ISSN 1443-850X

In this edition...
Times are tough and many stocks are experiencing price weakness. However, that also brings opportunity to investors who can discern quality investments. We focus attention on one stock in particular, Alchemia, that is worth buying on price weakness.
We also re-examine ChemGenex's Ceflatonin, which is emerging as a very attractive drug to treat Gleevec resistant leukemia. The more look, the more attractive this asset has become. Finally, we update readers on Acrux, and compare that stock with another company with activities in the transdermal drug delivery space, Phosphagenics.
The editors

Companies covered: **ACL, ACR, CXS, POH**

	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 (from 5 May '06)	-10.9%
Cumulative Gain	**148%**
Average Annual Gain	**22.1%**

Bioshares is published by Blake Industry & Market Analysis Pty Ltd. The company also provides market and company analysis of the Australian pharmaceutical and biotech industries for local and international funds management institutions, venture capital funds and other related industry groups. For further details contact David Blake (see details below).

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Individual Subscriptions (48 issues/year)
$320 (Inc.GST)
Edition Number 179 (11 August 2006)
ISSN 1443-850X

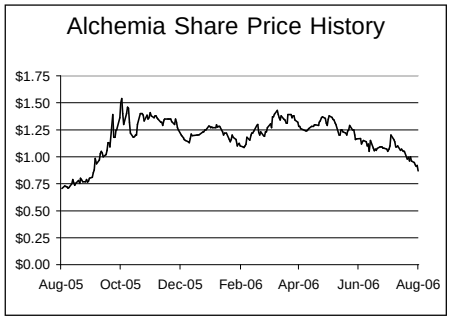
Bioshares

11 August 2006
Edition 179

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

Alchemia – Fundamentally a High Quality Stock; Use Price Weakness to Increase Exposure

Alchemia's (ACL: 87 cents) has weakened in recent weeks following recent sales figures released by **GlaxoSmithKline** for its synthetic heparin, Arixtra. In the second quarter of this year, Arixtra sales in the US fell slightly from US$12 million in the first quarter of this year to US$11 million in the last quarter.Alchemia will launch its generic version of Arixtra in the US in 2008.



Arixtra was launched at the end of 2004. It is into its second year and over the last 12 months has generated revenue of US$40 million in the US alone.Total sales for this period were US$70 million. GSK's Arixtra is attempting to take market share away from **Sanofi-Aventis**' Lovenox, which is generating in the order of US$3 billion of sales a year. It is worth noting the slow penetration of Lovenox when it was first released in 1993; after three years on the market (1995), Lovenox was generating sales of US$63 million in the US. However once the drug exceeded US$100 million of sales in the US market, sales ramped up very quickly and in 2002, Lovenox sales in the US exceeded US$1 billion.

Another point to note is that Arixtra has yet to be granted approval for the treatment indication of acute coronary syndrome (ACS). This constitutes approximately 30% of the heparin market and is where Arixtra has shown significant safety benefits over Lovenox in studies involving 20,000 patients. GSK is expected to received approval for ACS in the US by 2008, when Alchemia's generic version is anticipated to receive approval. It will take time for Arixtra to become included in existing guidelines for antithrombotic treatment with medical practitioners.

Bioshares maintains a firm **Speculative Buy Class A** recommendation on this stock. Within two years, Alchemia will be receiving 35 cents from every dollar of sales of its generic Arixtra in the US, which will be sold by APP. APP has a strong chance to obtain 50% market share in the US. It should also be launched in Australia in 2008, and can be sold in Europe in 2012 when market exclusivity for Arixtra ends. Alchemia is also investigating entry into the Chinese and Indian markets. Alchemia is capitalised at $122 million with $26 million in cash assets.

The Origins of Chemgenex's Ceflatonin

Chemgenex Pharmaceuticals (CXS: 46 cents) and its lead oncology drug, Ceflatonin, was recently covered in *Bioshares* (see edition 172). However with this compound potentially becoming an important drug for Chemgenex and also the Australian biotech sector, it's worth understanding the background of the development and the depth of development of this cancer therapeutic. Chemgenex has a number of other development programs, however, the focus in this article is on the Ceflatonin asset.

Ceflatonin origins from Chinese Medicine

Ceflatonin (homoharringtonine/HHT) has its origins from Chinese medicine. It is a natural plant extract from the evergreen tree *Cephalotaxus harringtonia K. koch var harringtonia* present in China. In the 1970s, researchers from China and the US extracted the active compound from the bark of this tree. The **National Cancer Institute** in the US conducted extensive testing with the compound and two companies, **Oncopharm** in France and **Stragen Pharma** in Germany, attempted to commercialise the drug, primarily for the treatment of chronic myeloid leukemia (CML). However when the drug Gleevec emerged in the late 1990s producing stunning results for CML achieving a complete hematological response (CHR) rate in CML patients of 96%, the development Ceflatonin quickly stalled.

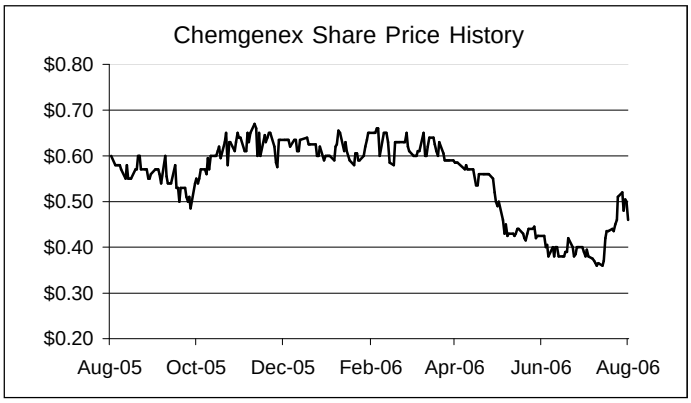
In 2001, Denis Brown, the founder of **Chemgenex Therapeutics** in the US (Chemgenex Therapeutics was acquired by the Australian biotech now renamed as Chemgenex Pharmaceuticals in 2004) realised there were resistance issues emerging with Gleevec and that a market for Ceflatonin may still exist. He gained access to the battery of data produced by the NCI and filed 'use' patents for Ceflatonin to be used in conjunction with Gleevec, and for use in patients who have developed Gleevec resistance.

Stragen an important alliance

In July 2005, Chemgenex secured the remaining portion of the intellectual property protection over Ceflatonin by forming an alliance with Stragen Pharma. Under the agreement, Stragen will manufacture Ceflatonin for Chemgenex and will receive 51% of profits from sales of Ceflatonin in Europe. Ceflatonin is manufactured through a semi-synthetic process and the access to this facility and process can not be underestimated. Stragen also has an established IP position over the manufacturing process and has also acquired IP from Oncopharm relating to Ceflatonin and follow-up analogues. Chemgenex maintains full rights to Ceflatonin outside of Europe. Importantly, the alliance has also removed a potential competitor for the company.

Patent position

Chemgenex does not have 'composition of matter' patents over Ceflatonin as researchers have been working on this compound for over 30 years. This does not prevent the company from establishing a protected franchise over the product. The highly successful oncology drug Taxol, extracted from the Pacific Yew tree, was developed by **Bristol-Myers Squibb** (BMS). In 2004 the drug generated sales of US$1 billion for BMS although was without composition of matter protection.



There are four granted patents that secure the Ceflatonin technology (US patent numbers 6,613,900; 6,734,178; 6,579,869; 6,987,103). Two of these patents were assigned to Stragen, one to Oncopharm and one to Chemgenex Pharmaceuticals). They cover the manufacture of Ceflatonin, analogues of Ceflatonin, the use of Ceflatonin in Gleevec resistance. The patents expire between 2019 - 2021.

The patents are supported by the Orphan Drug Status in the US and Europe awarded to Chemgenex for Ceflatonin. This certification delivers the company guaranteed seven years market exclusivity from market launch in the US against generic products and 10 years in Europe from the EMEA.

Path to market for Ceflatonin

Chemgenex is confident its current Phase II/III clinical trial underway with Ceflatonin will allow the company to be in a position to file for regulatory approval in the US at the end of 2007. This trial started in June this year and will enroll between 81 - 100 patients with CML who have what is termed a 'T315I bcr-abl point mutation'. Tyrosine kinase inhibitor drugs Gleevec and the recently approved Sprycel are ineffective against these mutations.

The approval of the BMS drug in June this year was an important event for Chemgenex. The drug Sprycel was approved as a second line therapy for patients with CML who have failed first line therapy, primarily Gleevec. What needs to be noted here is that BMS received 'accelerated approval' based on the surrogate markers hematologic and cytogenetic responses, not improvements in survival rates. There were also no control groups in the registration trials.

Chemgenex is following a similar trial design structure with its Phase II/III trial in 81 - 100 patients, using the same surrogate markers and no control group, as there are no alternative treatments available to patients with the T315I mutation. BMS presented efficacy data from four Phase II trials to gain approval which involved 445 patients. Whether Chemgenex's 81 - 100 patient trial size will be sufficient to gain FDA approval is uncertain, although the company has structured its trial following discussions with the FDA.

Cont'd over

The priority for Chemgenex is to gain regulatory approval for Ceflatonin for one indication and to continue to publish data on Ceflatonin from trials in other indications. These include in patients with CML in combination with Gleevec, in patients resistant to Gleevec, in patients with AML (acute myeloid leukemia) and MDS (myelodysplastic syndrome).

Once Ceflatonin is approved for one indication (CML), it will be able to be used 'off-label' for other indications by oncologists if there is published data available that supports its use. In 2005, Novartis generated sales for Gleevec of US$2,2 billion, although a considerable portion of this was from off-label use of Gleevec.

Competition

There are other drugs in development that seek to address Gleevec resistance, in particular, due to the T315I mutation. It's worth noting a deal that Novartis (which markets Gleevec) signed with **SGX Pharmaceuticals** (see Table, Bioshares edition 170 p3). SGX received US$25 million under a licensing and collaboration agreement that will give Novartis access to the company's CML drug that treats drug resistant mutations to Gleevec, including the most challenging T315I mutant. The total deal value is worth up to US$515 million.

Market Size

As a second line treatment, the BMS drug Sprycel is expected to generate sales in 2008 in the order of US$500 million. About 20% of CML patients treated with Gleevec develop the T315I mutation. There have also been recent reports linking Gleevec treatment with heart failure, published in the recent edition of *Nature Medicine*, that may encourage combination therapy with this drug at lower doses. We estimate the potential market size for Ceflatonin at initially US$150 million, increasing to as high as US$500 million as the pool of Gleevec resistant patients grows and as other Ceflatonin is expanded to treat other indications.

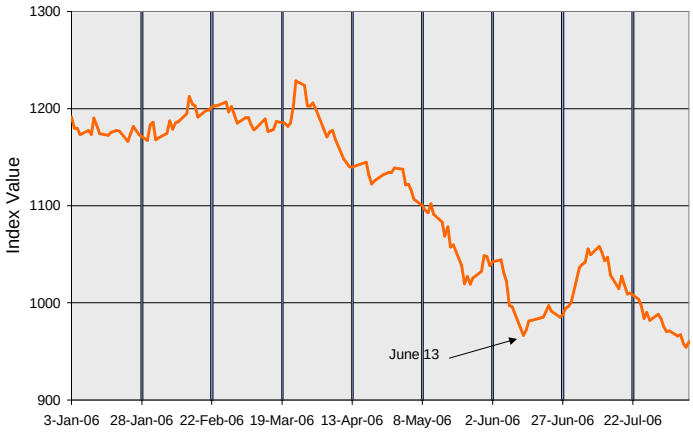
Recommendation

Chemgenex has systematically secured access to a oncology drug that can potentially become a very valuable asset for the company. A substantial amount of data has been generated with Ceflatonin and the company is hopeful it will be in a position to file for regulatory approval for this drug by the end of 2007, pending positive results from the current registration trial now underway. Chemgenex is capitalised at $70 million with $15 million in cash.

Bioshares Model Portfolio (11 August 2006)

Company	Price (current)	Price added to portfolio
Acrux	$0.83	$0.83
Agenix	$0.18	$0.22
Alchemia	$0.87	$0.67
Avexa	$0.245	$0.15
Biolayer	$0.13	$0.195
Bionomics	$0.16	$0.210
Biosignal	$0.22	$0.22
Cytopia	$0.720	$0.46
Chemgenex Pharma.	$0.46	$0.38
Evogenix	$0.480	$0.47
GroPep	$1.46	$1.43
Optiscan Imaging	$0.515	$0.35
Neuren Pharmaceuticals	$0.45	$0.70
Pharmaxis	$1.93	$1.90
Prima Biomed	$0.065	$0.09
Sirtex Medical	$2.30	$1.95

The Bioshares 20 Index



Change from June 30, 2006	**-4.0%**
Change - week ago	**-1.1%**
Change - 13 June (Low)	**-0.7%**

Recent Developments at Acrux

Acrux (ACR: 83 cents) has moved forward positively on several fronts recently. Acrux is a Melbourne based developer of transdermal drug delivery technology that originates from Monash University.

Business development focus

The company has strengthened its business development focus with the elevation of Nina Wilkins, and the appointment of Hugh Alsop, to the positions of Directors of Business Development. Alsop was formerly with **Mayne Pharma** and **Sigma** and will focus on the EU, Asia and South Africa, and Wilkins will focus on Australia, the USA and Japan. Alsop brings to the position a set of established business relationships in Europe and an established track record in deal making and completion. However, business development activities will be also shared and jointly conducted with the recently appointed CEO, Richard Treagus.

Evamist and Vivus

This newly formed team is also expected to devote careful attention to, and nurturing of Acrux's relationship with **Vivus**, which is developing Evamist (transdermally delivered estradiol for treatment of symptoms of menopause). Evamist is expected to be submitted for marketing approval by the end of September, and gain marketing approval in 2007. Another development with respect to Evamist is that Acrux now has access to New Drug Application (NDA) data that allows Acrux to move ahead with licensing the product for Australia and New Zealand.

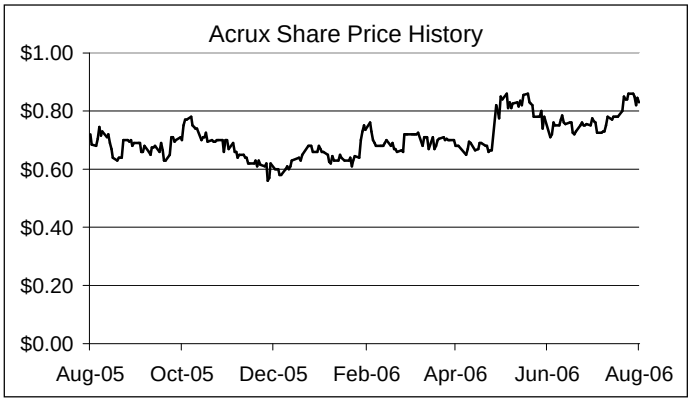
Testosterone

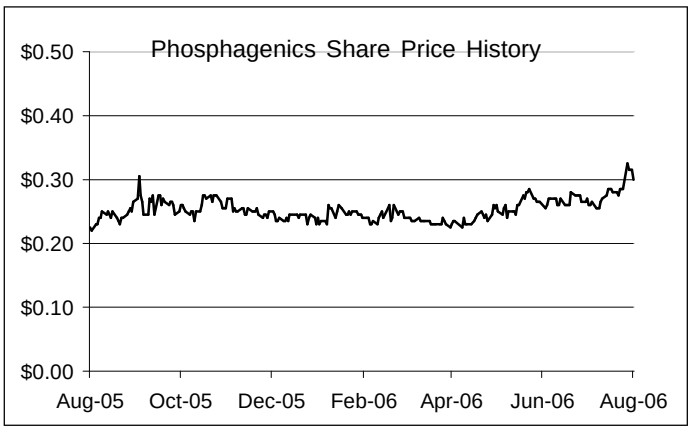
Vivus is also developing, under licence from Acrux, transdermally delivered testosterone for treatment of decreased libido in women. Vivus will file an IND for this product in the next week or so, with a Phase II study expected to commence in September.

Investors should keep in mind that Phase I, II and III phase clinical trials of drug delivery technologies, using known active pharmaceutical ingredients/chemicals, are vastly different, in terms of time, cost and overall risk, to trials conducted for new chemical entities and new therapies.

Nestorone

Another development announced by Acrux, concerns Nestorone, a fourth generation progestin contraceptive. In February 2006, Acrux licensed the world-wide rights to Nestorone from the **Population Council**, for use with Acrux's metered dose skin spray technology (MDTS). Acrux has now changed its plans to develop a Nesterone only MDTS product, including commencing a Phase II trial this year. Instead it will develop a suite of combination spray products and commence a clinical trial in 2007. The commercial argument is that the Nesterone only products represent only 4% of the US$4.4 billion global contraceptive market, and that such a product modification greatly increases the scope for Nesterone, or Nesterone plus other contraceptive MDTS products.





Although Acrux has experienced turbulence this year, it appears the company regained its composure and looks to be moving forward with a strong sense of purpose and focus.

Other transdermal companies

There are several other ASX companies that are developing transdermal drug delivery technologies. One that is a potential benchmark company is Melbourne based **Phosphagenics**, which is exploiting the phosphorylation (the adding of phosphor groups) of various chemical entities, such as morphine and insulin, to enable transdermal (across the skin) delivery of drugs. Phosphagenics is also developing and marketing (through partners) various nutraceutical applications of its proprietary phosphorylation technology.

History of Phosphagenics

Phosphagenics (POH: 30 cents) was formerly known as the investment company, **Greenchip Development Capital**, which changed its name to **Vital Capital** in April 1999. For a period it was registered as a Pooled Development Fund, but rescinded that status in December 2004. One of its first investments as Vital Capital was in **Tocovite Pty Ltd**, which was established in January 1999. Vital Capital's initial 25% stake was booked at $800,000, valuing Tocovite at the time at $3.2 million. Tocovite was renamed **Vital Health Sciences** (VHS) in August 2002.

On January 29, 2004, a general meeting of Vital Capital shareholders agreed to change the company's name to Phosphagenics

Cont'd over

and buy out the 63.33% stake in VHS it did not already have through a swap of Phosphagenics shares.

Comparing Acrux to Phosphagenics

Acrux is capitalised at $112 million. However, if cash held by the company is subtracted, a technology valuation of $92 million implied.

Phosphagenics is capitalised at $164 million. We estimate that the current cash at hand (at June 30) is a little over $11 million. An implied technology valuation for Phosphagenics cannot be derived by simple subtraction of cash from capitalisation because the company's nutraceutical asset has matured into an income generating division.

Phosphagenics' Nutraceutical business

However, the value of the nutraceutical business, or assets is an important point. Where once the division may have represented significant potential value, its current value has been severely diminished through setbacks that have occurred in the market for Vitamin E dietary supplement markets in the US.

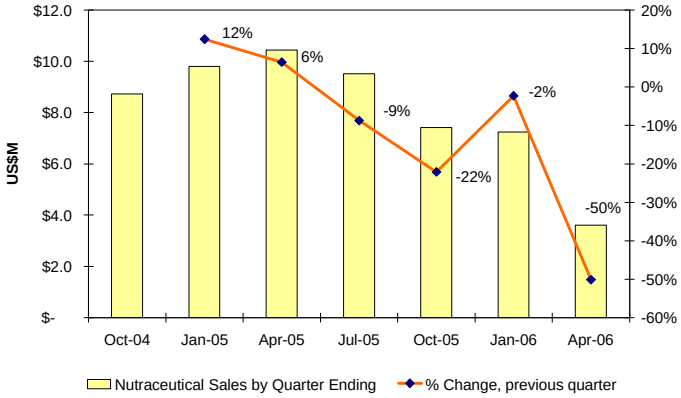
In October 2003, Phosphagenics licensed its tocopheryl (Vitamin E) phosphate technology to the listed US company, **Zila Inc** for exclusive rights in the human dietary supplement markets in the USA, Canada and Indonesia. The agreement was initially for a five year term, but included unilateral extension rights. Zila is also required to pay minimum annual royalty payments to Phosphagenics.

Company	**Acrux**	**Phosphagenics**
Code	ACR	POH
Date founded	19-Mar-98	21-Jan-99 (as Tocovite)
Date listed	29-Jul-04	29-Jan-04 Date gained 100% ownership through re-structure
Years established before listing	6	5
Years established	8.4	7.6
Shares (M)	135	547
CMP	$0.83	$0.30
Capitalisation ($M)	$112	$164
Cash June 30 (POH estimated) ($M)	$19.5	$11.2
Value Assumption - Nutriceuticals Business (Low) ($M)		$10
Technology Value ($M)	$92	$143
Value Assumption - Nutriceuticals Business (High) ($M)		$20
Technology Value ($M)	$92	$133
ACR discount to POH	**-31%**	
POH premium to ACR		**44%**
Funding - ACR IPO onwards; POH (2003-05) ($M)	$28	$23
Staff (EFT) (Num.)	40	<15 (est)

Troubles at Zila

However, recent sales of Vitamin E products slumped because of the lagged effect of the dissemination of a view presented at the American Heart Association conference in November 2004 that certain high doses Vitamin E of could be harmful. Sales from Zila's nutraceutical division totalled US$29.8 million for the nine months ending July 2005. For the nine months ending April 2006, sales had fallen 39% to US$18.3 million. Sales for the three months ending April 2006 were US$3.6 million, a 50% fall from the previous quarter. It must be noted that Zila's financial statements to not make a distinction between sales of Vitamin C and Vitamin E products, nor what sales emanated from undifferentiated Vitamin E products and the differentiated Vitamin product derived from Phosphagenics' technology.

Nutraceutical Sales - Zila Inc; Last 7 Qtrs



To date, Phosphagenics has received royalties of $1.5 million, booked to its calendar financial year of 2005. We assume these royalties would by and large relate to its relationship with Zila and be paid by Zila in arrears. They are likely to reflect sales activity before the widespread slump in Vitamin E sales set in. We do not know what minimum royalty payments Phosphagenics is entitled to and it would be surprising if any royalty income due from Zila exceeded any amounts received to date.

Implications for Phosphagenics

Zila is under some financial stress and has since announced plans to divest its nutraceutical division. The implications for Phosphagenics is that a major revenue stream has not only been dampened considerably, but future entitlements may be difficult to obtain. In addition, the company may have to seek a new marketing partner. Therefore, this part of Phosphagenics

Cont'd over

nutraceutical business has deteriorated in value considerably. In addition the company has not yet described any revenues flowing from its arrangement with **International Specialty Products**, which is the global distributor of Phosphagenics' personal care active ingredient, Vital ET. Sales may eventuate, however, the uptake for this ingredient has been slow, and the clear sense of value for this application in personal care market has yet to be confirmed.

In April 2006, Phosphagenics reached an agreement with **Nestle Nutrition** for the rights for to use phosphated tocopheryl as an additive in its food products. Despite this agreement, no products have yet been defined and it is too early to attribute any value of significance to this relationship.

Therefore, our conclusion (with out the benefit of more detailed sales and royalty income figures) is that the value of the nutraceutical division is probably worth somewhere between $10 million and $20 million. Deducting the greater of these figures generates an implied technology value for Phosphagenics' drug delivery and human therapeutic assets based on phosphorylation of $133 million.

If Phosphagenics implied technology value is assumed to be fair value, there are several arguments to be made that Acrux's 30% discount to Phosphagenics is unwarranted.

Acrux and Phosphagenics
- Points of similarity

Both companies were founded at a similar time (Acrux - March 1998, Phosphagenics as Tocovite - January 1999) and could be said to have listed at a similar time

Both companies are targeting a range of transdermal drug delivery markets that in aggregate represent significant established markets

Orbis Funds Management has invested heavily in both companies (ACR 12 %, POH 11 %)

Both companies have a comprehensive patent portfolio, with key patents granted in key jurisdictions, with similar times to expiration

Points of difference

1. Staff and depth in management

While both companies have engaged in the transition of senior management in the last 12 months, Acrux is better supported in terms of experience in its management ranks and overall staff numbers at Acrux of 40 personnel exceed our estimate of less than 15 at Phosphagenics. An issue for Phosphagenics is that has less collective experience in transdermal drug development and clinical trial management.

2. Stage of development

Acrux's technology is much further developed and validated than Phosphagenics. Vivus, Acrux's US marketing partner for Evamist (transdermally delivered estradiol for treatment of symptoms of menopause) is expected to submit a marketing application in the September quarter, 2006, with a marketing approval gained in 2007.

Alza, a business of **Johnson & Johnson** entered into an evaluation agreement with Phosphagenics in November 2005. Should Alza enter into a licensing agreement with Phosphagenics then the value of Phosphagenics drug delivery assets would be strengthened considerably. However, a licensing agreement is not guaranteed and the ability of Phosphagenics license the technology on the most favourable terms may be an issue going forward.

Another important point to note is that Acrux's technology is a comprehensive assembly of dermal penetrations and enhancers coupled to a metered dose delivery device. The result is a package capable of achieving higher royalty rates. In contrast, Phosphagenics' technology is a more simple chemical enabler, which more than likely would need to wrapped up with other drug delivery technologies that govern dose, formulation, release and administration. A concomitant effect would be lower relative royalty rates and a longer time to market as the optimal drug delivery system would have to be devised followed by clinical trials. (For example, questions to be resolved would be whether transdermal insulin would be better delivered with a patch, or if delivered as a gel, how would the optimal dose be formulated and what would be the best site of administration, what formulation would work best for self administering children?)

3. Funding risk

While all biotech companies are subject to funding risk, there are always relative differences. Phosphagenics' funding position has been dented by setbacks at Zila, and the company may need to raise funds in the next twelve months, if a licensing deal with Alza does not eventuate. We estimate the company's annual net burn rate to be $5.5 million, which implies a cash balance in twelve months of $5.7 million. The company has been funding a number of cell based and pre-clinical studies in the areas of insulin, artherosclerosis and cancer, and the advance of projects these human studies will place increased demands on its cash resources.

Although Acrux also has, like Phosphagenics slightly more than two years of cash at hand, it anticipates receiving US$4 million (within the next 12-18 months) from Vivus for the filing and marketing approval of Evamist.

Summary

Australian biotech investors have, in the form Acrux and Phosphagenics, the rare opportunity to assess two investments on a reasonably comparable basis. Should investors choose to use Phosphagenics as a 'normal' value, then a range of arguments exist that suggest that Acrux is undervalued by at least 30 percent, or could certainly command a premium to that part of the Phosphagenics business involved in drug delivery.

Bioshares recommendation:
Acrux - **Speculative Buy Class A**
Phosphagenics - **Under review**

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

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