ISSN 1443-850X

Bioshares

18 October 2013
Edition 525

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

	Bioshares Portfolio
Year 1 (May '01 - May '02)	21.2%
Year 2 (May '02 - May '03)	-9.4%
Year 3 (May '03 - May '04)	70.6%
Year 4 (May '04 - May '05)	-16.3%
Year 5 (May '05 - May '06)	77.8%
Year 6 (May '06 - May '07)	17.4%
Year 7 (May '07 - May '08)	-36%
Year 8 (May '08 - May '09)	-7.4%
Year 9 (May '09 - May '10)	50.2%
Year 10 (May '10 - May'11)	45.4%
Year 11 (May '11 - May '12)	-18.0%
Year 12 (May '12 - May '13)	3.1%
Year 13 (May '13 - Current)	69.4%
Cumulative Gain	**503%**
Av. annual gain (13 yrs)	**20.6%**

Bioshares is published by Blake Industry & Market Analysis Pty Ltd.

Blake Industry & Market Analysis Pty Ltd
ACN 085 334 292
PO Box 193
Richmond Vic 3121
AFS Licence
No. 258032

Enquiries for *Bioshares*
Ph: (03) 9326 5382
Fax: (03) 9329 3350
Email: info@bioshares.com.au

David Blake - Editor
Ph: (03) 9326 5382
Email: blake@bioshares.com.au
Mark Pachacz - Research Principal
Ph: 0403 850 425
Email: pachacz@bioshares.com.au

Individual Subscriptions (48 issues/year)
$400 (Inc.GST)
Edition Number 525 (18 October 2013)

US Biotech Boom Set to Infect Australia

The US biotech sector is going through an IPO boom, with 39 companies having listed this year to dated (see table on the next two pages). On average, these companies have seen share gains of a whopping 68% since listing, with a cumulative US$2.7 billion having been raised. The excitement has made its way to the Australian biotech sector, with a raft of local IPOs expected in the coming months.

The biotech boom in the US is the second largest in biotech investment history, still below the year 2000, which saw 63 companies list, raising US$6 billion. The 2000 boom year was followed by a biotech bull market in 2003. However as a result of the Global Financial Crisis, the IPO window in the US was largely closed until 2012, a year in which 12 companies made IPOs. The missed opportunity as a result of the GFC for venture capital companies to exit their investments has resulted in a powerful surge of biotech listings this year. And that wave of biotech IPOs is showing now signs of abating. In this month alone, 11 companies have filed for an IPO in the US.

The stunning average 68% gain was helped by four companies which have achieved more than a 200% gain from listing. These are Insys Therapeutics (up 400%), which has brought a sublingual fentanyl spray to market in the US, animal health company Aratana Therapeutics (up 367%), cancer stem cell company Stemline Therapeutics (up 252%), and GW Pharmaceuticals (up 227%), which is also listed on the AIM stock market in the UK. This company is developing cannabinoid medicines for the treatment of multiple sclerosis symptoms, cancer pain and neuropathic pain.

Removing these outliers from the calculations, the other 35 companies have still delivered a very impressive average gain of 40% above their listing prices. Since 1 July, that performance has fallen somewhat, with the 17 companies that listed in this half having achieved an average share price gain of 28.8%. Most of the companies that have listed (90%) either had products on market or at Phase II or Phase III stage of clinical development.

Australian Listings

At the end of last year, Alchemia had the right idea of spinning out its oncology business Audeo Oncology to list it in the US. Audeo would have been one of the first companies to list in the US and there is a good chance it would have made a very successful IPO.

Locally, we have seen stem cell company Regeneus list on the ASX last month at 25 cents a share, with that stock now trading at a small (6%) premium to its listing price. Oncosil made a successful backdoor listing through the Neurodiscovery shell, and that stock is up 15%. Eco Quest has also exercised its rights to acquire the remaining shares in US stem cell company Cynata Inc, with Ross Macdonald appointed as Managing Director.

Cont'd on page 3

US Biotech IPOs 2013

	Listing date	Code	Country of Origin	Company Name	Field	Status	Cap. US$M	Listing Price US$	Raised US$ M	Price 18 Oct $	Gain Since Listing
1	Apr-13	CGIX	USA	Cancer Genetics	Cancer diagnostics	On market	$91	$10.00	$7	$15.24	52%
2	Jul-13	ICEL	USA	Cellular Dynamics	Stem cell lines for R&D	On market	$278	$12.00	$46	$17.72	48%
3	May-13	INSY	USA	Insys Therapeutics	Pain drugs	On market	$853	$8.00	$32	$40.00	400%
4	Jun-13	KMDA	Israel	Kamada	Plasma-derived proteins	On market	$488	$9.25	$52	$16.44	78%
5	Jan-13	LPDX	USA	LipoScience	Diagnostics (low density lipo protein)	On market	$74	$9.00	$45	$5.00	-44%
6	Jun-13	NSTG	USA	NanoString Technologies	Diagnostic (molecular, breast cancer)	On market	$163	$10.00	$54	$11.15	12%
7	Sep-13	FMI	USA	Foundation Medicine	Cancer diangostics (for personalised treatment)	On market	$923	$15.00	$106	$34.00	127%
8	May-13	GWPH	UK	GW Pharmaceuticals	MS symptom treatment, pain	On market	$392	$8.90	$31	$29.12	227%
9	Apr-13	OMTH	USA	Omthera Pharmaceuticals	Cardiovascular. Co acquired by AstraZeneca	Filing NDA	$323	$8.00	$64	$12.70	59%
10	Jun-13	PTCT	USA	PTC Therapeutics	Duchenne's Muscular Dystrophy, Cystic Fibrosis	Phase III	$457	$15.00	$125	$19.24	28%
11	Mar-13	ENTA	USA	Enanta Pharmaceuticals	HCV inhibitors with AbbVie	Phase III	$363	$14.00	$56	$20.30	45%
12	Jun-13	BLUE	USA	Bluebird bio	Gene therapy, rare diseases	Entering Phase III	$561	$17.00	$101	$23.80	40%
13	Apr-13	CMRX	USA	Chimerix	Antivirals, prevention of CMV	Entering Phase III	$436	$14.00	$102	$16.82	20%
14	Jul-13	CNAT	USA	Conatus Pharmaceuticals	Liver diseases, ex-Pfizer drug	Entering Phase III	$155	$11.00	$66	$9.99	-9%
15	Aug-13	SPHS	Canada	Sophiris	(BPH) Prostate cancer	Entering Phase III	$14	$5.00	$65	$4.49	-10%
16	Mar-13	TTPH	USA	Tetraphase Pharmaceuticals	Antibiotics	Entering Phase III (x2)	$272	$7.00	$75	$13.20	89%
17	May-13	ADHD	Israel	Alcobra Pharma	ADHD	Late stage clinical	$215	$8.00	$25	$19.29	141%
18	Jul-13	ONTX	USA	Onconova Therapeutics	Oncology (kinase inhiobitor)	Phase III	$442	$15.00	$77	$20.68	38%
19	May-13	PTLA	USA	Portola Pharmaceuticals	Anticoagulant (Factor Xa inhibitor)	Phase III	$836	$14.50	$122	$23.75	64%
20	Aug-13	RGDO	USA	Regada Biosciences	Bleeding in heart surgery	Phase III	$121	$4.00	$43	$5.96	49%
21	Oct-13	OPHT	USA	Ophthotech	Combination eye drug therapy	Phase III	$836	$22.00	$167	$23.75	8%
22	May-13	RCPT	USA	Receptos	Relapsing-remitting MS	Phase II/Phase III	$598	$14.00	$73	$33.91	142%
23	Jun-13	RNA	Netherlands	Prosensa	Duchenne's Muscular Dystrophy (licensed to GSK)	Phase IIb	$124	$13.00	$78	$4.29	-67%
24	Oct-13	EVOK	USA	Evoke Pharma	GI disorders	Phase IIb	$72	$12.00	$25	$12.50	4%
25	Jan-13	KBIO	USA	Kalabios Pharmaceuticals	MABs, Cystic Fibrosis, asthma	Phase II	$107	$8.00	$70	$4.42	-45%
26	May-13	AMBI	USA	Ambit Biosciences	Various, kinase inhibitors	Phase II	$322	$8.00	$65	$18.02	125%
27	Oct-13	MGNX	USA	MacroGenics	Oncology (next generation antibodies)	Phase II	$610	$16.00	$92	$25.41	59%
28	Oct-13	FATE	USA	Fate Therapeutics	Adult stem cell therapies	Phase II	$134	$6.00	$40	$7.00	17%
29	Sep-13	XLRN	USA	Acceleron	Boost red blood cells (with Celegene)	Phase II	$605	$15.00	$97	$22.80	52%
30	Jan-13	STML	USA	Stemline Therapeutics	Oncology (cancer stem cells)	Moving into Phase IIb	$432	$10.00	$33	$35.20	252%
31	Jun-13	ESPR	USA	Esperion Therapeutics	Cholesterol, ex-Pfizer drug	Phase IIa completed	$251	$14.00	$70	$17.20	23%
32	Jul-13	HTBX	USA	Heat Biologics	Oncology, immunotherapy	Entering Phase II	$69	$10.00	$25	$11.13	11%
33	Jun-13	PETX	USA	Aratana Therapeutics	Animal health	Clinical	$613	$6.00	$35	$28.04	367%
34	May-13	EPZM	USA	Epizyme	Oncology, Celgene partner	Phase I	$1,040	$15.00	$89	$36.54	144%
35	Jul-13	OMED	USA	OncoMed Pharmaceuticals	Oncology (cancer stem cells)	Phase I	$410	$17.00	$82	$14.76	-13%
36	Jul-13	AGIO	USA	Agios Pharmaceuticals	Oncology	Preclinical	$886	$18.00	$106	$28.52	58%

Cont'd over

US Biotech IPOs 2013

Platform/Tools companies

37	Aug-13	XON	USA	Intrexon	Synthetic biology/tools company	Phase I, Phase II	$2,230	$16.00	$160	$23.00	44%
38	Sep-13	BIND	USA	Bind Therapeutics	Oncology (nanomedicine)	Phase II	$236	$15.00	$71	$15.00	0%
39	Sep-13	FPRX	USA	Five Prime Therapeutics	RA (with GSK), cancer, (protein libraries)	Phase I	$221	$13.00	$62	$13.82	6%
							Total Funds Raised		$2,733		
							Average Price Gain				**68%**

– US Biotech IPOs cont'd from page 1

BioLife Science was looking to conduct a backdoor listing through Acuvax however that deal fell through, and *Bioshares* understands BioLife is seeking to attempt a backdoor listing through a different vehicle. Dermatology drug developer Mimetica was seeking to conduct a backdoor listing through listed shell Telesso Technologies, and that deal was due to conclude on Friday 18 October. However it is unclear whether that deal will progress or not.

At least two local IPOs are underway. One is with New Zealand drug developer Innate Immunotherapeutics, which is developing a drug for secondary-progressive multiple sclerosis. The IPO is being managed by Pattersons Securities, with the company seeking to raise $16.5 million. Innate's lead drug candidate in Phase II development. Canaccord Genuity is also working on an undisclosed Victorian biotech IPO, seeking to raise $14 million.

We expect a number of additional IPOs to be announced in coming months. IPO candidates include Victorian company Ascend Biopharmaceuticals, which recently conducted a pre-IPO funding round and appointed Pete Smith as Chairman. Animal health company NexVet has said it will consider a listing in 2014.

Bioshares

Bioshares Model Portfolio (18 October 2013)

Company	Price (current)	Price added to portfolio	Date added
Oncosil Medical	$0.150	$0.155	September 13
Calzada	$0.080	$0.073	September 13
Invion	$0.090	$0.060	August 13
IDT Australia	$0.370	$0.260	August 13
Viralytics	$0.380	$0.300	August 13
Circadian Technologies	$0.250	$0.270	March 2013
Tissue Therapies	$0.280	$0.255	March 2013
Benitec Biopharma	$0.615	$0.40	November 2012
Somnomed	$1.20	$0.94	January 2011
Cogstate	$0.480	$0.13	November 2007
Universal Biosensors	$0.63	$1.23	June 2007

Portfolio Changes – 18 October 2013

IN:
No changes.

OUT:
No changes.

Is Pharmaxis a Takeover Target? At What Price?

Key Events 2012-2013

April 20, 2012 - Receives European Marketing Authorisation for Bronchitol for CF Patients > 18 years

January 31, 2013 - Receives a Negative Recommendation from the FDA's Pulmonary-Allergy Drugs Advisory Committee Concerning Bronchitol

January 31, 2013 - Receives US$20 Million from Financing Agreement with NovaQuest Pharma Opportunities Fund III; NovaQuest to Receive Payments based on the sale of Bronchitol for CF in the USA (for 7 years from launch) and Europe (for 8 years); A Further US$20 Million May be invested in January 2014

March 12, 2013 - Gary Phillips Appointed CEO; Alan Robertson Steps Down

March 19, 2013 - Receives Complete Responses Letter from the FDA for Bonchitol for CF

April 24, 2013 - Announced Bronchiectasis Phase III Trial Did Not Meet Primary Endpoint

May 23, 2013 - Reports Results of Business Review - Intention to Partner Bronchitol for CF in the US, Bronchiectasis Globally, Maintain Direct Interest in CF for Europe

Conference Call – Key Points

Pharmaxis (PXS: $0.125) held its September quarter conference call was this week. CEO Gary Phillips discussed progress made in the September quarter against the corporate restructuring plans set out earlier in the year.

The company submitted a draft protocol for its third Phase III trial of Bronchitol in cystic fibrosis patients to the FDA, with a response expected in the current December quarter. This trial is, it should be remembered, only being conducted in the adult population. Pharmaxis estimates the Phase III trial will cost $15 million and while the company is studying proposals from CROs, it expects trial to begin recruitment in 2014 H1.

Phillips also said that Pharmaxis had shortlisted potential North American licensing partners and that they had 'detailed discussions with quite a large number of significant partners'. He said that some of these companies were already in CF in the US but there were also some whom would like to enter the CF market in the US.

Pharmaxis is aiming to finalize a deal by 2014 Q1 once the company has been able to convert the current program of solicitation of interest into a formal bids process.

Phillips discussed progress made with Bronchitol sales in UK and Germany where he said they are 'now beginning to see results', describing the September quarter sales as solid. He said sales in Germany were 'going back to growth after a sluggish phase' and that UK sales show 'what can be done in well supported clinics when the funding issues are resolved.'

Bronchitol unit sales of approximately 1,600 were 25% higher in the September quarter from the previous quarter. Unit sales in Germany (~920 units) rose 14% from the previous quarter and in the UK (350 units), by 87% for over the same period. The strong growth in the UK was attributed in part to national pricing for Bronchitol coming into effect from April 1, 2013 and the change in the number of centres selling Bronchitol

Commentary

Pharmaxis raises several interesting investment considerations for investors, which revolve around what the likely effective prescription rate of Bronchitol (the percentage of the total CF population using the drug) will be in the US.

To set some benchmarks, the prescription rate for Pulmozyme (Dornase alpha) in the US is 82%, for hypertonic saline 55% and TOBI (tobramycin solution for inhalation) 66%. (These rates apply to CF patients aged six and over.)

What is emerging from five quarters of sales of Bronchitol in the UK and Germany is crude but important data for prescription use, and market access trends. It should be noted that with the UK only the two most recent quarters include sales made following the granting of UK national pricing.

If quarterly unit sales are converted into fully compliant patient prescription sales (FCPP), then Pharmaxis achieved an estimated market access in the September quarter in the UK of 1.1%. The equivalent figure Germany was an estimated 3.5%. (Note that Bronchitol is only approved for patients aged 18 and over in Europe.) (An FCPP can defined as the number of patients who are prescribed Bronchitol and use the drug and are fully compliant over the quarter. A fully compliant patient for example would use 6 units (i.e. 6 x 14-day packs) over a quarter.)

However, a problem with conversion of the unit sales data into an FCPP figure is that the unit sales figures are not broken down into actual per patient prescriptions and repeats. The FCPP assumes full compliance with the product label's instructions for use. It does not take into account units which are purchased but are not used. (A second limitation is that Bronchitol has not been available from all CF centres in Germany and UK, which it now reports access at 85% of centres in Germany and 65% in the UK.)

Pharmaxis has described adherence problems with Bronchitol, or to use another phrase, the 'cycling on and off' of medication. This means that the unit sales figure could actual mean that Bronchitol has been purchased and used by more CF patients than the FCPP market access rate implies.

Pharmaxis has put in place plans to improve the adherence problem in Germany by initiating a pilot physiotherapy led education program at nine centres and a pilot behavioural training program at four centres.

Cont'd over

The impact of these programs is expected to begin to be seen in 2013 Q4 and 2014 Q1. The company has remarked that adherence is stronger in the UK and Australia, estimated at about 60%-65%. In this case adherence means the percentage of patients which take the drug as indicated for use.

The problem facing Pharmaxis is where a market access rate for Bronchitol for CF might sit. Is it more likely to be 10%, or 80% and roughly in line with Roche's Pulmozyme? What might mitigate against Bronchitol achieving a market access rate of greater than 10% is a feature of the drug itself, which is that the drug must be inhaled 10 times twice a day [see box for an extract from the European product label for Bronchitol for CF].

This number of inhalation events may mean that CF patients make tradeoffs with the drug, possibly using Bronchitol as an ancilliary but not primary lung health medicine. In other words, it may become an optional or discretionary treatment. The extract from the product label also shows the complexity that occurs with the administration of cystic fibrosis medicines and therapies.

We estimate the break even market access rate for Pharmaxis' financing partner Novoquest to be about 15%. This is an important figure for investors because, if a market access rate of 15% is applied to a no-growth in patient number model for Bronchitol, priced at US$13,000, the adult CF market for the US is valued at about 15 cents per share (assuming FDA approval).

Extract from Bronchitol Product Label (Europe)

Therapeutic dose regimen

The therapeutic dose regimen should not be prescribed until the initiation dose assessment has been performed.

For patients receiving several respiratory therapies, the recommended order is:

1. Bronchodilator (must be administered 5-15 minutes before Bronchitol).

2. Bronchitol

3. Physiotherapy/exercise

4. Dornase alfa (if applicable)

5. Inhaled antibiotics (if applicable)

The recommended dose of Bronchitol is 400 mg twice a day. This requires the inhalation of the contents of ten capsules via the inhaler device twice a day.

An Investment Strategy

A strategy for investors to consider is to factor in the likelihood of a bid for the company by one of the companies currently investigating licensing Bronchitol. We outline some assumptions below that describe a potential bid price.

First we assume a market access rate of 15%, in line with our (hypothetical) estimate of Novoquest's break even rate. Assuming the company's cash balance reduces by $8 million over the December quarter to $45 million gives 15 cents per share.

Given that the European CF market is roughly equivalent to the US, then 15 cents a share can be applied to the stock for that asset. Valuation upside could also arise from expanding the labeling to include CF patients below the age of 18 in Europe. Pharmaxis is currently managing a pediatric trial (CF-204) to support this objective. However, we balance out the current absence of sales in many other European territories with the upside potentially gained from a pediatric label expansion.

We factor in Bronchitol for CF for the US at 17 cents (assuming a 90% chance of FDA approval), but also factoring out obligations to Novoquest relating to the second funding tranche.

Pharmaxis is a potentially a takeover target at up to 47 cents per share. Net of cash, an acquirer might pay up to $98-$99 million for Pharmaxis. However, the timing of a takeover to be optimal for an acquirer would have to be formally initiated before the end of the year because of the necessity to gazump the licensing process.

It is probable that a very significant number of shareholders of Pharmaxis would support a takeover given the tremendous loss of value that has occurred with this stock.

If an acquisition bid does not eventuate before the end of the year and the US rights for bronchitol are secured by a partner, investors speculating on the takeover play should sell the stock.

Pharmaxis is capitalised at $38.6 million.

Bioshares recommendation: **Speculative Buy Class C – Short Term Trade**

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: Starpharma Holdings, Cogstate, Bionomics, Impedimed, QRxPharma, LBT Innovations, Mesoblast, Tissue Therapies, Viralytics, Phylogica, pSivida, Antisense Therapeutics, Benitec BioPharma, Allied Healthcare Group, Calzada, Atcor Medical, Invion, Circadian Technologies

Subscription Rates (inc. GST)

48 issues per year (electronic distribution): **$400**

For multiple email distributions within the same business cost centre, our pricing structure is as follows:	$630	2-3 email addresses
	$855	4-5 email addresses
	$1090	6-10 email addresses

To subscribe, post/fax this subscription form to:

Bioshares
PO Box 193 Richmond VIC 3121
Fax: +61 3 9329 3350

I enclose a cheque for **$** made payable to **Blake Industry & Market Analysis Pty Ltd**, or

Please charge my credit card **$** MasterCard ☐ Visa ☐

Card Number ☐☐☐☐ ☐☐☐☐ ☐☐☐☐ ☐☐☐☐

Signature _____ Expiry date _____

Subscriber details

Name _____

Organisation _____

Ph ( ) _____

Emails _____

_____

_____