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In this edition...
The sentiment towards biotech stocks is suprisingly positive at the moment, but the focus is very selective. Companies with late stage products in development or nearing registration or market miletsones have experienced strong gains off their twelve month lows.

Investors are driving a path towards companies with more advanced programs with decreased funding and technical risk.

Will the capital squeeze on the rest of the sector end anytime soon? If investors start to make money with the 'late stage' stocks then perhaps some 'early' and 'mid-stage' stocks will receive a boost as well.

The Editors
Companies Covered: BTA, CXS,CUV

	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)	-12%
Cumulative Gain	**81%**
Av Annual Gain (7 yrs)	**17.8%**

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

Late Stage Biotechs Attract Strong Investor Interest

Arguably one of the most important milestones for the Australian biotech sector is approaching; at the end of this month **Pharmaxis** is due to report on the Phase III cystic fibrosis trial with its lead drug candidate, Bronchitol. Perhaps not unexpectedly, a selection of Australian biotechs that are approaching the final phase of drug development have been receiving strong investor interest this year. The period 2009-2010 had been slated in *Bioshares* as a busy time for the Australian biotech sector with an unprecedented number of companies expected to file their drugs for approval over this time. If the Pharmaxis trial result is positive, it may well trigger a surge of interest into the leading biotech stocks that are starting to building momentum.

From their recent 12 month lows, strong share price gains have been made by: **Pharmaxis** (113%), **Peplin** (114%), **Alchemia** (279%), **QRxPharma** (125%), **Chemgenex Pharmaceuticals** (61%), **Acrux** (82%), **Halcygen Pharmaceuticals** (90%), **Clinuvel Pharmaceuticals** (53%), **Biota Holdings** (124%) and **Avexa** (64%). All are in or approaching final registration trials. A number of these stocks have been well oversold. With positive news flow and a renewed interest in the sector from investors, we are likely to see many of these stocks continue to move higher over 2009.

Cont'd over

Late Stage Clinical Programs

	Company (Partner)	Drug	Indication	Regulatory Timing	Price change from 12 month low
	New Chemical Entities				
1	Chemgenex Pharmaceuticals	Omacetaxine	CML (315I mutation)	File in USA mid 2009	61%
2	Pharmaxis	Bronchitol	Cystic Fibrosis	File in Europe Q3 2009	113%
			Bronchiectasis	(Filed in Australia 2008) ✓	
3	Clinuvel Pharmaceuticals	Afamelanotide	EPP (sun intolerance)	File in Europe Q4 2009	53%
4	Biota Holdings (Daiichi Sankyo)	CS-8958	Influenza	File in Japan 2009	124%
5	Peplin	PEP005	Actinic Keratosis	File in USA by mid-2010	114%
6	Avexa	Apricitabine	HIV (M184 mutations)	File in USA 2011	64%
7	Circadian Tech. (Ark Therap.)	Trinam	Kidney dialysis (prevent graft overgrowth)	File in 2011	42%
	Super Generics/Technology Enabled Generics				
8	Alchemia (Dr Reddy's)	Fondaparinux	Anticoagulant	(Filed ANDA in March 2009) ✓	279%
9	Acrux	Axiron	Male testosterone gel (Super generic)	File in USA 2009	82%
		Ellavie	HRT spray (super generic)	(Filed in Europe 2008) ✓	
10	Halcygen Pharmaceuticals	SUBA-Itraconazole	Antifungal (super generic)	File in Europe 2009	90%
11	QRxPharma	MoxDuo IR	Pain relief	File in USA 2010	125%

Leading device/diagnostic companies have also fared well this year. **Nanosonics**, which started selling its ultrasound disinfection product in March, is up 171% from its 12 month low. **CathRx**, which is selling and developing a range of cardiac diagnostic and treatment catheters, is up 93% from its low, and **Universal Biosensors** (UBI) is up 117%. UBI is expected to renegotiate its agreement with **Johnson & Johnson's LifeScan** division for the manufacture of its improved version of glucose test strips. UBI expects the first 12 months of revenue once manufacturing starts to be between $20 - $30 million and for the company to be profitable.

However, the funding crisis remains dire for many struggling small cap biotechs, and many of these companies would be hoping that the positive sentiment being directed towards the sector leaders will filter through to less advanced companies.

ChemGenex – On Track for Market Launch in 2010

Recent capital raisings, including that by Chemgenex Pharmaceuticals (CXS: 45 cents), indicates that some investor appetite for higher risk investments is slowly returning. However, what is proving to be crucial is the quality of shareholders within biotechs, particularly institutional investors that are prepared to continue to support their investments.

Chemgenex has raised $10 million through a placement including to existing shareholders **GBS Venture Partners**, **Merck Serono** and **Orbis Funds Management**. It will raise up to a further $7.4 million from a non-renounceable rights issue which should see its other VC shareholder, **Alta Partners,** participate as well. All funds will be raised at 43 cents a share.

Chemgenex's lead drug candidate, Omacetaxine, is due to complete its NDA (New Drug Application) filing with the FDA mid-year and is expected to be launched in the first quarter of next year. The first application of the drug is for the treatment patients with chronic myeloid leukemia (CML) who have tested positive for the T315I mutation. This is a niche indication initially, with just under 10% of people failing existing treatments (TKIs) having this mutation and 7% of patients failing frontline Gleevec therapy. By our estimates, this places the market between US$50 - US$100 million a year for Omacetaxine, although the market is estimated to grow at more than 20% a year.

Getting the drug approved for the first indication is a speed-to-market strategy for the company. Once the drug is approved, further positive trial outcomes in other indications, in other situations and in combination use with existing treatments will likely follow. There is the potential to significantly expand the use and market size of this therapeutic.

The second indication for which Omacetaxine is expected to gain approval, in 2010, is in patients with CML who have failed two or more of existing tyrosine kinase (TKI) drugs such as Gleevec, Sprycel or Tasigna. Omacetaxine works with a mechanism of action that sets it apart from existing therapies. Hence, it has the potential to be used as either as a third line therapy, or in combination with existing therapies.

What differentiates Omacetaxine from existing therapies is its potential ability to kill off the leukemic stem cells in the bone marrow (which generate the leukemic cells that exist in blood). Existing TKI drugs only treat the leukemic cells in blood. While Gleevec has shown to be exceptionally effective in treating CML (its exceptional results are what stymied the Omacetaxine program initially) and better than Omacetaxine as a first line treatment, resistance to the drug is emerging (in 7% of patients a year) and the drug does not tackle the root cause of the disease (in the bone marrow). In a pre-clinical trial, Omacetaxine eliminated 90% of leukemic stem cells in a laboratory trial, compared to only 9% for Gleevec (and 25% for Sprycel).

According to Dr Luke Akard from the **Indiana Bone Marrow Transplant Center**, who specializes in CML, there is a lot of interest in looking at combining Omacetaxine with Gleevec, with the field of CML stem cells relatively young. Other indications being investigated in clinical trials for Omacetaxine or are in the treatment of myelodysplastic syndrome and in acute myelogenous leukemia.

Data so far...very good

So far the data all looks good for Omacetaxine. In the first 25 patients in the study in the chronic phase of disease (which then progresses to accelerated and blast phase), 80% had a complete response in clearing the cancer cells in the blood, and 16% had a complete response to clearing the cancer from the bone marrow from where it originates. These are good results in patients who have no other treatment options. This is why it is very likely Omacetaxine will get approval from being trialed in only a small number of patients. It doesn't need to be tested against other therapies and results can be viewed as the trial progresses because it is not blinded and there is no placebo. The drug is not a typical cytotoxic that causes severe nausea and hair loss. It is predominantly well tolerated. The main side effect is myelosuppression which can be safely managed by reducing the frequency of dosing during a cycle.

The first indication will likely be for patients with the T315I mutation with chronic and possible accelerated CML, and unlikely blast phase of the disease. The company has Orphan Drug status in Europe and the US, which allows the NDA to be filed in parts in the US, some cost advantages, and market exclusivity, five years in the US and 10 years in Europe, which helps further protect the proprietary ownership of the product in addition to patents.

Funding

The funds being raised will get Chemgenex to the approval stage of Omacetaxine in Europe and the USA. Chemgenex will look to license the drug in Europe in the second half of 2009, with any funds from a licensing deal going towards funding the commercial rollout of Omacetaxine in the USA. Excluding the rights issue, Chemgenex is capitalised at $118 million. With a new oncology drug likely to be on the market early next year, sufficient funding to complete development for the first indication and a dedicated investor base, the current share price offers an excellent opportunity to enter or increase exposure to this stock.

Bioshares recommendation: **Speculative Buy Class A**

Capital Requirements – A Hypothetical Study

Since the close of the March quarter, several companies have announced progress with capital raisings. **ChemGenex Pharmaceuticals** has raised $10 million through a placement, and may yet raise up to $7.4 million more through a rights issue. **Starpharma** has raised at least $4.3 million through a placement. **Medical Therapies** and **Biotron** have raised $700,000 and $800,000 a piece, through private placement and SPP respectively. Tallied up, it appears that another $15.8 million has found its way into the sector. However, investors are often left in the dark when it comes to capital raisings and the delicate matter of capital requirements. A company might for example raise $10 million, but investors can be left wondering if that is either too much or too little. Often, whatever is raised is less than what is required to achieve a particular commercialisation goal because clinical programs can often be pushed back due to problems with recruitment and because regulators can impose conditions that weren't initially budgeted for.

To illustrate the biotech capital budget problem we have analysed programs from a sample of ten drug development companies, for the most part where the program has not yet commenced its next anticipated phase of development. We have made estimates of funds required for each clinical project, and have also made assumptions about the number of patients required for each trial and the average cost per patient for each trial. We have attempted to derive, where possible, these costs from previous similar trials conducted by the company or by other companies operating in the same or a similar field. We accept that these estimates could vary from a company's own internal costings.

The hypothetical study shows a capital requirement on a project basis for these ten companies of $101 million, with the largest sum being $45 million for the completion for Avexa's Phase III trial of apricitabine to the 24 week mark. It is more than likely that these projects are unfunded (collectively, these ten companies held cash resources of $50 million as of December 31, 2008). However, clinical program costs are one of several areas of biotech company expense, with corporate overheads and salaries accounting anywhere from $2-$5 million per annum for a small biotech. Thus, any capital raising conducted to support the programs specified in the table below would generally include a working capital component, desirably funding corporate overheads for two years at least. This gives rise to an additional capital requirement (for two years) for the ten sample companies of between $20 and $50 million.

One factor ignored in this analysis is the flow of revenue from partnering or royalty arrangements that can offset development costs, and several companies in the table below enjoy the benefit of partnership and license income.

However, this hypothetical analysis illustrates the capital dimensions of the biotech sector, at least for the drug development subsector. In previous years, upwards of $500 million flowed into the sector each year from 2003 through to 2007, addressing the capital requirements of more than 100 companies.

With the funding tap barely dripping, it is likely that a significant number of pending development programs will remain that way until capital markets allocate more funds to the biotech sector, and as is also evident in the table below, to programs at the Phase II stage of development, or earlier.

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Hypothetical Clinical Trial Capital Requirements Analysis - 10 Sample Companies

Company	Code	Drug	Indication	Next Development Phase/ Complete Current Phase	Est. Cost ($M)	Assumptions	
						Num. Patients	Cost/patient
Antisense Therap.	ANP	ATL1103	Growth and sight Disorders	Phase Ib/IIa	$5.3	60	$88,000
Avexa	AVX	Apricitabine	HIV	Phase III (to 24 weeks)	$45.0		
Biotron	BIT	BIT225	HCV	Phase IIb	$3.0	60	$50,000
Bone Medical	BNE	CapTHymone	Osteoporosis	Phase IIb	$3.8	150	$25,000
Bionomics	BNO	BNC210	Anxiety	Phase I	$1.9	25	$75,000
Cytopia	CYT	CYT387	Myeloproliferative disorders	Phase I/II	$2.6	34	$75,000
NeuroDiscovery	NDL	NSL-043	Neuropathic Pain	Phase II	$1.3	50	$50,000
Prana Biotechnology	PBT	PBT-2	Alzheimers Disease	Phase IIb/III	$26.1	300	$87,000
Prima Biomed	PRR	CVac	Ovarian cancer	Phase II	$9.4	150	$125,000
Viralytics	VLA	Cavatak	Cancer	Phase II	$3.0	60	$100,000
Total					**$101.2**		

Notes

Avexa - Cost figure is sourced from Paragraph 106, Lonergan Edwards IER for PGL-AVX merger, Jan 29, 2009
Prana Biotech - assumes a two arm randomised placebo controlled trial, with costs based on costs for Phase II trial of $6.8M (78 pts)
Antisense - based on ATL1102 MS trial costs of $6.7 million (77 pts)
NeuroDiscovery - Based on MBP trial costs for ACV1 of $4.2 million (85 pts); 50% of total costs shared with Sosei
Bone Medical - pt number is BNE estimate 24/2/09; cost/patient derived from analysis of HGN SUBA-Itraconazole pk trials
Cytopia - pt number is CYT estimate from Bioshares Clinical Trials Survey 2008

NB: The estimates of the costs of programs presented in this table are hypothetical and any specified program may not necessarily be taken forward into a next phase of development.

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Clinuvel Pharmaceuticals – On Track for Market Launch in 2010

Clinuvel Pharmaceuticals (CUV: 27.5 cents), like ChemGenex, is looking to file its drug for approval this year. It is seeking to file in Europe by the end of the year with product revenue anticipated in 2010. Clinuvel is developing Afemelanotide, which increases the pigmentation of the skin and thereby providing increased protection to people severe intolerance to sunlight exposure.

Similar to Chemgenex, the initial market size is small, US$25 million in the US alone for the lead indication of EPP (erythropoietic protoporphyria). The second application, polymorphous light eruption (PLE) is also small, estimated at US$40 million in the USA in 2006. However as with Chemgenex, the game plan is to get the product onto the market, and then expand indications. The largest application is for organ transplant patients on immunosuppression treatment. These patients have a several fold increased chance of developing skin cancers and a regular injection of Afemelanotide could significantly reduce the risk of skin cancer disease. This market in the USA is estimated at US$240 million (in 2006).

Clinuvel has been granted Orphan Drug status in the US and Europe for EPP. Developing drugs to treat a small subset of the population, as defined by Orphan Drug designation, can be a very profitable business. The incentives are offered by regulators to encourage drug developers to pursue diseases that affect smaller numbers of people, and a premium pricing can generally be negotiated with payors.

Final Phase III results from the EPP trial are due to be reported in the December quarter this year. Data from the first 14 Swiss patients treated with Afemelanotide for EPP was positive and all 14 patients have elected to continue treatment under compassionate grounds, suggesting the drug is beneficial, well tolerated and in demand by people afflicted with this disorder.

Clinuvel is looking to license the product in various regions, and is also considering to slice and dice the commercial use of the product across different disease categories. This may be difficult to achieve with complications arising from how distinct disease areas may be partitioned between different licensing partners. Clinuvel may also keep some marketing rights for itself.

Clinuvel is well funded with an estimated $40 million in cash assets. It has made strong and disciplined progress over the last three years under its current CEO, Dr Philippe Wolgen. The company enjoys strong institutional support and we expect solid progress to market over the next 18 months. Major milestones include Phase III trial results, both interim results for PLE and final results for EPP, and commercial licensing agreements.

Bioshares recommendation: **Speculative Buy Class A**

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Biota – CDC Recommends Relenza for H1N1 Infection

The US Centers for Disease Control and Prevention (CDC) recently analysed the predominance of various flu strains circulating in the US in the period September 2008 to April 2009. It found that 67% were influenza A type viruses and 33% were influenza type B viruses. Of the type A, 90% were found to be H1N1 viruses and 10% were H3N2 viruses. The CDC found all of the H1N1 viruses were resistant to oseltamivir (tamiflu). The CDC stated that "when an influenza A (H1N1) virus or infection or expousre is suspected, zanamivir (Relenza) is the preferred medication". Tamiflu is essentially ineffective against 60% of all the flu strains that have circulated in the current US flu season. No resistance was reported for Relenza against currently circulating flu strains.

With Tamiflu declining in effectiveness, the CDC recommendation regarding Relenza (marketed by Biota's licensee **GlaxoSmithKline**) offers the potential for sales of Relenza to increase substantially, both on seasonal needs basis and a stockpiling basis.

Biota is capitalised at $113 million and last traded at 65 cents.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares Model Portfolio (17 April 2009)

Company	Price (current)	Price added to portfolio	Date added
ASDM	$0.40	$0.30	December 2008
QRxPharma	$0.45	$0.25	December 2008
Hexima	$0.45	$0.60	October 2008
Atcor Medical	$0.24	$0.10	October 2008
CathRx	$0.58	$0.70	October 2008
Impedimed	$0.73	$0.70	August 2008
Mesoblast	$0.81	$1.25	August 2008
Cellestis	$2.98	$2.27	April 2008
IDT	$1.63	$1.90	March 2008
Circadian Technologies	$0.77	$1.03	February 2008
Patrys	$0.08	$0.50	December 2007
Bionomics	$0.20	$0.42	December 2007
Cogstate	$0.20	$0.13	November 2007
Sirtex Medical	$2.36	$3.90	October 2007
Clinuvel Pharmaceuticals	$0.28	$0.66	September 2007
Starpharma Holdings	$0.30	$0.37	August 2007
Pharmaxis	$2.00	$3.15	August 2007
Universal Biosensors	$0.89	$1.23	June 2007
Biota Holdings	$0.65	$1.55	March 2007
Probiotec	$1.87	$1.12	February 2007
Peplin Inc	$0.60	$0.83	January 2007
Arana Therapeutics	$1.39	$1.31	October 2006
Chemgenex Pharma.	$0.45	$0.38	June 2006
Cytopia	$0.09	$0.46	June 2005
Acrux	$0.69	$0.83	November 2004
Alchemia	$0.36	$0.67	May 2004

Portfolio Changes – 17 April 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, 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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