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In this edition...
Another eventful week in biotech. Peplin completed a funding round, but a change at the top at Peplin left many investors wondering why and if anything had gone wrong. We explore these events in greater detail inside.
Progress has been strong on the trials front with positive results for Imugene's PRRS vaccine (for pigs) and Mesoblast's allogeneic stem cell product for bone fusion evaluated in sheep, were reported. QRxPharma has received valuable guidance from the FDA for its pain drug and Hexima has inked a significant deal with chemicals giant DuPont.

Companies covered: HXL, IMU, MSB, PLI, QRX

	Bioshares Portfolio
Year 1 (May '01 - May '02)	21.2%
Year 2 (May '02 - May '03)	-9.4%
Year 3 (May '03 - May '04)	70.0%
Year 4 (May '04 - May '05)	-16.3%
Year 5 (May '05 - May '06)	77.8%
Year 6 (May '06 - May '07)	17.3%
Year 7 (May '07 - May '08)	-36.3%
Year 8 (May '08 - current)	-8.0%
Cumulative Gain	**92%**
Av Annual Gain (7 yrs)	**17.8%**

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Blake Industry & Market Analysis Pty Ltd
ACN 085 334 292
PO Box 193
Richmond Vic 3121
AFS Licence
No. 258032

Enquiries for *Bioshares*
Ph: (03) 9326 5382
Fax: (03) 9329 3350
Email: info@bioshares.com.au
David Blake
Ph: (03) 9326 5382
Email: blake@bioshares.com.au
Mark Pachacz
Ph: (03) 9671 3222
Email: pachacz@bioshares.com.au

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Bioshares

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

VCs Take Control of Peplin Inc

Peplin Inc (PLI: 50 cents) this weak eased shareholder concerns about funding, by announcing a capital raising led by venture capital groups and existing major shareholders. Peplin will raise US$24 million at 35 cents a share, with a free warrant for every three shares acquired under this placement. Peplin's share price jumped on the news, to an intra-week daily high of 65 cents.

However, the Peplin board also took the opportunity to replace the CEO, Michael Aldridge. Thomas Wiggins, Peplin's Chairman will become both Chairman and CEO. This must be a disappointing outcome for Aldridge, who has been CEO for the last five years and recently relocated with his family to San Francisco, in conjunction with the redomiciling of the company in the USA. Aldridge was one of the quality CEOs in the sector and can be credited with successfully steering the company to the strong position it is in today.

The company's largest shareholder, **MPM Capital** in the US, is now firmly in control of the reigns at Peplin, with a 20% shareholding in the company, a board position (Jim Scopa) and board members Eugene Bauer and Thomas Wiggins who were both introduced to the company through MPM.

This capital raising will see MPM invest a further $10 million in Peplin, **GBS Venture Partners** in Melbourne will invest $10 million (for a 9.4% stake in the company) and existing shareholders **Asia Union Investments** and **Orbis Funds Management** also participated in the placement.

In September last year, Asia Union Investments held an 11.44% stake in the company, **Acorn Capital** owned 14.28% and Orbis Capital held 12.25% in Peplin.

Estimated substantial shareholdings in Peplin post capital raising:
- MPM Capital - 20%
- GBS Venture Partners - 10%
- Orbis Capital, Asia Union Investments & Acorn Capital - in excess of 24%

Approximately 30% of the company will be held by venture capital investors and about one quarter by local non-VC investment funds.

There are a number of themes that emerge from these events that are worth discussing. There is a strong likelihood that the removal of Aldridge from Peplin was an acrimonious decision, with until recently, Aldridge appearing very settled in the role of CEO. The new CEO joined the company as Chairman last year and in discussions with *Bioshares*, indicated he is very well suited for the role, having previously been CEO and Chairman of **Connetics Corporation,** which was sold to dermatology group **Stiefel Laboratories** for US$640 million (3 times sales). Aldridge's employee options have since been effectively cancelled (lapsed) by the company.

Cont'd over

Bringing on board a large investor such as MPM Capital, which is one of the world's largest life science investment firms, there was always the risk, and in fact evident from early on, that it would exert considerable influence on the company. That influence has increased significantly with the change in CEOs and the latest funding round.

In *Bioshares* view, the direction of Peplin is now clearly being driven by MPM Capital. GBS will have a board position, however the fact that MPM has installed its general partner Jim Scopa to the board indicates it is taking a very active role in this business.

Reason for management change?

Thomas Wiggins certainly has the credentials for running the Peplin business. However, the reason for the change in management is possibly due to differing views regarding the direction of the business. Aldridge was committed to building a fully integrated dermatology company, with the aim of building a sales force to sell PEP005 directly into the US markets. Wiggins has a successful track record in selling businesses and VC groups are always looking forward to how they will exit their investments. In *Bioshares* view, this company is now on the market, and we expect the business will be sold within 24 months possibly aligning with the registration of PEP005 for US regulatory approval. However, a sale could occur even sooner if an interested buyer with a keen appetite and deep pockets is waiting in the wings. So what is the expected price tag?

Peplin price tag?

For MPM Capital, a sale price of $2.50 a share (fully diluted market capitalisation of US$780 million) in 2010 would deliver an estimated 4.6 fold return on investment, or an internal rate of return (IRR) of 55%, based on all funds invested to date being slated for investment in Peplin back in 2006, the date of the initial investment. At $2.00 a share (fully diluted market capitalisation of US$625 million), we estimate MPM would generate a 3.4 fold return or an IRR of 44%. We speculate a sale price above $2.00 would generate a sufficient return for MPM in 2010.

Of interest for investors also is that 18.6 million options will expire by 30 June 2010, most with a strike price of 84 cents a share.

Summary

Peplin is now well funded with US$56 million to complete clinical trials for actinic keratosis for PEP005. The share price responded well this week to the improved funding position and with the validation of seeing a major Australian life science VC group take a substantial stake in the company.

Whilst loyal shareholders had previously been included in capital raisings through a rights issue with additional options or through share purchase plans, there was no such inclusion in this funding round or the previous funding round. The focus very much appears to be on how the investment return for major shareholders can be maximised.

For GBS Venture Partners, the investment is well-timed. The only surprising aspect is that local VC firms have not been more active in investing in listed Australian biotechs with the value of local stocks having plummeted over the last 18 months whilst progress has overall been strong. The advantage certainly is with institutional investors that have the ability to eliminate or significantly reduce funding risk that has been a contributing factor to the strong sell-off in biotech stocks this year.

One of the risks moving forward now is if the company is being primed for sale, then the focus is not on creating a sustainable business but on generating an investment return outcome. The performance hurdle for the new CEO will be very high, no doubt with an expectation that value will be better reflected in the company's share price and that a successful M&A transaction will be effected, by our estimates, within 24 months.

Bioshares recommendation: **Speculative Buy Class A** (unchanged)

Peplin Share structure following capital raising and Neosil acquisition

CDIs:	303.6 million
Listed options:	17.1 million (exercise price 84 cents, expire 30 June 2010)
Unlisted options:	15.0 million (exercise prices 70 cents - $1.00, majority expire 2010 - 2012)
Warrants from current issue:	to purchase 26.7 million shares at 45.5 cents a share

Bioshares

QRxPharma Boosted by FDA Guidance

QRxPharma (58 cents) has received positive news from the FDA regarding its Phase III program for its lead compound, Q8003IR, for the treatment of pain. The company is not required to conduct *long term* safety studies with its therapy. It is an unexpected bonus for the company, which now needs to conduct two further Phase III trials prior to submitting its drug for regulatory approval in the US.

QRxPharma has completed the first of its Phase III studies successfully. The trial, in 256 patients who had undergone bunionectomy surgery, found that 80003IR delivered a statistically significant improvement over placebo, which was not a surprise, and the optimum dose was determined (12mg morphine and 8mg of oxycodone in the one combined tablet).

However, the Phase III study also showed that only 2% of the patients in the Q8003IR arm experienced the severe drowsiness and no patients the euphoria normally seen with morphine or oxycodone treatment.

Phase II studies have shown that a 34% - 40% lower dose of morphine can be achieved for the same pain relief when a dual opioid combination of morphine and oxycodone is taken versus morphine alone.

QRxPharma is advised by the former Commissioner of the FDA, Dr Lester Crawford. His advice has been for the company to proceed with the FDA trials under a Special Protocol Assessment program, which will be gained over the next six to nine months. While recent discussions with the FDA have streamlined the regulatory process removing the need for long term safety studies, an SPA with the FDA gives certainty to QRxPharma that if predetermined efficacy and safety endpoints are achieved, the drug should gain approval from that regulatory body.

Second Phase III study - bunionectomy

The next Phase III study will compare Q8003IR against current opioid drugs in about 350-400 patients who have undergone a bunionectomy. Testing pain drugs in patients who have been through a bunionectomy procedure is the accepted standard for testing pain drugs. There is a small cottage industry that exists to cater for such testing, allowing pain drug trials to be conducted efficiently and quickly. A previous pain drug evaluation setting was wisdom tooth extraction.

Third Phase III study - knee surgery

A third Phase III pain trial will look at Q8003IR in knee replacement surgery. It will be a smaller trial, with about 60 patients per group, comparing Q003IR against a placebo. The reason for the third Phase III trial is that the FDA likes to see replication of results in another pain group.

Rescue medication

These trials are normally funded by the sponsoring company, giving patients incentive to enroll in such trials, even if there is a risk that they will receive a placebo for pain treatment. There is the opportunity for rescue medication should the level of pain become unbearable.

Both Phase III trials will have to wait until the SPA agreement is reached with the FDA, which should be in the first half of 2009. We expect trials to be completed in 2009, with an New Drug Application expected to be filed three to five months after the trials, most likely in the first half of 2010.

Average Phase III deal terms

A recent market analysis by the Licensing Executives Society indicates that companies that have completed Phase II trials and /or are conducting Phase III trials can expect average deal terms when partnering of an upfront payment of US$19 million with royalty payments of between 14% - 18% (on a tiered royalty basis). This is of relevance to QRxPharma, which has entered partnership discussions although is leaving open the option to bring its drug to market on its own. It is also relevant to other companies conducting Phase III studies that may seek to partner, including **Acrux**, **Halcygen Pharmaceuticals** and **Avexa**.

Summary

QRxPharma is capitalised at only $36 million with $29.6 million in cash at the end of June this year. The company has sufficient cash to complete its Phase III program. Events to monitor over the next year include potential licensing agreements, an SPA agreement with the FDA, and commencement of remaining Phase III trials.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Hexima Ties Up DuPont's Antifungal Assets

Agribusiness Hexima ($0.94) has advanced its position within the global crop sciences sector following the completion of a deal with **DuPont**, the owner of the **Pioneer Hi-Bred International** crop seed business.

The agreement covers certain biotech fungal resistance technology in corn, soybean and other crops. The deal involves an exchange of technologies between the two companies.

Through the deal Hexima accesses DuPont's gene shuffling technology, with DuPont accessing Hexima's multi-gene expression technology. Hexima also obtains access to DuPont's antifungal protein library. Significantly, the partnership agreement also allows Hexima to co-invest at later stages of plant trait development and commercialisation, enabling Hexima to double its percentage royalty rate it could receive from DuPont as the mareketing partner.

The deal involves DuPont assigning certain intellectual property and anti-fungal protein assets to Hexima, in exchange for shares in Hexima. Hexima has issued 4 million shares to Pioneer at $1.50 per share in consideration for the IP.

Hexima has effectively become DuPont's antifungal play. Interestingly the deal restricts DuPont's ability to initiate new internal competing anti-fungal programs.

However, the deal allows Hexima to partner and develop its antifungal technologies with third parties, outside of corn and soy product areas, but would be obligated to pay DuPont royalties on sales.

There are five main areas in which plant scientists work to develop economically beneficial traits i.e. specific functional properties. These areas include abiotic stress (such as relating to drought tolerance), herbicide tolerance, insect resistance, quality traits (such as relating to oil content) and fungal resistance. Other companies such as **Monsanto** have developed commanding positions for products in the herbicide tolerance and insect resistance areas (e.g. Monsanto's herbicide resistance Round-up Ready is available for corn, soybeans and canola crops among others).

Hexima is arguably now well positioned in the antifungal area of biotech crop protection technologies, with the company's defensin technology being successfully trialled in cotton against fusarium wilt and verticillium wilt, with yields double those obtained from control groups in both trials. Hexima believes it has addressed certain problems relating to phytotoxicity and yield drag.

Recently installed CEO

Hexima recently installed a new CEO, Joshua Hofheimer, a lawyer formerly with **Sidley Austin** in Los Angeles. Hofheimer had worked for Hexima on various matters for some time. However, his experience over the last seven and half years in deal making in the agbio area looks to have been instrumental in writing and concluding the DuPont deal. Hofheimer's skill base would also appear to be very beneficial going forward as the company does more deals in relation to its technology base, and possibly looks opportunistically outwards to complementary technologies.

Summary

The co-investment deal model adopted by Hexima and Dupont is a breakaway from typical deals enacted in the crop sciences sector. A more traditional approach is based on a large industry partner that exclusively licenses a technology allowing fully for internal programs to continue development and also denying the opportunity for the junior partner to contribute and share the risk and reward of later development. Both the stature of the deal partner and the character of the deal confirm there is significant commercial potential is be created with the Hexima vehicle.

Hexima is capitalised at $74 million and held $35.6 million in cash at the end of the financial year.

Bioshares recommendation: **Speculative Buy Class A**

Successful Trial for Imugene's PRRS Vaccine

Animal health technologies company Imugene (6.8 cents) reported interim results from its porcine reproductive and respiratory syndrome (PRRS) vaccine trial this week. The PRRS disease is causes significant annual losses to the pork industry. Clinical markers of the disease include the number of lesions that occur in the lungs of diseased animals. The vaccinated groups in the trial recorded average lung lesion scores 1.31 (oral) and 1.88 (injected) versus 9.76 for the control group.

Over 14 days, average weight gain compared to the control group was 10.1% for the oral vaccine group and 16.9% for the injected group. These interim results are very positive for the Imugene PRRS vaccine program.

Following the release of these successful results, Imugene will now expand its porcine adenovirus vector development program to include other pig diseases. Imugene will also commence discussions with animal health companies with a view to licencing the technology, once the full data package is available. However, Imugene would also aim to retain more development control in any future licensing agreements.

Comment

Success with the PRRS vaccine is very significant for Imugene as potential pig vaccine products should command higher prices relative to vaccine products for the poultry market. The global pork industry does not have a satisfactory PRRS vaccine and Imugene's current PRRS vaccine now appears to have passed an important proof of efficacy trial that should increase its chances of partnering and increases value of the company's assets.

Imugene is capitalised at $10 million, and held $1.6 million in cash at June 30, 2008.

Bioshares recommendation: **Speculative Buy Class B**

Mesoblast – A Window of Opportunity

There has been a steady flow of data emerging from Mesoblast ($1.25) over the last two months from preclinical and clinical studies with the company's adult stem cell technology (mesenchymal precursor stem cells). The company reported this week that its stem cells were safe and effective in treating cervical spine fusion, following a three-month animal study.

This is an important development for the company. Spine fusion is the leading application for Mesoblast with a Phase II study underway in the US. The spinal fusion market is valued at in excess of US$6 billion a year, with the leading biologic product, the BMP-2 product from **Medtronic,** generating sales of US$772 million last year. The most common procedure for spinal fusion is using an autograft, where bone is source from the hip of patients and use in the spine fusion procedure.

The problem with BMP-2 is that it can cause inflammation, which in cervical spinal fusion can result in a swelling around the neck and blockage of the airway requiring an emergency surgical procedure. It is this particular part of the market that may provide an ideal entry for the Mesoblast stem cell application.

The recent results released showed that there were no stem cell-related adverse events using Mesoblast stem cells in the preclinical cervical spine fusion trial involving 24 sheep. The rate of fusion was considerably better than the autograft procedure. According to Mesoblast's founder, Silviu Itescu, other biologic products had shown the problematic inflammatory effects in preclinical studies. The implication is the Mesoblast cells should be safe, in relative terms, in human cervical spine fusion procedures.

In about 20% of autografts used in spinal fusion, there is an unmet need where the autograft predictably will not work and where existing biologics such as BMP-2 should not be used, creating an unmet market need in a subset of the sizeable spine fusion market. The market for this 20% of the cervical spine fusion market in the US alone, assuming no pricing premium, we estimate at US$200 million a year.

Bioshares recommendation: **Speculative Buy Class B**

Bioshares

Bioshares Model Portfolio (22 August 2008)

Company	Price (current)	Price added to portfolio	Date added
Impedimed	$0.72	$0.70	Aug-08
Antisense Therapeutics	$0.07	$0.07	Aug-08
Mesoblast	$1.25	$1.25	Aug-08
Avexa	$0.31	$0.32	Jun-08
Cellestis	$2.34	$2.27	April 2008
IDT	$2.02	$1.90	March 2008
Circadian Technologies	$0.95	$1.03	February 2008
Patrys	$0.26	$0.50	December 2007
NeuroDiscovery	$0.10	$0.16	December 2007
Bionomics	$0.33	$0.42	December 2007
Cogstate	$0.12	$0.13	November 2007
Sirtex Medical	$2.30	$3.90	October 2007
Clinuvel Pharmaceuticals	$0.33	$0.66	September 2007
Starpharma Holdings	$0.24	$0.37	August 2007
Pharmaxis	$2.01	$3.15	August 2007
Universal Biosensors	$0.71	$1.23	June 2007
Biota Holdings	$0.69	$1.55	March 2007
Probiotec	$1.40	$1.12	February 2007
Peplin Inc	$0.50	$0.83	January 2007
Arana Therapeutics	$1.12	$1.31	October 2006
Chemgenex Pharma.	$1.00	$0.38	June 2006
Cytopia	$0.23	$0.46	June 2005
Optiscan Imaging	$0.23	$0.35	March 2005
Acrux	$1.21	$0.83	November 2004
Alchemia	$0.29	$0.67	May 2004

Portfolio Changes – 22 August 2008

IN:
No changes.

OUT:
No changes.

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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