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In this edition...
Whilst 2009 was a very strong year for the leading biotech stocks in the sector, it will be well worth monitoring some of the smaller biotechs this year as they approach major commercial inflexion points in 2010. Four of these companies are updated in this edition – Genera Biosystems, Tissue Therapies, CathRx and Antisense Therapeutics.

Pharmaxis has evened up the score with Canadian biotech after the Cytopia acquisition by YM Biosciences. In what could be argued as overdue, Pharmaxis has decided to use the value of its strong scrip to acquire Canadian-based Topigen pharmaceuticals and fill some of its pipeline gap. The funding crisis remains for many smaller biotechs which creates opportunities for better placed companies.

The Editors
Companies Covered: ANP, CXD, GBI, OIL, PXS, TIS

	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)	78.9%
Cumulative Gain	**247%**
Av Annual Gain (9 yrs)	**21.8%**

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Bioshares

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

Pharmaxis Capitalises on Strong Scrip & Small Cap Biotech Financial Stress

Topigen Acquisition

For small and private biotech companies, the global funding crisis remains a very large obstacle. For larger biotech and pharmaceutical companies, it represents an opportunity to acquire assets at severely discounted prices. Earlier this month Pharmaxis (PXS: $2.73) announced it would acquire private Canadian biotech **Topigen Pharmaceuticals**. Up to September 2007, Topigen had raised C$75 million. Pharmaxis will acquire Topigen for an initial payment of $8 million (in shares) with a further $14 million (also in shares) based on achievement of set milestones.

Current financial market conditions had made it difficult for Topigen to continue funding its programs, presumably with venture capital funding becoming more scarce, and with an IPO not a realistic pathway given the company's depth and continued caution in public equity markets. The acquisition was primarily to gain access to Topigen's lead asthma drug program with TPI ASM8, which Pharmaxis had been following for two years.

Topigen TPI ASM8 program

There are around three million people in the world with severe allergic asthma for which the corticosteroids do not sufficiently treat the condition. Only about half of that population can be treated adequately with the **Novartis** drug, Xolair. However, this drug, an antibody, requires an injection by a doctor every two to four weeks and causes severe allergic reactions in some people. In 2008, Xolair generated sales of US$720 million. The Topigen drug candidtate, TPI ASM8, in contrast,would be inhaled once a day.

TPI ASM8 is a combination of two oligonucleotides that seeks to inhibit two receptors on two overlapping inflammation-related pathways (CCR3 receptor and the beta-subunit of the IL-3, IL-5 and GM-CSL cytokine receptors). Inhalation directly to the target organ (lung) may overcome delivery issues with antisense drugs that tend to be absorbed by the liver spleen and kidneys. This is the first antisense drug delivered topically to the lungs that has shown to have an effect in treating asthma in clinical studies.

Pharmaxis pipeline (following Topigen acquisition)

Stage of development	Drug/Drug candidate	Application	Region
On Market	Aridol	Asthma diagnosis	Au/Eu/Korea
Registration	Bronchitol	Cystic fibrosis	Europe
Phase III	Bronchitol	Broncicctasis	Eu/USA
Phase II	TPI ASM8	Asthma	Canada
Phase I	PXS25	Lung fibrosis	Australia
Preclinical	ASSAO/VAP-1	Asthma	Australia
Preclinical	TPI 1100	COPD	Canada

A Phase IIa study with TPI ASM8 was completed in 2008 in seventeen patients with mild atopic asthma. The trial treated patients over four days with the one dose. It achieved some positive clinical results although the dose may have been low. A second Phase II trial is underway in 15 patients in Canada. Results from this trial are expected in the first half of this year. This trial is testing the drug at four different doses for four days of daily treatment in patients with mild-to-moderate allergic asthma.

Pharmaxis is likely to move this program into a third Phase II study in the second half of this year which will involve a longer duration (two weeks versus the current four day treatment). The program is close to a value inflexion point which was one of the appeals to Pharmaxis.

Synergies Between Pharmaxis & Topigen

Topigen's next drug candidate is in preclinical development for the treatment of chronic pulmonary obstructive disorder. Pharmaxis has an interest in both of these areas, with a Phase I trial underway with drug candidate PXS25 in asthma, and having previously completed a Phase I/II trial in COPD with Bronchitol. The acquisition helps fill Pharmaxis's pipeline gap, giving it now a product on the market, and products in Phase III, Phase II, Phase I and preclinical investigation stages. (See table)

Topigen is an antisense technology company. Pharmaxis had previously had some interest in ASX listed Antisense Therapeutics prior to that company's multiple sclerosis drug development deal with Teva Pharmaceutical Industries. (Both Antisense Therapeutics and Pharmaxis have or have had interests in MS and asthma).

Within days of signing the agreement, the Topigen website had been closed down and redirected to Pharmaxis, and a development agreement with **Nicox** in France had been terminated as a result of the acquisition. The deal is expected to be completed in the next two months. Topigen currently employs less than 20 people although it is uncertain how many will move across to Pharmaxis.

FDA Holds Off on Approval of Aridol

Pharmaxis's asthma test Aridol is approved for use in South Korea, Australia and Europe. However, at the end of last month in a surprising move, the FDA did not approve the test in its present form. This was surprising because in November an FDA Advisory committee recommended that the test be approved.

The deficiencies in the submission appear minor, relating to three subcontracting facilities, labeling and post-market surveillance, which we expect will not be difficult to resolve. No additional trials are required.

The Aridol market in the US is small, valued at only around US$10 million a year. Nevertheless, the opportunity there is for Pharmaxis to grow this market with a more user-friendly test. Launching this product in the US will also aid in developing an efficient distribution and launch of its lead product, Bronchitol, likely to be in early 2012 in the US. Bronchitol, for the treatment of cystic fibrosis, is on track for approval in Europe in the second half of this year, with a possible launch in early 2011.

Access to the European market should not be overwhelmingly difficult, with 80% of the CF market in Europe concentrated in five countries – UK, Germany, France, Spain and Italy.

Bioshares recommendation: **Speculative Hold Class A**

Bioshares

Antisense Therapeutics Update

Positive news may be just around the corner for Antisense Therapeutics (ANP: 5.4 cents). Antisense has licensed the commercial development and rights to its multiple sclerosis drug candidate to **Teva Pharmaceutical Industries**. ANP completed positive Phase IIa trials in 77 patients with MS in 2008. Teva licensed the drug candidate in the same year however wanted to conduct further preclinical safety studies before moving the program into a Phase IIb dose ranging study. A decision is expected very shortly on Teva's decision on the ATL/TV1102 MS drug program.

A forward indicator on Teva's decision may be found in a deal Teva completed with **Oncogenex** in late 2009. Teva has acquired a global license to an antisense compound from Oncogenex (OGX-011) as a potential cancer therapy (through the inhibition of the clusterin protein). OGX-011 will move into three Phase III trials for the treatment of prostate cancer (CRPC), metastatic colorectal cancer and Non-Small Cell Lung Cancer. Teva will pay US$60 million in initial payments as part of the deal.

That ANP's drug candidate and Oncogenex's drug candidate are both antisense compounds could suggest that Teva is gaining confidence in the antisense drug approach and that it may likely progress its MS program into Phase IIb studies.

That will trigger a milestone payment for ANP, it should trigger a valuation re-rating for ANP, and it should position ANP better for raising funds to move its ATL1103 drug candidate for acromegaly into the clinic.

Also of interest is that Pharmaxis has acquired antisense technology company, Topigen Pharmaceuticals, another indicator of increased interest in the antisense field.

Bioshares recommendation: **Speculative Buy Class B**

Bioshares

Tissue Therapies – Edging Closer to Success

Although it has taken longer than initially expected, about 18 months longer, Tissue Therapies is now on track to complete the final commercialisation stages of its VitroGro wound healing product. Using a combination of naturally occurring wound healing proteins, Tissue Therapies has potentially developed a unique product for which there is a major clinical need.

Spectacular Clinical Trial Results

In November last year, Tissue Therapies released results from a very successful clinical study conducted in Perth and Canada. The results from this trial were spectacular. There were 10 patients treated in Canada and 11 in Perth. The patients had medical complications that mostly contributed to chronic wounds that had been unable to heal using existing therapies, some wounds having not healed for over two years prior to the trial commencing.

In the Canadian trial, seven of the 10 patients achieved at least a 26% reduction in the wound surface area within six weeks. In one case, a 73 year old man whose foot wound was completely unresponsive for over two years and a foot amputation had been recommended, achieved a 29% closure of the wound within six weeks following the VitroGro treatment.

In another case in a 37 year old diabetic, 74% closure of the wound (epidermis) was achieved in eight weeks in one of the most challenging wound treatment cases. The dermis was completed healed at eight weeks. In two other very severe patient wounds, whilst there was no surface wound reduction, healing from the base (near the tendon) was achieved.

In the 11 patients under the Australian clinical study arm, the median area of wounds (all venous ulcers) was reduced from 9.85mm^2 to 2.41mm^2 in 24 days.

These results have triggered substantial interest from potential sales and distribution partners, some of whom do not even operate in the wound care market.

Commercialisation Plan

Tissue Therapies has chosen two wise options in the commercialization path for its product. As seen with many Australian biotechs (including Pharmaxis, Clinuvel Pharmaceuticals, CathRx, Nanosonics, Halcygen Pharmaceuticals, Genera Biosystems, ASDM and Avita Medical), Tissue Therapies is electing to gain approval and commercialise its product first in Europe, prior to entering the more heavily regulated market of the USA.

The second wise move is to maintain manufacturing rights for its product should it form a sales and marketing agreement with a third party. This allows the company to maintain more control over the product which is beneficial should any disputes arise with commercial partners.

Further Clinical Studies

Unlike a pharmaceutical product, which requires Phase I, II and III clinical testing, Tissue Therapies wound healing product falls under a device classification. The company can potentially gain approval with one pivotal study. That study will begin in the UK in the second half of 2010 and the plan is the have the study completed by the end of this year.

Re-engineered Formulation

This trial will use a re-engineered protein formulation that combines the active regions of the growth factors, binding proteins and activation proteins from VitroGro into the protein product. Tissue Therapies has decided that to make the VitroGro product commercially viable, a more efficient manufacturing process involving only a single protein was required.

The manufacturing of this product has been contracted out to Eurogentec in Belgium. Eurogentec produces more than 80 biopharmaceutical products.

The construction of this new VitroGro formulation has been a major achievement by the company. The company has repeated preclinical studies with the new formulation and with live human skin samples achieving excellent results.

Delays to Date

Tissue Therapies is running about 18 months behind its clinical trial schedule. The delay has been caused by product contamination during manufacture and by clinical enrolment sites and regulatory hurdles. The company maintains reliance on external principal investigators and the risk that the forthcoming trial will not be completed on time remains. Professor Keith Harding, who is potentially the leading wound care clinician in the world, is the principal investigator for the forthcoming trial at Cardiff University.

Licensing

Tissue Therapies is currently in licensing discussions, having achieved strong interest from potential partners. The aim is to license the product by the end of September 2010, with the preference for an exclusive worldwide licensing agreement.

Capital/Funding

In the last quarter of 2009, Tissue Therapies raised just over $7 million net of costs through a private placement ($5 million at 15 cents a share) and share purchase plan ($2.7 million at 11.84 cents a share). We estimate Tissue Therapies has just over $7 million in funding. The company is seeking to achieve a breakeven point in the business by the end of calendar year 2011.

Risks

The funding risk for the company has been alleviated for the next two years following the recent capital raising. The near term risk is not being able to negotiate a licensing agreement, or not on favourable terms, however the interest following the release of the clinical studies has been very strong. Co-ordination and completion of the forthcoming clinical program in the US remains a risk as does a possible poor trial result from the re-engineered formulation, although studies with the new formulation have yielded similarly positive results.

Cont'd on page 5

Genera's Paptype HPV Test Receives TGA Approval

The Australian Therapeutic Goods Administration (TGA) has approved Genera Biosystems' (GBI: $0.80) human papillomavirus (HPV) test, Paptype. HVP is implicated as the predominant causative agent of cervical cancer.

The approval is a positive advance towards the commercialisation of the product in the local market. The test is currently available in Australia through the Gribbles Pathology network. At the same time, Genera is working towards partnering the test with a company capable of penetrating international markets.

The inclusion of the test of the Australian Register of Therapeutic Goods now allows, through reciprocation rights, for the company to gain European CE mark approval and launch the test into 26 European countries.

The Paptype Test

Genera's HPV test detects HPV but more importantly detects 14 high risk strains of the virus and two low risk types. Where the test differs from some of the rival products on the market is that it simultaneously detects and genotypes the virus. Genotyping is a desirable quality in a HPV test as women infected with types 16 and 18 are five times more likely to develop HCV than if infected with other high risk strains.

And while the test performs on par with Qiagen's HC2 test and Cervista's ThinPrep test in terms of processing time and handling steps, the Paptype test requires significantly less sample by volume (800 micro-litres, compared to 4 mls and 2 mls respectively).

Two Studies

Genera is set to conduct two further studies of Paptype on clinical samples. One will use Australian screening samples; the other will use 2000 US samples that have already been assessed using the current leading test in the market, the HC2 hybrid capture test marketed by Qiagen.

The Australian samples will be taken from the WHINURS study which was overseen by Professor Suzanne Garland from the Royal Women's Hospital in Melbourne, in which 3000 rural and urban, indigenous and non-indigenous Australian women were screened for the prevalence of HPVby genotype.

Genera hopes to use data from both studies to extrapolate Paptype performance metrics into existing published data on HPV infection and detection.

Forthcoming Milestones

For Paptype, Genera's forthcoming milestones will be to conclude a partnering deal and to gain reimbursement for the test in Australia (under the auspices of MSAC, the Medical Services Advisory Committee). Gaining reimbursement is a longer-term milestone with much more uncertainty attached to it. Part of the challenge will be persuading the Australian reimbursement authority to 'plug-in' data derived from the two studies mentioned above into a health economics model already devised by the authority.

Genera is also seeking a development partner for its RTI-Plex product, a test which is designed to simultaneously detect respiratory tract infections including RSV, influenza, parainfluenza, metapneumovirus, rhinovurus, adenovirus, corona virus and SARS.

Commentary

With the major milestone of a partnering deal approaching in the next few months, Genera should see itself in a much more de-risked position once a deal has been cemented.

Since its listing in July 2008, Genera has made steady progress in the development of Paptype, a test that has clear points of difference with rival products. In time, with an appropriate partner in the right markets, Paptype could succeed some of these tests as the HPV test of choice.

It must also be recognised that Genera Biosystems could easily become an acquisition target for one of its rivals in the HPV testing space, should it present itself as a clear commercial threat.

Genera Biosystems is capitalised at $49 million and holds estimated cash resources of $3.5 million.

Bioshares recommendation: **Speculative Buy Class B**

Bioshares

CathRx Update

CathRx (CXD: $0.60) has supplied its cash flow statement for the quarter ending December 31, 2009. The company failed to achieve the sales it had forecast of $800,000 for the period, receipting $151,000. It now expects current year sales will also be less than the previously forecast of figure $5.4 million for FY2010.

The company cited the strong Australian dollar as one factor, but sales were also weak due to the issues with a distributor in Germany and slow progress in finalising a distributor in France.

While the sales results are disappointing by the company's admission and our assessment, they are not of a terminal nature, with the French distributor appointment simply a matter of a time. Distributors have been appointed in all other major European countries.

The real driver for CathRx sales will come from the launch of its therapeutic catheters (both irrigated and standard) against which sits far less competition. These products have been submitted for CE mark approval, with approval for the irrigated device expected by 2010 Q2 and the standard device by 2010 Q3.

CathRx is capitalised at $43 million with cash of $5.4 million at hand.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

– Tissue Therapies cont'd

Summary

Tissue Therapy's technology has always appeared to have a strong chance of technical success. However, the challenge has been for a small company to successfully commercialise this product, and not unexpected, there have been considerable delays. Tissue Therapies listed on the ASX in 2004, raising $3.5 million in 2004. To date the company has raised $24.6 million from public capital markets. Tissue Therapies is capitalsed at $29 million.

Bioshares recommendation: **Speculative Buy Class B**

Tissue Therapies has been added to the Bioshares Model Portfolio.

Bioshares

Optiscan Imaging - Ominous Signs Continue

Another ominous sign emerged for Optiscan Imaging this week with the departure of CEO Vicki Tutungi. Chairman Angus Holt will become Executive Chairman, presumably taking on the CEO responsibilities. Holt joined the board in February. He is a long time investor in Optiscan, representing 6.1 million shares in Optiscan through indirect interests.

In January last year, Optiscan announced it was downsizing its work force. In March it terminated its second generation endomicroscope development project with **Hoya** in Japan. In May its Chairman Grant Latta stepped down. And at June the company had only $1.6 million in cash after generating a net loss of $6.4 million for the 2009 financial year. In November last year the company raised just under $1.2 million through a share purchase plan.

Optiscan has a very challenging time ahead.

Bioshares recommendation: **Avoid**

Bioshares

Bioshares Model Portfolio (22 January 2010)

Company	Price (current)	Price added to portfolio	Date added
Tissue Therapies	$0.21	$0.21	January 2010
Biodiem	$0.20	$0.15	October 2009
QRxPharma	$0.94	$0.25	December 2008
Hexima	$0.44	$0.60	October 2008
Atcor Medical	$0.18	$0.10	October 2008
CathRx	$0.60	$0.70	October 2008
Impedimed	$0.75	$0.70	August 2008
Mesoblast	$1.99	$1.25	August 2008
Circadian Technologies	$0.70	$1.03	February 2008
Patrys	$0.12	$0.50	December 2007
Bionomics	$0.34	$0.42	December 2007
Cogstate	$0.32	$0.13	November 2007
Sirtex Medical	$6.89	$3.90	October 2007
Clinuvel Pharmaceuticals	$0.25	$0.66	September 2007
Starpharma Holdings	$0.66	$0.37	August 2007
Pharmaxis	$2.73	$3.15	August 2007
Universal Biosensors	$2.05	$1.23	June 2007
Probiotec	$2.13	$1.12	February 2007
Chemgenex Pharma.	$0.93	$0.38	June 2006
Acrux	$1.95	$0.83	November 2004
Alchemia	$0.76	$0.67	May 2004

Portfolio Changes – 22 January 2010

IN:

Tissue Therapies 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

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

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