ISSN 1443-850X

In this edition...
We look at Sirtex's aggressive plans to achieve a 'step-change' in its business performance. More positive information continues to emerge for Atcor Medical and the wider adoption of its central blood pressure measurement system.
Pharmaxis delivers more positive data, with 18 month results from Bronchitol use showing a sustained effect that modifies the course of CF. Final Phase III study results are due out shortly.
We also provide an update on Progen and Mesoblast. And more coverage from this months BIO coverage, looking at the nuts-and-bolts of the Follow-on Biologics legislation to be implemented in the US.

The Editors
Companies Covered: ACG, MSB, PGL, PXS, SRX, BIO coverage

	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 - May '10)	49.2%
Year 10 (May '10 - Current)	-5.1%
Cumulative Gain	**175%**
Av Annual Gain (9 yrs)	**18.5%**

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

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

Individual Subscriptions (48 issues/year)
$350 (Inc.GST)
Edition Number 360 (21 May 2010)
ISSN 1443-850X

Bioshares

21 May 2010
Edition 360

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

Sirtex Medical Launches Aggressive Growth Plan

Sirtex Medical (SRX: $4.84) has pressed the button on an aggressive investment in growth for the continuation of its business. "We are pursuing a step-change to move all parts of our business above and beyond previous levels and performance", said CEO Gilman Wong in a release to the market last week. Having established a very profitable business that is generating a net profit of around $18 million a year and having only penetrated 1.6% of the addressable liver cancer market with its Sir-Spheres cancer treatment, it is a timely decision.

However, looking at the Sir-Spheres sales chart (see next page) over the last seven years clearly explains the rationale for this decision. From 2004 to 2009, Sirtex achieved an impressive sixfold increase in dose sales from around 500 units a year to over 3,500 units a year. Nevertheless, over the last year dose sales have slowed considerably, to only 15% growth in the first nine months of this financial year over the previous corresponding period.

A 15% growth in sales is still a reasonable result for most businesses a but it's well short of the 30%-50% annual growth that could be achievable and should be achievable over the next four years from the now well established Sir-Spheres liver cancer therapy. The tapering off in sales has largely been due to a slowing in the US market, with the US (and Asia pacific) growing at only 8%, compared to the 33% growth in Europe. The head of US operations was replaced at the end of last year, presumably due to the slowing performance in the US market.

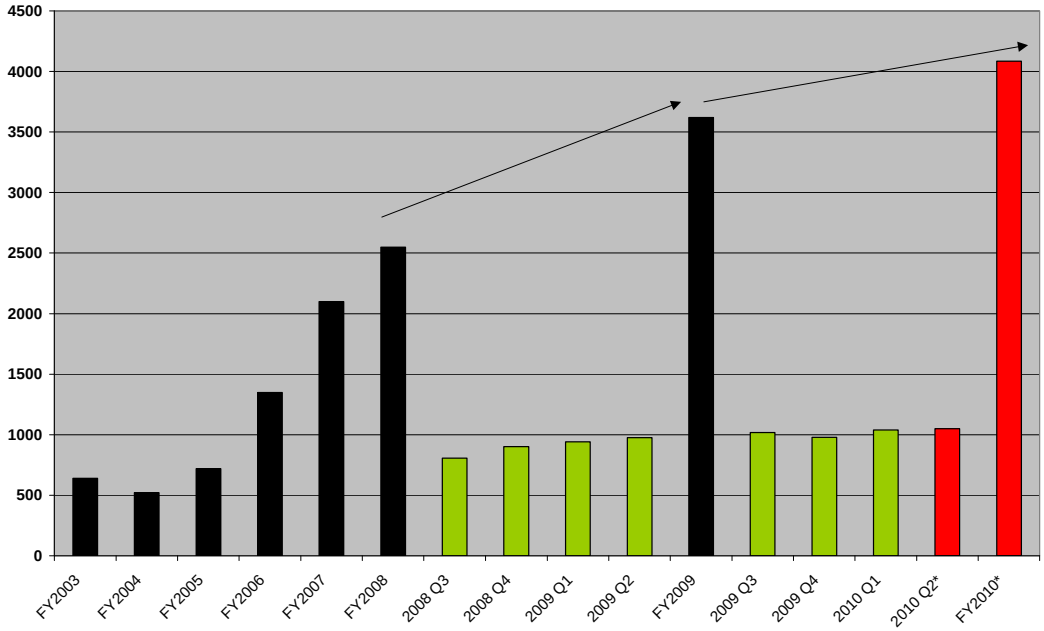
Sales Growth Dynamics

The company stated that the sales growth dynamics of the business are such that when strong growth is achieved in one year (2007 and 2009) the subsequent years tend to show more modest growth. This would suggest that FY2011 should see stronger growth in unit sales, with around 5,000 doses being our minimum target, and around 5,500 doses if things go well.

Short term growth, in financial year 2011, is expected to come from a more aggressive investment in sales and marketing in the USA, and also from expansion into other areas of Europe and the Asia Pacific region. The company currently employs 75 staff and this number should grow significantly over the next 12 months, with the company prepared to invest in aggressive expansion of the business now that a very profitable base has been established.

The company is also investing in longer-term growth through investment in ongoing clinical studies. The aim here is to expand the treatment for use further up the line rather than as currently being used as a treatment of last resort for salvage therapy. This includes treatment in combination with existing therapies for primary liver cancer. In January Sirtex announced it would combine its treatment with **Bayer**'s Nexavar in 375 patients with intermediate-to-advanced primary liver cancer.

Sirtex Dose Sales History & Forecast



** Forecast sales*

Another study, announced in March this year, will investigate Sir-Spheres in combination with the standard chemotherapy regime as a first line treatment in 490 patients with bowel cancer that has spread to the liver. Sirtex's treatment was initially approved for metastatic bowel cancer that has spread to the liver but is now also being used for primary liver cancer outside of the USA.

If these trials can show a statistically significant added benefit in combining Sir-Spheres with current treatments, then it presents an opportunity for a quantum leap in usage of the Sirtex product. (It may also be an appealing acquisition for a company such as Bayer to sell its drug in conjunction with the Sirtex product down the track). However results from these trials will take three to five years to complete.

In the first nine months of this financial year, Sirtex generated sales of $47 million and delivered an EBIT of just under $13.7 million. It had $38.7 million in cash. The deteriorating Australian currency against the US dollar delivers a considerable boost to operational profit with around two thirds of sales generated from the US.

Sirtex is capitalised at $270 million. It is currently tracking at delivering a net profit of $13.6 million (excluding abnormals), which corresponds to a tracking PE ratio of 19.9 times. Whilst there is some slowing in sales this year, with only 1.6% of the addressable market reached, Sirtex remains a high growth business. We expected strong growth to return in financial year 2011.

Bioshares recommendation: **Buy**

Bioshares

Atcor Medical – More Evidence for Central Blood Pressure Measurement

The evidence keeps mounting that physicians need to measure not just standard cuff blood pressure, but also central blood pressure, which reflects arterial stiffness and therefore the health of a person's arterial system. Earlier this month the prestigious Mayo Clinic in the US published a scientific review on non-invasive central blood pressure measurement on articles published between 1995 – 2009.

The key conclusion was that central blood pressure is a better predictor of cardiovascular outcome than cuff pressure. The author of the article, Dr Jan Stepanek, has posted a video (see Atcor's website under clinical discussion) showing two cases of using Atcor's Sphygmocor technology, which is the gold standard in central blood pressure.

Stepanek explains the importance of measuring central pressure (which can be done simply in a 5-10 minute procedure) in that central blood pressure is "truly the pressure against which the heart has to work". Stepanek also comments on the high fidelity readout of the central blood pressure that can be achieved non-invasively using the Sphygmocor device.

Perhaps one of the most important publications that has emerged was in October last year in the Journal of American College of Cardiology. This publication has quantified and set a level, 50 mmHg of central blood pressure, that if exceeded, indicates that person has a sharp increase in the chances of experiencing a cardiovascular event (such as a heart attack).

– Cont'd over

The presentation from Stepanek shows how central pressure could be used in clinical management of patients. In the first person tested in the video, his cuff pressure was 108/70 mmHg, which is not high, and his central pressure was 23 mmHg, indicating a healthy arterial system.

In the second case, the person had a slightly high cuff pressure of 135/77 mmHg, which would not normally trigger pharmaceutical treatment with anti-hypertensives. However that person had a central blood pressure measurement of 51 mmHg, which put him into the cardiovascular risk category, and pharmaceutical intervention would then be prescribed.

These types of publications continue to assist Atcor in rolling out its gold standard central blood pressure measurement system and the awareness and recognition will assist the company in gaining reimbursement and wider adoption of its technology, eventually into the primary care clinical market.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Publications/reports on central blood pressure testing in last 12 months

Date	Indication	Publication/Trial	Study size
May 2010	Review of scientific literature 1995-2009 highlights benefit of central blood pressure measurement	Mayo Clinical Proceedings	Years 1995-2009
March 2010	Significant difference in central but not cuff pressure when comparing different drug treatment regimes for hypertension	Presented at American College of Cardiology conference	232 African Americans
February 2010	Accurate effect of drugs to treat pre-eclampsia measured with central but not cuff pressure	University of Illinois Medical Center Study	-
February 2010	Central blood pressure testing more important than cuff pressure as indicator of left ventricular	Journal of Hypertension	2585 people
October 2009	Greater than 50mmHg in central pressure, sharp increase in cardiovascular event. No link to standard cuff pressure test.	JACC	2405 people

Corrections

Bioshares 357 - In the table on page 4 we indicated that Xceed Capital had a convertible note and put option arrangement. This was incorrect.

Bioshares 357 - In the article on Biota Holdings, it should have stated that the US market is the largest seasonal market for influenza drugs, at just under US$500 million, not Japan. The japanese seasonal flu market is valued at around US$240 million a year.

Pharmaxis – More Positive Data For Bronchitol

Pharmaxis released the first of two pivotal sets of data for this month, with the 18-month extension data from its first Phase III trial in people with cystic fibrosis. The good news was that benefit of treatment at 18 months was maintained, with a 7.9% overall improvement in lung function. This was up from up from 6.5% after six months, and down marginally from 8.1% at 12 months. The average person with cystic fibrosis can expect to lose 1-2% of lung function every year with current treatments.

The company is pleased because Bronchitol has shown that it can modify the course of the disease, which is quite an achievement, given the last real innovation in this disease came 14 years ago when Pulmozyme was approved.

At an RBS Morgans conference held earlier this month, CEO Alan Robertson discussed the huge treatment burden that people living CF have. This can include 20 minutes of Pulmozyme treatment on a nebuliser, taking 50 tablets a day, and antibiotics twice daily for 20 minutes each time also on a nebuliser. Bronchitol by comparison is portable and can be taken in a couple of minutes in the morning and at night.

Robertson said the addressable market in Europe is worth $390 million, with Bronchitol expected to sell for around the same price as Pulmozyme, $13,000 per year of treatment per patient. Pharmaxis will get a 12 year market exclusivity for its drug in Europe if approved. It could cover the five key countries with only 25 sales representatives. An answer from European regulators is expected around October this year.

The company is anticipating filing its drug for approval in the US by October this year, pending positive results from the second Phase III trial which are due to be released this month. The FDA is looking for reductions in exacerbations (around 20% we believe is what's needed). If all goes well, the approval in the US could be received by September/October 2011.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

BIO 2010 Session Report

Follow-on Biologics Legislation: The Impact on Your Patent Portfolio

This session was chaired by Sanya Sukduang, a Partner with **Finnegan, Henderson, Farabow, Garrett & Dunner, LLP**. Presenters included Bruce Leicher, Senior Vice President and General Counsel at **Momenta Pharmaceuticals** and Brian Barrett, Senior Director and Assistant General Patent Counsel at **Eli Lilly**.

Sanya Sukduang commenced proceedings by presenting an overview of the Biologics Price Competition and Innovation Act of 2009 (BPCIA) which was passed on March 23 as part of the Patient Protection and Affordable Care Act.

One quite basic thing the legislation changed was the definition of a biological product, to which the word "protein" was added.

Sukduang said that as proteins are large molecules that have proven difficult to characterise, the BPCIA was unable to adopt the concept of equivalence as used in generic drug development.

Two Standards

The legislation sets forth a bio-similar standard and an interchangeability standard (IS). To be a bio-similar, the biologic has to be highly similar to the reference product. No clinical meaningful difference should exist between the reference product and the Follow-On Biologic (FOB).

IS a higher standard, where the biologic is expected to be a bio-similar but also must achieve the same clinical result, plus there should be minimal risk when switching from the reference product to the FOB.

Clinical studies are intended, but the FDA has the discretion to waive them. The FDA can issue guidance, and the public has the right to comment. However, the FDA can also forego guidance.

The Exclusivity Period (BPCIA)

An FOB cannot be approved until 12 years after the initial approval of the reference product, with a further six months applying for pediatric exclusivity. This term is independent of patents covering the biologics.

However, follow-on biologics developers do not need to wait 12 years before initiating their program. This can begin four years into the 12 year term.

What incentives are there for FOB developers to file early, asked Sukduang? The legislation allows for the first FOB that aims for the interchangeability standard to get one year of exclusivity.

Patent Information Exchange

The PBCIA creates a patent information exchange, which is a complicated system. Within first 20 days of an FOB filing being accepted by the FDA, the FOB sponsor must provide the reference biologic sponsor a copy of their application and essential manufacturing information.

Within next 60 days, the reference product (RP) sponsor must supply a list of patents that cover the reference biologic, including third party patents that they may need to license. The duty to provide patent information is ongoing throughout the process.

If the reference product sponsor fails to provide such information they may be precluded from asserting those patents in future disputes.

Within the next 60 days after the FOB sponsor receives the patents list from the RP sponsor, the FOB applicant has to provide an opinion as to why they don't infringe those patents, or are invalid and unenforceable.

The FOB sponsor can also inform the RP sponsor that they don't intend to launch a FOB until the expiration of the last patent of the RP sponsor.

Within 60 days after that, the RP sponsor has to provide a detailed statement as to why the FOB biologic infringes.

After all this exchange of information, a law suit is still not permitted. The two parties have a duty to negotiate and try to come up with a list of patents that would be part of any dispute.

Assuming both parties don't agree, the RP sponsor can assert one patent in a law suit.

Unlike the Hatch-Waxman rules for generics which allow for a 30 month stay by the FDA before the generic can be approved, there is no such rule for biologics under the BPCIA, which is designed to see that any litigation can be completed within the 12 year period.

The timing of any lawsuit is important. Once the RP sponsor and the FOB sponsor have completed negotiations, the RP sponsor has 30 days to sue. If they do not sue in a timely manner, they forego their right to obtain an injunction in the event they win. All they could retain is a reasonable royalty.

If the RP sponsor sues within the 30 days but the suit is dismissed without prejudice, then again the RP sponsor can only obtain a reasonable royalty.

Sukduang said that he believed this system of dismissal without prejudice provides an incentive to litigate on the issue of jurisdiction. Especially if you are a follow-on applicant, perhaps you might be willing to pay a reasonable royalty to get once the 12 year period is up, rather than face the possibility of being completely stopped.

Bruce Leicher – Momenta Pharmaceuticals

Leicher posed the question: "Are we reducing the value of patentable inventions? It may be that the entities that finance small biotech will be more interested in financing moderate risk projects."

Leicher said that Momenta is focused on developing analytical technologies to characterise proteins to 'unlock the black box'.

– Cont'd over

– Follow-on Biologics cont'd

Today companies have not yet developed analytical technologies to address those differences between branded products and bio-similars. This is why the new legislation has provision for clinical trials.

Patent Strategy Implications

Although Liecher expects there will be continuous life cycle management, around formulation and manufacturing, characterisation methods IP will be important, but that could benefit branded drugs as well as FOBs.

Will characterisation IP that gets developed raise the bar for getting FOBs approved that don't have the same characterisation data was another question proffered by Leicher.

And finally Leicher suggested that because it is possible that to have IP around those structure-function relationships that will lead to knowing you have the same product, you might also be able to develop exclusivity as a follow-on and keep other bio-similars away

Brian Barrett – Eli Lilly

Barrett said he was "not jumping in the air" about the new legislation. "There are some good things about it, some not so good things, but also a lot of uncertainty. Expect a lot of litigation."

Barrett said that he spends much of his time thinking about Hatch-Waxman legislation that introduced the generic drug industry. Lilly lost $50 billion when Prozac went off patent. "There are no shortage of people waiting to challenge our patented drugs" he said. But what interests Barrett is how the new bio-similars legislation will be different.

The Hatch-Waxman act that supported the development of small molecules generics allowed companies to exist without discovering anything, which will be the same with the BPCIA. Hatch-Waxman has meant companies avoided massive spending on R&D, but with the BPCAI how much spending will be required.

Generics could be approved solely on bio-equivalence, but that won't be the case for a long time for biologics.

Generic drug costs are driven by manufacturing and not branding, promotional or physician education costs which are additional costs for branded drug makers. As an aside, Barrett said that he expected some of these costs will be soon be borne by bio-similar producers.

Barrett said that with the new legislation what they wanted were predictable exclusivity periods, so that Lilly could maximise its investments.

"When you are in Hatch-Waxman law suit and you are trying to put some percentage on whether you are going to win that law suit, are you going to invest hundreds of millions of dollars in a three year clinical trial or are you going to wait? You want some certainty."

"I think the BPCIA is a step in the right direction. We have a twelve year data protection period that provides some prospect that innovators can recover their R&D investment. There is also a pediatric data extension on the 12 years. However, we were looking for longer than 12 years. Hatch Waxman set the clock at 14 years, when you add extensions."

Barrett noted that there will be no data protection for new routes of administration and other types of improvements. It appears that argument is that with the 12 years of data protection, a sponsor should maximise all indications, all routes of administration from the beginning. The problem is, he said, that the research process uncovers new indications over time, so what would be the incentive to bring them to market?

Barrett did not think the new legislation would increase competition. With more development risk involved, biosimilar sponsors will seek greater rewards.

Barrett identified a range of uncertainties that he perceived exists with new legislation:

When does a product have no clinically meaningful differences in safety and potency?

How often will the FDA use the guidance process?

How often will the FDA waive the discretionary study requirements which many believe will be important for establishing safety?

Will the cost to receive the interchangability designation be worthwhile, when all that is gained with a one year advantage?

Are the anti-evergreening aspects so extreme that they might discourage innovation?

Given that biosimilars will be reviewed by the same division of the FDA that reviews innovators biologics, how will confidentiality be assured for innovators?

Will innovators rely more on using trade secrets going foward? If you have the one assay and an FOB sponsor finds out about it, then can you trust the regulator?

What role will third party patents play, and there are many out there, including process patents?

How much marketing and education will be required?

In summary, Barrett said the legislation provides an opportunity maxmise innovation, ensures patient safety and over time saves payors and patients money. However he also said it was a compromise legislation that was not perfect.

Bioshares Model Portfolio (21 May 2010)

Company	Price (current)	Price added to portfolio	Date added
Biota Holdings	$1.09	$1.09	May 2010
Tissue Therapies	$0.18	$0.21	January 2010
Biodiem	$0.12	$0.15	October 2009
QRxPharma	$1.16	$0.25	December 2008
Hexima	$0.29	$0.60	October 2008
Atcor Medical	$0.13	$0.10	October 2008
CathRx	$0.16	$0.70	October 2008
Impedimed	$0.60	$0.70	August 2008
Mesoblast	$2.04	$1.25	August 2008
Circadian Technologies	$0.63	$1.03	February 2008
Patrys	$0.09	$0.50	December 2007
Bionomics	$0.28	$0.42	December 2007
Cogstate	$0.26	$0.13	November 2007
Sirtex Medical	$4.84	$3.90	October 2007
Clinuvel Pharmaceuticals	$0.25	$0.66	September 2007
Starpharma Holdings	$0.53	$0.37	August 2007
Pharmaxis	$3.03	$3.15	August 2007
Universal Biosensors	$1.36	$1.23	June 2007
Probiotec	$1.34	$1.12	February 2007
Acrux	$1.88	$0.83	November 2004
Alchemia	$0.55	$0.67	May 2004

Portfolio Changes – 14 May 2010

IN:

Biota Holdings has fallen to very attractive levels, and is now capitalised at $195 million. It has been added to the portfolio at Friday's close of $1.09.

OUT:

No changes.

Mesoblast Update

Mesoblast ($2.04) this week received the go ahead to start a Phase II trial in the US and Australia in 36 patients for a procedure involving cervical fusion of the spine. Two doses of the company's Neofuse allogeneic stem cells will be compared against the standard of care.

The opportunity for Mesoblast is to show that its product is safer than an existing product on the market, Infuse from **Medtronic**. This product has led to a blockage of the airway from inflammation which can have a fatal affect. If Mesoblast's therapy can be shown to be safe and effective then it opens the door to an almost billion dollar spinal fusion product market.

No Share Purchase Plan?

Last week the company announced it had raised $37 million together with an agreement to merge with its investee company Angioblast Systems. Some shareholders are not pleased that the discounted offering was made only to institutional investors and not smaller retail shareholders. This is a valid point, with smaller shareholders who often provide the day-to-day liquidity for the company's shares on market and many having been loyal supporters of the stock.

In our opinion, companies should include smaller shareholders in capital raisings through share purchase plans. This has often been the case with capital raisings in this sector.

Bioshares recommendation: **Speculative Hold Class A**

Bioshares

Progen Pharmaceuticals Update

Progen (PGL: $0.415) is making progress in clearing up many of its issues of its past. The company has recently appointed an experienced biotech manager Sue Macleman as CEO. In April the company terminated its license agreement for PI-88, now called muparfostat, to **Global TransBiotech**. This week the company announced it was granted a manufacturing and use patent for Muparfostat in Europe.

It's unclear why the drug candidate was outlicensed in the first place but the company believes the compound may still have potential as a cancer therapeutic, re-analysing results from previous Phase II trials. At the end of last month Progen signaled it may license the compound to **Medigen Biotech Corporation**, which owns 8.48% of Progen.

Bioshares recommendation: **Not formally covered**

Bioshares

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: Pharmaxis, Starpharma Holdings, Cogstate, Bionomics, ChemGenex Pharmaceuticals, Circadian Technologies, Biota Holdings, Halcygen Pharmaceuticals, Impedimed, QRxPharma, Patrys, LBT Innovations, Hexima, Tyrian Diagnostics, Mesoblast, Atcor Medical, CathRx, BioMd, Tissue Therapies, Viralytics

Subscription Rates (inc. GST)

48 issues per year (electronic distribution): **$350**

For multiple email distributions within the same business cost centre, our pricing structure is as follows:	$550	2-3 email addresses
	$750	4-5 email addresses
	$950	6-10 email addresses

To subscribe, post/fax this subscription form to:

Bioshares
PO Box 193 Richmond VIC 3121
Fax: +61 3 9671 3633

I enclose a cheque for **$** made payable to **Blake Industry & Market Analysis Pty Ltd**, or

Please charge my credit card **$** MasterCard ☐ Visa ☐

Card Number ☐☐☐☐ ☐☐☐☐ ☐☐☐☐ ☐☐☐☐

Signature _____ Expiry date _____

Subscriber details

Name _____

Organisation _____

Ph ( ) _____

Emails _____

_____

_____