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In this edition...
Change is afoot in the biotech sector as effects of the global financial crisis take a deeper root, and the future of an increasing number of companies becomes uncertain. Despite that, a number of companies, such as ChemGenex Pharmaceuticals, continue to knock down the hurdles on the way to getting products to market. The company presented more positive clinical trial data at the recent American Society of Hematology conference.
In conjunction with a recent site visit, we discuss the Sydney-based orthopeadic implant manfufacturer ASDM. Market conditions now make this profitable company an increasingly attractive investment target. And to wrap up we include some notes from the annual CSL R&D Day.

Companies Covered: AMT, CSL, CXS, PGL

	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)	-39.0%
Cumulative Gain	**26%**
Av Annual Gain (7 yrs)	**17.8%**

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Bioshares

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Edition 293

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

The Australian Biotech Sector – Rationalisation Begins

The rationalisation of the Australian biotech sector has well and truly commenced thanks to the prompting by the global financial crisis. It is extremely likely that in 12 months time there will be fewer listed biotech companies rather than more, and perhaps as many as 20 less if the funding blockade continues well into 2009.

Ventracor For Sale

Ventracor missed the funding window in mid 2008, which has now placed the company in a dire financial position with only a few months of funding left. The share purchase plan offered by the company as an almost last resort for funds failed and the company has now placed itself up for sale or alternatively is seeking a strategic investor.

The company has spent $170 million developing its heart pump system. The product is approved for use in Australia, parts of Asia and in Europe with US approval expected in 2010. Last financial year Ventracor generated revenue of $17 million from VentrAssist sales. The company is now capitalised at $10 million. While it may be an appealing acquisition at these prices, further development costs, perhaps as much as $60 million, will be required to bring the company to profitability, with obligations to implanted patients another cloudy issue.

Stem Cell Sciences in M&A Discussions

Stem Cell Sciences has stopped trading on the ASX as it continues with discussions with a potential acquirer, divestment of technologies or refinancing. SCS is capitalised at only $5 million, possessing a suite of stem cell technology IP and expertise. SCS recently signed a five year master service agreement with Pfizer.

Ambri Finally Exits Sector

Former biosensor technology company Ambri, now called Diversa Ltd has finally exited the biotech sector. Ambri has acquired a retail superannuation trust with $275 million under management.

Cogstate Partner Continues to Increase Stake

The Cogstate cognitive testing business has performed exceptionally well over the last two years and is moving towards a position of profitability. It has a formed a strategic partnership with **United Biosource Corporation** in the US. The two companies will share pharmaceutical testing contracts, with UBC conducting the on-site testing of patients with its 1000 person work force and Cogstate analyzing the data and providing its software platform. The partnerships allows Cogstate to bid for major Phase III trials involving up to 3000 patients.

UBC has increased its stake from 13% to 16.5% since it invested $800,000 into Cogstate at the time the partnership was formed.

Chemgenex Pharmaceuticals Knocks Down The Barriers

The market approval of Chemgenex Pharmaceuticals' (CXS: 45.5 cents) lead compound, omacetaxine, may now only be around 12 months away in the US. The compound is in final clinical trials for the treatment of chronic myeloid leukemia, and specifically, those patients who have failed treatment with Gleevec and have the T315I mutation. This week Chemgenex released further positive information from its registration trial at the **American Society of Hematology** (ASH) conference in San Francisco.

Data from Another 14 Patients

Previous data reported was from the first 30 patients in this trial. The data presented this week included an additional 14 patients and was in line with previous results. A complete hematologic response was achieved in 80% (82% previously) of chronic patients. In 20% of patients (18% previously) the patients were effectively cured, with a major cytogenetic response, killing the CML stem cells that generate the peripheral leukemic cells in the blood. Unlike other drugs on the market such as Gleevec, omacetaxine appears to be the most advanced drug that actually destroys the stem cells that produce the leukemic blood cells.

In other data presented, 45% of the patients with accelerated form of disease experienced a hematologic response (50% previously) and 13% of patients in the blast phase of disease. Of the patients in this trial, 25 had chronic phase disease, 11 accelerated and eight in blast phase.

Progression Free Survival

Primary endpoint assessment of the drug will be on hematologic and cytogenic responses. However, the company also presented data on progression free survival in chronic phase patients, which was 80% at year one and 70% at year two.

Benefits of Open Label Trial

The obstacles to bringing this drug continue to be removed. The data being generated is consistently positive. There are no other treatment options for patients in this trial, which means it is an open label trial and is not measured against any other treatment. There are several benefits that result from this design. One of those is that the company can report on results as they are received before the trial is completed. This has significant benefits for licensing discussions, with potential licensors able to monitor the progress of this program closely. This is increasing in importance with recent Phase III failures in the oncology field, which has heightened the importance of close assessment of pivotal trial progress.

At the ASH conference, Chemgenex had 10 staff present, sponsoring a symposium on mutation testing in CML that was well attended by 350 people. Chemgenex is building the profile of its lead compound that appears to be gaining strong interest in the oncology field.

NDA Filing On Track for June 2010

It is not an unrealistic aim for Chemgenex to build the business into a billion dollar company (current capitalisation $109 million), although that aim depends on seeing omocetaxine approved for the treatment of broader set of indications.. The company is on track to complete its NDA filing with the FDA in June next year with an FDA Advisory Committee Meeting to assess the drug potentially occurring in late 2009. If positive, the drug should be on the market in the US in the first half of 2010. A European regulatory submission is expected in the third quarter of 2009.

Whilst the first application is for CML patients with the T315I mutation who have failed Gleevec therapy, a second trial is continuing with patients who have failed multiple (Tyrosine Kinase Inhibitor) existing therapies and do not have the T315I mutation. This will expand the application of omacetaxine. The registration trial underway for this second indication will enrol up to 100 patients in a similar open label study. The company is anticipating filing this additional indication for approval in 2010 in the US. The annual cost of treatment in the US with existing TKI therapies (Gleevec, Sprycel and Tasigna) ranges between US$46,000 - US$120,000 per year per patient.

At present, there are an estimated 1000 new patients a year for who omacetaxine would be prescribed under the first indication. With both indications, Chemgenex estimates the potential market for omacetaxine in 2012 to be valued at US$336 million.

At 30 September this year, the company held $20 million in cash, which is sufficient to fund the company for the next 12 months. The company has a strong shareholder base with VC investors **Alta Partner**s and **GBS Venture Partners** on the register, which should enable the company to continue to support the commercialisation of its lead compound. However, an option for the company to consider in the next six months is licensing of marketing rights for European or US regions, should it see the need to do so.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Advanced Surgical Design and Manufacture – An Robust Business Trading at Large Discount

One of the benefits of the current global credit crisis is that quality stocks can be acquired at significant discounts to what they were trading at 12 months earlier. Another case in point here is Advanced Surgical Design and Manufacture (ASDM) (AMT: 30 cents). It is a little known orthopaedic implant manufacturer based in Sydney. ASDM has been operational for 14 years and runs at a profit neutral position. It is a small but attractive company with considerable blue sky potential, aside from its core business.

ASDM makes around 20 product lines of orthopaedic implants such as knee replacements, and in total around 1000 different pieces. *Bioshares* recently visited its manufacturing facility in Sydney which an extremely impressive facility. The company generated sales in the financial year past of $7.1 million, a 21% increase over the previous year, and generated a small profit of $180,000. Just under $1 million was spent on R&D.

The company is capitalised at $10.5 million, and is trading at 1.5 times sales, with $1.5 million in cash assets and $4.1 million in property, plant and equipment. The company is well managed, focusing on the Australian market but has recently expanded operations to the UK.

Peripheral Access Device

One of the appealing upsides of the business is the Peripheral Access Device (PAD) that the company is commercialising in conjunction with private company AllVascular. This device is currently being tested in a 20 patient trial for the prevention of amputations. It appears to be extremely effective in preventing limb amputations.

How the technology works

The PAD system uses a catheter system that blocks the vein supplying the limb, allowing the lower limb to be pressurized at three times normal pressure in a process lasting several days. When the vein is depressurized, the theory is that vascular cells are stimulated, with genes up-regulated to rebuild the blood vessels that have near collapsed and threatening limb amputation.

It is potentially a revolutionary way to treat vascular damage. This technology was licensed from AllVascular Pty Ltd for a period of 15 years and provides ASDM with a manufacturing arrangement, whereby ASDM will receive 25% of sales for manufacturing the device, should it successfully make it to market.

The device has been tested primarily in Australia with the first procedure conducted in Germany in October. Over 1000 limbs are amputated each day in the Western world due to vascular disease, largely as a result of smoking or diabetes. This technology has the potential to prevent amputations and it would appear to be generating success in this regard.

The device may pricesd be in the order of $5000 and could be on the market as early as 2009. However, market launch depends on regulatory approval, with the first body to assess the technology being the TGA. Given the massive demand for such a device, the debilitating illness both before and after amputation and high probability of success that might be achieved with this treatment (to be proven in the current trial), there could be significant demand to bring the device to market quickly. However, it's entirely possible that regulatory authorities may require more extensive tests, and this is a development risk to keep in mind.

The market for such a device, at 1,000 devices a day, is potentially very large, at over $1 billion a year. ASDM has sufficient manufacturing capacity to cater for global demand at its current facility.

ASDM appears to have been careful not to lose sight of its core business and become too distracted by the lucrative potential of the PAD product. It has five of its 40 plus staff working on this project. ASDM is coordinating the clinical trials and the regulatory submissions. However, its development arrangements with AllVascular over the PAD product are somewhat flexible could be therefore be tightened.

ASDM has been operational for 14 years and has built an impressive business. Its ability to respond rapidly to the needs of surgeons coupled with its excellence in biomedical engineering has been behind its success to date. The core business at its current stock price represents very good value to investors and the blue-sky potential of the PAD product provides enticing appeal to this stock.

Bioshares recommendation: **Speculative Buy Class A**

ASDM has been added to the Bioshares Model Portfolio.

Bioshares

Progen's Future To Be Decided

Background

Progen Pharmaceuticals was founded in September 1989 as Almagest Pty Ltd, changing its name to Progen Industries in April 1990. Progen Industries listed on the ASX in December 1995 and again changed its name to Progen Pharmaceuticals in May 2007.

The company's principal project has been the development of the anti-cancer compound PI-88, which commenced clinical trials in September 1999. Progen intended commencing a Phase III trial of PI-88 in the December quarter of 2007, but did not enrol its first patients until March 2008. In July 2008 Progen terminated the trial, citing "slower than expected regulatory processes in China, Korea and Vietnam; slower than expected initiation of clinical sites; slower than expected recruitment of patients into active sites; and the recent launch of a competitive Phase III trial, assessing Bayer/ Onyx Nexavar in the same indication (of use as an adjuvant in post-resection liver cancer)."

Funding History

Progen has raised $170 million since 1997, including $99 million in FY2007 to support that Phase III trial. Progen Pharmaceuticals holds cash resources in the order of $70 million. The company has also been the recipient of several Commonwealth grants.

Advisors Appointed

Progen appointed **Beerworth and Partners** to assess the company's business and operations and develop strategic options for review by the board. Following the completion of the Beerworth report, the board of Progen is now considering its options. The board is considering that it should return all cash to shareholders (approximately $1.10 per share) or alternatively that it should return some (probably $0.50 per share) as a capital return to shareholders and apply the remainder to new pharmaceutical development activities, most likely achieved through an M&A process. The board describes the second option as delivering a value in excess of $1.10 per share. The board has set a deadline on this decision of January 14. The board has appointed **PriceWaterhouseCoopers** to assist with this task.

Progen Shareholders Group

A number of shareholders, the Progen Shareholders Group (PSG), have requisitioned a meeting for January 9, 2009. The meeting's items of business call for the removal of Dr Malvin Eutick, Robert Williamson, Stephen Jun Chi Chang, Patrick Burns, and Justus Homburg as directors and the election of Robert Moses, Alison Coutts and Woei-Jia Jiang as directors. The only director whose position is not being sought to spilled is that of John Lee.

The PSG is seeking to release value locked up in PI-88, release value in the 500 series, release value locked up in other Progen assets, provide access and rights to new, more potent and less toxic compounds incorporating highly sulphated polysaccharides, restructure and refocuse Progen, and return millions of dollars of surplus capital to shareholders.

The PSG has obtained an in-principle agreement from a third party covering basic terms that would lead to a collaboration and licensing agreement for PI-88. The PSG also states that expressions of interest have been received for a second generation sulphated polysaccharide compound '524'.

In this situation where strong interest abounds for Progen's assets, it is timely to ask questions of both the Progen board and the PSG. This is because not all shareholders will necessarily be aligned to the PSG and not all shareholders would necessarily be satisfied with the Progen board, in its current or previous incarnations. The reasons given for the termination of the Phase III trial of PI-88 are less than satisfactory. At the same time, the information provided by the PSG for the development of PI-88 in the hands of a third party are vague and non-specific.

We list below questions for both Progen board and the PSG in the hope that shareholders may become better informed while the company's future is debated and discussed.

Questions for the Progen board

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?

Questions for the PSG

1. What is the identity of the Taiwanese company that has expressed an interest in PI-88, who are its backers and shareholders and what are its financial resources?
2. If there is such strong interest in second generation compounds, including '524', which are supposedly less toxic, why persist with the development of PI-88?
3. Why is an unsecured $US3 million loan required from Progen by the un-named Taiwanese company to fund the Phase III clinical development of PI-88?
4. How much capital would the PSG aim to return to shareholders?
5. If the PSG did not wish to develop any second generation compounds (500 series compounds), what would be the focus of the company?

Comment

In our view, PI-88 is now a damaged asset and the application of further funds on its development is not warranted, given the failure to prosecute a Phase III trial and given the side effect data that was reported in the Phase II prostate cancer trial, in which high incidences of febrile neutropenia and thrombocytopenia were reported.

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CSL R&D Day – Selected Notes

CSL, at $17.6 billion, the ASX's 13th largest company by capitalisation, held its annual R&D Day in Sydney on Thursday.

CSL spent $240 million on R&D in FY2008 (6.3% of sales) and expects to increase that to $270 million in FY2009. CSL divides it R&D spend into three sections, including spending on new product development, spending on market development and spending on life cycle management. About $90 million is spent on new product development.

A significant proportion of CSL's R&D spend will go towards post marketing studies of its flu vaccine, now approved in the US, with three studies expected to absorb between $20-$30 million per year over the next two years.

CSL is gradually expanding its capabilities and products that are made using recombinant engineering technologies.

An interesting appearance in the company's portfolio chart was the addition of two recombinant blood factor products rFVIIa-FP (CSL-689), and rFIX-FP (CSL-654). Now at the pre-clinical stage, these two clotting factors have been fused with the albumin protein to extend their half life and therefore decrease the number of injections required per bleeding event to one (for FVIIa patients) or to one injection per week (for hemophilia patients).

The next steps in the development of these fusion proteins is the establishment of cell lines, development of analytical and manufacturing processes, production of GMP material and initiation of clinical trials. Much of this is still relatively new territory for CSL.

The company has for some time been developing a product from discard fractions of human plasma, reconstituted high density lipoprotein, as a treatment for coronary artheroslcerosis (in heart attack patients). In studies to date, the current formulation was found to have transient (i.e. negative) effect on liver function. CSL is now re-formulating the product to maintain the positive biological effect of reducing plaque but improve the toxicity profile, hopefully returning to the clinic in 2009.

CSL's lead in-house monoclonal antibody drug, CSL-360, is being developed to treat acute myeloid leukemia. The drug targets leukemic stem cells, through the IL-3 alpha receptor. The 26 patient Phase I trial is reported to have progressed well, with a complete response observed in one of 8 patients in the 3mg/kg-10mg/kg group. A second component of the study is ongoing with twenty patients being administered the highest dose of 10mg/kg.

CSL now has 65 staff located at the Bio21 facility in Parkville, Melbourne. These staff specialise in cell biology and physiology, molecular biology and protein biochemistry, but focused on cytokine research. We consider this a reasonable research commitment, for what is likely early stage research and certainly only something a company the size of a CSL can do.

Bioshares Model Portfolio (12 December 2008)

Company	Price (current)	Price added to portfolio	Date added
ASDM	*$0.30*	*$0.30*	*December 2007*
QRxPharma	$0.23	$0.25	December 2008
Hexima	$0.38	$0.60	October 2008
Atcor Medical	$0.14	$0.10	October 2008
CathRx	$0.60	$0.70	October 2008
Impedimed	$0.70	$0.70	August 2008
Mesoblast	$0.83	$1.25	August 2008
Cellestis	$1.87	$2.27	April 2008
IDT	$1.75	$1.90	March 2008
Circadian Technologies	$0.65	$1.03	February 2008
Patrys	$0.10	$0.50	December 2007
Bionomics	$0.20	$0.42	December 2007
Cogstate	$0.18	$0.13	November 2007
Sirtex Medical	$1.72	$3.90	October 2007
Clinuvel Pharmaceuticals	$0.21	$0.66	September 2007
Starpharma Holdings	$0.23	$0.37	August 2007
Pharmaxis	$1.10	$3.15	August 2007
Universal Biosensors	$0.55	$1.23	June 2007
Biota Holdings	$0.32	$1.55	March 2007
Probiotec	$1.39	$1.12	February 2007
Peplin Inc	$0.29	$0.83	January 2007
Arana Therapeutics	$0.83	$1.31	October 2006
Chemgenex Pharma.	$0.46	$0.38	June 2006
Cytopia	$0.22	$0.46	June 2005
Acrux	$0.49	$0.83	November 2004
Alchemia	$0.10	$0.67	May 2004

Portfolio Changes – 12 Dec 2008

IN:

ASDM has been added to the portfolio. It is a profitable business with strong upside and a share price that has fallen 70% from its peak.

OUT:

Antisense Therapeutics has been removed from the portfolio. There are a lack of short term drivers for the stock that would translate to share price gains in the short-to-medium term in the current investment environment.

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

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