

In this edition...

A falling US dollar has implications for global biotech. This week Japan's Takeda snapped up Millennium Pharmaceuticals for US\$8.8 billion, aided by a 20% appreciation of the Yen against the USD. The Aussie dollar is 30% higher from two years ago, so what might the local giant CSL do?

Acquisitions are a fact of life in biotech. And while other sectors of the economy might weaken in coming months, some of the bright spots for investors will be found amongst Australian biotechs that are singled out and bought by multi-national pharmaceutical firms that can manage currency fluctuations. No company is sacred, but it will be the solid businesses that will become take-over targets.

The editors

Companies covered: 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 (from 4 May '07)	-37%
Cumulative Gain	103.0%
Av Annual Gain (6 yrs)	26.8%

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Bioshares

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

Extract from *Bioshares* –

The Commercial Context for QRxPharma's QR8003IR

QRxPharma (QRX: \$1.02) is developing the pain drug candidate Q8003IR as an immediate release dual-opioid pain therapy. The company has initiated two Phase III trials, the first of which commenced in November 2007 in 250 patients experiencing acute post surgical pain. The second (an extension study) started in December 2007, for the purpose of evaluating the longer term use and effects of Q8003IR over 28 days.

Q8003IR combines two well known compounds, morphine and oxycodone, that bind to the *mu* opioid receptors. Other compounds that act on these targets include codeine, tramadol, fentanyl, naltrexone, heroin and hydrocodone among others. Opioid drugs have been used to quite successfully treat moderate to severe pain for decades. However, limiting side effects stem from tolerance, dependency and abuse, nausea and very significantly, constipation. This has instigated the development of drugs such as Entereg (**Adolar, GlaxoSmithKline**) and MNTX (**Progenics, Wyeth**), which block the activation of certain opioid receptors in the gut but allow it act on those in the CNS (see table, page 3).

Many morphine-based drugs have been off-patent for years, which means that any commercial considerations must be based on the new patented combinations or formulations, or based on new combinations and novel delivery systems, especially those that discourage abuse. New molecular entities that target the opioid receptors with superior efficacy and diminished side effect profiles have been hard to find. Another area of development has been the development of a sub-class that focuses on break through pain, which is the pain that occurs when the pain drug patients are receiving (e.g. morphine) for chronic pain fails. This sub-class is dominated by the opioid drug fentanyl, with at least eleven formulation/delivery systems approaches in development based on that compound. (*Note, Acrux is developing a Metered Dose Transdermal Spray delivery system for fentanyl.*)

QRxPharma's combination of compounds have been shown to achieve an analgesic effect equivalent to approximately half of a standard dose of morphine.

The QRxPharma approach is not dis-similar to that developed by **Elite Pharmaceuticals** and **Pain Therapeutics**, which have developed products that combine oxycodone and naltrexone (although in the different release formats of extended and immediate release respectively).

Cont'd over

For companies working with known chemical entities, the path to market is typically shortened with often only one pivotal Phase III study required. (e.g. Pain Therapeutics' Remoxy – twice daily oxycodone – only required one Phase III study.)

Pain drug markets represent a classic drug market paradox. They are replete with many approved compounds that over many sub-sectors garner billions in sales. At the same time, there exist major opportunities to generate sales from improvements to existing medicines or introduce new chemical entities.

QRxPharma is capitalised at \$77 million and holds cash assets of \$40 million at December 31, 2007.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Opioid receptor targeted pain drugs in development [excluding fentanyl products]

Company	Drug Candidate	Indication	Description	Status	Comments
Adolor Corporation	Entereg (Alvimopen)	Post-operative illeus	peripherally acting mu opioid antagonist	NDA	Partnered with GSK
	Entereg (Alvimopen)	Opioid Bowel Dysfunction	peripherally acting mu opioid antagonist	Phase III	Partnered with GSK
	ADL5859			Phase II	Partnered with Pfizer
	ADL5747			Phase I	Partnered with Pfizer
Javelin Pharmaceuticals	Rylomine	Acute pain	Intra-nasal morphine	Phase III	
Progenics	MNTX (Methyl-naltrexone sub-cutaneous)	OIC Palliative care	peripherally acting mu opioid antagonist	NDA	Partnered with Wyeth
	Methyl-naltrexone i.v.	Post-operative illeus	peripherally acting mu opioid antagonist	Phase III	
	Methyl-naltrexone oral	OIC	peripherally acting mu opioid antagonist	Phase II	
Neuromed	OROS Hydromorphone	Chronic medium to severe pain	Controlled release	Phase III	US rights lic. from ALZA; marketed in EU by Janssen Cilag
Elite Pharmaceuticals	EL-216	Pain Management	Oxycodone ER and naltrexone (once-a-day, abuse resistant oxycodone)	Phase III pending	
	EL-154	Pain Management	once daily oxycodone	Phase III pending	
Theraquest	TQ-1015	Chronic cancer/ non-cancer pain	abuse deterrent, sustained release opioid agonist	?	
LaboPharm	Tramadol Contramid OAD	Chronic medium to severe pain	Has extended and immediate release components	NDA	Under mediation with FDA; approved in Australia, Sth Korea and 22 EU countries
Penwest	Nalbuphine ER	Medium chronic pain	TIMERX drug delivery system	Phase IIb	
Acura Pharmaceuticals	Acurox	acute moderate to moderately severe pain	Oxycodone IR	Phase II	
Pain Therapeutics	Remoxy	Chronic pain	Twice daily oxycodone - abuse deterrent system	NDA (exp Q2 2008)	Partnered with King Pharmaceutical
	Oxytrex	Persistent severe chronic pain	Oxycodone IR and naltrexone	Phase III	
Zogenix	ZX002	Mod. to severe chronic pain	Oral hydrocodone IR and ER	Phase II	
CeNeS	M6G	Post-operative pain	Morphine-6-glucuronide	Phase III	
Alpharma	Kadian NT	Chronic pain	Morphine and naltrexone Extended release	Phase III	
QRxPharma	Q8003IR (Oral)	Moderate to severe pain, acute pain	Morphine and oxycodone extended release	Phase III	4 dosage strengths;post-surgery, acute pain setting
	Q8003IR (Oral)	Moderate to severe pain, acute pain	Morphine and oxycodone extended release	Phase III Safety extension study	collection of additional 28 days data
Phosphagenics	TPM-01/Morphine		Transdermal morphine	Phase II completed ??	
	TPM-01/Oxycodone		Transdermal oxycodone	Phase I completed	

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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