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In this edition...
The last 12 months has been a year of deal making for Australian biotechs. The common theme is that most are going away from dealing with Big Pharma. Tissue Therapies was first, then QRxPharma, and the latest is Bionomics with its deal with Ironwood Pharmaceuticals. It's a very good deal for a number of reasons.

Another group of companies have progressed their clinical programs, with Viralytics, Alchemia and Circadian all commencing cancer drug studies recently.

The Editors
Companies Covered: ACG, ACL, BNO, CGS, CIR, VLA

	Bioshares Portfolio
Year 1 (May '01 - May '02)	21.2%
Year 2 (May '02 - May '03)	-9.4%
Year 3 (May '03 - May '04)	70.0%
Year 4 (May '04 - May '05)	-16.3%
Year 5 (May '05 - May '06)	77.8%
Year 6 (May '06 - May '07)	17.3%
Year 7 (May '07 - May '08)	-36%
Year 8 (May '08 - May '09)	-7.3%
Year 9 (May '09 - May '10)	49.2%
Year 10 (May '10 - May'11)	45.4%
Year 11 now commenced	-23.0%
Cumulative Gain	**224%**
Av. annual gain (10 yrs)	**21.2%**

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Bioshares

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

Bionomics Signs Licensing Deal with Ironwood Pharmaceuticals

Bionomics (BNO: 48 cents) has signed a research and licensing deal for its second lead program, BNC210, for the treatment of anxiety. The deal is not with a major pharmaceutical group, but with a smaller drug development company, **Ironwood Pharmaceuticals**. The deal involves a US$3 million upfront payment to Bionomics, a further US$10 million in the first two years, and a total potential deal value of US$345 million for upfront payments, milestone payments and research payments. It's not the big upfront biotech deal investors were hoping for but it's still a very good deal for Bionomics for a number of reasons.

There are three reasons why this is a good deal for Bionomics. The first is that Ironwood is a very suitable partner for Bionomics. Ironwood appears to be an aggressive biotech company on the cusp of commercial success. Its lead candidate, Linaclotide, has been recently submitted for regulatory approval in the US and Europe for the treatment of irritable bowel syndrome and constipation. Ironwood may use some of the same sales force for Linaclotide to market BNC210 to high prescribing general practitioners if it gets BNC210 to market.

There are also advantages in dealing with a smaller company over a large pharmaceutical company including potentially a more expedient progression of the BNC210 clinical program. Bionomics CEO Deborah Rathjen believes there is an alignment in entrepreneurial culture between the two companies.

On the downside, if Ironwood stumbles, for instance with its lead program with Linaclotide, and more finances need to be invested into that program, then this could adversely affect the BNC210 program.

The second reason that this is a good deal for Bionomics is that Ironwood is committed to investing $60 million a year in the BNC210 program. According to Mark Currie, Ironwood's head of R&D, this is a high priority program for Ironwood.

Ironwood will pay for all of the development costs associated with BNC210 going forward. Ironwood will conduct another Phase I trial with BNC210 this year with a more specific group of subjects. A phase IIa trial could start as early as the end of this year. It will take several hundred million dollars to bring BNC210 to market and Ironwood will be well placed to fund this program if Linaclotide becomes a very successful product for it. BNC210 could get to market as early as 2019.

The third reason this is a good deal is that it appears Bionomics will receive a very good royalty from future sales. As late as October last year, Bionomics was hopeful it could transact a deal that would yield in the order of a US$50 million upfront payment, highlighting another comparable drug development deal between **Amgen** and **Johnson & Johnson**. That deal, also for a compound to potentially treat anxiety and depression, had

just completed Phase I trials. The milestone payments totalled US$385 million, similar to the BNC210 deal.

Royalty Rate

Without knowing the precise royalty Bionomics has negotiated, we would suggest Bionomics has traded a large upfront payment for a higher royalty fee. Rathjen indicated the company was targeting a mid-teens royalty rate and was very pleased with the outcome. It appears there was the interest but not yet sufficient evidence about the drug capability of BNC210 to transact a larger upfront licensing deal.

Bionomics will receive its set royalty from future BNC210 sales regardless of which company sells the drug, for instance if Ironwood is acquired by a larger pharmaceutical group. Rathjen would not comment on whether the royalty rate was on a sliding scale, depending in sales. Its potential milestone payments are not linked to future sales.

The trials for BNC210 will be large, with Phase IIb trials likely to involve around 1,000 patients. Ironwood has experience in running such trials, with one of the Linaclotide trials involving 3,000 patients.

For Ironwood's Linaclotide trial, Ironwood has has successfully developed the subjective patient reported outcomes approach to measuring efficacy. Rather than using biomarkers, Ironwood used feedback from patients, with around 60 endpoints used and all being successful. In will look into using a similar approach with BNC210 following consultation with the FDA.

Ironwood has a market value of US$1.4 billion and it last reported having US$175 million in cash.

BNC105 Timeline

Bionomics is seeking to complete its Phase II renal cancer trial BNC105 by the end of 2012 with results out in the first half of 2013. The company will now wait until those results are in before it seeks to partner the program. Its Phase II study with the drug in ovarian cancer is expected to start by mid year.

Bionomics is capitalised at $166 million. It had $18.9 million in cash at the end of September.

Bioshares recommendation: **Speculative Hold Class A**

Bioshares

Atcor Strikes Alliance with SunTech Medical

Atcor Medical (ACG: $0.09), the non-invasive central blood pressure monitoring company, has established a product development collaboration with **SunTech Medical**, a manufacturer of blood pressure monitoring devices. The alliance will seek to develop a product that incorporates Atcor's central blood pressure technology.

SunTech's expertise lies in blood pressure monitoring devices used in the ambulatory setting and for 24 hour monitoring as well as for general blood pressure monitoring. UK-registered SunTech is a privately-held OEM manufacturer supplying either blood pressure algorithms, sub-assemblies, or badged products to more than 75 companies.

Atcor Medical had previously signed as distributor of SunTech's products into the pharmaceutical research market, a market in which SunTech had no presence but one in which AtCor has built a presence with its central blood pressure measurement product and services.

Atcor has indicated a new SunTech product may be available in 2012 H1, or at least advanced details will be available in that period.

Revenue arrangements for the alliance will be shared according to market boundaries, with Atcor capturing revenues from sales in the pharmaceutical research (clinical trials) market and SunTech in its existing market.

The tie-up with Suntech as a distributor and new product partner should improve Atcor's sales reach giving it a foot in the door to present its central blood pressure technology products to customers while it sells brachychial (cuff) based products sourced from Suntech. The tie-up also means, as we see it, that both parties can sell a product that can measure both central and brachyial blood pressure, with the potential to power sales by categorically demonstrating the variation of blood pressure that occurs between both places, increasing the confidence of medical practitioners who are less familiar with the arguments for central blood pressure measurement.

The alliance was initiated by Atcor Medical on the back of the distribution deal signed in July 2011.

AMA Coding Update

Atcor Medical has been pushing ahead with the gaining of a Common Procedural Terminology (CPT) code from the American Medical Association. Such codes are needed for reimbursement purposes. A submission regarding the use of the Sphygmocor device for managing complex hypertension was made in November 2011 so that it that it could be considered at the February meeting of the AMA's special CPT committee (the Editorial Panel). The submission was made by the Renal Physicians Association, as companies do not do this directly.

If granted a CPT I code, the code would then become applicable from January 1, 2013. If granted a CPT III code (made available for new and emerging technologies) it would become available from July 1, 2012. Responses to submissions are made in May of each year.

A complicating factor with the granting of the CPT III code is that it must progress through what is called the RUC (or Relative Units Committee) which defines the relative value in units of a physicians time and experience in performing a test or procedure or treatment which is then linked to a recommended level of payment.

In parallel with gaining a CPT code, Atcor will also manage the task of gaining coverage from health insurance providers. In the longer term, achieving a specific CPT I code and payment coverage would allow Atcor to generate significantly greater revenues from its Sphygmocor product than what is does now from sales into the clinical trials market.

Summary

Atcor has booked contracts worth US$4 million this financial year. Other contracts are in the pipeline, however, progress in executing agreements is slow. Atcor recorded sales of $7.5 million in FY2011 However, meaningful revenues from the SunTech arrangement are not expected to occur until FY2013.Atcor is capitalised at $12 million.

Bioshares recommendation: **Speculative Buy Class B**

Bioshares

Cogstate Reports Record Sales for First Half

Cogstate (CGS: 25 cents) has delivered a cracker of a half year. Sales for the first half of this financial year were $6.9 million, which we estimate should see it generate a profit before tax of around $2.6 million for the half, excluding any foreign exchange losses or investments in its Axon Sports venture, of which the company now owns 100%.

The company had just under $3.5 million in cash at the end of December with a further $3.6 to be collected from its debtors. Its liabilities were only $1.6 million, which should leave it with $5.5 million in cash.

It's been an unusually strong half for the company and that growth is unlikely to be sustainable. But it sets the company up for a very good profit result for the full year. The company has also hedged much of its income into Australia (after US costs) around $1.00 for 2012, which will cap the negative impact from a strengthening Australian dollar.

Events to look out for outside its core clinical trials cognitive testing work are progress in the Axon Sports product, which is a concussion management tool, and more importantly licensing arrangements of its cognitive test as a tool for broad population dementia screening.

Cogstate is capitalised at $19 million.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Three Clinical Trials Commence: Alchemia, Circadian & Viralytics

Three companies have initiated clinical trials this month with all three trials representing important advances for the companies concerned, as well offering the chance to provide clinical data that investors are likely to respond to.

Alchemia – HA-Irinotecan, 390 Pts, Phase III

Alchemia (ACL: $0.33) announced that its first of 390 subjects in its Phase III trial of HA-irinotecan commenced treatment at the beginning of January.

There is an established treatment regime for second and third line metastatic colorectal cancer which combines irinotecan with leucovorin and 5FU, better known as FOLFORI. Alchemia will compare FOLFORI with its formulation of irinotecan that has been embedded in hyaluronic acid, in addition to leucovorin and 5-FU.

The potential advantages of HA-irinotecan are that side effects (e.g. nausea) from irinotecan could be reduced and that efficacy is increased due to HA's preference for binding with CD44 receptors that are highly expressed on cancer cells. A further benefit occurs from the more efficient delivery of irinotecan into the cell. Irinotecan is a topoisomerase I inhibitor, which means it an interferes with cell DNA.

The endpoint for the trial is progression free survival (around 2013 Q3) when about 350 patients will have been treated.

The trial will recruit from 55 sites in Australia and Eastern and Western Europe, with 27 sites active so far.

Alchemia has received advice from both the FDA and the EMA that only one Phase III trial may be required to support a registration application.

In one respect the trial is a proof-of-platform trial since a number of other anti-cancer agents could also be combined with HA.

Alchemia is capitalised at $92 million. It raised $20 million net of costs in late 2011.

Circadian – VGX-100, 40 Pts, Phase I

Circadian (ACL: $0.54) had hoped to initiate its first in human trial of its own VEGF-C monoclonal antibody in 2011. However, the first monotherapy phase of the trial is now finally underway at the **MD Anderson Cancer Center** in Texas.

The novelty with this trial is that despite its Phase I status it will combine two anti-angiogenesis inhibitors, being Circadian's VEGF-C monoclonal antibody with **Genentech**'s Avastin, a VEGF-A monoclonal antibody. This combination phase of the study will commence in 2012 Q3.

A pre-clinical xenograft study showed that VGX-100 combined with Avastin reduced tumour burden by 42% compared to a control at 49 days post-implant, and by 33% compared to Avastin alone.

While the trial will evaluate VGX-100 across a range of tumour types, the planned indications for the drug include glioblastoma (aggressive malignant brain tumours) and metastatic colorectal cancer. It is also expected that VGX-100 would ultimately be administered alongside anti-angiogenic agents such as Avastin, Nexavar and Sutent.

Although patient numbers are small but typical of a Phase I program, the trial can be expected to yield meaningful data on the reduction in tumour burden.

The trial should be completed by December 2012.

Circadian is capitalised at $25 million and retained cash of $18.5 million at December 31, 2011.

Circadian shares have gained ground this month, rising 20% since the close of the last quarter.

Cont'd over

Company	Therapeutic Agent	Indication	Phase	Pts	Est. Data Complete Date	Design	Primary endpoint	Secondary endpoints
Alchemia	HA-Irinotecan	Metastatic colorectal cancer (2nd and 3rd line)	Phase III	390	Jan-14	Randomised, double blind; **Treatment arm**: HA-Irinotecan + 5FU+ leucovorin; **Comparator arm:** Irinotecan + 5FU+ leucovorin	Progession Free Survival (assessed when 350 pts treated ~ 2013 Q3)	Safety (diarrhea and hematology)
Circadian Technologies	VGX-100 (VEGF-C monoclonal antibody)	Advanced or Metastatic Solid Tumours	Phase I	40	Dec-12	Open label, dose escalation, alone and co-administered with bevacuzimab (Avastin)	Safety	Tumour response (measured by MRI)
Viralytics	CAVATAK (wild type Coxsackievurus A21)	Stage IIIc or IV melanoma	Phase II	63	Dec-13	Single arm; 10 intratumoural injections	Immune-related PFS at 6 months	Durable response rate at 6 months; 6 mo PFS, 1 yr OS, safety, QoL

Company	Price (current)	Price added to portfolio	Date added
QRxPharma	$1.55	$1.66	October 2011
Mayne Pharma Group	$0.345	$0.435	September 2011
Genetic Technologies	$0.14	$0.18	August 2011
Acrux	$3.36	$3.37	June 2011
Bioniche	$0.72	$1.35	March 2011
Somnomed	$0.98	$0.94	January 2011
Phylogica	$0.042	$0.053	September 2010
Biota Holdings	$0.83	$1.09	May 2010
Tissue Therapies	$0.38	$0.21	January 2010
Atcor Medical	$0.09	$0.10	October 2008
Impedimed	$0.56	$0.70	August 2008
Bionomics	$0.48	$0.42	December 2007
Cogstate	$0.25	$0.13	November 2007
Sirtex Medical	$4.74	$3.90	October 2007
Clinuvel Pharmaceuticals	$2.30	$6.60	September 2007
Pharmaxis	$1.02	$3.15	August 2007
Universal Biosensors	$0.76	$1.23	June 2007
Alchemia	$0.330	$0.67	May 2004

Portfolio Changes – 27 January 2011

IN:
No changes

OUT:
No Changes

Viralytics – CAVATAK, 63 Pts, Phase II

Viralytics (VLA:$0.37) has commenced its IND-backed Phase II trial of its novel cancer therapy CAVATAK. The trial will enrol 63 patients with Stage IIIc or IV malignant melanoma.

CAVATAK therapy involves the injection into tumours of doses of wild-type Cocksackievirus strain A2, a virus that has a wide distribution in human populations and is relatively benign. The virus binds to several receptors highly expressed on cancer cells, triggering destruction of the cell and secondly conditioning an immune system response against the cells.

The appeal of the technology is the potential to greatly reduce side-effects relative to many other cyto-toxic therapies.

The Phase II trial is not a randomised trial which will see CAVATAK compared to another agent. However, the primary endpoint will measure immune-related progression free survival at six months. This is an important design point, since it is a new endpoint criteria which recognises the immunotherapeutic character of the treatment. Immune-related criteria consider changes in net tumour burden across different points in time (as opposed to a single point in time compared to base line), to more accurately reflect the kinetics of the effects of immunotherapies on tumours.

Viralytics expects to utilise six US sites for the trial with two recruiting at present.

Final data from the trial is expected to be obtained by December 2013.

The trial will provide the most valuable data to date for Viralytics' virotherapy asset by providing an indication of the efficacy of the technology from a more statistically relevant group of patients. Two other trials underway involve much smaller numbers (nine patients each) consistent with trials being run to explore safety parameters.

Viralytics is capitalised at $27 million and retained cash of $4 million at September 30, 2011, but raised $4.7 million from a share purchase plan completed in December, 2011.

Bioshares recommendations:
ACL - Speculative Buy Class A
CIR - Speculative Buy Class B
VLA - Speculative Buy Class B

Bioshares

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. For both groups, the rating "Take Profits" means that investors may re-weight their holding by selling between 25%-75% of a stock.

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, Starpharma Holdings, Cogstate, Bionomics, Circadian Technologies, Biota Holdings, Impedimed, QRxPharma, Patrys, LBT Innovations, Mesoblast, Atcor Medical, Tissue Therapies, Viralytics, Phosphagenics, Immuron, Phylogica, Bluechiip, pSivida, Antisense Therapeutics, Benitec BioPharma, Allied Healthcare Group, Genetic Technologies

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