ISSN 1443-850X

In this edition...
Not all is doom and gloom for biotech stocks. While it takes time for companies to bring products to market and even more time to see strong revenues emerge, there are companies posting growth in sales and profits. An example is Cellestis which looks to have found that spot on the J-curve (or hockey stick) where growth appears set to accelerate with the dollars streaming through to the bottom line. Likewise Cogstate is shifting into profitability and monitoring of its quarterly figures is a 'must do' task.
We also note positive progress with Antisense Therapeutics ATL1101 in preclinical studies. This compound may have benefit as treatment for cancer.
And with funding a major problem looming for many companies, we canvass some options available to biotechs to help them deall with the funding drought.

Companies covered: ANP,CGS,CST

	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)	-31.0%
Cumulative Gain	**43%**
Av Annual Gain (7 yrs)	**17.8%**

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

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Individual Subscriptions (48 issues/year)
$320 (Inc.GST)
Edition Number 286 (24 October 2008)
ISSN 1443-850X

Bioshares

24 October 2008
Edition 286

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

Cellestis Hits the 'Hockey Stick' Sweet Spot

Cellestis (CST: $2.18) recorded a strong first quarter result for the current financial year. Recipts from customers increased by $1.1 million over the previous quarter to $6.65 million. What is impressive about the result is that it appears the company has hit the sweet spot in its business where most of the revenue is now moving through to the bottom line.

The net operating cash flow for the quarter increased by $954,000 to $1.9 million, and that is without much of the effect of the falling Australian currency. The average AUD/USD exchange rate for the last quarter was 89 cents. The current exchange rate is 65 cents with the Australian dollar having fallen both against the Euro and the Yen, which make up the three major trading regions for Cellestis.

Annualising the last quarter's receipts from customers and converting at the current exchange rate for the relevant currencies in proportion to sales in those regions, then Cellestis appears set to generate sales in the current financial year, as approximated by receipts from customers, of $33 million, up from $19.5 million last financial year. This assumes no sales growth over the September quarter, which is unlikely (we expect to see continued strong sales growth).

Taking into account the cost base increase of the year due to lower exchange rates and assuming 70% of the costs are incurred overseas, then our estimates indicate that Cellestis could achieve earnings before tax in this year in excess of $10.4 million, without increasing the number of tests sold over the September quarter. This equates to a net profit of $7.3 million by our estimates as a minimum (excluding any amortisation and depreciation charges).

Cellestis is trading on an annualised PE ratio of 28.7, based on the last quarter sales figure and the current foreign currency exchange rates. The company had $15.9 million in cash at 30 September.

Cellestis has brought to market a diagnostic test for latent tuberculosis, in a range of formats. The company sells the test through its own sales network in the US, Australia and parts of Europe (UK, France, Germany, Switzerland, Austria and Poland) and through distributors into other parts of Europe, Japan and South and Latin America.

Bioshares recommendation: **Buy**

Antisense Therapeutics – Third Shot on Goal Progresses

Antisense Therapeutics (ANP: 4.9 cents) has reported a positive result from the company's third program which is in preclinical studies. The compound, ATL1101, is being tested for the treatment of solid tumours, in this case in prostate cancer in mice studies.

ATL1101 was previously tested as a topical treatment for psoriasis although was unsuccessful. The new application for the drug candidate comes about followed a renewed interest in the target, IGF-1 in the oncology area. IGF-1 makes tissue grow, hence the interest by Antisense Therapeutics in using this IGF-1 antisense inhibitor to stop the excessive and uncontrolled skin growth associated with psoriasis. However, psoriasis is an extremely difficult disease target, with all psoriasis programs undertaken by Australian biotechs over the last ten years having failed.

In the treatment of cancer, IGF-1 receptors have been found in solid tumours including breast and colon cancers. In 1998, it was found that men with elevated levels of IGF-1 had a higher chance of developing prostate cancer. There are now at least six major pharmaceutical groups (**Pfizer**, **Imclone Systems**, **Roche**, **Merck**, **Amgen** and **Sanofi-Aventis**) with clinical cancer programs aimed at knocking out the IGF-1 receptor, all using monoclonal antibodies. Pfizer is leading the race with its monoclonal candidate having recently entered Phase III trials.

Antisense has the only known program that is looking at not blocking the IGF-1 receptor on the outside of cancer cells, but by preventing the production of IGF-1 within the cell, which is how antisense drugs work. It possible that an antisense drug could work will in combination with an antibody drug to knock out the same downstream target.

Preclinical results

The study involved 10 mice. Human prostate cancer cells were implanted (subcutaneous) into all mice and then an antisense construct was injected into the bloodstream, either of ATL1101 or a control of scrambled antisense sequences.

Prostate cancer (androgen-dependent) is initially treated with androgen ablation. But when that therapy fails, it progresses to a very difficult and dangerous form called androgen independent (castration resistant) prostate cancer.

It this trial, although in mice, it comprehensively showed the potential of this type of therapy at a number of levels.

Firstly, ATL1101 was shown to slow down the rate at which the prostate cancer cells (LNCaP, which are sensitive to androgen ablation) progressed to the more serious castration resistant form. Secondly, it completely stopped the growth in the tumours when treated with ATL1101 with all mice, compared to growth in all of the control mice. And lastly, the trial showed that ATL1101 was significantly effective in reducing the rate of tumour growth over the control in the castration-independent prostate cancer cells (called PCS).

What also gave Antisense Therapeutics confidence in this program is a previous prostate cancer clinical trial conducted by another company, **Oncogenex**, which targeted the protein clusterin with another Isis made second generation antisense drug. Antisense Therapeutics' drug is also a second generation Isis made antisense drug. However, what was of particular interest is that in the Oncogenex trial, where the prostate had been removed in some patients undergoing antisense therapy, the prostate organ was found to have absorbed the Oncogenex antisense drug. One of the main issues with antisense drugs is delivery, and whether the target tissue takes up the drug compound.

Clinical trials with this drug candidate are expected to commence in 2010. Antisense may consider partnering this program earlier, depending of funding availability. At the end of September Antisense had $7.4 million in cash. The company has a capitalisation of $28 million.

Bioshares recommendation: **Speculative Hold Class B**

Business Strategies for Listed Biotech Companies Facing an Investment Markets Freeze

Shortly, many ASX listed life science firms will be releasing their quarterly cash flow statements. Approximately twenty companies have done so prior to the end of the month deadline that follows the close of the quarter.

Our expectation is that an increasing number of companies will be reporting cash positions that will be insufficient to meet their requirements for the next six months (until March 31, 2009). With capital markets closed for the foreseeable future, it is a moot question whether a number of listed biotechs (perhaps as many as twenty) will survive beyond June 30, 2009.

It is also worth noting that **Apollo Life Sciences** was placed under administration this week, following a period when the company sought unsuccessfully to re-finance the business.

So what options do biotech companies have in the face of what looks like the worst financial market conditions ever to hit the sector? There are several options available to companies with badly depleted cash positions, which are explored below and summarised in a table on the next page.

One key point worth noting is that time is of the essence; as more companies defer accepting the reality of imploded investment markets, the fewer and worse the options become.

1. Hybrid Cashflow and R&D Business

This familiar strategy revolves around the merger of an R&D biotech company with a reagents, manufacturing, contract research, agency services or other cash-generating business that have a strong domestic focus.

The principal advantage is that a cash generating business becomes a source of income that can support an R&D business through a funding drought.

A downside is that the terms of a merger may not favour the R&D business. However, the strategy is one that can possibly mean a product in development is kept alive.

There are some examples of hybrid businesses in Australia. For many years **Progen Industries** operated an agency services business and a contract manufacturing business alongside its drug development activities. Likewise **Agenix** (Agen Biomedical) operated several trading businesses alongside its Thromboview diagnostic program.

One problem with this strategy, however, is that life science trading businesses may also be set to experience some softening in trading performance.

2. Merger – Hibernation – Spin-out

This strategy involves a biotech effectively parking itself under the wings a better resourced and presumably larger firm. What makes this strategy somewhat unusual is that an agreement is struck that after a 2-3 year period the company re-lists when a more favourable investment climate returns. Importantly, the business is treated as a standalone unit. Upside for the friendly senior company would come in the form of investment gains.

It would be rare to see such a strategy adopted because there are very few cashed-up biotech companies capable of acting as strategic, let alone benevolent, investors.

The concept does attend to the challenge of preserving drug development assets and personnel in the one place for a period of time. Arguably, much of biotech is people-based and the loss of key human resources can result in the diminution and decay of drug and medical product assets in development.

3. Privatisation

In this situation the R&D focused biotech business is delisted. Ownership and management stay the same. However, cost savings occur because the company's listing fees and related compliance and investor relations costs disappear or are greatly diminished. The strategy might suit a company that has a development milestone pending that could include the receipt of income from a development partner. Another key advantage is that by 'going off the radar' certain commercial advantages could be hidden from view from potential competitors for a period of time.

There are limitations to taking a company private. Firstly investors lose one of the attractive features of a listed security: liquidity. But right now, liquidity for biotech stocks has plummeted. And the privately held company loses the opportunity to learn from market feedback, which can be negative and positive.

4. Sale as a Going Concern

A final strategy is to sell the businesses as it is in a fairly rapid fashion, subject to shareholder approval. The sale price might well be considered a fire-sale price, but that simply reflects the parlous conditions that ride over markets at present. While it might see the crystalisation of substantial losses, a marginally positive outcome could be that some cash becomes available for investors to re-invest elsewhere.

Summary

With a number of ASX listed biotech companies at risk in the short term, the boards of these companies face the unenviable task of not only canvassing these options mentioned above but also considering administration and wind-up.

It may be that for some companies, it is too late to do anything. However, a merger with a trading business may still be an attractive and realistic possibility for some companies in this current market climate.

Bioshares

Business Strategies for Listed Biotech Companies facing an Investment Markets Freeze

1. Hybrid Cashflow and R&D Business

Strategy: An R&D business merges with a reagents, manufacturing, contract research or agency services or other cash-generating business

Pros	Cons
• Access to cashflows that *may* support R&D or corporate overheads	• Diminishment of management focus
• Reduced governance and listing costs where two listed businesses are merged	• Decreased investment clarity for investors
• A broader business profile may enlist investors previously uninterested in pure R&D play	• Resource allocation conflicts can occur between the various business units
• Connection to trading businesses may tighten R&D focus	

2. Merger - Hibernation - Spin-out

Strategy: Company merges with a friendly senior company An agreement is struck that after a 2-3 year period the company is spun out when a more favourable investment climate exists. Businesses is treated as standalone unit

Pros	Cons
• Preservation of staff and corporate knowldge is obtained for 2-3 year period	• There are few if any companies in a position to act as friendly acquirors (as strategic biotech-aligned investors)
• Reduced governance and listing costs where two listed businesses are merged	• Acquiror must be comfortable with managing the cost of the business
• Acquiror business stands to benefit as investor	

3. Privatisation

Strategy: The R&D focused biotech business is delisted

Pros	Cons
• Significant reduction in public company compliance costs	• Shareholders now hold an illiquid asset
• Significant reduction in investor relation costs	• Foregoes positive aspects of public markets' feedback
• Reduced public visibility (ie going off the radar) may aid the development of a company's commercial position	• Limited pricing mechanisms exist to price the value of the business
• Private status may enhance partnering chances with a company that values a low public profile	• If biotech investment markets suddenly thaw, the company would not be in position to access those markets in the rapid and timely manner that is typical of equities markets

4. Sale as a Going Concern

Strategy: The company is marked for sale as a going concern

Pros	Cons
• Returns capital to shareholders for re-investment	• Crystalises losses/gains
• May see the release of some management and staff for employment in other businesses	• Potential loss of key staff and corporate knowledge
	• Likelihood of sale of business at price that significantly understates fair value in a 'normal' market

Cogstate Moves to Profitability

Another company in the sector that looks to have turned the corner into profitability is Cogstate. The company recently reported its best quarter result, generating sales of $2.0 million, a 170% increase over the previous corresponding quarter. The company is delivering good consistency in its revenue growth, with trailing 12 months revenue of $5 million. The falling Australian dollar has also been benefiting Cogstate with that benefit set to continue.

The company now appears to be a profitable business. Over the last 12 months it has generated a net operating cash flow of $0.5 million when the increases in debtors for the same period are included, which is a valid measure given the company has negligible bad debts to its business.

Cogstate provides cognitive testing services for pharmaceutical companies conducting clinical trials. Its clients are primarily top 20 pharmaceutical businesses and this business is expected to be unaffected by the current financial market turmoil.

The growth in the business has come from improved branding of the company's services and improved capabilities. In the last financial year the company was provided services for 37 clinical trials compared to just 17 in the previous year. In the first quarter of this financial year Cogstate has signed contracts to conduct 16 clinical trials, including one Phase III trial and four phase II trials, valued at $3.5 million.

A predictability is emerging with the company's business. The company has an order book valued at $3.1 million, with $2.2 million expected to be recognised as revenue in this financial year. The company is forecasting revenue in excess of $1.5 million for the current quarter with a profitable first half of this financial year. At 30 September the company held cash assets of $1.9 million with trade debtors of $1.5 million and liabilities of just over $550,000.

Potential market size for clinical trial cognition testing

As the company is aggressively growing the business, it is of benefit to look at the potential market size for cognitive testing in the clinical trial setting. The above table lists the number of drug trials registered with the National Institutes of Health in the US for central nervous system diseases and disorders. The disease categories below include those for which the Cogstate product has found regular use. Based on the estimated proportion of these disease categories that would use cognitive testing and the average cost of conducting these trials, we estimate the potential market for this service to be around $190 million a year.

The competition to the Cogstate product comes from pencil and paper tests and from competitors **The Brain Resource Company** (also listed on the ASX), **Cambridge Cognition**, **Cognitive Drug Research** and **Cogtest**.

Cogstate has continued to build its scientific profile. In addition to founder and neurologist Dr David Darby, neuropsychologist Professor Paul Maruff and Professor Peter Snyder, who was formerly with **Pfizer**, the company recruited CNS specialist Dr John Harrison in December last year who is highly recognised in cognition testing in the Alzheimer's disease field.

NIH registered CNS trials

Disease category	Phase I	Phase II	Phase III	Phase IV
Alzheimer's disease	29	36	21	22
Schitzophrenia	17	55	59	86
Depression	18	86	62	104
Insomnia	2	8	17	15
ADHD	1	14	16	35
Traumatic brain injury	10	30	42	25

Given the strong branding and improving capability, we estimate that Cogstate has the potential to build its sales to in excess of $30 million a year within the pharmaceutical testing market. The partnership with pharmaceutical services group **United Biosource Corporation** (UBC) entered into in July this year will allow Cogstate to bid for larger Phase III programs without expanding its clinical trials teams. In the last two years the company has only secured one Phase III trial contract. UBC will conduct the on-site assessments using the Cogstate product with data to be managed by Cogstate.

Cogstate is capitalized at $10.5 million. We anticipate continued strong growth with sustained profitability moving forward. Of interest to follow will be how the UBC partnership progresses, and whether the company successfully moves into larger Phase III trial contracts with its larger partner.

Bioshares recommendation: **Speculative Buy Class A**

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Bioshares Model Portfolio (24 October 2008)

Company	Price (current)	Price added to portfolio	Date added
Hexima	$0.70	$0.60	October 2008
Atcor Medical	$0.11	$0.10	October 2008
CathRx	$0.70	$0.70	October 2008
Impedimed	$0.70	$0.70	Aug-08
Antisense Therapeutics	$0.05	$0.07	Aug-08
Mesoblast	$0.88	$1.25	Aug-08
Cellestis	$2.18	$2.27	April 2008
IDT	$1.80	$1.90	March 2008
Circadian Technologies	$0.66	$1.03	February 2008
Patrys	$0.12	$0.50	December 2007
Bionomics	$0.25	$0.42	December 2007
Cogstate	$0.16	$0.13	November 2007
Sirtex Medical	$2.18	$3.90	October 2007
Clinuvel Pharmaceuticals	$0.26	$0.66	September 2007
Starpharma Holdings	$0.25	$0.37	August 2007
Pharmaxis	$1.66	$3.15	August 2007
Universal Biosensors	$0.66	$1.23	June 2007
Biota Holdings	$0.34	$1.55	March 2007
Probiotec	$1.24	$1.12	February 2007
Peplin Inc	$0.35	$0.83	January 2007
Arana Therapeutics	$0.83	$1.31	October 2006
Chemgenex Pharma.	$0.59	$0.38	June 2006
Cytopia	$0.11	$0.46	June 2005
Acrux	$0.70	$0.83	November 2004
Alchemia	$0.22	$0.67	May 2004

Portfolio Changes – 24 Oct 2008

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

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48 issues per year (electronic distribution): **$320**

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