ISSN 1443-850X

In this edition...
The concept of a "Commercialise in Australia First" strategy for biotech companies is beginning to take hold, with Mesoblast and Pharmaxis looking to launch products in Australia prior to entry into EU or US markets. One argument for this strategy is that an Australian launch is a means to iron out the bugs in the market strategy. And speaking of bugs, we profile Ondek, a private company founded by Nobel Prize winner Dr Barry Marshall, that is developing a drug delivery platform based on the bacteria *H. pylori*. The technology could revolutionise vaccination. We also update readers on progress at Starpharma and note a fundraising underway at Sunshine Heart.
The Editors
Companies Covered: MSB, SHC, SPL, Ondek

	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 - May '09)	-7.3%
Year 9 (May '09 - Current)	22.0%
Cumulative Gain	**137%**
Av Annual Gain (8 yrs)	**14.7%**

Bioshares is published by Blake Industry & Market Analysis Pty Ltd.

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Individual Subscriptions (48 issues/year)
$320 (Inc.GST)
Edition Number 322 (31 July 2009)
ISSN 1443-850X

Bioshares

31 July 2009
Edition 322

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

Mesoblast – An Australia First Strategy

One company that has not been hampered by the deterioration in financial markets over the last 12 months is **Mesoblast**. The company continues to accelerate its commercialisation of its adult stem cell technologies and expand the applications.

Last week the company announced it would apply for regulatory approval in Australia for the first application of the stem cells, for the treatment of non-healing long bone fractures. There are a number of sensible strategic objectives in getting the product first approved in the local market.

Too often Australian biotech companies see the first objective in commercialising their technologies as breaking into the US market, the largest healthcare market in the world. If the company has sufficient cash resources and if all goes as planned, then following this most direct path can work, but it often requires the assistance of a large partner.

By commercialising a product in Australia first, even though a small market, allows revenue to begin sooner, and product rollout to be controlled more closely. According to Mesoblast's founder, Professor Silviu Itescu, "Australian regulatory approval will enable us to formulate a template that could be duplicated in other jurisdictions on a country by country basis."

Pharmaxis has also adopted a similar strategy. Bronchitol is expected to be first approved in Australia this year for the treatment of bronchiectasis, to be followed by approval in Europe, anticipated next year, and anticipated approval in the US in 2011.

Earlier this month **CathRx**, which is commercialising a new range of cardiac catheters, announced the appointment of its fourth distributor in Europe, with 20 sales people now selling its products into 75% of the European market. Entry into the US market will be at least 12 months behind Europe, when product sales can fund the more expensive regulatory approval process in the US.

Getting the template right first in Australia has shown to be a successful strategy. **CSL** first started its toll fractionation business in Australia before acquiring large blood fractionation businesses overseas. **Sonic Healthcare** first got its pathology business consolidation template right in Australia before expanding to the UK and the US. **ASDM**, a local orthopaedic implant manufacturer built up a profitable business in Australia before it expanded into the UK two years ago. **Portland Orthopaedic** is one company that went direct to the US and failed. It is an expensive process with a challenging regulatory system and a highly competitive market.

Another advantage for Mesoblast is that commercial success in the market in Australia will help build interest from investors and partners to help fund commercialisation in larger markets.

Cont'd on page 4

Biotech Divide Continues

The divide between those biotechs that are looking likely to succeed and those that don't to continues to broaden. What the Tier-1 biotechs are doing right, or the smaller biotechs that look to have their business plans on track with commercial and financial viability, is becoming clearer each month. This divide is being accentuated by the difficult market conditions imposed by the global financial crisis which now looks to be easing.

Over the next 12-18 months we will see several of the leading biotechs in the sector bring their products to market. **Alchemia**'s generic fondaparinux should be released in the US in the first half of 2010, with profit share income we estimate at over $30 million a year with rapid market penetration. **Universal Biosensors** will start manufacturing its glucose strips for **Life Scan** towards the end of this year, bringing in around $25 million of revenue in the first 12 months. **CathRx** has released its forecast for the next two years with sales expected to reach $5.4 million in this financial year and $21.3 million in FY2011.

Pharmaxis, **Chemgenex Pharmaceuticals**, **Clinuvel Pharmaceuticals**, **QRxPharma**, **Acrux** (with its male testosterone product Axiron), **Halcgygen Pharmaceuticals**, **Biota Holdings** (with its LANI product in Japan, co-developed with **Daiichi Sankyo**) and now Mesoblast are on track to see their drug products and therapies reach the market over the next 12-24 months. There are 23 profitable companies in the sector (see Bioshares 306) with a number of other companies building sales with recently released products. These include **Acrux** (Evamist), **Labtech Systems**, **Atcor Medical**, **Nanosonics**, **Impedimed** and **Tyrian Diagnostics**, with sales traction progress worth following.

Starpharma – Getting it Right

Starpharma (SPL: $0.37) is one company which seems to getting it right, with the main focus on the microbicide application for condom coating. It's partner **SSL International**, which continues to build its dominance in the global condom market, is expected to start selling microbicide coated condoms using a microbicide developed by Starpharma.

This will be the only microbicide on the market when the product is released in the second half of 2010. Product uptake should be rapid after the initial introduction, with SSL now commanding a 40% share of the global condom market. (SSL recently purchased a major share in two market leading condom makers in Eastern Europe and Russia.) Starpharma initially expected that its deal with SSL will bring in over $100 million in revenue over the life of the deal. However, it looks likely that the product application of the microbicides for the condom market may be broader than earlier anticipated, and by our estimates significantly larger.

In May Starpharma raised $7.1 million, confirming the heightened interest in this company. The proximity to market for Starpharma has seen not only the more traditional biotech investors taking an interest in Starpharma, but more general fund interest according to the company's CEO Dr Jackie Fairley.

At the end of June, the company had $11.6 million in cash and had reduced its cash burn considerably, from $6.1 million in FY2008 to $2.9 million in the last year. The difficult market conditions has seen a deliberate reduction on expenditure, with more of a focus on late stage product applications, such as the condom coating product, and funded R&D collaborations such as those with Stiefel Laboratories (now part of GlaxoSmithKline) and Elanco (Eli Lilly).

In December, Starpharma entered into a collaboration with Stiefel to apply its chemistry platform to improve the properties of dermatology treatments. And in May it teamed up with Elanco to apply the same technology to develop improved animal health products. Incorporating the company's dendrimer chemistry scaffold has the potential to increase the half life of drugs and the way the drugs are distributed and absorbed in the body.

The DNT subsidiary business in the US has also for the first time become cash flow positive, currently generating US$500,000 positive cash flow on an annualised basis.

Regulatory Approval

It is not expected that efficacy trials will be required by regulators to have the microbicide condom product approved for sale, although there is continuing dialogue with regulators, and small safety studies will be a requirement, along with stability testing and durability testing. The raw material manufacture is contracted out to third parties. Commercialisation of the standalone Vivagel microbicide product is continuing, however the focus has been on lead product and revenue generating aspects of the business.

Summary

As we approach the end of this decade, we expect to see companies such as Starpharma generate a very real return from the investments made in product development over this period. Highly profitable businesses are emerging in the sector such as **Biota Holdings**, **Sirtex Medical**, **Arana Therapeutics** (majority owned by **Cephalon**) and **Cellestis**. The next two years should see this list expand significantly.

Bioshares recommendation: **Speculative Buy Class A**

***C*larification:**
Hexima has indicated that the development of its technology was also undertaken at La Trobe University.

In *Bioshares* 321, page 6, right hand column, the following paragraph replaces the first sentence in the second last paragraph.

"The Hexima technology was developed by researchers at the **University of Melbourne** and **La Trobe University** in Victoria**.** The founding scientists include Professor Adrienne Clarke, Professor Marilyn Anderson, and Dr Robyn Heath. The team at Latrobe University focuses on research and discovery and is managed by Hexima's Chief Scientist, Professor Anderson. The team at the University of Melbourne focuses on product development and is managed by Dr Heath."

Private Company Profile

Ondek – Developing the HPPT Platform

From time to time we come across private companies that warrant discussion in the pages of Bioshares. Such discussion may help ASX investors should the private company seek a listing on the ASX in the future.

Ondek is a Perth-based technology platform company, founded in 2005 by Dr Barry Marshal, who, along with Dr Robin Warren were awarded the Noble Prize for Medicine in 2005, for the discovery of the role *H. pylori* plays in causing gastric illness and disease, including gastric cancer. Ondek is developing genetically engineered strains of *H. pylori* for the oral delivery of vaccine antigens or other disease modulating peptides, protein or hormones.

H. pylori is a common bacteria which infects 50% of the world's population but which causes illness in 10%-20% of those with long term infection. Infection can occur from very young ages and the bacteria can reside in the gut for years without causing problems. However, the bacteria can cause stomach ulcers, particularly in subjects with a strong or 'over responsive' immune system over many years of persistent infection. It has been observed that subjects with weak immune systems (e.g. HIV positive subjects) do not get stomach ulcers, with the long term attack by the immune system being responsible for the ulcers. *H. pylori* infection can be treated successfully with antibiotics.

The Technology

Ondek has badged its technology as the Helicobacter pylori platform technology (HPPT). Genetically modified *H. pylor*i can be designed to express antigens or peptides on the surface of the bacteria. The bacteria live on the mucosa of the gut where they are visible to the immune system, which means that it can cause the immune system to produce antibodies and other cells of the immune system.

A single dose infection could deliver antigens for a vaccine or therapeutic proteins over a set period of time, until the *H. pylori* is switched off using a 'suicide gene' mechanism or survive only for a short period when in the presence of delivery nutrients included in a liquid formulation.

Safety Consideration

A possible concern about the use of genetically modified *H. pylori* as a drug delivery system is its potential to cause cancer in patients. This appears to be less a risk than at first glance. A study of gastric cancer incidence following eradication therapy [Wong, Lam and Wong (*JAMA*, 2004)] reported that no patients with precancerous lesions developed gastric cancer.

Opportunity

The HPPT has the potential to displace a number existing vaccine technologies. One feature of HPPT-derived vaccines is that they can be delivered orally in preference to needle administration, a feature especially welcome when vaccines must be administered to infants.

A potential advantage of a HPPT derived flu vaccine is that it could be manufactured more quickly in much greater quantities than vaccines traditionally made in chicken eggs. Such manufacturing features are sought after by public health authorities seeking measures to rapidly vaccinate populations at risk from influenza pandemics. The HPPT platform could also be used to construct vaccines for cholera, tetanus, diptheria, pertussis and Hepatitis B.

Trial

Ondek is planning a 36 patient trial, which involves administering five different strains of *H. pylori*. The object of the study is determine a strain that is symptom-free in 99% of human subjects. This trial would pave the way for a Phase I/IIa proof of concept trial in 2011 or 2012 with the preferred strain that has been genetically modified to deliver influenza antigen. Such a trial would require approval by the Office of the Gene Regulator, in addition to approvals by clinical trial authorities such as the TGA and hospital ethics boards. Clinical trial data may be available in three years time.

Development Issues

Eradication Management

Ondec must complete the development and validation of a gene based mechanism that turns off the bacteria's reproduction cycle at a given point in time (i.e.a suicide gene).

Delivery format, dosage data

Ondek envisages that a HPPT based flu (or other) vaccine could be delivered using a Yakult-style drink. However, is more than likely that considerable development effort and patient preference research will need to be devoted to properly understand the subtleties and limiting factors to what might appear to be simple a administration system. Another challenge likely to be set by regulatory authorities is for the company to quantify the amount of active drug in a patient, since the drug is delivered by a living organism that continues to reproduce. Benchmark studies in different patient groups may be sought by drug regulators.

Why is vaccination or drug delivery using genetically engineered H. pylori feasible?

Ten years ago, it would have been considered fanciful to develop a vaccine or therapeutic platform based on genetically engineering *H. pylori*. However, knowledge of *H. pylori* and its genome has increased considerably, aided by the steadily falling costs of gene research tools and databases. This has helped Ondek researchers to pull apart the genome and identify genes that are essential to its survival. Using what are now everyday genetic engineering techniques, Ondek researchers can place genes that code for antigens needed for vaccination to be reliably 'housed' by being placed alongside genes essential to the bacteria's survival. The *H. pylori* genome has around 1000 core genes but also another 500 that are shuffled about.

Summary

Ondek is developing a technology that could give rise to a major advance in vaccine development in terms of ease of administration, faster manufacturing times and reduced costs. Although the HPPT technology platform is unproven in human subjects it will be worth monitoring very closely.

Bioshares

Mesoblast cont'd

Expanding applications

Mesoblast's stem cells are now in trials or have completed clinical trials in five applications. These are:
– Long bone fracture repair (to be submitted for TGA approval)
– Spinal fusion (in Phase II trials in the US)
– Knee joint cartilage regeneration (in Phase II trials in Melbourne)
– Congestive heart failure trials (through sister company Angioblast) continues with very encouraging early results (Phase II trial in 20 patients in the US)
– Bone marrow transplant trials underway (through sister company **Angioblast**) to improve engraftment using the company's stem cells to expand haematopoietic stem cells and progenitor cells. First five of 20 patients showed two week improvement in engraftment time. (Phase II trial in US under orphan drug status)

Mesoblast owns 38.4% of Angioblast. Mesoblast has rights to the stem cell technology for use in orthopaedic applications, with Angioblast the rights for re-growth of cells in cardiac, vascular and eye diseases. The companies are making exceptional clinical progress, with the move to file for regulatory approval in Australia a measure of the surprising rate of progress being achieved.

Mesoblast is capitalised at $155 million with $16.5 million in cash at the end of June, or two years cash at the current spend rate.

Bioshares recommendation: **Speculative Buy Class A**

Update – Sunshine Heart

Sunshine Heart (SHC: 6.1 cents) is conducting a funding round to raise $7-$8 million. Key investors **CM Capital** and **GBS Ventures** have committed to provide approximately $5 million of the total amount being sought.

The fundraising is needed to support the completion of the US feasibility trial of its C-Pulse non-blood contacting heart assist device in heart failure patients. The funds would also be applied to the analysis of data from the trial, submission of the data to the US FDA in preparation of a US 150 patient pivotal trial and for costs associated with filing for European approval.

The current US trial has now seen two patients implanted with the device. Company provided video footage of one of these patients offers evidence of noticeable improvements to this patient's health based on breathing effort and mobility.

Sunshine Heart now has five out of six hospital sites open for recruitment and expects to complete enrollment of 20 patients by 2010 Q1 and have six month follow up completed by 2010 Q3

Sunshine Heart is capitalised at $18 million and had $2 million cash at hand as of June 30, 2009.

Bioshares recommendation: **Speculative Buy Class B**

Bioshares Model Portfolio (31 July 2009)

Company	Price (current)	Price added to portfolio	Date added
ASDM	$0.33	$0.30	December 2008
QRx Pharma	$0.55	$0.25	December 2008
Hexima	$0.60	$0.60	October 2008
Atcor Medical	$0.19	$0.10	October 2008
CathRx	$0.31	$0.70	October 2008
Impedimed	$0.60	$0.70	August 2008
Mesoblast	$1.14	$1.25	August 2008
Cellestis	$3.62	$2.27	April 2008
IDT	$1.66	$1.90	March 2008
Circadian Technologies	$0.77	$1.03	February 2008
Patrys	$0.11	$0.50	December 2007
Bionomics	$0.25	$0.42	December 2007
Cogstate	$0.29	$0.13	November 2007
Sirtex Medical	$4.50	$3.90	October 2007
Clinuvel Pharmaceuticals	$0.31	$0.66	September 2007
Starpharma Holdings	$0.37	$0.37	August 2007
Pharmaxis	$2.44	$3.15	August 2007
Universal Biosensors	$0.91	$1.23	June 2007
Biota Holdings	$1.92	$1.55	March 2007
Probiotec	$2.10	$1.12	February 2007
Peplin Inc	$0.61	$0.83	January 2007
Chemgenex Pharma.	$0.60	$0.38	June 2006
Cytopia	$0.08	$0.46	June 2005
Acrux	$1.21	$0.83	November 2004
Alchemia	$0.38	$0.67	May 2004

Portfolio Changes – 31 July 2009

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

Corporate Subscribers: Phylogica, Pharmaxis, Cytopia, Arana Therapeutics, Starpharma Holdings, Cogstate, Bionomics, ChemGenex Pharmaceuticals, Circadian Technologies, Biota Holdings, Halcygen Pharmaceuticals, Peplin, BioMD, Impedimed, QRxPharma, Patrys, Labtech Systems, Hexima, Tyrian Diagnostics, Mesoblast, Atcor Medical, CathRx

Subscription Rates (inc. GST)

48 issues per year (electronic distribution): **$320**

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