

In this edition...

How intense is M&A activity around the globe at the present time? Acquisitions of smaller life science firms looks to be on the up and this may mean that some Australian companies will be on the radar of larger firms looking to infill their pipelines or add attractive technologies to their asset stables. The fact that asset prices have fallen to very low levels should surely spice things up.

We also update readers on recent events at Alchemia.

The editors

Companies covered: ACL

	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)	-11.1%
Cumulative Gain	85%
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.

A Survey of Recent Life Science Acquisitions

A theme that is expected to be discussed with even greater urgency and frequency by Australian biotech investors is that of mergers and acquisitions. This discussion is being driven by a profound drop in value of many companies in the sector, with the sector essentially having lost half its value from a year ago. And recently in *Bioshares* (see #269) we set forth our suggestions on a range of companies that we argued would be reasonable candidates for acquisition by other firms, generally larger international companies.

While various companies skirt the M&A issue and jockey for a position of superiority – an odd situation if cash is short – it is worthwhile to reflect on acquisition trends in the wider global life sciences sector. On the following pages we have tabulated basic information pertaining to 69 acquisitions amongst life science companies that have been initiated in the last twelve months or so. This data is not complete.

The most salient fact for investors to observe is the sheer bulk of activity, and this survey for the most part excludes device companies. Acquisitions occur frequently, illustrating an essential fact about the life science sectors. Larger pharmaceutical companies have a steady appetite for smaller businesses. To a lesser extent, acquisitions of more similarly sized companies occur as well. Some companies, such as **Inverness Medical Innovations** could be said to have an insatiable appetite, having acquired twelve companies in the last twelve months or so, including Brisbane-based **PanBio**.

Of late, there have been some big ticket acquisitions made, with **Takeda's** purchase of **Millennium Pharmaceuticals** for US\$8.8 billion standing as a recent high water mark. And recently, **Fresenius AG** has bid US\$3.7 billion for **APP Pharmaceuticals**, a generic injectables business that had formerly partnered with Alchemia to market generic fondaparinux.

Surprisingly, drug development companies have fetched reasonably high prices considering the early stage of development at which some companies are at. For example, **GlaxoSmithKline** paid US\$720 million for **Sirtris Pharmaceuticals**, a company just starting to build up steam at the Phase I stage. And **Bristol Myers Squibb** paid US\$430 million

Cont'd on page 4

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Selected Life Science Acquisitions: June 2007- July 2008

Month	Target Company	Acquirer	Value (US\$M)	Contingent Value and other terms (US\$ M)	Target Company - Category	Comments
Apr-08	Millenium Pharmaceuticals	Takeda	\$8,800		Pharmaceutical	
Jun-08	Applied Biosystems	Invitrogen Corporation	\$6,700		LS products and reagents	17% premium on closing price
Dec-07	MGI Pharma	Eisai	\$3,900		Pharmaceutical	
Jul-08	APP Pharmaceuticals	Fresenius AG	\$3,700		Pharmaceuticals - generic injectables	
Feb-08	Ventana Medical Systems	Roche	\$3,400		Diagnostics	
Nov-07	Pharmion	Celgene	\$2,900		Pharmaceutical -oncology	
May-08	Matria Healthcare	Inverness Medical Innovations	\$1,180	Included \$280M in assumed debt	Health and disease management	see also Bioshares 224
Jul-08	Speedel Holding AG	Novartis	\$880		Drug development - cardiovascular and metabolic	one drug FDA and EMEA approved
Apr-08	Sirtris Pharmaceuticals	GlaxoSmithKline	\$720		Drug discovery	
Jun-08	Tercica	Ipsen	\$663	Acq. outstanding shares for \$403M	Biologic - Marketing Stage - Endocrinology	Originated from NZ; to US in 2000
Jul-08	Jerini AG	Shire Limited	\$518	Staged process	Pharmaceutical (peptides)	199% premium
Oct-07	Adnexus	Bristol Myers Squibb	\$430		Drug discovery - protein fragments	
Jun-07	Ilypsa	Amgen	\$420		Drug development	see also Bioshares 219
Feb-08	CoGenesys	Teva Pharmaceutical	\$400		Biologics	
Nov-07	Agensys	Astellas Pharma	\$375	plus \$150	Drug discovery	
Jul-07	Novocardia	Merck	\$350		Drug development - cardiovascular	
Jun-07	Cholestech	Inverness Medical Innovations	\$326		Diagnostics - heart disease	see also Bioshares 224
Oct-07	Alere Medical	Inverness Medical Innovations	\$302		Healthcare management services	see also Bioshares 224
Jun-07	Alantos Pharmaceuticals	Amgen	\$300		Drug development	see also Bioshares 219
Oct-07	ViaCell	Perkin Elmer	\$300		Cord blood stem cells	
Apr-08	Innogenetics	Solvay SA	\$277		Diagnostics and genetic testingf	
Jul-07	NimbleGen	Roche	\$273		LS Instruments (Microarrays)	
May-08	U3 Pharma	Daiichi Sankyo	\$235		Drug discovery - antibodies	see also Bioshares 265
Nov-07	Paradigm Health	Inverness Medical Innovations	\$230		Disease management services	see also Bioshares 224
Feb-08	Encysive	Pfizer	\$195		Drug development	117% premium

Selected Life Science Acquisitions: June 2007- July 2008

Month	Target Company	Acquirer	Value (US\$M)	Contingent Value and other terms (US\$ M)	Target Company - Category	Comments
May-08	KOSAN Biosciences	Bristol-Myers Squibb	\$190		Drug developer - oncology	
May-08	Iomai	Intercell	\$189		Vaccine development - travellers diarrhea	Needle free
Aug-07	HemoSense	Inverness Medical Innovations	\$168		Handheld blood coagulation monitoring systems	see also Bioshares 224
Nov-07	Coley Pharmaceutical	Pfizer	\$164		Drug development - immunomodulatory drugs	Also vaccine adjuvants
Feb-08	Piramed	Roche	\$160	\$15	Drug development	
Sep-07	Renovis	Evotec AG	\$152		Drug discovery	Renovis held US\$87M in cash
Jun-08	LipoSonix	Medicis	\$150	plus \$150	Body aesthetics - body contouring	
Jun-08	Barrier Therapeutics	Stiefel Laboratories	\$148		Pharmaceutical - dermatology	73% premium
Dec-07	BBI	Inverness Medical Innovations	\$123		Manufacture of non-invasive later flow tests	see also Bioshares 224
Oct-07	Symphony Genisis	Isis Pharmaceuticals	\$120		Drug development (antisense)	
Aug-07	New Brunswick Scientific	Eppendorf	\$110		LS Instruments	
Dec-07	Redwood Toxicology	Inverness Medical Innovations	\$99		Diagnostics - drugs of abuse	see also Bioshares 224
Jul-08	Corbett Life Science	QIAGEN Inc.	\$66	\$4 in escrowed stock; plus \$65.5 over 4 yrs	LS Tools (PCR)	Sydney-based
Jul-08	SGX Pharmaceuticals	Eli Lilly	\$64		Drug discovery - structure-guided	
Feb-08	CellzDirect	Invitrogen	\$57		Cells for testing services	
May-08	Xanthus Pharmaceuticals	Antisoma	\$52		Dug development - Phase III - Oncology	
May-08	Oryx Pharmaceuticals	Sepracor	\$50	plus \$20	Pharmaceuticals - CNS & pain	
Oct-07	Panbio	Inverness Medical Innovations	\$37		Diagnostics - infectious diseases	see also Bioshares 224
Dec-07	Matritech	Inverness Medical Innovations	\$36	\$2	Diagnostic - cancer detection	see also Bioshares 224
Oct-07	BioStat	Inverness Medical Innovations	\$33	Earn out of US\$ 14.6 M	Distributor	see also Bioshares 224
Mar-08	Cytogen	Eusa	\$23		Pharmaceutical - Pain and Oncology	
Feb-08	FineTech	RxElite	\$18		API manufacturer	
Jan-08	Ester Neurosciences	Amarin	\$15		Drug development	
Feb-08	Hunter-Fleming	Newron	\$12		Drug development - CNS	
Jun-08	Inlog	Global Med Technologies	\$12		Blood centre donor center and transfusion management systems	

Selected Life Science Acquisitions: June 2007- July 2008

Month	Target Company	Acquirer	Value (US\$M)	Contingent Value and other terms (US\$ M)	Target Company - Category	Comments
Jun-08	MCR American Pharmaceuticals	Neuro-Hitech	\$10	3M in escrowed shares	Pharmaceutical (OTC)	
Jul-08	Bio Med Sciences	ULURU	\$10		Specialty wound and burn care	
Jul-08	MacroChem Corporation	Access Pharmaceuticals	\$9		Drug discovery - oncology and dermatology	
Jan-08	Illumigen	Cubist	\$9	\$333	Drug development	
Jun-08	Amnestix Inc	SYGNIS Pharma AG	\$6		Genomics - CNS diseases and conditions	
Feb-08	Cellgate	Progen Pharmaceuticals	\$2.5	plus \$19.5	Drug discovery - oncology	
Jun-08	Actimis Pharmaceuticals	Boehringer Ingelheim	Not Disc.	\$515	Drug development - respiratory	Phase I program
Jun-08	INNOVIVE Pharmaceuticals	CytRx Corporation	Not Disc.		Drug development - clinical stage oncology	
Jan-08	Immunotope	Immunovaccine Technologies	Not Disc.		Immuno-therapy developer	
Jun-07	Quality Assured Services	Inverness Medical Innovations	Not Disc.		Anti-coagulation monitoring	see also Bioshares 224
May-08	amaxa	Lonza Group	Not Disc.		Non-viral transfection technologies	
Apr-08	Virium Pharmaceuticals	MacriChem Corporation	Not Disc.		Drug discovery - oncology	
Jan-08	Precision Therapeutics	Oracle Healthcare Acquisition	Not Disc.		Personalised medicine/ diagnostics	Reverse merger
Apr-08	Calgenex Corporation	PanGenex Corporation	Not Disc.		Nutraceuticals ?	
May-08	ABR (and ABR Invent)	Stiefel Laboratories	Not Disc.		Dermal filler products	
Jul-08	Open Biosystems	Thermo Fisher Scientific	Not Disc.		LS Tools (RNAi)	
Oct-07	NanoDrop Technologies	ThermoFisher Scientific	Not Disc.		LS Instrumentation (UV-Vis instrumentation)	
Jan-08	La-Pha-Pack	ThermoFisher Scientific	Not Disc.		LS -chromatography products	
Sep-07	Pacific Pharma	Upstream Biosciences	Not Disc.		Drug Discovery Platform	

for **Adnexus**, a drug discovery company that has developed a novel protein fragment approach to drug discovery. In both cases, the large pharma companies have placed bets either on a novel technology or biological intervention concept.

Locally, Sydney-based but privately-held **Corbett Life Science** was acquired by **QIAGEN** earlier in July for US\$66 million, with another \$65 million to follow in performance and development milestones. Corbett developed the world's first rotary real time PCR cyclers system.

In the second half of 2007, 21 acquisitions were initiated, compared to 36 in the first six months of 2008. Eight transactions have occurred so far in July, following nine in June and eight in May.

It looks as though M&A activity is intensifying globally and it is only a matter of time before aggressive and hungry pharmaceutical firms place bids on some of the quality Australian biotech firms, whose share prices are languishing.

Bioshares

Correction –

In the sector tables in last week's edition, Living Cell Technologies' share price, quarterly and per cent changes and capitalisation at June 30 were incorrect. The correct figures were 25 cents, -21%, 96% and \$58 million respectively. We apologise to LCT for this error.

Update – Alchemia

Alchemia's (ACL: 31 cents; Cap'n \$50 million) lead program is the development of a generic version of the blood thinning drug, Arixtra (fondaparinux), sold by **GlaxoSmithKline**. The original plan by Alchemia was to submit its generic version of fondaparinux for approval with the FDA in December 2006, with anticipated market launch in early 2008. That timeline has slipped by just over one year but we remain confident Alchemia's generic will reach the market in 2009, possibly in the first half of 2009.

Similar to when the fondaparinux was being manufactured by **Dow Chemical**, there were delays in completing the final purification step. We understand that Alchemia's new manufacturing partner, **Dr Reddy's**, has also met with similar challenges resulting in delays although the company announced that it now expects the drug to be launched in the US in the first half 2009. With the FDA taking around six months to approve generics from submission of the application, we are confident Alchemia's partner will file its ANDA (abbreviated New Drug Application) before the end of this year. There remains a small risk that the FDA will not approve Dr Reddy's application for an unknown reason.

Once the drug receives FDA approval, penetration into the market should be fairly rapid, which is the case for first generics, unlike new drugs that need to establish a market. By way of example, when Dr Reddy's released its generic version of simvastatin in the US in 2006 (an authorized generic from **Merck**) it achieved sales of US\$310 million in the first seven months with peak sales achieved after only one month. Once other generics entered the market, its sales fell by 90%. At this stage there do not appear to be any other

generics companies working on fondaparinux. According to Alchemia's CEO, Pete Smith, fondaparinux is one of the most difficult drugs in the world to manufacture. We understand Alchemia's patented process has reduced the manufacturing steps for fondaparinux by half, to around 25 steps.

In the last set of data to emerge, sales of fondaparinux in the US are currently tracking at US\$150 million a year, up 54% from 12 months earlier. Our expectation is that Alchemia should be able to gain at least 40% of this market next year, which equates to a net revenue for Alchemia of between \$20 - \$25 million on current sales, although we expect sales of fondaparinux to continue to grow.

The clinical drug development process can take seven years to complete and delays are invariably likely to occur. Most recently the **Pharmaxis** market launch of Bronchitol in Europe has been put back by about six months, **Avexa's** launch of its HIV drug has been delayed due to the increased size of its Phase III trials required, and **Peplin** has seen the expected launch of its lead compound, PEP005, for the treatment of skin cancers, move out by one year to 2011 with a different-dose Phase III trial required for head & neck skin cancers (actinic keratosis) compared to the rest of the body. If Alchemia's launch into the US is just over one year late following a change of manufacturer and marketing partner, it will be viewed as quite an accomplishment.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Bioshares Model Portfolio (11 July 2008)

Company	Price (current)	Price added to portfolio	Date added
Avexa	\$0.31	\$0.32	Jun-08
Cellestis	\$2.40	\$2.27	April 2008
IDT	\$1.63	\$1.90	March 2008
Circadian Technologies	\$0.90	\$1.03	February 2008
Patrys	\$0.31	\$0.50	December 2007
NeuroDiscovery	\$0.10	\$0.16	December 2007
Bionomics	\$0.33	\$0.42	December 2007
Cogstate	\$0.12	\$0.13	November 2007
Sirtex Medical	\$2.80	\$3.90	October 2007
Clinuvel Pharmaceuticals	\$0.35	\$0.66	September 2007
Starpharma Holdings	\$0.31	\$0.37	August 2007
Pharmaxis	\$1.47	\$3.15	August 2007
Universal Biosensors	\$0.80	\$1.23	June 2007
Biota Holdings	\$0.77	\$1.55	March 2007
Probiotec	\$1.25	\$1.12	February 2007
Peplin Inc	\$0.39	\$0.83	January 2007
Arana Therapeutics	\$1.01	\$1.31	October 2006
Chemgenex Pharma.	\$1.00	\$0.38	June 2006
Cytopia	\$0.20	\$0.46	June 2005
Optiscan Imaging	\$0.23	\$0.35	March 2005
Acrux	\$1.06	\$0.83	November 2004
Alchemia	\$0.31	\$0.67	May 2004

Portfolio Changes – 11 July 2008

IN:

No changes.

OUT:

No changes.

How Bioshares Rates Stocks

For the purpose of valuation, *Bioshares* divides biotech stocks into two categories. The first group are stocks with existing positive cash flows or close to producing positive cash flows. The second group are stocks without near term positive cash flows, history of losses, or at early stages of commercialisation. In this second group, which are essentially speculative propositions, *Bioshares* grades them according to relative risk within that group, to better reflect the very large spread of risk within those stocks.

Group A

Stocks with existing positive cash flows or close to producing positive cash flows.

- Buy** CMP is 20% < Fair Value
 - Accumulate** CMP is 10% < Fair Value
 - Hold** Value = CMP
 - Lighten** CMP is 10% > Fair Value
 - Sell** CMP is 20% > Fair Value
- (CMP–Current Market Price)

Group B

Stocks without near term positive cash flows, history of losses, or at early stages commercialisation.

Speculative Buy – Class A

These stocks will have more than one technology, product or investment in development, with perhaps those same technologies offering multiple opportunities. These features, coupled to the presence of alliances, partnerships and scientific advisory boards, indicate the stock is relative less risky than other biotech stocks.

Speculative Buy – Class B

These stocks may have more than one product or opportunity, and may even be close to market. However, they are likely to be lacking in several key areas. For example, their cash position is weak, or management or board may need strengthening.

Speculative Buy – Class C

These stocks generally have one product in development and lack many external validation features.

Speculative Hold – Class A or B or C

Sell

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