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In this edition...
Biotech companies in Australia have lost a key funding support from the Federal Government through following the first budget from the Rudd Government. We look at the impact Government funding has had on the sector and the implications of that decision for Australian biotechs going forward.
The pharmaceutical industry is struggling to find enough new chemical entities. Generic margins will continue to fall. But the gap in the middle leaves room for companies developing improved chemical entities, such as Halcygen Pharmaceuticals. We take a look at developments with that company. And like many smaller biotechs, Healthlinx, which is developing a much needed diagnostic for ovarian cancer, is moving through a difficult but crucial funding round.

The editors
Companies covered: HGN, HTX

	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)	-1.00%
Cumulative Gain	**106%**
Av Annual Gain (7 yrs)	**17.8%**

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Bioshares

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

Commercial Ready Program Axed – What it Means for Biotech

The Rudd Government delivered its first budget on May 13 2008. One move that has clearly shocked the biotech sector was the axing of an industry support program, the Commercial Ready scheme. The scheme has provided direct assistance to many small-to-medium sized Australian companies looking to progress products and services they have developed towards commercial outcomes. The budget papers marked the axing of the CR program as contributing a saving of $700 million up to 2011-12. The program, which was announced in 2004 by the Howard Government, had been expected to provide over $200 million per year in matching grants to program recipients. Successful applicants received up to 50 cents for each dollar they spent on eligible activities.

The Commercial Ready program replaced the R&D Start program, the Biotechnology Innovation Fund (BIF) and elements of the Innovation Access program. The R&D Start program offered matching funding, but maximum grant size was reduced under the CR program, from $15 million to $5 million. The R&D Start program commenced in 1996 and was changed in July 1998 to allow larger companies to participate. It concluded in September 2004. The Commercial Ready program began in October 2004.

From 1996 to 2007, $1.365 billion in funds had been provided through the R&D Start grant program. *Bioshares* has not been able to gain access to all AusIndustry R&D Start grant data, but since FY2000, we have calculated that $1.396 billion of federal funds have been approved for the support of eligible firms, through *both* the R&D Start program and the Commercial Ready program.

Value of R&D Start and Commercial Ready Agreements Signed 2000-2008 ($M)

Year (FY)	Total	Life Sciences	%
R&D Start			
2000	$149.7	$23.5	16%
2001	$207.8	$33.1	16%
2002	$190.7	$41.6	22%
2003	$55.6	$8.8	16%
2004	$207.2	$52.1	25%
2005	$137.7	$29.9	22%
Commercial Ready			
2005	$29.0	$6.4	22%
2006	$160.0	$63.4	40%
2007	$155.3	$45.4	29%
2008	$103.5	$17.4	17%
Total	$1,396.4	$321.7	23%

Since FY2000, roughly one-quarter of funds ($322 million) have been provided to support life science firms. Life science firms received 20% of funding under the R&D Start Grant program and 30% under the Commercial Ready program. However, these figures do take into account funding provided under the BIF program.

On a sub-sector basis for life science firms for the period 2000-2008, 42% of funds or $134 mil-

Cont'd over

Life Science R&D Start Grant and Commercial Ready Agreements Signed 2000-2008

Sub-sector	Num.	Value ($M)	%	%
Ag-bio	18	$13.1	4%	
Cosmeceutical	3	$1.2	0%	
Device	36	$44.0	14%	
Diag./Detect.	35	$38.9	12%	
Drug Delivery	8	$16.4	5%	
Drug Discovery & Engineering	6	$7.0	2%	
Industrial or enabling tech.	17	$38.9	12%	
Nutraceutical	4	$3.2	1%	
Th. - Biologic	8	$12.8	4%	10%
Th. - Cell	3	$8.1	3%	6%
Th. - Immune	5	$4.1	1%	3%
Th. - NatPdt	3	$2.6	1%	2%
Th. - Peptide	6	$13.0	4%	10%
Th .- SmMol	47	$85.2	26%	63%
Vaccine	8	$8.5	3%	6%
Subtotal - Therap. & Vaccine	80	$134.3	42%	100%
Other	25	$24.7	8%	
Total	232	$321.7		

Classifications have been devised for analytical purposes only by Bioshares, not AusIndustry

lion were made available to Therapeutic Product and Vaccine firms. Small molecule drug developers received the largest proportion of funds, a total of $85 million, distributed to 47 projects at an average grant value of $1.8 million. Device companies received $44 million, distributed to 36 recipients at an average value of $1.22 million.

We estimate public listed companies received approval for $137 million in funds or 43% of total life science funds. Including grants received prior to listing, grants received by associated entities or from merged entities included, that estimate increases to $184 million or 57% of total life science funds and representing 101 grants. To put that in context however, more than $3.3 billion has been supplied since the beginning of 2002 to fund the commercialisation activities of public listed life science firms by private investors.

Comment

The AusIndustry R&D Start and Commercial Ready programs have been designed as merit based assistance programs that have disbursed modest amounts of money reasonably widely. While the axing of the current program may, on the face of it, appear to be a set-back for life science firms relying what appeared to be a 'guar-

Cont'd over

HealthLinx Aims for Australia First

Healthlinx (HTX: 7.5 cents) is commercialising a new diagnostic test for the early detection of ovarian cancer. It is currently conducting a funding round to raise $4 million. At the end of March this year the company had only $635,000 in cash.

The Healthlinx test combines the existing ovarian cancer biomarker (CA125) which is about 60% accurate, with a series of proprietary biomarkers. An independent analysis of validation of its test battery showed the test was 89.2% sensitive (i.e. the test missed picking up the disease in just under 11% of samples) and 93.9% specificity (about 6% without disease in fact received a positive result). This trial was conducted from 152 samples, of which 115 were control (known to be healthy) and 37 samples were known to contain early stage disease. In *Bioshares* view, a 90% test accuracy level is a remarkable result for such a difficult to detect disease.

There are both positives and negatives to this investment. On the down side, the company has low cash reserves and the non-renounceable rights issue being conducted is not underwritten. The test battery has been validated with only a small sample population, 268 samples in total, and to gain widespread acceptance the company will likely need tests conducted on thousands of samples. And from a corporate point of view, the board could be strengthened.

However, there are a number of positives with this company. Firstly it is widely accepted that there is no good early stage ovarian cancer diagnostic test available. In Australia last year there were 1300 new cases of ovarian cancer diagnosed. In the USA the number was 23,000. If detected early enough, the disease is curable, but if it's detected late then the mortality rate is very high (20% five year survival). Over 75% of women diagnosed with ovarian cancer find out once they are in an advanced stage of the disease.

The existing ovarian cancer marker CA125, which generates global sales of $260 million a year, is not accurate enough at detecting early stage cancer although is a reasonably good indicator of disease progression in advanced cancer stages.

One of the appeals of this company is the company's business model, which involves commercializing the test first in Australia. It is expected the test will be commercially available in the third quarter of this year, selling for $200 per test. It's an approach rarely seen here but one that is very credible in Bioshares view and should occur more often. Too frequently small biotechs become US-focused without the patience and the capital to enter that extremely competitive and difficult market. Getting a track record in smaller markets should eventually see success in larger markets if the test is sufficiently accurate, following a growth path that is within the capabilities of a small biotech.

In Australia and New Zealand the test will be sold in coming months by ARL Pathology. It will be directed to at risk women with the aim to introduce testing with the existing Pap Smear testing procedure.

Healthlinx is currently capitalised at $7.5 million prior to the capital raising.

Bioshares recommendation: **Speculative Buy Class C** (to be revised following capital raising)

Investors looking to invest through the rights issue should contact Guy Aird at Aragon Capital (03 9600 0788/0411 767 177).

Bioshares

Federal Budget - from previous page

anteed' line of funding, it is not the most important funding issue for listed Australian firms. That issue is the ongoing market malaise which has caused heavy discounting of biotech stocks.

The Rudd Government has indicated a commitment to lifting innovation in the Australian economy. One possible scenario is that the Federal government reintroduces a very targeted commercialisation support program following the completion of the current Innovation Review. It is also worth noting that industry support continues through the Innovation Investment Fund program, whichhas seen $220 million committed in Rounds I (1997) and II (2000). In 2006, another $200 million was committed for Round III which commenced in 2007. Round III funding involves the government committing $40 million each year to license two fund managers per year over five consecutive years, with funding matched on a 1:1 basis.

The biotech sector was also shocked by the axing of the Commercial Ready program because no warnings were given, and the program was cancelled immediately. While such suddenness may have some negative impact on the government, the action comes as a warning signal to those in the sector conscious of capital constraints and limitations. The biotech sector needs to marshal its arguments for assistance and place them in front of the relevant ministers in a timely manner, which has been poorly conducted by the sector as a whole in recent times. The irony is that the biotech sector probably has the best informed access it has ever had in the guise of former BioMelbourne network CEO, Tim Murphy who is now Senior Adviser - Innovation to Senator Kim Carr, Minister for Innovation, Industry, Science and Research (tim.murphy@innovation.gov.au - 0417 330 219).

Bioshares

Data Sources: AusIndustry Annual Reports and documents titled respectively R&D Start Grant and Loan Agreements signed in 1999-2000, ...2000-2001, ...2003-2004, ...2004-2005, Commercial Ready grant recipients for 2004 - 05, ...2005-06, ...2006-2007 and Commercial Ready grants signed 2007-2008 (to Mar).

The Increasing Appeal of 'Improved Chemical Entities'

As the pharmaceutical industry struggles to find sufficient numbers of new chemical entities (NCEs) to bring to market, and as margins in the generics industry continue to fall because of the rapid global penetration by low cost Indian generic drug makers, the gap in the middle is emerging for value adding generic developers. Call them SuperGenerics, Improved Chemical Entities or Technology Enabled Generics, Australian biotech companies have been quick to move into this space.

Alchemia, **QRxPharma**, **Acrux**, **Phosphagenics**, **Giaconda**, **Psivida**, **Bone Medical** and **Halcygen Pharmaceuticals** all have businesses based upon the improvement of, or novel combinations of existing generic drugs. The advantage of improved chemical entities (ICEs) is that the company can secure intellectual property protection over its invention, but also that the time to market is significantly shorter, less risky and less costly than for the development of NCEs.

Testament to this claim is the number of ICEs approaching the market from Australian biotechs. Alchemia is expecting to be the first to file a generic fondaparinux in the USA in coming months; Acrux's marketing partner recently launched the first of its compounds onto the market, Evamist for the treatment of HRT, with a transdermal male testosterone product expected to be file for approval in the US in the second half of next year; QRxPharma expects to file its opioid combination drug for approval in the US late next year; and Halcgygen should be in a position to file its leading product, SUBA-Itraconazole, for approval either this year or in 2010, depending on the outcome of forthcoming trials.

Halcygen – Update

Halcygen Pharmaceuticals (HGN: 50 cents) listed on the ASX last year at 50 cents a share, raising $12.5 million. The company has accessed an oral drug reformulation technology from **Mayne Pharma** that can significantly increase the absorption of oral pharmaceuticals. The lead compound, SUBA-Itraconazole, is an improved chemical entity of the antifungal drug Sporanox (itraconazole) developed and marketed by Johnson & Johnson. The second less advanced program is an improved version of the antibiotic Minocycline.

Regulatory update

In recent months Halcygen has been seeking to clarify its regulatory pathway for the US market with the FDA. The company's initial expectation was that it would require only bioequivalent studies against Sporanox. Following a meeting with the FDA in November last year (with the Division of Special Pathogen and Transplant Products, subdivision Office of Antimicrobial Products), it was expected that the company would be required to conduct Phase III efficacy studies.

The company was advised however that the FDA Division of Dermatology would be the more appropriate governing body within the FDA for the application chosen by Halcygen. Following a recent meeting with that division, the outcome was twofold. Firstly, the company will conduct bioequivalent studies in the US in around 80 patients. If the trial shows bioequivalence against Sporanox, then a Phase III efficacy studies should not be required. If its absorption is not bioequivalent to Sporanox then a Phase III study will likely be required.

Clinical studies to date have shown that Halcygen's SUBA-Itraconazole is absorbed twice as well as Sporanox. The forthcoming trial will compare SUBA-Itraconazole (2x50mg tablets once a day) against Sporanox (2x100mg tablets once a day), so half the active ingredient in Halcygen's formulation.

The trial will look at a single dose of drug, a rising dose of drug and a steady state dose of drug over 90 days. The study will also compare the absorption in patients who have been fed and those who have fasted. Each category will compare SUBA-Itraconazole against Sporanox. It's expected the trials will take nine months to complete.

Halcygen recently filed an IND for its program with the FDA with the US regulator having 30 days to respond. If all goes well, the company could expect to start its trial next month, and be in a position to file its drug for approval by mid 2009. If further efficacy studies are required, then we expect the company would be in a position to file its drug for approval with the FDA at the earliest by late 2010.

The company has fallen behind by at least six to 12 months from its prospectus forecast, which listed expected registration filing as 2008. The company is maintaining dialogue with potential marketing partners for the technology for various regions throughout the world.

Complications

Trials to date show that SUBA-Itraconazole's absorption profile is significantly better than that of Sporanox. Sporanox is required to be taken with a high fat meal to improve its absorption. This is not a suitable characteristic for long term use, which is the case with some fungal infections. There is definite merit in Halcygen's improved reformulation. A half dose of itraconazole that may not need to be taken with a high fat meal may not only result in better patient compliance and more consistent treatment results, but the level of intestinal side effects should be considerably reduced. Around 22% of patients taking itraconazole suffer gastrointestinal side effects.

However if the above holds true, then it is likely that the absorption profile of SUBA-Itraconazole against Sporanox in the fasted state might not match up, even at half the Halcygen drug dose. How the FDA will respond such a result is unclear.

Cont'd over

The Mayne Pharma link

The intellectual property surrounding Halcygen's programs originates from a commercial arrangement with Mayne Pharma (formerly FH Faulding, now Hospira) including access to its oral reformulation technology. Over the last 40 years, Mayne Pharma has become a leading drug reformulation group since it started work on sustained release of pharmaceuticals in the late 1960s. It has developed technologies that improve drug characteristics in the following ways:

1. Sustained release drug delivery
2. Pulsed release delivery
3. Modified release
4. Delayed release
5. Taste masking
6. And improved solubility

Mayne Pharma has a 2.5 billion capsule production capacity at its manufacturing site in Adelaide which is FDA and TGA approved. *Bioshares* recently visited this facility. It currently manufactures a number of improved chemical entities for international pharmaceutical clients which generate annual sales of around $400 million a year.

These include Doryx and Eryc (modified release antibiotics), Astrix (enteric coated aspirin) and Kapanol (sustained release morphine).

The arrangement with Halcygen is an important test for a business development model adopted by Mayne Pharma, whereby it can leverage its expertise in drug reformulation through corporate relationships such as the one with Halcygen. SUBA-Itraconazole will be the first internally developed product from this site from which Mayne has rights over and according to Mayne, has the potential to be a bigger seller than the Doryx product manufactured for **Warner Chilcott**.

Under the contract between Mayne Pharma and Halcygen, Halcygen has licensed the drug, SUBA-Itraconazole and Minocycline, reformulated by Mayne Pharma. In return for this license, Mayne has first right of refusal to manufacture any approved drugs. The appeal to Mayne is that it wants to continue to expand its manufacturing base in Adelaide. If another manufacturer is chosen, then Mayne will receive 30% of all income received by Halcygen from its distributors in relation to sales of developed products. Obviously there is a strong incentive to negotiate a manufacturing contract with Mayne.

Reformulation of pharmaceuticals is substantially more difficult than it appears. According to Mayne, SUBA-Itraconazole is a very insoluble drug. Mayne's technology disperses the drug into a hydrophilic polymer which enhances the dissolution level by creating an interaction between the drug and polymer that does not crystallise. Mayne Pharma expects to continue to leverage from its reformulation experience and to look at existing (or new drugs) that can benefit from improved delivery characteristics providing life cycle management benefits.

Competition

Barrier Therapeutics is currently conducting a Phase III trial with its once daily version of a single tablet, a 200mg version of itraconazole. If the trial is successful, the company expects to file its version for approval in the US in the first quarter of 2009. The only advantage this formulation appears to have over Sporanox is the convenience of taking only one tablet rather than two. If Halcgygen can show SUBA-itraconazole has a significantly better absorption profile, then it would offer clear advantages over these competing products.

Sales of Sporanox and other generic versions currently exceed $600 million worldwide. It is acknowledged that the drug is poorly absorbed, that gastrointestinal side effects are common, and the drug has the onerous requirement to be taken with a high fat diet. An improved version, that is smaller and provides an improved absorption profile thereby would be arguable well received by regulators and the market.

Improving the bioavailabilty of Itraconazole is extremely difficult with its solubility being extremely poor. Mayne's reformulation technology, that has been developed with over 30 years of drug reformulation experience, is a very valuable asset (see box at left). Mayne has a track record of adding considerable value for its clients through drug reformulation.

Summary

Halcygen is well financed, with $12.7 million in cash resources at the end of March this year. There remains some level of regulatory uncertainty, which is one of the key risks going forward. Halcygen Pharmaceuticals is capitalised at $20 million.

Bioshares recommendation: **Speculative Buy Class B**

Bioshares

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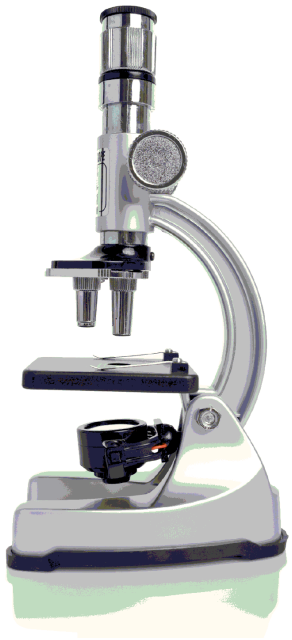

Bioshares 2008 Thredbo Biotech Summit

Second Conference Early Bird Offer Closes Saturday May 31
www.bioshares.com.au/thredbo2008.htm

Bioshares Model Portfolio (23 May 2008)

Company	Price (current)	Price added to portfolio	Date added
Cellestis	$2.58	$2.27	April 2008
IDT	$2.10	$1.90	March 2008
Circadian Technologies	$0.94	$1.03	February 2008
Patrys	$0.29	$0.50	December 2007
NeuroDiscovery	$0.14	$0.16	December 2007
Bionomics	$0.36	$0.42	December 2007
Cogstate	$0.13	$0.13	November 2007
Sirtex Medical	$3.89	$3.90	October 2007
Clinuvel Pharmaceuticals	$0.40	$0.66	September 2007
Starpharma Holdings	$0.36	$0.37	August 2007
Pharmaxis	$1.54	$3.15	August 2007
Universal Biosensors	$0.90	$1.23	June 2007
Biota Holdings	$1.10	$1.55	March 2007
Probiotec	$1.20	$1.12	February 2007
Peplin Inc	$0.49	$0.83	January 2007
Arana Therapeutics	$1.04	$1.31	October 2006
Chemgenex Pharma.	$0.92	$0.38	June 2006
Cytopia	$0.25	$0.46	June 2005
Optiscan Imaging	$0.25	$0.35	March 2005
Acrux	$0.99	$0.83	November 2004
Alchemia	$0.41	$0.67	May 2004

Portfolio Changes – 23 May 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

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