extended by five years.

In the US, the patent will expire before the data exclusivity period ends, thus extending the term of protection for the product. Additionally the data exclusivity period will not expire even if a patent is revoked.

Simply speaking, the US legislation appears bad for generics and good for innovators. The lobbyists said it would encourage more biologic innovation as more companies would be encouraged to invent. There will still be a need for patents to protect an invention and have value at an early stage (even before a lead biologic is determined). Patents generally seek to protect more than one entity.

While some Australian companies will be seeking approval from the FDA many more will be seeking investment or to sell their product on before it is approved.

Patents allow companies to do this, as without them there is limited protection. Ideally companies should seek to get marketing approval at an early stage, but what the biosimilars legislation does is offer some protection if the approval process is long or if patents are revoked.

Amanda Stark
Principal, Griffith Hack Patent & Trade Mark Attorneys

IMPEDIMED

Impedimed has lodged an application with the US Food and Drug Administration to expand the indications for its L-Dex U400 to lower limb lymphoedema.

Impedimed said the L-Dex U400 was the first device with FDA clearance for unilateral arm applications applied to breast cancer patients and if successful, the new claim would allow it "to target a far broader range of healthcare professionals including general surgeons, oncologists and physical therapists, all of whom could be involved in the much larger market of the prevention of lower limb lymphoedema".

Impedimed chief executive officer Greg Brown said the application for lower limbs was a milestone.

"The leg market for lymphoedema represents around 80 percent of all secondary lymphoedema cases, and of these 60 to 70 percent are unilateral cases," Mr Brown said.

"It has long been suspected that the early identification and treatment of lymphoedema can prevent the progression of the condition in patients with leg involvement," Mr Brown said.

"Studies are underway to demonstrate the effectiveness of pre-emptive care in pelvic related cancers and the number of patients who could benefit is significant," he said.

Mr Brown said Impedimed was well-positioned to target coverage by insurers on the new American Medical Association current procedural terminology (CPT) reimbursement code for arms and legs (BD: Mar 8, 2010).

Mr Brown said these factors implied an increase in potential revenues.

Impedimed medical director Dr Walton Taylor said he wanted to use the L-Dex test as a clinical tool to assess the lymphatic systems in all of his cancer patients.

"Lymphoedema has historically been a significant issue in melanoma and some of the pelvic cancers," Dr Taylor said.

"With this claim, surgeons can now simply, clinically assess patients for the earliest signs of lymphoedema and start treatment and education earlier," Dr Taylor said.

Impedimed fell 9.5 cents or 12.5 percent to 66.5 cents.

LIVING CELL TECHNOLOGIES

Living Cell says that at two years post-implant several Russian type 1 diabetes patients had reduced insulin doses and there were no serious adverse events.

Living Cell said that the first patient in the phase I/II trial was enrolled in June 2007 and at 34 months after receiving the Diabecell encapsulated porcine islets of Langerhans cells all patient blood samples tested negative for any pig-to-human transmission of diseases.

The company said that six of the eight patients had improvements in blood glucose control as reflected by reduction in glycated haemoglobin (HbA1c %) levels and reduction of the required daily dose of insulin injections.

Two patients discontinued insulin injections entirely; the longest period was for a span of 14 weeks.

Living Cell said the data analysis “confirmed that the trial has successfully met its end points of demonstrating safety and tolerability”.

The company said the treatment had shown proof-of-principle of efficacy in humans with insulin-dependent or type 1 diabetes.

Living Cell said the results had been accepted for oral presentation at the scientific meeting of the American Diabetes Association in Orlando, Florida, June 25-29, 2010.

The eight Russian patients, aged 21 to 68 years, with insulin-dependent diabetes received between one and three implants of Diabecell with only minor adverse events.

Living Cell said two patients reported adverse events of abdominal discomfort occurring up to five days post-implant, although both of these patients fully recovered without experiencing any residual effects.

Living Cell said that all trial patients at the Sklifosovsky Institute in Moscow would continue to be monitored to establish the duration of clinical benefit and safety.

The company said the data, taken together with positive progress in its phase II trial in New Zealand, “provided encouragement to progress Diabecell further towards commercialization” and said it was investigating additional trials in other jurisdictions.

Living Cell medical director Prof Bob Elliott said the company was “pleased that our treatment has shown so far to be safe and well-tolerated”.

“We are encouraged that we have demonstrated that Diabecell may be safely administered up to three times and that we have seen evidence of continuing efficacy exemplified by the patients clearly showing reduced HbA1c levels as well as the daily dose of insulin injections, with better control over their blood glucose levels,” Prof Elliott said. “Patients volunteered that they sensed greater well being.”

The director of the adult diabetes program at the University of Colorado in Denver Prof Boris Draznin said it was “the first time that anyone with long term insulin-dependent diabetes has come off insulin injections following islet cell implants without using immunosuppressant drugs”.

Living Cell chief executive officer Dr Paul Tan said the New Zealand phase II trial would help determine the optimum dosing regimen.

Living Cell was up one cent or 3.45 percent to 30 cents.

BIOMD

Biomd says its non-renounceable rights issue of options raised $581,837 through the issue of 38,789,168 options, a 45.2 percent take-up of the offer (BD Feb 26, 2010).

Biomd said the shortfall was 47,092,907 options and the underwriter Bell Potter Securities will allocate the options to sub-underwriters.

On completion, a total of $1.288 million will be raised.

Biomd was untraded at 4.8 cents.

BIOSIGNAL

Biosignal says it has completed its 25 for one share consolidation, reducing its shares on offer from 130,416,353 shares to 5,217,026 shares.

Biosignal is in transition to the RGM entertainment company, but retains its original biotechnology assets (BD: Mar 19, 2010).

Biosignal was untraded at a notional 37.5 cents.