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In this edition...
The 4th annual Bioshares Thredbo Biotech Summit was held on July 25 and July 26.

A wide range of biotech investment and commercialisation topics were discussed, of which a selection are reported on in this conference wrap edition of Bioshares.

The editors
Companies covered: Conference Wrap

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Delivering independent investment research to investors on Australian biotech, pharma and healthcare companies.

Roche Lands in Thredbo – Will it Trigger a Biotech Avalanche?

The 4th annual Bioshares Thredbo Biotech Summit was held last Friday and Saturday, with approximately 100 delegates attending this year. The conference ended on a surprisingly optimistic and positive note, surprising because over the last 15 months the Australian biotech sector has recorded five consecutive quarters of negative stock market performance and is down almost 50% since the start of last year.

The climax at this year's event came at the second last open session, when Ajan Reginald from Roche presented to delegates. Ajan is the Global Head of Emerging Technologies for Roche and arrived in Thredbo from New York just prior to his presentation. That this big pharma representative was prepared to make such an effort to attend and present at the conference was somewhat of a mystery that was revealed very quickly.

Roche has set up a CHF 500 million evergreen fund (i.e. the fund can continue to operate indefinitely without having to make a return to shareholders within a specific timeframe) that is being managed by Ajan. By the end of next year, his team plans to complete 40 deals investing in 'transformational technologies', as opposed to technologies that seek to make incremental changes to existing products.

The fund was set up three years ago although it appears the company has just begun promoting its strategy over the last two months. The group has looked at 1800 companies to date, of which Ajan indicated 300 have very interesting technologies. The Roche team's visit to Thredbo includes meetings with several Australian biotechs working with emerging technologies.

The message was perhaps heard very clearly by delegates because just this week, Roche announced two biotech acquisitions – **Mirus Bio Corporation** (RNAi delivery platform) in the US for US$125 million, and **Arius Research** in Canada (an antibody platform that allows antibodies to be selected on their functional ability to modulate disease) for C$191 million – and it announced a bid to acquire the remaining 44% of Genentech for US$43.7 billion. Has Roche just kicked opened the door to set the global biotech sector bolting again?

The fund will look at six technology areas. These are:

- Next generation RNAi (implication: positive news for **Benitec**)
- Stem cells, including adult stem cells (implication: positive news for **Mesoblast** and **Stem Cell Sciences**)
- Next generation antibodies
- *In silico* production
- Peptides (implication: positive news for **Phylogica** and **Xenome**)
- *In vivo* molecular biomarkers

Cont'd over

The group has access to 130 key opinion leaders on various scientific advisory boards, who according to Ajan, are immediately available to the Roche team to allow decisions to be made very promptly.

It is expected the 40 deals will be structured as follows:

- 20-30 option deals
- 3-5 licensing deals
- 2-3 new company deals
- 3-5 strategic portfolio deals where up to a 19.9% investment in the company will be made
- 2-3 M&A deals where a majority interest (50.1%) will be acquired
- 2-3 M&A deals where 100% of the business will be acquired

According to Ajan, the approach at big pharma towards partnering has changed considerably. These major companies have lost up to half of their value in recent years. The original model was to access programs at the Phase IIb state. However that has now changed and pharmaceutical companies are now looking at earlier deals, presumably because of the lack of options, suggesting that it may be becoming more of a sellers market for good quality assets. With biotech company share prices having fallen heavily in Australia, it is almost certain we will see accelerated M&A deals in Australia over the next 12 months. In Bioshares view, this sector has well and truly bottomed!

Roche currently spends 19% of its revenue on R&D. Ajan indicated the company has a full pipeline to 2016 and 25% of its R&D budget will spent on emerging technologies.

(Emerging technology deals completed recently (2007) by Roche include the $331 million deal (upfront and equity) in RNAi with **Alnylam** (completed by Ajan), the acquisition of **Therapeutic Human Polyclonals** for US$56.5 million, and the **Transgene** alliance for a Phase III HPV therapeutic vaccine program, with the deal including 23 million Euros in upfront and near term payments).

So what is the aim of this CHF 500 million evergreen fund? The answer is very simple according to Ajan: to find the next Genentech!

Biotech year in review

In additional to the halving in stock prices over the last 18 months, this week delivered more disappointing news for biotech investors, with **Progen Pharmaceuticals** cancelling its PI-88 Phase III program and **Biota Holdings** settling with **GlaxoSmithKline** for only $20 million, half of its legal costs on the failed action.

Capital markets have reduced capital inflow in the sector to only $99 million in this first half, compared to $943 million last year. IPOs have slowed to a trickle, with only two listings this year, **Genera Biosystems** and **Austofix**, although there are at lease 13 companies identified by Bioshares as possible candidates for an IPO when the market turns.

Overall the clinical results have been largely positive over the last 12 months, with three Phase II failures during the year, two from **Metabolic Pharmaceuticals** and one from **Biodiem**.

Although the milestone table for 2008 looks a little vacant, it is expected that 2009 will be a very busy period for the Australian biotech sector, with at least three companies expected to launch products next year and five companies are expected to file their drugs for approval.

An extensive international year-in-review was provided by senior **Wilson HTM** analyst, Shane Storey. For the first time mid cap US stocks (capitalisation between US$1-5 billion) were profitable and Storey expects the gap in the US to widen between large/mid cap stocks and the small/micro cap stocks. The biotech blockbuster list is currently dominated by relatively old products that reached the market in 2004 or earlier.

In terms of deals in the biotech sector, 2008 so far has already surpassed the total the total deal flow seen in the sector in 2007. Storey attributed the increased interest by Japanese pharmaceutical companies in international biotech assets to the patent expiry pressure those firms are under.

On average, Australia should be doing one major M&A deal (over $200 million) every 2.5 years. With the last $200 million plus deal completed in Australia in 2006 (Vision Biosystems), Australia is due to see another major acquisition according to these historical numbers.

Analysing the stock purchase trends, Storey said that current graphs indicated the boom in the energy sector may have run its course and we might see some of those funds move into the biotech sector. Storey expects a resurgence in small cap M&A in Australian biotech stocks with the number of ASX listed biotechs expected to erode. He believes there are early signs from institutional clients of a recovery in investor interest in biotech stocks. But product sales must deliver conclusively over 2009-2010.

An insight into the FDA from Dr Lester Crawford

The overwhelming highlight of this year's event was the Key Note Address by former US Food and Drug Administration (FDA) Commissioner, Dr Lester Crawford. Bioshares was delighted that Dr Crawford was prepared to travel to Australia to attend this year's event (supported by **QRxPharma** and **Arana Therapeutics**) and delegates were not disappointed.

Dr Crawford described the unique nature of the US FDA, which employs 10,000 people and has an annual budget of US$2 billion. One of the problems with the FDA are budget constraints, which in real dollar terms has not increased since the 1970s.

The FDA is divided into five Centers. These are:

1. Foods
2. Drugs (Drug Evaluation & Research)
3. Veterinary medicines
4. Biologics
5. Medical devices

Cont'd over

These five Centers are not the Divisions and do not govern regulatory policy within the FDA. The Directors and Deputy Directors in these Centers hold considerable power at the FDA and have the final say on drug approvals. These Centers work somewhat independently. The current Director of the Center for Drug Evaluation and Research is Dr Janet Woodcock, who is also Deputy Commissioner of the FDA.

The FDA has three main roles. These are to ensure safety of products, efficacy of drugs, and to maintain manufacturing controls. Assessing efficacy of pharmaceuticals did not start until the early 1960s although took another 14 years to be enforced well. More recently, Dr Janet Woodcock has made a priority of improving GMP enforcement and foreign inspection, with 400 staff having been added to these areas in recent times.

Presumably as with the growing importance of emerging markets as a source of low cost manufacture of global pharmaceutical products, there will shortly be eight FDA offices outside of the US, in China (3), India (2), South America, North Africa and Europe, with this number expected to increase to 12 by 2010.

One facet of the FDA that needs to be kept in mind is the election year malaise and its effect on the FDA. Informally, six months before an election in the US, there are very little changes that occurs at the FDA. When the average of NCE approvals might be around 20 per year, in an election year there are likely to be around only four NCE approvals. The worst time is just after the election, when the transition team comes in and essentially 'paralyses' the FDA. Presidential ordination occurs on January 20. However it can take some time before a new Commissioner is installed. Under Bush (W) it took two years, under Clinton, 18 months, compared to the old days when the process only took around four months.

The relationship between the FDA and CMS is, strangely, not a close one, with Dr Crawford having talked to CMS just once during his time in office!

On the topic of comparative drug analysis, companies should not give up if their drug in development does not appear to compare with existing therapies on the market.

On using FDA consultants, it's important to choose the right type of consultant that understands the culture at the FDA. But there may be two types of FDA consultants that will need to be employed; one a strategist the other a technician, the latter being very capable in day-to-day dialogue with the FDA, while the strategist may be better at liaising with the FDA on broader issues.

Most useful technical session – reimbursement

Judging from discussions with delegates, one of the most useful sessions during the event for delegates was on the topic of reimbursement and pricing in US and European markets. It's a topic that is seldom discussed at investor meetings, yet it is a part of the commercialisation pathway that is crucial to success. Greg Brown, CEO of **Impedimed**, shed some light on the complex reimbursement system in the US.

Prior to Impedimed, Brown spent eight years at **Digene Corporation** as VP of Global Strategic Marketing. Digene was sold to **Qiagen** for US$1.6 billion. Brown looked at another acquisition last year, that of **Cytyc** for US$6.2 billion by **Hologic**. The key to understanding Cytyc's acquisition price was its reimbursement strategy. Cytyc had developed an improved process for processing pap smears. According to Brown they did their homework early. The company went under the existing pap smear code. However, it was able to argue a $14 increase in reimbursement over the standard pap smear. What companies need to look at very early in the commercialisation process is to find out what it is that differentiates a product in order give a company a unique reimbursement position.

Even before clinical trials start, companies need to perform an initial reimbursement assessment, conduct reimbursement due diligence, form a reimbursement team and develop a reimbursement comprehensive strategy!

Alan Robertson from **Pharmaxis** gave an equally insightful review of the intricacies of the European reimbursement and pricing system. In Europe, it is critical to chose the right path for gaining approval of your product in the 30 countries that make up the European Economic Area.

For Aridol, Pharmaxis pursued the decentralised avenue, whereby it used Sweden as its reference member state, then used the mutual recognition procedure to gain approval in other member states. However it took Sweden 18 months to review its application, then a further 12 months for the mutual recognition to occur in other countries.

The centralised procedure is much quicker and should be considered first, where one application is submitted to the EMEA to gain marketing authorization across Europe. The centralised procedure is mandatory for biologic products, and NCEs for AIDS, cancer, CNS disorders, viral diseases and orphan drugs.

Robertson suggested the preferred launch sequence in Europe being the UK, Germany, then Sweden Austria and Switzerland together, followed by France, Spain, then Italy and Norway together.

Germany and the UK have a free pricing system. The UK has the highest prices for pharmaceuticals yet spends 7% less per capita than the remainder of Europe on average because of its obsession with generics. On the 1st of January this year, France indicated it would cut pharmaceutical prices by 10% across the board. There is currently a price freeze in Germany and Spain. Germany is the world's third largest drug market although is rated 25th by the WHO from a healthcare perspective.

A pharmacoeconomic study is crucial if a company desires **IQWiG**, the German equivalent of **NICE** in the UK, to recommend a product for reimbursement. If a company's product is unable to pass the superiority boundary test in Germany, then the submitted drug will not achieve reimbursement.

Cont'd over

There is a pricing referencing system in Europe, where one country will consider the pricing of a product in a neighbouring country when establishing its own reimbursement. Prices of drugs in Greece are one of the lowest in Europe, and given that Portugal references Greece, then Spain, France and Italy reference Portugal, there could be an argument for not immediately seeking reimbursement of a drug in Greece.

Analyst & Investor Panel – Surviving the Capital Market Squeeze

Comments from **ABN AMRO Morgans'** senior analyst Scott Power provided perhaps the most optimism for delegates. Power and his team believe the broader market has now bottomed. The Australian equity market has fallen almost 30% since November 2007 however the market has provided two quarters of positive growth and their analysts believe the broader market is 1000 points undervalued. Power also noted that US bank stocks had bounced back 31% in recent weeks.

And importantly for the sector, Power indicated that high net worth investors and institutional investors are now returning to the biotech space, including founding investors of Wotif investing in **Metabolic Pharmaceuticals** and the Walker family taking a significant chunk of **Acrux** stock.

In this session, Bioshares invited two fund managers that had recently raised dedicated biotech funds, to present on their investment strategies. David Fisher, a partner and investment manager at **Brandon Capital Partners** in Sydney, has recently raised $80 million for an early stage fund and a venture capital fund.

The first is a $30 million Medical Research Commercialisation Fund (MRCF). Its first close was in 2007 with funds contributed by superannuation groups **Statewide** and **Westscheme**. It has a first right of review of biotechnologies emanating from its 18 medical research members (including **WEHI**, **WAIMR**, the **Garvan Institute**, and the **Baker Medical Research Institute**). The fund receives support from the Victorian, NSW and WA Governments for operational costs. It can invest up to $2 million per investment. Whilst there are 25 committee members who must vote on each investment decision, the process is working surprisingly well, providing a constructing medium for collaboration between the 18 member groups.

The second fund is a traditional VC fund with investment support through the Federal Government's IIF program. It is a $50 million fund and the managers are aiming to raise an additional $30 million. The fund managers expect to make between 8-10 investments, allocating $4-5 million each. It will diversify from early to mid stage companies, and by development areas, being medical devices, human therapeutics and life science platform technologies. Fisher expects the fund to be fully invested in the next 12-18 months.

In June this year, Matt McNamara and his team in Melbourne completed the first close of the IB Australian Bioscience Fund I. A final close is expected over the next year with a goal of raising up to $100 million in total. The fund will invest in Australian and New Zealand companies at the mid stage of commercial development (i.e. in or near clinical development). It will invest across the board in medical and life sciences. The fund currently has six investments. These are in: **Alchemia**, **Sunshine Heart**, **Bionomics**, **Arana Therapeutics**, **Heartware** and **Neuren Pharmaceuticals**. An important consideration for McNamara's fund is that it intends to provide for follow-on capital to continue to support its investments.

Dates for the 2009 Thredbo Biotech Summit have yet to be announced.

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How Bioshares Rates Stocks

For the purpose of valuation, *Bioshares* divides biotech stocks into two categories. The first group are stocks with existing positive cash flows or close to producing positive cash flows. The second group are stocks without near term positive cash flows, history of losses, or at early stages of commercialisation. In this second group, which are essentially speculative propositions, *Bioshares* grades them according to relative risk within that group, to better reflect the very large spread of risk within those stocks.

Group A

Stocks with existing positive cash flows or close to producing positive cash flows.

Buy	CMP is 20% < Fair Value
Accumulate	CMP is 10% < Fair Value
Hold	Value = CMP
Lighten	CMP is 10% > Fair Value
Sell	CMP is 20% > Fair Value

(CMP–Current Market Price)

Group B

Stocks without near term positive cash flows, history of losses, or at early stages commercialisation.

Speculative Buy – Class A
These stocks will have more than one technology, product or investment in development, with perhaps those same technologies offering multiple opportunities. These features, coupled to the presence of alliances, partnerships and scientific advisory boards, indicate the stock is relative less risky than other biotech stocks.

Speculative Buy – Class B
These stocks may have more than one product or opportunity, and may even be close to market. However, they are likely to be lacking in several key areas. For example, their cash position is weak, or management or board may need strengthening.

Speculative Buy – Class C
These stocks generally have one product in development and lack many external validation features.

Speculative Hold – Class A or B or C

Sell

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