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In this edition...
A detailed understanding of the world of pain therapies and pain drug development is worth pursuing because, at first glance, this drug sector appears saturated by too many drugs. However, this is one area of drug development in which the introduction of modifications and improvements, and introduction of combination products, have made inroads into dealing with pain. And healthy revenues have flowed to a number of winners in this area of drug development. Our analysis of QRxPharma's combination drug, now called MoxDuoIR, sets out the challenges and the potential opportunity.

In the area of regenerative medicine, it appears that Big Pharma is starting to take a keen interest, and this has implications for two companies in the space, Mesoblast and Stem Cell Sciences.
Companies Covered: MSB, QRX, STC

	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%
Year 8 (May '08 - current)	-39.0%
Cumulative Gain	**26%**
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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QRxPharma and Pain Drugs – Niche Opportunities or Major Markets?

QRxPharma is developing a novel formulation of a pain therapeutic. The idea is relatively straightforward: to use a combination of morphine and oxycodone in the single tablet, which physicians are currently not allowed prescribe together. Phase II studies have delivered positive results, showing importantly that the same pain relief can be achieved with 34% - 40% less morphine when used in combination with oxycodone.

The company is currently trading at around 30% below cash assets, with $29.9 million in cash at September 30 this year, and is currently capitalised at $19 million. QRxPharma is in the midst of Phase III studies which are expected to be completed towards the end of 2009 with market launch anticipated in the US in 2011. To understand this investment potential requires an assessment of the pain therapeutic market, both in the commercially successful products that have been developed, and the dynamics that govern this sector.

Background

The core technology behind QRxPharma, which is the combination use of oxycodone and morphine, came from research conducted by Dr Maree Smith and her scientific team at the University of Queensland. The company was formed in 2002. In 2007 the company merged with **CNSCo**, a US company associated with the current Managing Director, Dr John Holaday. CNSCo acquired rights to pain technology from the University of Alabama relating to intellectual property around the torsin protein found in the brain. This protein prevents mutations of proteins found in the brain that cause neurological disorders.

Combination pain products

The focus in the pain therapeutics market is on improving the profile of existing drugs through improved delivery methods, either as a patch, gel, extended release, sub-lingual or inhaled. However the combination of pain drugs into the one table has a long history (see table). The combination of pain drugs with abuse deterrents is being explored by several groups. **Johnson & Johnson** has just received approval for Tapentadol, a combination tablet of oxycodone with the antidepressant norepinephrine reuptake inhibitor, which appears to provide a synergistic effect by combining two CNS mechanisms of action.

Morphine, which acts on the mu-type opioid receptor and oxycodone, which acts on the kappa-opioid receptor, is also thought to provide a synergistic pain relief effect, whereby less opioid can be delivered when combined to achieve an equivalent pain relief with resulting fewer side effects.

In 2006, **Pozen** signed a US$40 million up front deal with **AstraZeneca** for its Phase II combination product of an NSAID (naproxen) and a proton pump inhibitor (esomeprazole) into the single table fore the treatment of pain and inflammation. The study is progressing well with positive Phase III results released.

Cont'd over

Pain therapeutics - Combination products

Company	Combination	Date released	2007 Sales	Branded/Generic	Name
Endo Pharmaceuticals	Oxycodone + aspirin	1950	< US$11M	Branded	Percodan
Endo Pharmaceuticals	Oxycodone + acetaminophen	1976	US$122M	Branded	Percocet
Abbott Laboratories	Hydrocodone + ibuptofen	1997	n/a	Generic	Vicoprofen
Abbott Laboratories	Hydrocodone + acetaminophen	1984	n/a	Generic	Vicodin
Forest Laboratories	Oxycodone + ibuprofen	2005	US$4M	Generic	Combunox
J&J	Oxycodone + antidepressant	Approved Nov 2008	-	Branded	Tapentadol
King pharmaceuticals	Oxycodone + abuse deterrent	Expected 2010	-	Branded	Acurox
AstraZeneca/Pozen	NSAID + proton pump inhibitor	Phase III underway	-	Branded	PN 400
QRxPharma	Oxycodone + morphine	2011	-	Branded (2017+)	MoxDuoIR

The intense interest in developing topical NSAIDs explains the recent decision by **Acrux** to utilise its transdermal delivery platform and begin its own transdermal NSAID program

Acquisitions in the pain space

The most significant M&A deal in the pain therapeutics field was agreed to just last month with the US$1.6 billion acquisition of **Alpharma** by **King Pharmaceuticals**. Companies appear to be either European or US-centric in their operations. The heightened interest in this sector would suggest more M&A activity will occur over the next three years. The interest in the sector is being driven by the stunning commercial successes of new product variations over the last decade such as Duragesic, Lipoderm, Oxycontin, Lyrica, Opana ER and Kadian.

QRxPharma Clinical Trial Update

To bring the company's lead product to market, Q8003IR (recently renamed MoxDuoIR), QRxPharma will need to complete three Phase III studies. The first of these studies has been successfully completed.

Pivotal Study 1

That Phase III study involved 256 patients who had undergone bunionectomy surgery and was completed quickly in only four months. The findings showed that MoxDuoIR delivered a statistically significant improvement over placebo (not surprising) and the optimum dose of 12mg of morphine in combination with 8mg of oxycodone was determined. The study also showed that only 2% of patients experienced severe drowsiness and no patients the euphoria normally seen with morphine or oxycodone treatment.

Special Protocol Assessment

The two final pivotal studies will be conducted under a Special Protocol Assessment with the FDA. The SPA is a process whereby both the FDA and the company agree to study design terms. If the endpoints are successfully achieved, the compound should receive approval. It is a process that delays the start of the final clinical studies, however if received, delivers surety to the company over its regulatory development pathway. We anticipate the SPA will be received by mid 2009, the pivotal studies will be completed in the second half of 2009, and the drug MoxDuoIR will be file for approval in the US in the first half of 2010. Product launch should then occur in 2011 if all goes well.

Pilot Studies

In the meantime, the company will conduct two pilot studies that will deliver further information on the ideal dose for the pivotal studies and will seek to provide more evidence of the improved combination drug profile of MoxDuoIR. These studies will not be powered for significance, however, the data will help in partnering discussions for MoxDuoIR.

Partnering

Although the company is maintaining the option of bringing its product to market independently, the current global funding crisis is a factor in the company placing more emphasis on partnering/co-development discussions prior to commencing the pivotal studies. While well funded with $30 million in cash at 30 September, QRxPharma, as have most companies in the sector, reduced its burn rate. It has modified its clinical trial program, to ensure it has sufficient funding for the next two years with a partnering option being considered earlier rather than later.

Pivotal Studies – Forthcoming

Two pivotal studies are expected to begin in the second half of 2009. The first will compare MoxDuoIR against the individual components of MoxDuoIR, morphine and then against oxycodone in patients having undergone bunionectomy surgery (this has been a common patient group used by the major pain drug developers because of the large patient population and the trial facilities that are in place for this particular patient group).

The second pivotal study will look at a second patient group, in patients having undergone knee replacement surgery. It will compare MoxDuoIR against the existing standard of care, such as Percocet (oxycodone).

Controlled release (MoxDuoCR) and Intravenous (MoxDuoIV) versions

QRxPharma is also developing an extended release and an intravenous version of its oxycodone and morphine combination. The MoxDuoCR program is expected to move into Phase I studies in 2009 and the MoxDuoIV program is expected to move into Phase II studies in the first quarter of 2009.

Cont'd over

Pain Market Dynamics – Highly Reliant on In-Licensing

The pain therapeutic market is dominated by seven companies. These are **Johnson & Johnson**, **Pfizer**, **Purdue Pharma** (private), **Endo Pharmaceuticals**, **Cephalon**, **Alpharma** and **King Pharmaceuticals**. Recently Alpharma and King Pharmaceuticals have agreed on merger terms. Purdue and Endo are highly focused pain therapeutic businesses.

Licensing of technologies is very common practise in the pain area. By way of example, Endo Pharmaceuticals,which has a 700 person dedicated pain drug sales force, has built its business almost entirely from in-licensing technologies with the aim of becoming the dominant pain therapeutics player in the US. It has in-licensed Lidoderm (from **Hind Healthcare**), Opana ER (**Penwest Pharmaceuticals)**, Frova (**Vernalis Development**), Rapinyl which is a sub-lingual fentanyl tablet in Phase III studies (from Orexo), a ketoprofen patch in Phase III studies (licensed from **ProEthic Pharmaceuticals**, a sufentanil transdermal patch in Phase II trials (from **Durect Corporation**), the acquisition of **RxKinetix** in 2006 for the product En3285 for prevention of oral mucositis in patients undergoing chemotherapy, and the in-licensing of an inhaled fentanyl program from **Alexza Pharmaceuticals** which is in Phase I trials.

The point to this example is that it is an established practise for specialised pain therapeutic players to in-license technologies that can be rapidly adopted by pain treatment specialists and sold by existing sales teams if there is sufficient improvement over existing products that can be clearly shown.

There has been considerable in-licensing interest in the pain therapeutics space over the last two years, with at least seven significant licensing deals being completed (see table). All of these deals have been for improved delivery of existing pain drugs, either through extended oral release, patches, gels, inhaled delivery or abuse deterrent technologies.

The deal terms over the last year have a linear quality, dependent of the stage of development. A Phase I program was licensed for US$10 million up front, a Phase IIa program for a US$20 million up front payment, two phase III programs were licensed for US$30 million up front, and three approved products were licensed for between US$60-US$100 million. Most of the deals included royalty payments as well and most deals were for the North American region alone.

Pain therapeutic deals in 2007 - 2008

Company	Technology developer	Date	Details	Region	Terms
Alpharma	Institut Biochimique (Swiss)	August 2007	Diclofenac patch (NSAID) called Flector, **Approved**	USA	**US$100M** up front
Endo Pharmaceuticals	Novartis	May 2008	Diclofenac (NDAID) gel (Volataren). **Approved.**	N.America	**US$85M** up front + royalties. (Novartis to manufacture)
Alpharma	IDEA (Germany)	September 2007	Ketoprofen gel (NSAID) in **Phase III**	USA	**US$60M** up front + milestones + royalties
King Pharmaceuticals	Acura Pharmaceuticals	October 2007	Abuse deterrant technology. For lead product Acurox (oxycodone) in **Phase III** and platform access.	N.America + Canada	**US$30M** up front + milestones + royalty (5%-25%)
Neuromed	Alza Corporation (J&J)	April 2007	Extended release hydromorphone in **Phase III**	USA	**US$30M** up front + royalties
Alpharma	Durect	September 2008	Bupivacaine (amino amide) patch in **Phase IIa**	Worldwide	**US$20M** up front + milestones + royalties
Endo Pharmaceuticals	Alexza Pharmaceuticals	December 2007	Inhaled fentanyl in **Phase I**	N.America	**US$10M** + royalties

Risks

The near closure of capital markets for development programs has placed a greater emphasis for QRxPharma on a partnering or licensing deal before the completion of Phase III studies. In-licensing deals are very common for some of the leading companies in this sector and there should be strong interest for the novel QRxPharma pain therapy. However there is a risk that the company will not be able to secure a licensing deal and that the global economic crisis continues for a prolonged period that will challenge the company's ability to commercialise its programs.

Regulatory risks remain and the company is seeking to temper this risk through a Special Protocol Assessment with the FDA. There is also technology risk with remaining pivotal trials to be successfully completed. And there is the risk that the drug profile of MoxDuoIR will not please pain treatment specialists. However, all trials completed to date show that the combination of oxycodone with morphine allows less morphine to be delivered and resulting in an improved side effect profile, which should appeal to patients and doctors.

There is also the risk that pain specialists will prescribe generic forms of morphine and oxycodone in combination, rather than a

Cont'd on page 5

Successful Pain Drugs Over the Last Two Decades

The drug development area of novel pain therapeutics is extremely difficult. This is best highlighted by the successful new pain products released over the last 20 years. Most successful new drugs have involved modifications to existing classes of pain drugs, primarily opioids, with one exception, that being the serendipitous discovery that an epilepsy drug was effective in the treatment of neuropathic pain.

The dynamics of this industry are important when evaluating new therapeutics in development, and understanding that minor changes to existing drugs have delivered stunning commercial successes as described below. (The estimated sales listed below are based on annualised third quarter 2008 figures.)

1. Duragesic – US$2.1 billion peak sales (2004) – Fentanyl Patch

In 1995, Johnson & Johnson released its patch version of the opioid analgesic fentanyl. Fentanyl was first made in 1959 by Paul Janssen, who formed Janssen Pharmaceutica which was acquired by J&J in 1961. In 1963 Fentanyl, which is 81 times more potent than morphine, was released onto the market. J&J combined its fentanyl knowledge with is drug deliver expertise from its Alza subsidiary, to produce the fentanyl patch, Duragesic. Duragesic generated peak sales in 2004 of US$2.1 billion before it became generic.

Success in the non-neuropathic pain therapeutic space is achieved through delivering the right pharmcokinetic profile with pain treatment that suits the chronic and acute pain treatment segments of the market. Reduced side effects (including constipation and sedation), ease of use, instant, delayed or extended release drug profiling and a reduced ability for drug abuse are the key secondary parameters that govern prescribing doctors' selections after primary outcome of pain reduction. Pain specialists are quick to adopt novel variants of pain therapeutics that are released to market.

2. Lyrica – US$2.7 billion sales (2008) – Improved gabapentin version

In the neuropathic pain area, the treatment options are more limited and provide less effective pain relief. The most successful drug for neuropathic pain was originally developed as an anticonvulsant for the treatment of epilepsy, gabapentin. The drug was also found to be quite effective (30%-50% on cases) in the treatment of neuropathic pain. In 2005, Pfizer released a more potent version of this drug, called pregabalin (trade name Lyrica) for the treatment of seizures and neuropathic pain.

Gabapentin (as Neurontin) was a highly successful drug for Pfizer, first released in 1983 for the treatment of seizures, and with the market effectively doubled when it was found to be effective for the treatment of neuropathic pain. Opioid-based drugs and NSAIDs are not effective for neuropathic pain. The release of a more potent version of gabapentin in 2005 as Lyrica has been highly successful for Pfizer in evergreening its franchise with this drug. This year, Lyrica will sell in excess of US$2.7 billion, close to a 50% increase on 2007 sales. Its patent on Lyrica expires in 2018!

3. Lidoderm – US$776 million sales (2008) – Lidocaine patch

There are pockets in the pain therapeutic space that if you provide the right solution, the rewards can be extremely high. Lidocaine is an amino amide local anesthetic that was first brought to market in 1948. In 1999 Endo Pharmaceuticals released a patch version of this drug (called Lidoderm) for the local topical treatment of shingles. Most of the drug is localized with only a small amount being systemically absorbed. The product was developed under an orphan drug status. The product has been a stunning success generating sales now of around US$770 million year.

4. Kadian – US$200 million sales (2008) – Extended release morphine

Kadian is an extended release version of morphine sulphate. It is in fact an Australian success story. The drug was re-engineered at the **F.H. Faulding** facility in Adelaide which is the same site that has re-engineered the drugs licensed to **Halcygen Pharmaceuticals** (the antifungal drug SUB-Itraconazole and the antibiotic minocycline). What has made this drug successful is that it has an excellent pharmacokinetic profile that fits exactly into pain specialists concept of pain control, according to Phil Magistro, who is now VP of Commercial Operations for QRxPharma in the US. The novelty on this drug was to deliver a sustained release of morphine to patients.

Cont'd over

Highly Successful Pain Therapeutic Products

Company	Product	Date released	Peak sales	Branded/generic	Name
Endo Pharmaceuticals	Lidocaine patch	1999	US$776M (2008)*	Branded	Lidoderm
J&J	Fentanyl patch	1995	US$2.1 billion (2004)	Generic	Duragesic
Purdue pharma	Extended release oxycodone	1996	US$800M***	Generic/branded	OxyContin
Alpharma	Extended release morphine sulphat	1996	US$204M (2008)*	Branded	Kadian**
Pfizer	More potent gabapentin	2005	US$2.7 billion*	Branded	Lyrica
Endo Pharmaceuticals	Extended release oxymorphone	2006	US$199M (2008)*	Branded	Opana, Opan ER

**Annualised*

***Licensed from FH Faulding*

****Market estimates*

Succesful Pain Drugs cont'd

It was first released onto the market in 1996 and later the rights to the drug were sold to **Endo Pharmaceuticals.** From 2001 to the end of 2003, Magistro was the marketing manager for the drug at Faulding and later **Alpharma,** building it to a US$80 million a year product. The drug now generates sales of over US$200 million a year.

Initially it was released with a 24 hour extended release claim. However, the drug only really lasted for around 12 hours and was not well received. It was re-launched under Magistro as a 12 hour version and has since become a standout success. Once again success in this industry is driven by minor changes that deliver the right drug profile characteristics to the end user that are understood and accepted by patients and doctors.

5. Opana ER – US$199 million sales (2008) – Extended release oxymorphone

Opana ER is the first extended release version of oxymorphone in an oral form. It was released only two years ago only two years ago by **Endo Pharmaceuticals** and is now generating sales of US$200 million a year.

6. Oxycontin – Est. US$800 million sales (2008) – Extended release Oxycodone

An extended release version of oxycodone, called Oxycontin, was developed by **Purdue Pharma** and brought to market in 1996. (Oxycodone is a semi-synthetic opioid first developed in 1916). The drug has a combine immediate and sustained drug release profile, where 40% of the drug is released immediately, with the remaining 60% giving a sustained release effect. It's a good drug that works well and is liked by pain specialists. This year the drug is expected to generate massive sales of around $800 million.

The drug has been licensed to generics, however with the drug's patent estate being upheld, agreements with generic companies will cease and the drug will go back to being a branded proprietary product, which should see sales of around US$1.7 billion in 2009.

Oxycontin opened up the chronic pain market to oxycodone by developing the world's first sustained release version of oxycodone.

Oxycodone, morphine, oxymorphone and fentanyl are all strong opioid drugs. The market for this drug class in the US alone is estimated at around US$5 billion a year. QRxPharma's products will be competing in this market.

Cont'd from page 3

combined tablet from QRxPharma. This will limit the premium at which QRxPharma or its partner will be able to price its product (possibly 20%) to existing generic forms of oxycodone and morphine.

Patents

The core technology for QRxPharma, and the focus of this assessment, is the combinational use of morphine and oxycodone. The company's patents however are less specific, and extend to the use of oxycodone with other opioid drugs, including fentanyl, sufentanil, alfentanil, hydromorphone and oxymorphone. The core patent has been granted in Australia, Europe, New Zealand and the US, and is pending in Japan and Canada. The patents will expire from 2016, although can be extended in the US for up to five years under the Hatch-Waxman Act. Patent extensions of between two to three years are common in the US under this legislation.

A biotech A-team

QRxPharma has put together an A-team in drug development and life science commercialization. The company's chairman is Dr Peter Farrell, founder and CEO of **Resmed**. The CEO, Dr John Holaday, has founded three biotech companies, its advisory board includes former FDA chief, Dr Lester Crawford and Solomon H. Snyder who identified the opioid receptor in 1973. The company's head of drug discovery Dr Warren Stern has previously led two CNS drug NDA submissions (for Wellbutrin and Celexa) and Phil Magistro, VP of Commercial Operations, who built up the successful Kadian product was then involved with the launch of Pfizer's Lyrica.

Summary

The parallel channels through which the body regulates and experiences pain is highly complex. Hence, the successes in this field have largely been based on improved delivery or combinations of existing opioid-based medicines, or through serendipitous discoveries of existing medicines that have crossover benefits for the pain area.

Stunning commercial successes in this sector have been achieved through drug reprofiling that has found favour with prescribing pain specialists, primary care doctors and importantly with patients.

QRxPharma is commercialising a seemingly straightforward observation that a combination of two opioid drugs provides a synergistic outcome can deliver similar levels of pain relief with less morphine and a reduction in negative side effects.

Bioshares recommendation: **Speculative Buy Class A**

(QRxPharma has also been added to the Bioshares Model Portfolio)

Regenerative Medicine Moves Ahead

The election of Barack Obama to the office of President of the United States of America is expected to see a positive shift in policy regarding stem cell research and medical therapies based on cell-based technologies. Such technologies and products are likely to benefit from more funding flowing to early stage research and latter stage product development is likely to benefit from a more conducive regulatory pathway.

So it was no surprise following the US elections on November 4, 2008, that **Pfizer** announced the establishment of a global regenerative medicine unit, **Pfizer Regenerative Medicine** on November 14, 2008. Regenerative medicine is a descriptor for therapies that are based on stem cell technologies. The unit is expected to function as one of four new small independent research outfits for Pfizer, organised to replicate the innovative culture typical of biotech start-ups. Pfizer Regenerative Medicine will have operations in Cambridge, UK and Cambridge, Massachusetts and will eventually employ 70 staff. The UK team will focus on neural and sensory disorders and the US team will focus on diabetes and cardiac diseases.

However, Pfizer is not the only major pharmaceutical company to initiate a regenerative medicine capability either directly through partnerships, with **Johnson & Johnson**, **GlaxoSmithKline**, **Roche** and **Novartis**. Pharmaceutical companies, while cautious, recognize that failure to embrace emerging technologies can be costly in terms missing competitive advantages from being on the 'technology' learning curve and the 'new therapy' learning curve early in the piece. The outstanding success of a number antibody drugs has gradually changed the willingness of large pharmaceutical marketing firms to adopt and develop technologies and products that often depend on different regulatory paths, reimbursement and marketing models, interventional techniques and changes to the views and opinions of physicians and patients. The real incentive however, comes from the creation of new intellectual property and domination of knowledge domains.

The regenerative medicine area received a stimulus when **Genzyme** and **Osiris Therapeutics** revealed in early November they created a partnership to develop two mesenchymal stem cell products, Prochymal (a Phase III stage product) and Chondrogen, developed initially by Osiris. Genzyme made an up-front payment to Osiris of US$130 million. (see *Bioshares* 288)

A Recent Development…

A female patient, who had been suffering from tuberculosis induced dysphonia and cough, recently received a bio-engineered bronchial tube*. A human trachea donor scaffold was seeded with epithelial cells and mesenchymal-stem-cell derived chondrocytes. Four months after the operation, the patient has been observed to have a functional airway, no anti-donor antibodies have been detected and immune-suppressive drugs are no longer required.

Positive clinical developments such as the one just mentioned are among some of the factors that are stimulating the interest of large pharmaceutical companies in regenerative medicine.

GlaxoSmithKline

In July, GlaxoSmithKline signed a five year, US$25 million plus deal with Harvard Stem Cell Institute, to support stem cell research at Harvard University and several affiliated hospitals. The areas covered by the agreement include neuroscience, heart disease, cancer, diabetes, musculoskeletal diseases and obesity. What was interesting about the GSK announcement was the following statement: "We have carefully chose the Boston biomedical community to collaborate with on this important venture. It has the highest concentration of leading stem cell scientists and the Harvard Stem Cell Institute is the epicentre of that community."

Johnson & Johnson

Johnson & Johnson, through its venture capital unit has invested in **Tengion**, a company that is aiming to regenerate tissues and organs, using autologous uncommitted progenitor cells and tissue scaffolds. Tengion is conducting three Phase II clinical trials of its Neo-Bladder Augment in neurogenic bladder in spina bifida, neurogenic bladder following spinal cord injury and for treatment of urge incontinence.

On November 19, the company completed a Series C funding round, raising US$21 million. The completion of a funding round in the midst of a major meltdown in global finance markets is possibly a sign of just how attractive cell therapy investments are becoming.

Novartis/Roche

Novartis and Roche, through their respective venture capital arms have invested in Spanish cell therapy company, **Cellerix**. Novartis Venture Fund and Roche Venture Fund invested in a •27 million round in September 2007. Cellerix is developing a suite of products derived from expanded adipose tissues (fat cells). Its most advanced product, Ontaril FATT 1, is in a Phase III trial for patients with complex perianal fistulas with a cryptoglandular origin. Ontaril is an autologous cell product. However, Cellerix is developing allogeneic products targeting the same indications that Ontaril is directed at.

ASX Regenerative Medicine Company Briefs

Mesoblast

Developments at Mesoblast (MSB: 79 cents) were covered recently in *Bioshares* 288. However, several further items of interest emerged at the company's AGM held in late November. The company stated that to date, it had conducted over 400 large animal studies with no adverse events recorded.

The company also revealed that recruitment in the randomized Phase II congestive heart failure is proceeding very well with 17 out 20 patients recruited, in a 3 x 20 cohort trial. Interim results will be available at three monthly intervals for the 12 month trial, which should see the first data appear in around March 2009. The trial involves implantation by catheter of allogenic (single human donor) mesenchymal precursor stem cells (product name - Revascor).

Cont'd over

** The Lancet, Nov. 19, 2008*

Mesoblast also discussed its commercialisation options which includes the option of taking products to markets under its own efforts. However, such a strategy would require the highest capital commitments and the greatest execution risk. The second option is partnering of specific products. The third option is broad-based partnering of the platform technology, similar to the Genzyme-Osiris deal.

Mesoblast's view is that Osiris was about 18 months ahead when it signed up Genzyme. However, Mesoblast also believes that while there is growing interest from large pharmaceutical companies in cell therapy products and technologies, an attractive partnering deal will not occur until the technology has been sufficiently de-risked and that it works across multiple applications.

In our view, 2009 will be a pivotal year for Mesoblast, and the stock is a very attractive investment.

Mesoblast is capitalised at $94 million.

Bioshares recommendation: **Speculative Buy Class A**

Stem Cell Sciences

Stem Cell Sciences (STC: 15 cents) signed a Master Services Agreement for up to five years duration with **Pfizer**. The agreement involves Stem Cell Sciences supplying Pfizer with research services, cell lines, media and reagents.

With the recent commitment of Pfizer to regenerative medicine in the creation of Pfizer Regenerative Medicine, the agreement appears to be a crucial company saving event for Stem Cell Sciences, and should see it placed to weather the current meltdown in biotech financing.

The announcement follows several other recent announcements including a service agreement with the CHDI foundation, which supports the development of drugs to treat or delay Huntington's disease. This agreement will see Stem Cell Sciences create standard culture conditions for twenty CHRI mouse embryonic stem cell lines using Stem Cell Sciences serum-free and feeder-free ESGRO Complete media.

The research benefit will be that researchers around the world who use the CHDI mouse stem cell lines will all use the same media, which is expected to reduce variability in research results.

Stem Cell Sciences is capitalised at $5 million.

Bioshares recommendation: **Speculative Buy Class B**

Bioshares Model Portfolio (5 December 2008)

Company	Price (current)	Price added to portfolio	Date added
QRxPharma	$0.25	$0.25	*December 2008*
Hexima	$0.36	$0.60	October 2008
Atcor Medical	$0.13	$0.10	October 2008
CathRx	$0.60	$0.70	October 2008
Impedimed	$0.70	$0.70	August 2008
Antisense Therapeutics	$0.04	$0.07	August 2008
Mesoblast	$0.79	$1.25	August 2008
Cellestis	$1.83	$2.27	April 2008
IDT	$1.66	$1.90	March 2008
Circadian Technologies	$0.60	$1.03	February 2008
Patrys	$0.10	$0.50	December 2007
Bionomics	$0.21	$0.42	December 2007
Cogstate	$0.17	$0.13	November 2007
Sirtex Medical	$1.70	$3.90	October 2007
Clinuvel Pharmaceuticals	$0.21	$0.66	September 2007
Starpharma Holdings	$0.19	$0.37	August 2007
Pharmaxis	$1.12	$3.15	August 2007
Universal Biosensors	$0.58	$1.23	June 2007
Biota Holdings	$0.31	$1.55	March 2007
Probiotec	$1.41	$1.12	February 2007
Peplin Inc	$0.29	$0.83	January 2007
Arana Therapeutics	$0.80	$1.31	October 2006
Chemgenex Pharma.	$0.47	$0.38	June 2006
Cytopia	$0.18	$0.46	June 2005
Acrux	$0.47	$0.83	November 2004
Alchemia	$0.13	$0.67	May 2004

Portfolio Changes – 5 Dec 2008

IN:

QRxPharma has been added to the portfolio.

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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