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In this edition...
Infection control is major challenge for hospitals and medical practices. Nanosonics is set to roll out its lead product, a device to disinfect ultrasound probes. Its technology is non-toxic and can treat instruments that can't be disinfected by high temperature autoclave systems.
Pharmaxis is making steady progress with Bronchitol, with enrollment for one Phase III trial completed and another underway. The cystic fibrosis indication is now clearly established as primary market for Bronchitol.

We also provide a further update on the Progen/Avexa merger.

The Editors
Companies Covered: AVX, NAN, PGL, PXS

	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)	-35%
Cumulative Gain	**35%**
Av Annual Gain (7 yrs)	**17.8%**

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Bioshares

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

All Clear For Nanosonics Market Launch

Nanosonics has been given the green light from the TGA to start selling its ultrasound probe disinfection system in Australia. The devices are expected to be released at the end of this month into the Australian and New Zealand markets. There have been a number of delays with the release of this product. However, the company has been extremely cautious in making sure the product was right for commercial release.

The company also has a sensible rollout strategy. The device is approved for sale into Europe and Canada. However, it will resolve any device or customer issues closer to home before it launches into the larger and further a field markets.

Nanosonics' invention is a nebulized solution of hydrogen peroxide that disinfects medical probes in a closed container (The Trophon EPR). This technology platform, termed NanoNebulant, allows secure disinfection that produces innocuous byproducts of water and oxygen. It is a clean and neat system that should find favour within the hospital system.

Problems with existing systems

Existing disinfection systems include low temperature liquids, with the most common being glutaraldehyde. However glutaraldehyde is toxic and carcinogenic. Its use is restricted to within fume cupboards and countries such as the UK are seeking to ban its use. High temperature autoclaving is suitable for non-plastic devices, which excludes most ultrasound devices, and takes between 20-60 minutes to disinfect. Gas sterilization uses ethylene oxide or hydrogen peroxide plasma, however both systems also have their shortfalls. Ethylene oxide can take up to 24 hours and can leave residue, and hydrogen peroxide plasma requires more elaborate equipment which has a higher initial and ongoing cost.

The Nanosonics system

Nanosonics' Trophon EPR ultrasound probe disinfection system will cost around $10,000 for the system, and ongoing costs, hydrogen peroxide cartridges for the system, will cost over $2 each. Aside from the clean nature of this system, the other major benefit is the disinfection will take only 4-6 minutes. Its also causes no damage to the probe.

Distribution

One risk with this company is the distribution pathway. Nanosonics has elected to sell its products through third party distributors. The risk here is that there is limited control on how actively their products can be marketed to the end users (hospitals, pathologists and clinics).

In October last year the company announced the appointment of seven distributors, five in Europe and one in Australia and one in New Zealand. The company is mindful that the first year will be a learning period for both company and distributors. The distributorship agreements all include the achievement of key milestones, which if are not met, the

agreements can be terminated. Invariably, the use of distributors becomes a trial and error process. Whilst there are less running costs in using distributors, there is also less input in to how aggressively the product can be sold.

Working in Nanosonics' favour is the incentives it can offer distributors. Not only is there a percentage of the capital equipment cost (list price around $10,000) going to the distributor, the distributor will also receive a reasonable portion of the tracking consumable cost of the hydrogen peroxide cartridge (list price of over $2 per disinfection procedure), which will give the distributor a reason to stay in touch with the customer.

The Trophon EPR unit may also be purchased by OEMs who produce the ultrasound units, and package it all together. There is an incentive to the OEM groups to ensure their products are well maintained with proper cleaning procedures to reduce product returns.

Business model

The combination of an affordable, low end capital cost for the disinfection Trophon EPR unit in combination of tracking sales from the patented, hydrogen peroxide cartridges has been well structured and should provide more consistent and a higher quality earnings stream for the company. The company has a strong IP position with patents going out past 2020.

Manufacturing

The company manufacturers the product at its headquarters in Sydney. By July the company will be making 300 units a month. It has the capacity to make 4,000 units a year on a double shift and could increase this manufacturing output by outsourcing.

Product rollout

Nanosonics has been very diligent in ensuring the first commercial product would be well received by customers. There have been numerous product development iterations, making minor improvements such as reducing the size marginally, improving the ergonomics of the device, reducing the noise levels to that of a personal computer and reducing the cycle time to within six minutes. The Nanosonics management has been acutely conscious of getting the product rollout right.

The first product, Trophon EPR for the disinfection of ultrasound probes (both external use and internal) will be released in Australia and New Zealand at the end of February, then into Europe in April and Canada in May. The company already has forward orders for the Trophon EPR system.

Subsequent products

The company is also working on disinfection units for various endoscopes which the may come onto the market later in 2009. Nanosonics estimates that the annual market size (in 2005) for ultrasound probe disinfection is in excess of $600 million and in excess of $650 million for endoscope disinfection.

Summary

Infection issues in hospitals are a major concern at present with new regulations forcing the adoption of better disinfection processes. Nanosonics offers a clean, safe and affordable system for the disinfection of ultrasound probes and this application is expected to be extended into the disinfection of endoscopes. Existing systems are either toxic, time consuming, require significant capital costs or all of the above.

The company has developed a smart business model where tracking consumable sales from the patented cartridges will generate a high quality of earnings. The one weakness is that the company is reliant on third party distribution relationships to sell its product, although strong incentives have been structured into these agreements which should provide sufficient incentive to sell the Nansonics products.

The much awaited market release of the company's first product launch will occur in the next two weeks. The company is well funded with $19 million in cash. This will be a stock well worth monitoring closely.

NAN: 29 cents

Cash position (31/12/08)	$19 million
Market capitalization	$56 million
Bioshares recommendation	Speculative Buy Class A

Bioshares

Bioshares Thredbo Biotech Summit Dates
28 – 29 August, 2009

Registration for this year's conference will open in March

Pharmaxis Targets CF as Lead Indication for Bronchitol

Commercialisation activities at Pharmaxis continue to progress well with the path to market for the company's key asset, Bronchitol, becoming progressively clearer. Bronchitol has potential applications in many respiratory diseases however the principle, immediate driver for the company appears to be in the cystic fibrosis market.

The issue for Pharmaxis when trying to sell Bronchitol into two different markets, such as for the treatment of cystic fibrosis and bronchiectasis (a broader degenerative lung condition), is what the company refers to as 'pricing pressure'. Bronchiectasis is a far larger market in terms of patient numbers but is likely to command a lower price than what can be achieved for the treatment of cystic fibrosis.

It looks like Pharmaxis will concentrate on the cystic fibrosis market first in the major markets, with there already being an established market for mucous clearance in CF patients, valued in excess of US$400 million a year (for Pulmozyme, marketed by Genentech).

The first Phase III cystic fibrosis trial in 325 patients has completed enrolment with results expected in March/April of this year. The primary endpoint will be improvement in lung function (FEV1) and if the results are positive, Pharmaxis anticipates filing for approval in Europe in the third quarter of 2009, with the longer 12 month safety data to be submitted once available. This is expected to be the largest cystic fibrosis trial result to be reported in the world for this year.

Although the commercial return from the company's first product, Aridol (lung function test) may be very low at this stage (sales of $206,000 in the fourth quarter of 2008), the experience gained in negotiating through the complex European regulatory pathway will be incredibly valuable. And some of the distributors in place for Aridol may also be suitable for selling Bronchitol into Europe once that drug receives approval, which we estimate to be at the earliest the second half of 2010.

Pharmaxis has become clearer on pricing, anticipating that Bronchitol will be priced similar to Pulmozyme in Europe, which is US$13,000 for a year's treatment.

To gain approval for cystic fibrosis in the US, Pharmaxis will need to complete a second trial in around 300 patients. That trial has already started with around 40 patients enrolled so far. Early data from this trial is expected in 2010.

The company's new manufacturing facility is expected to be operational by year's end, including receipt of the necessary regulatory certificates. The capacity of that facility is over 30 million doses, or enough to treat 41,000 patients. At US$13,000 for a year's treatment, this equates to a production output value of US$533 million.

Bronchiectasis

In Australia, the company has filed Bronchitol with the TGA for approval with a verdict expected in the second half of this year. The first Phase III trial, data on which the Australian submission is based, was completed last year. The second Phase III trial has been designed in consultation with the US and European regulators. However the initiation of this trial has been pushed back to allow resources to focus on the cystic fibrosis trial.

Funding

At the end of last year, Pharmaxis had $94 million in cash. At the end of this year, the company should have around $60 million in funds, at which stage the product should be ready for launch in Australia and a European regulatory submission underway. For launch into the US, if the company is continuing to market Bronchitol directly, it will need to either raise further funding or consider a co-marketing arrangement, unless product acceptance in Europe beginning 2010 is rapid. In Europe, it is expected Bronchitol will be sold via distributors. We anticipate Bronchitol will reach the US market in 2011.

Summary

The path to market for Pharmaxis' Bronchitol has become clearer in the last twelve months. How Pharmaxis will fund the commercial rollout into the US market remains to be seen, although will depend on the state of financial markets in two years time and the success that Bronchitol (and Aridol) can garner in Australia and Europe. Pharmaxis remains in a strong position to become Australia's first home grown specialty pharmaceutical business.

PXS: $1.285

Cash position (31/12/08)	$94 million
Market capitalization	$250 million
Bioshares recommendation	Speculative Buy Class A

Bioshares

Why Progen Shareholders Should Vote Against the Progen-Avexa Merger

On December 22, 2008, the board of **Progen Pharmaceuticals** announced that it would proceed, subject to shareholder approval, with a merger with **Avexa**, developer of the HIV drug candidate, apricitabine (ATC). ATC is a nucleoside reverse transcriptase inhibitor (NRTI). The merger would, if agreed by shareholders, be effected through a court approved scheme of arrangement

Since the announcement of the merger, Melbourne-based cancer drug developer **Cytopia** has, along with a significant number of other Progen shareholders, requisitioned a shareholders meeting.

The Cytopia-led group of shareholders, constituting more than 18% of shareholders, is seeking to offer a full $1.10 buy-back to shareholders (not capped, but subject to available net cash reserves), removal of the current board and replacement with three directors not associated with Cytopia. The Cytopia group has also asked for its meeting to be held at the same time as the meeting called to vote on the proposed merger of Progen with Avexa. The scheduled date of this meeting is March 11, 2009.

While the merger with Avexa may appear as a positive opportunity for Avexa shareholders, it is negative on several counts for Progen shareholders. Progen shareholders do not get the opportunity to be offered a full $1.10 buy back, with the existing Progen board offering a $1.10 per share capped at $20 million.

A most perplexing issue for Progen shareholders are the capital requirements of the entity that results from a merger with Avexa. Merger documents indicate that the merged entity would require $110 million to complete the current Phase III ATC study beyond the week 24 primary endpoint (expected mid-2010), complete extension studies following regulatory approval, conduct a second Phase III study and market launch preparations.

At issue are the economic merits of ATC. This compound was assessed by Lonergan Edwards as being worth between $151.4 million to $225.8 million. This valuation can be compared to a licensing transaction that was announced on February 6 in which **GlaxoSmithKline** licensed a non-nucleoside reverse transcriptase inhibitor (NNRTI) IDX899 from **Idenix Pharmaceuticals** for a total deal value worth up to US$450 million. This deal figure excludes the royalty stream that would flow to Idenix if IDX899 reached the market.

IDX899 completed a Phase II study in 2008, achieving mean viral load reduction of 1.8 $\log^{10}$ [32 patients]. Avexa achieved a mean viral load reduction of 0.8 $\log^{10}$ in a Phase II trial [47 patients].

IDX899 is designed to be orally administered *once a day*. ATC is also an orally delivered compound, but taken *twice a day*. This is a significant but arguably unfavourable point of difference for ATC in that a competitor compound has emerged with a potentially superior drug profile. It is one of a number of factors that explain, in our opinion, the niche potential for ATC. Other factors include the emergence of newer classes of drugs, including integrase inhibitors and CCR antagonists.

Progen shareholders can rightly ask if there can be any substantial net economic gains by further investing in a compound that will take another $110 million to get to market and which does not appear to have taken as yet the interest of potential licensing partners. This is an issue about which there should be a properly informed debate.

A further issue for Progen shareholders is that of confidence in the existing Progen board. The Progen board has presided over the termination of a Phase III trial of PI-88, yet in our opinion has offered less than satisfactory reasons for the cessation of the development of PI-88.

We posed the following questions to the Progen board *in Bioshares* 293:

1. How many licensing proposals were rejected by the Progen board for PI-88 and what was the value and terms of those offers?
2. Why was recruitment in the Phase III trial so difficult to achieve, given that a global contract research company was employed and that liver cancer is a disease that has a high prevalence?
3. Was the Phase III trial protocol changed in such a way that recruitment was hampered?
4. Was negative side effect data from the Phase II prostate cancer trial, released in February, a major contributing reason for the cessation of the Phase III trial?
5. Were any senior executives of the firm found to responsible for the failure to progress the Phase III trial?

It is reasonable for shareholders to expect fair and honest disclosure by boards of directors on matters of a material nature.

We maintain an **Avoid** recommendation on both stocks (Progen Pharmaceuticals and Avexa) in the context of proposed merger.

Bioshares

Sector Restructuring – A Progress Report

As the global financial crisis unfolds and problems are identified and economic solution proposed and adopted, a capital drought envelopes the global biotech sector. The prospects of equity markets being closed for three years is not out of the question for early stage development companies. We expect the September quarter of 2009 to be a period when investors will be able to more clearly understand the extent of losses and write downs incurred by banks and large multi-nationals, and whether economic rescue plans are beginning to grip. It is possible that the December quarter is when investors will be able to better gauge any change in sentiment towards biotech companies without cash flow.

We estimate there are 45 biotechs from a pool of approximately 95 cash burning biotechs that have less than one year's cash to support operations. Two companies **Portland Orthopaedics** and **Apollo Life Sciences** entered administration in 2008. As many as twenty biotechs are on the verge of collapse and could be insolvent. The absence of M&A activity is puzzling, but could be explained by the proposition that some companies have worthless assets. What is the catalyst for change for these companies and by change, we mean the internal and external recognition that a company's days are over?

Some companies have initiated re-structurings (see table), but interestingly, they are not necessarily companies facing an imminent threat.

Recent Restructuring Announcements

Company	Date	Actions	Latest cash ($M) est.
Alchemia	28/10/08	Staff reduced from 50 to 20; suspended various projects	$11.1
Benitec	20/11/08	Terminated several staff positions	$1.5
Incitive	23/12/08	Cutting back on R&D programs; Adj. executive agreements	$0.1
Optiscan	23/01/09	Staff reduced from 34 to 23	$2.0
Tyrian Diagnostics	30/01/09	Headcount down from 42 (30/6/08) to 25; re-focusing on diagnostics	$6.6
Novogen	13/02/09	Staff reduced from 62 to 51; focus to be on oncology	$44.0

Bioshares Model Portfolio (13 February 2009)

Company	Price (current)	Price added to portfolio	Date added
ASDM	$0.35	$0.30	December 2008
QRxPharma	$0.25	$0.25	December 2008
Hexima	$0.30	$0.60	October 2008
Atcor Medical	$0.17	$0.10	October 2008
CathRx	$0.54	$0.70	October 2008
Impedimed	$0.72	$0.70	August 2008
Mesoblast	$0.78	$1.25	August 2008
Cellestis	$2.00	$2.27	April 2008
IDT	$1.58	$1.90	March 2008
Circadian Technologies	$0.68	$1.03	February 2008
Patrys	$0.05	$0.50	December 2007
Bionomics	$0.21	$0.42	December 2007
Cogstate	$0.22	$0.13	November 2007
Sirtex Medical	$2.55	$3.90	October 2007
Clinuvel Pharmaceuticals	$0.22	$0.66	September 2007
Starpharma Holdings	$0.20	$0.37	August 2007
Pharmaxis	$1.29	$3.15	August 2007
Universal Biosensors	$0.55	$1.23	June 2007
Biota Holdings	$0.47	$1.55	March 2007
Probiotec	$1.32	$1.12	February 2007
Peplin Inc	$0.60	$0.83	January 2007
Arana Therapeutics	$0.82	$1.31	October 2006
Chemgenex Pharma.	$0.34	$0.38	June 2006
Cytopia	$0.10	$0.46	June 2005
Acrux	$0.45	$0.83	November 2004
Alchemia	$0.14	$0.67	May 2004

Portfolio Changes – 13 Feb 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: Pharmaxis, Cytopia, Arana Therapeutics, Starpharma Holdings, Cogstate, Xceed Biotechnology, Optiscan Imaging, Bionomics, ChemGenex Pharmaceuticals, Circadian Technologies, Biota Holdings, Stem Cell Sciences, Halcygen Pharmaceuticals, Peplin, BioMD, Impedimed, QRxPharma, Patrys, Labtech Systems, Hexima, Tyrian Diagnostics, Mesoblast, Atcor Medical

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