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In this edition...
QRxPharma's management was stunned this week when it received from the FDA a Complete Response Letter concerning its new drug application for its acute pain drug MoxDuo IR. While not a rejection, a CRL typically asks for additional information or other issues to be addressed before the FDA will give approval. QRxPharma was blindsided by the FDA request for information relating to the 'combination rule' which comes into play when two active ingredients (APIs) are combined in the one formulation and must be shown to better than the individual APIs. The company will meet with the FDA in August to get to the root of the FDA's concerns. Cogstate has signed a dementia screening partnership with Merck of Canada. And pSivida has commenced a trial of its lead product in posterior uveitis.
Companies Covered: CGS, PVA, 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)	70.6%
Year 4 (May '04 - May '05)	-16.3%
Year 5 (May '05 - May '06)	77.8%
Year 6 (May '06 - May '07)	17.4%
Year 7 (May '07 - May '08)	-36%
Year 8 (May '08 - May '09)	-7.4%
Year 9 (May '09 - May '10)	50.2%
Year 10 (May '10 - May'11)	45.4%
Year 11 (May '11 - May '12)	-18.0%
Year 12 (May '12 - current)	-11.5%
Cumulative Gain	**205%**
Av. annual gain (11 yrs)	**17.8%**

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Bioshares

29 June 2012
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Delivering independent investment research to investors on Australian biotech, pharma and healthcare companies.

FDA Delays QRxPharma's MoxDuo IR

QRxPharma's (QRX: $0.585) share price was shattered this week when the US FDA delivered a Complete Response Letter (CRL) in response to the company's New Drug Application for MoxDuo IR. QRxPharma shares fell as low as $0.50 cents, a fall of 70% from its previous closing price.

MoxDuo IR is an immediate release pain medicine that combines the opioid drugs morphine and oxycodone in a specific 3:2 ratio (e.g. 12mg morphine with 8mg oxycodone or 6mg morphine with 4mg oxycodone) for the treatment of moderate to severe acute pain.

A CRL is a statement by the FDA to a drug sponsor that its drug is not approvable given the information supplied to date. A CRL will set out changes or clarifications to be made to the new drug submission or describe deficiencies which must be rectified.

QRxPharma CEO John Holaday said that the FDA had requested more information in relation to the 'combination rule'. This rule required QRxPharma to demonstrate that MoxDuo was safer or more effective than comparable doses of oxycodone and morphine.

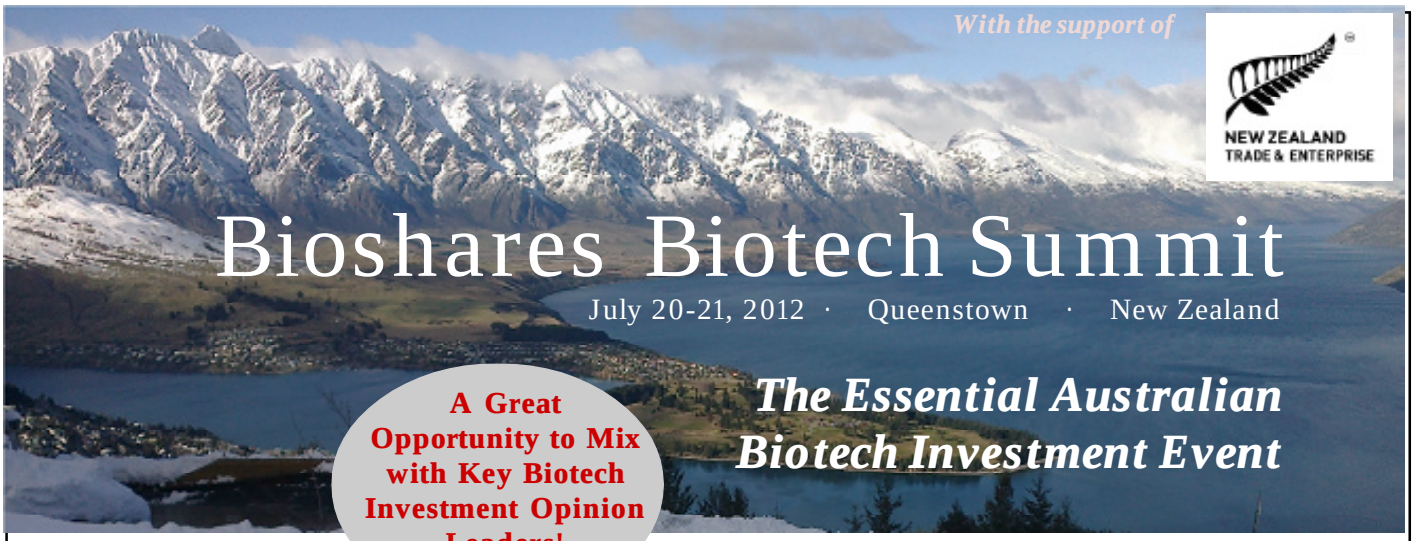
"We were surprised at the subject matter of the request given our past discussion with the FDA, which gave us sound reason to believe that these requirements had been met," said Holaday. The issue of the 'combination rule' (as set out in the CRL) had not been raised when the company held its end of Phase II meeting, nor at its pre-NDA meeting, nor at the filing of the NDA when the NDA was accepted in an approvable format, and was not mentioned in a '74 day' letter received by QRxPharma.

The 'combination rule' was addressed in Study 008 which showed that MoxDuo IR (morphine 12mg/ oxycodone 8mg) was superior to equal analgesic doses of morphine 12mg and oxycodone 8mg, on both the primary endpoint pain score and the secondary endpoint pain score, with statistical significance achieved for these endpoints.

In our view, it was not surprising that Holaday said the decision was "unexpected and disappointing to all involved", whose words were echoed by the company's COO Ed Rudnic who said the decision "caught us by surprise".

The company's next step is to hold a post-PDUFA meeting with the FDA where it can clarify details of the CRL and determine the next steps. The meeting has been set down for a date in August.

Cont'd on page 3



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We are pleased to record the support of Wilson HTM, Nexia Australia, Piper Alderman, QRxPharma and CSL.

We would also like to thank New Zealand Trade and Enterprise for its support of this event in New Zealand for a second year.

– QRxPharma cont'd

QRxPharma does not know for sure if further clinical trials will be required. The company does however, have additional data and analyses from Study 022 (Respiratory Depression) to forward to the FDA prior to the August meeting.

It is common for CRLs from the FDA to contain requests for sponsors to rectify manufacturing deficiencies. In QRxPharma's case no manufacturing deficiencies were cited. Additionally, no risk management (REMS) concerns were raised because MoxDuo IR has been developed for the acute pain setting for which REMS are not required.

What Could Happen Next? (Post August 2012 Meeting with the FDA)

There are several possible scenarios that could follow QRxPharma's meeting with the FDA in August. There are two aspects to predicting when the next FDA decision on MoxDuo IR might occur. The first factor relates to what QRxPharma must deliver to the FDA in terms of new information; the second is how long the FDA will take to respond to the revised drug submission.

Scenario 1 - Best Case Approval Time Line – 6 Months

QRxPharma submits additional data alongside reformatted data from its initial submission with the FDA.

Estimated time line: Resubmission in October 2012 (i.e. 2 months of applicant time); FDA decision by February 2013 (i.e. 4 months of FDA time).

The assumption that the FDA takes four months to make a decision is based on the average time taken by the FDA to assess CLRs from 2010 that were finally approved in 2011.

Scenario 2 - Mid Case Approval Time Line – 12 Months

QRxPharma repeats Study 008 at the same trial size (~500) (estimated time from commencement to data analysis through to resubmission: 8 months); FDA decision by August 2013 (i.e. 4 months of FDA time).

The assumption that the FDA takes four months to make a decision is based on the average time taken by the FDA to assess CLRs from 2010 that were finally approved in 2011.

Scenario 3 - Worst Case Approval Time Line – 19 Months

QRxPharma repeats Study 008 but with bigger numbers (~1000) (estimated time from commencement to data analysis through to resubmission: 12 months); FDA decision by March 2014 (i.e. 7 months of FDA time).

The assumption that the FDA takes seven months to make a decision is based on the average time taken by the FDA to assess CLRs from 2009 that were finally approved in 2011.

Commentary

QRxPharma has received a major setback with the receipt of the CRL from the FDA for MoxDuo IR. We estimate the company's time table for accessing the US market has been set back by 6 months based on optimistic assumptions and 19 months based on a less optimistic assumption.

Implications for Biotech Investment Strategy

There are several schools of thought on how investors should manage their investment in a biotech stock as it passes through major clinical and regulatory milestones.

One view is to hold the stock up until the time of a decision or clinical trial announcement is made (the event period) but not hold the stock during the event period, then possibly re-acquire the stock after the event. The risk for the investor is that the stock could rapidly appreciate if the regulatory decision or trial result is unambiguously positive.

The time of entry into a stock is another factor that plays into the decision to hold a stock through an event period. The set of investors that can potentially weather a negative trial result or negative regulatory decision are those who entered the stock at very low prices, perhaps in the very early days of the company or from acquisition at a time when a deep trough in stock prices across the board has occurred.

What must be remembered is why the most biotech sector stocks are awarded speculative ratings. While some biotechs are better structured, better managed and better funded than others, they all grouped together because the possibility exists that much of the value in the business can be lost if pivotal trials fail or if a regulator does not approve the medical product (representing the dominant asset in the company) in development. And biotech stocks even warrant a speculative rating until consistent positive cash flows appear.

The most common approach to managing inherent risks in biotech stocks, or all equities for that matter, is through portfolio management with major considerations given to weighting.

However, following QRxPharma's receipt of a CRL from the FDA, and Pharmaxis' and Mayne Pharma's recent experiences with the European regulator of first-cycle non-approval followed by a later approval , there is an increasingly strong argument to not hold positions in the shares of biotech companies just prior to the release of regulatory decisions.

The company has been clearly surprised by the decision although investors should note that MoxDuo IR has not been rejected by the FDA (as 'unapprovable'). However, the company's share price is unlikely to begin to regain lost ground until the company meets with the FDA in August and obtains clarification from the FDA regarding the necessary steps to make MoxDuo IR an approvable drug.

Other ASX listed companies including Pharmaxis and ChemGenex Pharmaceuticals (acquired by Cephalon in June 2011) have been the recipient of CRLs. In the case of Pharmaxis, it received a CRL for Aridol 9.8 months after its submitted its NDA; it then resubmitted 3.5 months later with the FDA approving Aridol 6 months further on. ChemGenex Pharmaceuticals Omapro was the subject of a CRL in April 2010. However, the drug candidate has yet to be submitted for re-appraisal.

pSivida's Lead Product Moves into Uveitis Trial

pSivida's (PVA: $2.20) lead drug product for the treatment of eye diseases has now progressed into a clinical trial for the treatment of posterior uveitis. The condition affects around 175,000 people in the US with around 30,000 of those now blind as a result of the condition.

This drug candidate, a three year implant of a corticosteroid, is the same drug and device as Iluvien, which has now been approved in several parts of Europe (Portugal, Austria and the UK) for the treatment of diabetic macular edema (DME). The therapy was developed by pSivida and pSivida has rights to apply it to the treatment of other eye diseases. For the treatment of DME it has licensed the product to **Alimera Sciences**.

Last year Alimera's New Drug Application for Iluvien for the treatment of DME was knocked back (in the form of a Complete Response Letter) by the FDA. The FDA sought additional clinical data (from the 36 month evaluation point) not included in the original submission as well as additional information regarding controls and specifications concerning the manufacturing, packaging and sterilisation of Iluvien.

It is expected that Alimera will start selling Iluvien into Europe at the end of this year. pSivida is entitled to a 20% profit share from Iluvien sales, which translates to around a 15% royalty. If Alimera licenses the product in Europe, pSivida is entitled to 33% of any revenue received by Alimera.

pSivida has another product, Retisert, which has been approved for the treatment of uveitis. This product was licensed to **Bausch and Lomb**. However, it generates very low sales because the device needs to be surgically implanted, is expensive and lasts for only 18 months.

By comparison, the Iluvien product lasts for three years, will be substantially lower priced, and can be injected by a needle. pSivida is hopeful that these more appealing product advantages will make it a commercially viable and successful product.

The clinical trial just started is an investigator sponsored trial. Although Iluvien was knocked back by the FDA, pSivida believes the same product may have a better chance of getting FDA approval for the treatment of uveitis because it has a better side effect profile that the approved Retisert product. pSivida has 100% rights to commercialise the product for the treatment of uveitis.

pSivida is capitalised at $46 million. At the end of March it had US$16.5 million in cash.

Bioshares recommendation: **Speculative Hold Class B**

Bioshares

– QRxPharma cont'd

Is the FDA Cracking Down on Pain Drugs?

The FDA has taken a stronger stance on pain drugs in recent times as evidenced by the introduction of risk management plans for pain drugs (although they also ask for REMS for drugs in other categories as well). The FDA has been focused on making certain pain drugs less amenable to tampering in particular. The phase-out of higher dose forms of acetaminophen (paracetamol) drugs is also evidence of the FDAs desire to manage liver toxicity issues with that drug.

However, there is less evidence to suggest that the FDA has been deliberately slowing down the introduction of pain drugs through the provision of complete response letters. CRLs written by the FDA in the last two years have been evenly spread across drug classes and indications and class of company by size of company.

Investment Considerations

The FDA's CRLs concerning MoxDuo IR illustrates that regulatory risk should remain a major consideration for investors even where company is utilising the 505(b)2 pathway (i.e. is not a new molecular entity which has meant generally that less risk is attached with the development pathway for the drug.) Without the benefit of a necessary and vital clarification from the FDA, we recommend investors wait until details of the August meeting with the FDA become available before considering which direction an investment decision for this stock should take.

A further consideration for investors is that until this meeting is held, the capital requirements of the company are uncertain. If the FDA indicates that QRxPharma must conduct an additional study then it will be more likely that the company will need to raise funds to support the trial in the absence of income from the licensing of MoxDuo IR for ex-USA regions. (**Actavis**, which is being acquired by **Watson Pharmaceuticals** is the licensee of MoxDuo IR for the US.)

QRxPharma is capitalised at $85 million and retained cash of $27 million at March 31, 2012.

Bioshares recommendation: **Speculative Hold Class A**

Bioshares

Cogstate Partners with Merck in Canada for Dementia Screening

Cogstate (CGS: 30 cents) has moved its cognitive testing platform into a third commercial application. The first application is for assessing changes in cognitive function in the testing of novel medicines in clinical trials run by biotech and pharmaceutical companies. The second area is using its test as a concussion management tool in sports. And the third area is moving the test into general practice medicine.

This week Cogstate announced a partnership with **Merck Canada** to sell the test into the GP network in that country. Merck is very active in the CNS drug area and will presumably use its existing primary care sales force to sell this new product. Sales are expected to start before the end of 2012.

For Cogstate it's an important first market entry, with the company having plans to roll out the test into other countries. The deal with Merck is only for Canada. Cogstate is in discussions with other pharmaceutical companies according to CEO, Brad O'Connor, including for rights to market the test in the US.

O'Connor believes the global cognitive testing screening market is valued in excess of $500 million a year. Alzheimer's disease associations, including Canada's, believe there is a need for early detection of Alzheimer's disease as early detection allows disease progression to be managed effectively by the doctor, family and the patient. This is independent of whether disease modifying drugs available or not.

At the moment there are no disease modifying drugs for Alzheimer's disease approved. However if that changes, the market and the demand for an accurate, early-stage screening tool should expand rapidly.

Results from Two Major Phase III Alzheimer's Disease Trials Expected in 2012

In the third quarter of this year, **Eli Lilly** and **Pfizer** expect to release results from large Phase III studies with Alzheimer's disease drug candidates. The two antibody drugs, bapineuzumab from Pfizer and solanezumab from Eli Lilly, bind with beta amyloid.

Wall Street analysts are not giving the two drug candidates a high chance of success. According to a recent article in Reuters, 146 investors surveyed gave solanezumab only a 14% probability to meet its primary endpoints in its two Phase III trials.

Pfizer's bapineuzumab is only viewed with slightly more optimism, with a 21% probability of success in its two Phase III trials. However a positive result could deliver a massive blockbuster to these big Pharma, with some analysts forecasting Eli Lilly's share could increase by 50% (equating to US$24 billion).

A success from either of these drugs would also have a major impact on Cogstate, with these companies then requiring an accurate cognitive screening test for this disease.

Cogstate's test has been used in hundreds of clinical trials in the CNS area, and it has most commonly been used in the Alzheimer's area. Its test has been shown to detect cognitive impairment linked to the early stages of Alzheimer's which has correlated with amyloid beta plaque deposits detected using new imaging technologies.

New imaging technologies for detecting the presence of beta amyloid plaque include the Amyvid test from **Eli Lilly** which was recently approved by the FDA. This test will be used to confirm plaque build up in patients with cognitive impairment who are being assessed for Alzheimer's disease, and also to monitor disease progression. And **GE Healthcare** has released positive Phase III results with its PET technology, Flutemetamol. These tests however still require measurement of cognitive impairment first, which is where the Cogstate test fits in.

Long Term Cognitive Impairment Study

Cogstate claims its test can detect early cognitive impairment linked to Alzheimer's disease. This is because of positive data coming out of its involvement with a major long-term study in Alzheimer's disease, called the Australian Imaging Biomarker Lifestyle Flagship Study of Aging (AIBL). Cogstate has been involved with the AIBL study since he study started in 2007.

Last year Cogstate was able to show a distinct correlation between cognitive decline (using its test) with amyloid deposits in the brain imaged using the PET test. This data would explain the interest from Merck in partnering with Cogstate.

The launch of a population-based screening test into the GP sector represents an attractive commercial opportunity for both Cogstate and Merck. Pricing of the test will be revealed upon launch of the product later this year. We expect that the companies will seek to gain reimbursement for the test.

Cogstate is capitalised at $23 million. It had just under $5.6 million in cash at the end of March. For the first half of this year, the company generated sales of $6.9 million and a profit of $3.4 million.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Bioshares Model Portfolio (29 June 2012)

Company	Price (current)	Price added to portfolio	Date added
Nanosonics	$0.510	$0.495	June 2011
Osprey Medical	$0.40	$0.40	April 2012
QRxPharma	$0.59	$1.66	October 2011
Mayne Pharma Group	$0.350	$0.435	September 2011
Somnomed	$0.88	$0.94	January 2011
Phylogica	$0.044	$0.053	September 2010
Biota Holdings	$0.69	$1.09	May 2010
Tissue Therapies	$0.48	$0.21	January 2010
Atcor Medical	$0.06	$0.10	October 2008
Bionomics	$0.30	$0.42	December 2007
Cogstate	$0.300	$0.13	November 2007
Sirtex Medical	$6.09	$3.90	October 2007
Clinuvel Pharmaceuticals	$1.59	$6.60	September 2007
Pharmaxis	$1.03	$3.15	August 2007
Universal Biosensors	$0.63	$1.23	June 2007
Alchemia	$0.450	$0.67	May 2004

Portfolio Changes – 29 June 2012

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. For both groups, the rating "Take Profits" means that investors may re-weight their holding by selling between 25%-75% of a stock.

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

Corporate Subscribers: Pharmaxis, Starpharma Holdings, Cogstate, Bionomics, Circadian Technologies, Biota Holdings, Impedimed, QRxPharma, LBT Innovations, Mesoblast, Tissue Therapies, Viralytics, Phosphagenics, Immuron, Phylogica, Bluechiip, pSivida, Antisense Therapeutics, Benitec BioPharma, Allied Healthcare Group, Genetic Technologies, Calzada, Bioniche