ISSN 1443-850X

In this edition...
This week two Melbourne-based biotechs were moving in starkly different directions. Avexa has closed its lead HIV program, which should not come as any real surprise given the failure to secure a licensing deal over the last two years. In contrast, Mesoblast is transforming itself into a global adult stem cell technology powerhouse by acquiring the remaining interests of its investee company, Angioblast Systems.
We also provide more coverage from the BIO 2010 conference from Chicago earlier this month, hearing from four biotech CEOs who had successfully sold their platform technology companies in recent years for very hefty multiples.

The Editors
Companies Covered: BIO coverage, AVX, MSB

	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 - Current)	1.7%
Cumulative Gain	**194%**
Av Annual Gain (9 yrs)	**18.5%**

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
Ph: (03) 9326 5382
Email: blake@bioshares.com.au
Mark Pachacz
Ph: (03) 9671 3222
Email: pachacz@bioshares.com.au

Individual Subscriptions (48 issues/year)
$350 (Inc.GST)
Edition Number 359 (14 May 2010)
ISSN 1443-850X

Bioshares

14 May 2010
Edition 359

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

Avexa Winds Down; Mesoblast Consolidates Global Stem Cell Business

This week Avexa (AVX: 2.6 cents) announced it would be closing its lead HIV program for the drug candidate apricitabine. The reason announced for closing the program was due to an inability to conclude a licensing deal for the compound. The company's CEO, Julian Chick resigned from the board immediately and will step down as CEO at the end of this month. The company's share price came crashing down this week, falling 78% to end the week at 2.6 cents. The main surprise for investors should have been that the closure of this program took so long to eventuate.

Apricitabine program falls off rails, November 2007

Following successful Phase IIb results in treating patients with HIV announced in early 2007, Avexa immediately raised $79.5 million to fund its Phase III pivotal program. This was supposed to be enough to complete clinical development and file the drug for approval. However, the commercial viability of this program became questionable in late 2007 at the company's AGM, just eight months after the capital raising was announced.

At that AGM, the company announced that the FDA had requested Avexa to include a higher dose in the Phase III trials. This effectively made the trial a combination of a Phase II dose ranging study and a Phase III trial. The outcome was that patient numbers would have to increase from 800 patients to 1800 patients, which alarmingly, Avexa could not fund with the money raised earlier that year.

Bioshares opening comments following that AGM (in *Bioshares* 242 in November 2007) were "Warning signs are emerging with this stock". At the time the stock was trading at 64.5 cents and we placed a **Sell** recommendation on the stock with a three-month price target of 40 cents. In hindsight that price target was generous. Other concerns remained over the patent life over the program, with composition of matter patents expiring in 2013, and we ended our note by saying "the outlook for this program is dimming".

In August 2008, we placed a **Speculative Buy Class B** on the stock after it had fallen to 31.5 cents, but the stock had further to fall with concerns about securing a partnering deal increasing. After two years of running a Phase III trial the company could not complete on its own, Avexa was unable to partner its lead program. In October 2009 the company announced it would stop its Phase III trial, un-blind data and assess the progress. The aim was to attract a partner with the additional data, although a new trial would then need

– cont'd over

to be conducted to get the drug candidate to market.

Surprisingly the company was able to raise a further $15 million in November/December last year having to scale back subscriptions for stock.

When the Phase III results were released in February of this year, the results were disappointing because they did not match the very good Phase IIb results from 2007. This prompted another **Sell** recommendation from *Bioshares.*

Reasons for apricitabine development failure

On May 6 (last week) Avexa received news that the last party involved in partnering discussions did not want to proceed with licensing Apricitabine. Avexa listed three reasons for an inability to partner its Apricitabine program. The first was the large commitment required in view of other factors, including US market exclusivity. This relates back to the short patent life on apricitabine, an issue raised by *Bioshares* in at least 2007.

The second factor was the high dosage required of apricitabine, making it difficult to combine into one pill with other HIV drugs. **Datamonitor**'s analyst, Hedwig Kresse, said this week once daily, cross class, fixed dose combinations, such as Atripla (a combination of two **Gilead** drugs and one **BMS** drug) will drive the market growth in the HIV space. Datamonitor expects Atripla sales to peak next year and US$2.4 billion, and will be followed by Gilead's QuadPill, which includes four drugs into the once daily pill. Datamonitor says the shelving of apricitabine does not come as a surprise in the competitive HIV market, and the twice-daily dose impeded the combination with other retroviral drugs limiting its scope.

The third factor cited by Avexa for ending apricitabine development was the inability to assess the level of activity of apricitabine when used in combination with new active drugs on the market (which presumably reflects the effective treatment regimes available for combating HIV infection).

Avexa expects to have $23 million in funds at the end of this financial year. It is conducting a review on current projects and M&A opportunities.

The lessons to be learned from Avexa are: the intellectual property position of a program remains a key investment parameter; the strategic market positioning of a novel therapy is crucial and one that needs to be regularly revised and questioned; and companies should not start pivotal clinical studies unless there is the financial capacity to complete that program.

Bioshares recommendation: **Under Review**

Bioshares recommendations on Avexa

Date	Price	Recommendation
23 November 2007	64.5 cents	Sell
15 August 2008	31.5 cents	Speculative Buy Class B
13 February 2009	8 cents	Avoid
5 February 2010	13.5 cents	Sell

Mesoblast Sizes Up With Angioblast Acquisition

Mesoblast has reached agreement to acquire the remaining assets of its investee company, Angioblast Systems Inc, forming one of the leading and possibly the largest adult stem cell companies in the world. In a complicated structure previously that has seen Mesoblast with commercial rights to orthopedic applications of the same mesenchymal precursor cell platform, and Angioblast owning rights for cardiac (and other) applications, the proposed merged business will provide investment and operation clarity.

Mesoblast has also raised $27 million ($13 million of which is committed but subject to shareholder approval), which based on Friday's closing price, will give Mesoblast a market capitalisation of $537 million. The acquisition values Angioblast at $239 million and the core Mesoblast assets (excluding the 33% ownership in Angioblast) at $161 million.

Angioblast has more advanced clinical programs, with a pivotal study anticipated starting in cord blood expansion for bone marrow transplant in the next 12 months. That product is being developed under an orphan drug designation. A pivotal trial could involve as few as 100 people with a three month endpoint. Angioblast also has delivered positive interim Phase II data in the treatment of heart failure. Mesoblast is conducting a Phase II trial in spinal fusion and is due to start a Phase II trial in the regrowth of spinal disc cartilage. Mesoblast is also looking to have its product for the repair on non-union long bone fractures available in Australia this year under the Special Access Scheme.

Under the sale agreement, Angioblast shareholders are entitled to receive 15% ($24 million) of their consideration in cash, which the company says is to fund capital gains tax requirements in the US for US shareholders in Angioblast.

The combined entity gives investors in Mesoblast greater clarity in their Angioblast investment and reduces the risk profile of the stock with a greater breadth in clinical programs. It will also allow the company to more objectively prioritise the commercial programs and streamlines the management of the businesses. With a capitalisation of around $500 million, future capital raises of up to $70 million would be possible without requiring shareholder approval. That level of investment would allow the company to significantly expand its clinical trial activity which should continue to build shareholder value if positive results can be achieved. There appears to be sufficient interest in Mesoblast's work to support acceleration of the company's activities.

Bioshares recommendation: **Speculative Hold Class A**

Bioshares

BIO 2010 Coverage: The Deal Makers – M&A Success Stories

This session brought together the CEOs from four biotechs that were acquired for attractive multiples between 2005 and 2007. The panel comprised Bob Connelly (ex-Domantis), Duncan Higgons (ex-Transform Pharmaceuticals), Tillman Gerngross (ex-Glycofi) and John Mendlein (ex-Adnexus).

Bob Connelly, Domantis (currently CEO Pulmatrix)

Bob Connelly was instrumental in growing the Domantis business, which culminated in its sale to GlaxoSmithKline in 2006 for US$454 million. (Former Arana Therapeutics/Peptech shareholders will remember this transaction, since Arana as a 31% shareholder and received an estimated $170 million from the sale. (Current shareholders of Pharmaxis would also be keen to follow the development of Pulmatrix, a company developing drugs to treat lung conditions such as COPD).

Domantis was sold six years after its inception. Greg Winter and Ian Tomlinson founded the company. Greg Winter was previously a founder of Cambridge Antibody Technology and a key inventor of antibody humanization technologies.

In 2000, Domantis was established as a virtual company and one employee, Bob Connelly. In 2001, the decision was made to focus on the most risky of a range of potential applications, that of domain antibodies, which are smaller fragments of antibodies. The goal was to engineer a single molecule that could bind to multiple targets, that did not need to be administered by injection, and could be directed to new targets due to the much reduced size of the molecules.

In its virtual phase of existence, US$20 million was raised. But by 2005, Domantis had raised $75 million, mostly from strategic partners, with staff numbers growing to 65. Connelly said that early on, Domantis moved away from the service provider model. The reason Domantis was bought, in the end, was because it had a lot of unpartnered products in development.

Prior to sale, Domantis had closed a Series C round, with three years worth of cash in the bank and was probably three years away from establishing proof-of-concept of the dab technology. At the time Domantis had one pre-clinical asthma program as its most advanced product.

"Timing is everything" said Connelly. In the year before its acquisition, Glycofi and CAT had been acquired. "People were jumping on companies in the space". Then the company was put in play, with an unsolicited proposal, although there had never been any discussion previously about selling the company, because (board and management) never thought they could get the values that warranted its sale. There were five companies that did diligence, but this fell back to two. Connelly believed that GSK wanted Domantis primarily for the people, its toolkit and freedom to oper-

ate in the antibody space, but having an unencumbered pre-clinical program was also important.

Duncan Higgons, Transform Pharmaceuticals (currently Agios Pharmaceuticals)

Transform Pharmaceuticals was founded in 1999 by Nick Galakatos, who was formerly with Millennium Pharmaceuticals. Investors originally were MPM and Polaris, although strategic investors came to include Johnson & Johnson and Eli Lilly. Duncan Higgons came on board as CEO in early 2003.

By the time of its acquisition in 2005 for US$230 million cash, it had raised US$60 million, achieved revenues of US$35 million and employed about 80 people.

The original technology started out as a form and formulation platform, with core competencies in physical chemistry, materials science and high throughput screening, with the focus in the beginning on lower value service provision. However, it progressed to higher value higher risk areas including transdermals, biologics and convergence products. By the time of acquisition, the company had some significant deals in the pipeline. And it had started a products initiative. The company eventually took a liquid formulation product from a lead to Phase II in 18 months.

Leading up to the acquisition, Transform Pharma found a new crystal form of topiramate (an epilepsy medicine) but did not realize they had beaten J&J in patenting the chemical. Transform set out to do a deal on topiramate, however, this progressed into a full acquisition. The acquisition process began nine months after the topiramate deal. A portion of the US$230 million was withheld for 18 months as contingency for any liabilities that might arise. The return to investors was between one and five fold.

Higgons said that the sale of Transform should be been done much earlier and should have moved to developing higher value assets much sooner and been more aggressive in doing so.

Tillman Gerngrass, Glycofi (currently Adimab)

Glycofi was founded in 2006 and sold to Merck for US$400 million in March 2006. Investors included Polaris, SV Life Sciences, Eli Lilly, Merck, and Boston Millennia Partners. Total invested capital was $28 million, with the return on investment fourteen fold. The sale process was run as a limited auction managed by Morgan Stanley.

Glycofi was a platform technology company that developed a yeast system to make glyco-proteins. The firm's technology was targeted at making more effective biologics by controlling the sugars that decorate proteins in a way that was superior to that achieved by using CHO cells.

The sale originated in a deal with Eli Lilly, who wanted to expand the arrangement. However, the company said to Lilly that it was too busy working on projects for Merck. This stimulated a proposal to acquire the company from Lilly. However, under the state laws that governed the company, other shareholders were to be notified of any bid, and this is what led to the acquisition by Merck, since Merck was a shareholder.

Gerngrass said in retrospect, they had been 'lousy' in articulating the value of Glycofi to investors, with the capitalisation of the company not reaching $70 million when a capital raising was conducted in year six with the company being sold four months later for $400 million. He remarked that he didn't make that 'mistake' with his current company Adimab, founded in 2007, which has had five rounds of financing, with investors coming to Adimab and not the reverse.

John Mendlein, Adnexus (currently CEO Fate Therapeutics)

Adnexus was sold to Bristol Myers Squibb in September 2007 for US$430 million plus a US$75 million earnout. All up, US$50 million had been invested in the company. In setting the scene, Mendlein said that at the time biologics companies were developing a scarcity value, sometimes leading to auction processes with large pharma companies. " There was some concern that they would not be able to participate in biologics the way they needed to build out a robust pipeline."

Significantly, Adnexus completed a 'very important' pre-clinical deal with BMS which allowed the company skip a financing round. The company was initially founded as Adzymes. Investors included Polaris, Atlas and Flagship. However, in 2004-05 it absorbed the assets of Phylos, for its Adnectins and Profusion technologies.

Initially the company, like Domantis, was developing a hybrid model of service provision and partnerships. However, it shifted towards drug development. Mendlein commented that the company employed people who had been associated with bringing 20 prod-

Bioshares Model Portfolio (14 May 2010)

Company	Price (current)	Price added to portfolio	Date added
Tissue Therapies	$0.19	$0.21	January 2010
Biodiem	$0.16	$0.15	October 2009
QRxPharma	$1.20	$0.25	December 2008
Hexima	$0.29	$0.60	October 2008
Atcor Medical	$0.13	$0.10	October 2008
CathRx	$0.16	$0.70	October 2008
Impedimed	$0.67	$0.70	August 2008
Mesoblast	$2.09	$1.25	August 2008
Circadian Technologies	$0.70	$1.03	February 2008
Patrys	$0.11	$0.50	December 2007
Bionomics	$0.30	$0.42	December 2007
Cogstate	$0.26	$0.13	November 2007
Sirtex Medical	$5.36	$3.90	October 2007
Clinuvel Pharmaceuticals	$0.23	$0.66	September 2007
Starpharma Holdings	$0.57	$0.37	August 2007
Pharmaxis	$3.29	$3.15	August 2007
Universal Biosensors	$1.53	$1.23	June 2007
Probiotec	$1.44	$1.12	February 2007
Acrux	$1.95	$0.83	November 2004
Alchemia	$0.60	$0.67	May 2004

Portfolio Changes – 14 May 2010

IN:
No changes.

OUT:
No changes.

ucts to the market and had been responsible for 50 INDs. "We had the DNA inside the company to take us to the long haul." The goal was to build a pipeline but also keep part of the pipeline.

Mendlein noted that the pressure began to grow to have human clinical data to show that this new class of biologics was safe, since concerns had been expressed that the technology might create mutagenic compounds. In February 2007, the company began its collaboration with BMS. By July it closed a Series C round, raising $15.9 million, and by August it had filed for an IPO.

However, by September the deal with BMS took place. At about the time of the acquisition was initiated, Adnexus had begun preparations for a Phase II trial, and also begun development of manufacturing capabilities. "There was a lot of operational execution at about the same time as we were starting to explore our strategic options."

"BMS was quite smart" Gerngrass said. "There was a very strong joint program execution. In other words we were executing on targets we had already agreed to with BMS and already generated very interesting data they hadn't seen before. This happened very quickly and in a very capital efficient manner."

Summary

Several themes emerged from the discussion that followed. Each company, prior to its acquisition, either had a collaboration or was establishing one with its acquirer. All companies had a platform technology of some description, several offered strong IP positions and freedom to operate within current monopoly areas, all were bought by aggressive, sophisticated buyers. And in several instances, the acquisition allowed the buyer to complement and infill its technology and product base.

Another theme was that all companies were, in general, aiming to build a robust, stand alone business, in other words, they weren't built as a 'spec house' in the hope that a buyer would come along. And finally, the move from the service provision model to product development model, qualified with the objective of getting a product in the clinic to validate the technology was also an important factor in generating a higher sales multiple.

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.

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, ChemGenex Pharmaceuticals, Circadian Technologies, Biota Holdings, Halcygen Pharmaceuticals, Impedimed, QRxPharma, Patrys, LBT Innovations, Hexima, Tyrian Diagnostics, Mesoblast, Atcor Medical, CathRx, BioMd, Tissue Therapies, Viralytics