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In this edition...
In what has been a terrible week for equities and a dreadful week for biotech, the sector has had at least three positive announcements that have had no, or next to no share price impact. Cytopia signed a deal with Novartis and Phylogica partnered with Johnson & Johnson. Gardasil, a University of Queensland/CSL cervical cancer vaccine partnered with Merck was approved by the FDA.

However, in time we expect these developments to be recognised by the market.

We also update readers on Biotech Capital and Sunshine Heart.

The editors
Companies covered: BTC, CYT, PYC, SHC

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

Cytopia Partners JAK-3 Program with Novartis

Cytopia (CYT: 87 cents) has secured **Novartis** as a development partner for its JAK-3 kinase assets. The licensing and collaboration deal signed by the two companies is worth $287 million (US$215 million) in total potential revenues to Cytopia. The deal includes an upfront and research payments component of $13 million. The goal of the partnership is to develop orally active small molecule therapeutics that can be used in the treatment of rheumatoid arthritis and other auto-immune diseases, and in preventing transplant rejection. This is the first deal reached by Novartis with an Australian biotech company.

An 'all in' deal

The two companies will manage the program under a legal agreement. The deal is characterised as an 'all in' deal, in which both parties subscribe their molecules and expertise, and should a 'Novartis' compound be selected for clinical development and eventually reach the market, then Cytopia will still stand to collect milestone and royalty payments as appropriate.

The deal is the fourth major out-licensing event for junior Australian biotech since **Zenyth Pharmaceuticals** (then Amrad) partnered with **Merck** in June 2003, in a deal with a total potential value of US$112 million. Zenyth has since then received US$16.5 million or roughly $22 million in upfront and milestone payments. The Cytopia-Novartis deal is the biggest of all these deals to date, although a qualification is that **Biota** deal with **Medimmune** for the development of small molecule inhibitors of respiratory syncytial virus saw Biota retain rights for Australia, New Zealand and Asian territories other than Japan.

Deals by Australian drug developers with larger pharmaceutical partners do deserve the attention and support of investors, because they represent risk being removed from the business.

Source of validation

Deals of the stature as listed in the table on page 2, even though they have all been signed at the pre-clinical stage, given significant validation of a company's capabilities. It is notoriously diffucult to get a larger company interested in a product or technology, let alone to consumate that interest with a licensing or acquisition arrangement on fair and reasonable terms. Investors can take a great deal of comfort in investing in biotech stocks where a small company has partnered its technology to a leading international pharmaceutical firm, whose due diligence considerations go well

Cont'd over

beyond analysis of clinical potential and include thorough assessments of cost of goods and marketing requirements. They can take even greater comfort where one of a number of possible applications has been out-licensed, leaving other compounds or assets for further exploitation.

Driver for the deal

Competitive pressure appears to have been an important motivator for Novartis to complete this deal. **Pfizer** is developing a compound, CP-690,550, as a transplant rejection drug and treatment for rheumatoid arthritis. CP-690,550 is also JAK-3 kinase inhibitor and is currently being evaluated in three Phase II studies, one for rheumatoid arthritis and two for kidney transplant patients. Novartis markets Neoral/Sandimmune for the prevention of organ transplant rejection. This drug achieved global sales of US$950 million in 2005 and it ranks as Novartis' sixth biggest drug by sales. Two other drugs compete with Neoral/Sandimmune, including Cellcept (**Roche**)[Sales of US$1.1 billion] and Prograf (**Astellas**) [US$1 billion].

A vindication

The deal with Novartis represents a vindication of the original plan for the development of Cytopia. This was to resource the company to build a drug discovery and development company, in its own corporate setting and away from academic research labs, although it must be said that the company has successfully collaborated locally with academic drug designers. The strategy also included significant investment in specialised drug design software in the order of $3 million, and in medicinal chemistry capabilities. This has resulted in a platform capability, of which the first asset to yield value or recognition is the JAK-3 asset. In relative terms, this is the least valuable, with the JAK-2 kinase program and the cancer drug CYT-997 still with the development control of Cytopia. Cytopia has a proprietary position over the JAK-2 kinase, which makes it all the more valuable as a licensable asset. The company was careful to quarantine JAK-2 assets from the deal it reached with Novartis.

Cytopia is also capable of applying its drug discovery know-how to other kinases, which with some modest increase in resources, it should be able to expand in the short-to-medium term.

Context of the Novartis-Cytopia deal

Novartis has in recent times engaged in a high level of in-licensing activity, in order to maintain and build its competitive position in its key product areas. The deal with Cytopia is one of at least thirteen completed since the beginning of 2005 (see table on page 3). Roughly eight of these deals have been initiated at the pre-clinical or discovery phase of development. The deal with Cytopia is similar to a number of others, incorporating a low-order up-front payment, and research payments. Interestingly, many of these partner companies appear to operate from a strong technology base or platform. Cytopia's total potential deal value of US$215 million is, generally speaking, in the middle of the range of deals struck by Novartis. It is possibly the only 'all in' deal, and is certainly the only organ transplant rejection drug deal struck by Novartis.

Change of CEO

Following the announcement of the deal with Novartis, Cytopia has announced a change in management with founding CEO Kevin Healey, stepping down to make way for the current CFO, Andrew Macdonald. Healey will remain on the board and will act as a consultant to the firm on strategy and business development. Macdonald, who was formerly the CFO at Biota, is well equipped to lead a management team at Cytopia through its next phase of development. The transition of CEOs at Cytopia is an example of a well managed approach to leadership succession at an Australian listed biotech company.

Cytopia is capitalised at $64 million, and following this latest deal should have cash assets at its disposal of that we estimate lies between $13 and $15 million. There is a possibility that the first milestone payment from the Novartis deal may eventuate sooner rather than later. This would be because of work that progressed while the deal was still being finalised by Novartis. Cytopia also holds a 10% stake in Alchemia (assuming the merger with Meditech Research completes), that on current prices is valued at $16.8 million.

Bioshares recommendation: **Speculative Buy Class A**

Selected Licensing and Collaboration Deals by Australian Companies

Date	Out-licensor	In-licensor	Deal Value $US (M)	Up-front $US (M)	Marketing Rights	Research & Materials $US (M)	Royalties	Asset or Technology Description	Phase	Indication/s
23/06/2003	Zenyth (Amrad)	Merck	$112	$5			Yes	Antibodies for IL-13 receptor	Pre-clinical	Asthma, other respiratory conditions, oncology
15/12/2005	Biota	Medimmune	$112.5	$5	**Merck**:US, Europe, Japan; **Biota**: ANZ, Asia	Yes- but not stated	Yes	Respiratory Syncitial Virus inhibitors	Pre-clinical	Respiratory
8/02/2006	G2 Therapeutics	Novo Nordisk	$102	$6		Yes- but not stated	Yes	Antibodies for C5a receptor	Pre-clinical	Inflammation, Auto-immune
5/06/2006	Cytopia	Novartis	$215	$5 (estimated)	CYT retains ANZ rights	$4.75 (estimated)	Yes	JAK3 kinase inhibitors	Pre-clinical	Inflammation, Transplantation

G2 Therapeutics is a private company, which was spun out of the Garvan Institute in Sydney

Novartis' Recent Licensing and Collaboration Deals

Date	Out-licensor/Seller	Deal Value $US (M)	Up-front $US (M)	Equity $US (M)	Research & Materials $US (M)	Royalties	Asset or Technology Description	Phase	Indication/s
13/04/2005	Arakis, Vectura	$375	$30			Yes	NVA237, once daily, long acting antimuscariinic agent for COPD	Phase II	Respiratory
28/04/2005	Avanir	$200	Not disc.		$10	Yes	Macrophage inhibitory factor (MIF) inhibitors	Not disc. (Pre-clinical?)	Inflammation
1/06/2005	Idera Pharmaceuticals (ex Hybridon)	$136	$4		Yes	Yes	Toll-like Receptor 9 (TLR9) inhibitors (oligonucleotide technology)	Pre-clinical	Asthma and allergy
2/06/2005	Anadys Pharma-ceuticals	$570	$20			Yes	ANA975 and additional Toll-Like Receptor 7 (TLR7) oral prodrugs, HCV and HBV	Phase I	Anti-infective
12/06/2005	Astex	$520	Not disc.	$25		Yes	AT9311, oral cell cycle inhibitor; AT7519, parenteral cell cycle inhibitor	Pre-clinical, Phase I	Cancer
30/06/2005	Arrow Therapeutics	$227	$20			Yes	A60444, treatment of RSV infection	Phase II	Respiratory
7/09/2005	Alnylam Pharma-ceuticals	$700	$10	$46		Yes	Multiple products, broad technology collaboration	Discovery	Various
18/03/2006	Ablynx	Not disc.	Not disc.		Yes	Yes	Nanobodies - various	Discovery	Various
6/03/2006	Infinity Pharmaceuticals	$400	$30	Yes	Yes- (for 2 yrs)	Yes -& Infinity retains option over US marketing rights	BCL-2 inhibitors (small mol)	Discovery	Cancer
27/03/2006	SGX Pharmaceuticals	$515	$25	Yes	Yes- (for 2 yrs)	Yes -& SGX retains option over US marketing rights	BCR-ABL inhibitors (small mol)	Pre-clinical	Drug resistant Chronic Myelogenous Leukemia (CML).
5/06/2006	**Cytopia**	**$215**	**$5 (estimated)**		**$4.75 (estimated) - over 3 years**	**Yes -& CYT retains ANZ rights**	**JAK3 kinase inhibitors**	**Pre-clinical**	**Inflammation, Transplantation**
5/06/2006	Genelabs Technologies	$175	$12.5		$7.50	Yes	Hepatitis C non-nucleoside inhibitors	Pre-clinical	Hepatitis C
6/06/2006	Human Genome Sciences	$508	$45			Yes; Profit share US market	Albuferon (albumin interferon alpha 2a)	Phase II	Hepatitis C and all other uses

Stock Updates

Biotech Capital (BTC: $0.45)
Biotech Capital is a listed life sciences investment fund, which holds stakes in six listed companies (**Alchemia, Clinical Cell Culture, Phylogica, Prima Biomed, Starpharma** and **Stem Cell Sciences,** which is listed on London's AIM market) and four private companies (**Biocomm, Continence Control Systems, Pacific Knowledge Systems and XRT**). Biotech Capital is currently capitalised at $40 million, with $8 million in cash in the bank. The company is trading at 22% discount to its net tangible assets (by its own calculations) for May 31, 2005.

With the majority of Biotech Capital's ASX listed investee companies well known to Bioshares' readers, a short update on Stem Cell Sciences is warranted.

Investee Company Profile - Stem Cell Sciences
Stem Cell Sciences is seeking to build a comprehensive stem cell company, which takes in the supply of reagents and cell lines for research purposes, conducting screening work for pharmaceutical companies, and developing cellular therapies using most types of stem cells, including adult-based stem cells derived from fat tissue (hMADS) and stem cells harvested from the central nervous system. By collaborating with leading stem cell academic centres on four continents, the company's goal is to remain at the forefront of stem cell research at the same time being at the forefront of commercialisation of this advanced medical technology.

Stem cell therapy, *if successful*, will deliver a transformational therapeutic advance that arguably will define the change in medicine for the first half of the 21st century, in particular for the treatment of certain degenerative and genetic diseases. Although embryonic stem cell therapy remains many years away from a therapeutic reality, the clinical development of adult stem cells (and other cellular therapies) are making rapid advances. Locally, Mesoblast is one of those companies, with patients being treated with autologous adult stem cells (mesenchymal precursor cells) to repair long bone fracture and also for the prevention of heart failure.

Stem Cell Sciences was founded in 1994 and last year listed on the AIM stock market in the UK. The company's management team are all Australians. However, the parent company is a UK entity with wholly owned subsidiaries in Australia, the US and Scotland, with a 25% equity interest in a Japanese stem cell group.

Stem Cell Sciences KK - Japanese joint venture
The Japanese interest is important and exemplifies the approach SCS takes - that of forming strategic collaborations in countries or regions that best support the field of stem cell R&D. Called Stem Cell Sciences KK, it's a joint venture between SCS and the Japanese biotech company, **Sosei**, which was formed in 2002. Based in Kobe, Japan, the centre houses 220 basic researchers, a GMP cell production facility, and an 85 bed hospital that is designed to move products from the research bench into patients as quickly as is possible.

SCS provides the intellectual property assets and has no ongoing funding commitments. It is entitled to 100% of any revenue streams generated in Europe arising from the technologies being developed under the JV and is entitled to 50% of any future revenue from the US.

There are 30 people working in the JV team in Japan. The SCS KK joint venture last year in-licensed technology from the **University of Nice** in France for multipotent adipose-derived stem cells (hMADS) which the team will apply towards cellular therapy for the treatment of Duchenne Muscular Dystrophy.

Bioshares recommendation: **Speculative Buy Class A**

Sunshine Completes Third Implant

Sunshine Heart (SHC: 14 cents)
The Sunshine Heart C-Pulse device could potentially be the most commercially successful heart assist device in development. It consists of a sleeve that wraps around the aorta to improve cardiac output and in the process, improving the health of the heart muscle itself. It has three main advantages over mechanical heart pump devices. Firstly, it does not come in contact with the blood, so there is negligble clotting risk and anti-coagulant medication is not required in relation to the use of the device. Secondly, the device can be turned off; and thirdly, implantation of the device is considerably easier, with patients not required to go on heart bypass.

Another attractive feature of the product is the market size, which is considerably larger than for patients suitable for left ventricular assist devices (LVADs) such as the **Ventracor** or **Heartware** products. It is expected that the device will also be substantially less expensive than the LVADs, probably selling for about US$50,000 each, half the price of LVADs. The C-Pulse is mostly suitable for Class III heart disease patients, of which there are 1.4 million in the US. In contrast, LVADs are more suited to Class IV patients, and there are about 400,000 Americans that would fit into this category.

Third implant completed
Sunshine Heart is less advanced than Ventracor in its development of a heart assist device.. Sunshine Heart has implanted its device into two patients in New Zealand with disappointing results, but whichc are not necessarily related to the device. Both were Class IV patients. In the last month, the company has completed its third implant, this time in Australia, and up to 10 patients will implanted in this pilot trial in Australia by year's end. It's expected data from this trial will support the company's IDE submission to the FDA, in support of trials to be conducted in the US next year. The US trial will involve between 100-200 patients.

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Sunshine Heart has some other development work to complete before the US trials begin. It is currently using a third party driver unit and development plans are underway to build a smaller unit in house. This should not be a difficult process, given the driver is simply a membrane solenoid pump that delivers air to inflate the cuff around the aorta. Currently, the driver and battery pack is considerably bulky. The new driver should weigh less than 2kg, about half the weight of the existing driver, and the company is hoping to increase battery capacity from 2 hours to over 6 hours.

The main risks for the technology are firstly infection, and secondly damage to the aorta wall. To date, no damage has been detected to the aorta from clinical or human studies. Infection was an issue with the second patient implanted in New Zealand, resulting in the device being removed. The company is hopeful that the infection risk has been reduced, with changes to the lead implant through the abdomen and it's likely operating procedures will be more stringent. Application of antibacterial coating to the plastic leads and cuffs could potentially benefit the program.

The current trial will involve four hospitals in Australia, with the first hospital being conducted in St Vincent's in Sydney. The Sunshine Heart approach is a lower risk option and could be more attractive for acquisition to a global medical devices group and it has differentiated itself from the crowded LVAD field. It will be a pivotal year for Sunshine Heart and it will be a stock to monitor very closely. If it can generate some positive results from its first few implants in Australia, it could potentially be one of the surprise performers for the year. Sunshine Heart is capitalised at $10 million and had $5.6 million in cash at the end of March this year. Funding risk is high for this company. However, as and when signs of clinical success and safety emerge, then this component of risk with the stock should recede.

Bioshares recommendation: **Speculative Buy Class C**

	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)	-9.0%
Cumulative Gain	**153.5%**
Average Annual Gain	**22.4%**

Phylogica Signs J&J

Phylogica (PYC: 69 cents)
Perth-based Phylogica this work signed a research and collaboration and licence agreement with the Australian research subsidiary of international pharmaceutical and medical device company, **Johnson & Johnson**.

Almost no substantive details pertaining to the deal were announced, although the deal did include upfront and milestone payments. The CEO of Phylogica, Stewart Washer, was disappointed he could not say more about the deal. The deal was in development for more than a year and involved J&J undertaking an initial analysis to see if Phylogica's phylomers (peptides) could replace antibodies in certain disease areas. The deal is exclusive around a specific target, which leaves Phylogica free to pursue the development of phylomers against numerous other targets.

A benefit of the deal is to deliver welcome revenue that now gives the company a comfortable 12 months of cash, extending to 18 months if necessary. Another equally important benefit is that the company's phylomer technology is now validated by a large pharmaceutical firm, as a technology worthy of research and exploration for potential to meet drug development goals. This validation is expected to aid other partnering opportunities the company is exploring.

The phylomer technology was attractive to J&J because of the absence of a 'royalty stack' and relative ease of synthetic manufacture as compared to biologics or other fragment based drugs. Phylogica is capitalised at $75 million.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares Model Portfolio (9 June 2006)

Company	Price (current)	Price added to portfolio
Acrux	$0.78	$0.83
Agenix	$0.15	$0.22
Alchemia	$1.17	$0.67
Avexa	$0.23	$0.15
Biolayer	$0.20	$0.195
Bionomics	$0.20	$0.210
Biosignal	$0.15	$0.22
Cytopia	$0.87	$0.46
Evogenix	$0.52	$0.47
GroPep	$1.56	$1.43
Optiscan Imaging	$0.51	$0.35
Neuren Pharmaceuticals	$0.48	$0.70
Pharmaxis	$2.00	$1.90
Prima Biomed	$0.075	$0.09
Sirtex Medical	$2.20	$1.95

Changes to portfolio
Cogstate's share price has increased by almost 200% since it was added to the portfolio. We will take some profits and remove it from the portfolio

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

Corporate Subscribers: Phylogica, Neuren Pharmaceuticals, Pharmaxis, NeuroDiscovery, Prima Biomed, Biotech Capital, Cygenics, Psivida, Cytopia, Biodiem, Peptech, Starpharma Holdings, Cogstate, Xceed Biotechnology, Healthlinx, Incitive

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