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In this edition...
Avexa shareholders have met and voted out the board chaired by Nathan Drona. With a new board in place, Avexa's ATC program may be re-started. But whether major shareholder Calzada supports this decision is a quesion to be answered.
Alchemia shares have come under pressure when it was revealed that a another generic of fondaparinux is being developed by Apicore of India.
On a positive note Atcor Medical has now received two favourable rulings from the CMS in the US that recommend the reimbursement of its Sphygmocor systems in four US states. And Biotron now has ethics approval for its HCV Phase II trial of BIT225.

The Editors
Companies Covered: ACG, ACL, AVX, BIT

	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)	-5.9%
Cumulative Gain	**172%**
Av Annual Gain (9 yrs)	**18.5%**

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Bioshares

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

Heated Discussion at Avexa EGM

Avexa (AVX: 3.7 cents) held an extraordinary general meeting this week which was truly extraordinary. The meeting was requisitioned by a group of unnamed shareholders, who combined own 5.3% of the company. The aim of the meeting was to vote on the removal of two of the company's three directors, Nathan Drona and Uri Ratna. It was a very heated meeting with both alternatives offering poor options for Avexa shareholders.

Background

Avexa was formed in 2004 when the anti-virals assets were spun out of Amrad. In January 2005 the company in-licensed the HIV drug candidate, now known as apricitabine, from **Shire Pharmaceuticals**. The drug had achieved positive Phase IIa results under Shire and Avexa went on to deliver positive trials in a Phase IIb trial in 2007. On the back of those positive results, the company raised $75 million, which was intended to be sufficient to fund the Phase III program for apricitabine.

However, in November 2007, the company announced at its AGM some devastating news, the weight of which was not to be appreciated by many shareholders for another two years; the Phase III program which was previously meant to involve only 800 patients, would need to be expanded to 1800 patients.

This was a game changer for the company. It would mean it was not able to complete the Phase III program for apricitabine for which it had just raised $75 million. In October 2009 the company announced that its uncompleted Phase III program would be closed and unblinded, in what can only be seen as a last desperate attempt to gain further data to partner the program.

The flaws with this asset were the composition of matter patent that expires in 2013, a double digit royalty that would need to be paid to Shire, the relatively small market size that struggled to justify development of the drug when the previous two factors are taken into account, the requirement to dose apricitabine twice daily rather than once a day, and the control that the major pharmaceutical companies have over the HIV drug industry, where a combination pill of once daily medication of three drugs place massive barriers to new entrants. From 2004, Avexa has spent around $130 million on its programs, the majority for apricitabine.

EGM Coverage

From our perspective, various Avexa shareholders at the AGM appeared to be very well briefed, posing many difficult questions to Avexa chairman Drona. It was an opportunity for various shareholders to vent their anger at the company in not being able to successfully develop the company's HIV drug candidate apricitabine. The main issue between the board and various shareholders was the discontinuation of the apricitabine program, which had been announced on 10 May this year.

The call to have Drona removed from the board was not surprising or unreasonable given the failure of the company to commercialise apricitabine. Investors had already seen the

– Cont'd on page 3

Biotron's Phase II Go-Ahead

Biotron (BIT: $5.8 cents) has received ethics approval for a Phase II study of BIT225 as a treatment for Hepatitis C to be conducted in Argentina. The trial is expected to be completed this year, although the dosing stage should be completed by September, with results available in the December quarter. This is a crucial study for the company, in which BIT225 will be evaluated as a combination therapy with interferon and ribavarin. The control will be standard of care.

The trial will enrol 24 treatment naive subjects that test positive for HCV genotype 1, the most common strain of HCV. They will be administered standard of care in conjunction with BIT225, with dosing taken place over 28 days. Two doses will be evaluated, 200 mg and 400 mg.

Development of HCV Medicines

As previously discussed in *Bioshares* #353 there are many drugs in development for the treatment of HCV, driven by an infectious agent that hibernates over decades in subjects and a disease that is poorly served by current drugs. However, many of these next generation drug candidates are designed to work against the same intra-cellular targets, such as the NS3 and NS4a proteases and the NS5a and NS5b polymerases. In contrast, Biotron's BIT225 targets a cell wall ion channel that is vital to cell replication and production.

Pharmaceutical companies that operate in the HCV space are likely to be interested in compounds with novel and differing modes of action. Anti-viral medicines can over time become ineffective as resistant strains emerge and the potential to co-administer a drug that has a different mode of action has merit.

Comparison with Debio 025

Biotron would be pleased if it achieved a result similar in its Phase IIa study to that gained by **Debiopharm** in its Phase IIa study of Debio 025. In a 28 day study, Debio 025 when co-administered with pegylated interferon alpha 2a, achieved a 4.6 log 10 reduction in viral load, compared to a 3.6 log 10 when trialled as a monotherapy over 15 days in a Phase I study. Debio 025 is a polypeptide-based cycolosporine A but has been engineered to remove certain immune suppressing features. It may be possible that Debio 025 can be dosed once a day.

Debio 025 is now being evaluated in a randomised Phase IIb trial, enrolling 290 patients and comparing three different treatment regimes of Debio 025 in combination with interferon and ribavarin. The compound was licensed to **Novartis** in February 2010. Terms were not disclosed.

Challenge

As is the case with many drug development companies, Biotron has had to focus its resources on the HCV program at the expense of others. A Phase I trial of its BIT225 in HIV patients could be initiated if it had an additional $500,000 at its disposal. Despite the current failure of Avexa to commercialise ATC (which we argue is due to commercial considerations), Biotron's BIT225 has in fact begun to receive renewed interest from pharmaceutical companies according the CEO Michelle Miller.

– Cont'd on page 3

Atcor Medical Receives a Boost

Atcor Medical (ACG: $0.14) received a boost this week for its goal of gaining re-imbursement for the use of its Sphygmocor system when another ruling was made in its favour by an administrative law judge associated with the US Centers for Medicare and Medicaid Services (CMS). The CMS is the US government health insurance provider and provides coverage to around 45 million people in the US.

Previously the Medicare health plan applicable to the US State of Michigan had sought to classify Atcor Medical's Sphygmocor central blood pressure measurement technology as experimental, and by implication, not something that warranted reimbursement. However, the judge disagreed with this view and said that the Michigan Medicare plan must cover use of the Sphygmocor system, where a physician is using the system to manage both hypertension and chronic kidney disease

The significance of the ruling is that it covers more than the State of Michigan but also extends to Illinois, Iowa and Wisconsin, where, according to Atcor Medical, Medicare covers 5 million people.

The ruling follows a similar positive ruling handed down in May in Michigan that was based on the successful treatment of a female patient with hypertension only.

An important implication of the CMS judge's ruling is that it will allow Atcor Medical to focus sales staff in the four-state region so that it can capitalise on the positive decision. Another implication is that it should give doctors in other regions the confidence to purchase Atcor's systems and in a similar way, push their regional CMS body to award reimbursement for use of the systems, especially given the perception that Atcor will support doctors that commit to that challenge.

Reimbursement Strategy

Currently, Atcor Medical is pursuing a reimbursement strategy that involves securing regional acceptance prior to moving more comprehensively to a national approach. Much of US healthcare management and coverage is organised on a state or regional basis.

Doctors in the US can apply to get reimbursed under a miscellaneous code but the objective is to gain a specific code. This is not automatic and is subject to a push-back process by the health insurance bodies.

Recent Clinical Trial and Service Contracts

Also this week Atcor Medical signed another contract with an existing customer, an unnamed pharmaceutical company, in which the company will use Sphygmocor in its clinical trial programs. This US$1.77 million contract contributes to a total of US$2.9 million of contracts signed since March.

In the first half of FY2010, Atcor recorded $4.3 million in sales and posted a loss of $1.2 million. On a cash basis, Atcor Medical received income of $1.9 million in the March quarter

– Cont'd on page 3

– Avexa cont'd

resignation of CEO and director Julian Chick in May this year. Chick did not attend the meeting.

Nathan Drona's preparation for the meeting was very poor, given that he was not able to answer some important questions. Drona, and the board were unsure as to whether patients were still taking apricitabine in clinical trials. Drona was unclear about whether he was aware of a request from one or two HIV organizations to reconsider the development of apricitabine. There were inconsistencies about whether and when directors were able to buy shares in Avexa. One shareholder was attempting to infer that former CEO Julian Chick was not in favour in ending the apricitabine program although Drona maintained that the board unanimously agreed to end the program. Drona was also questioned over how stated 'extensive interactions' with the FDA were relevant to the early closure of the Phase III program.

Uri Ratner no doubt would have been questioning his decision to take a board position at Avexa in May of this year. Ratna travelled from New York to attend the meeting. However, shareholders were angry and legitimately perplexed as to why Ratna had chosen to take the position after his group (Passport Capital) had previously sold all of its Avexa stock (and taking more than three years to disclose its substantial shareholder stake sell-off to the market).

Many of the questions posed at the EGM were particularly insightful. With most of the shareholders calling the meeting not disclosing their identities, we are left to guess that some of the former management of Avexa may have been included in that group. Former head scientist at Avexa, Jonathan Coates, was one that was spotted mingling with some of the aggrieved shareholders.

The Alternative

The alternative for Avexa shareholders to vote on was similarly uncompelling. The two directors who were seeking appointment to the board both declined to address the meeting. And only after a request from one shareholder did one of the directors briefing address the meeting however offering no more than an introduction – a combined 50 years pharmaceutical industry experience – and no details of their planned direction for Avexa.

The meeting became particularly heated when well respected biotech executive Ian Nisbet, who was also an investor in Avexa, addressed the meeting in support of his viewed credibility of Drona on to be shouted down by an angry shareholder and labelled a 'stooge'. Nisbet said he found it insulting that people would put themselves up for election as directors without stating what their intentions were, and rightly so. Former Avexa director Lawrence Gozlan, also present, then attempted defend Nisbet but his comments were also not appreciated as he was immediately identified for his former role in the company. Nisbet was seen after the meeting having some 'last words' with some of the Avexa shareholders.

EGM Outcome

With a resounding vote, Nathan Drona and Uri Ratna were both removed from the board of Avexa. The two directors proposed, Bruce Hewett and Steven Crowley, easily won election to the board. The only other director prior to the EGM, David Bottomley, resigned the day after the meeting. And that day Joe Baini was elected chairman, after having previously stepped down nine days after the apricitabine program was closed. The fate of apricitabine may once again have unanimous support.

Calzada Interest

Listed biotech investor **Calzada** has been building up its interest in Avexa, having acquired funds management group **Orbis**' stake at 3 cents per share and it now owns 16.06% of Avexa. The Calzada team was present at the EGM and was seen exchanging business cards with the new directors. Calzada did not vote at the meeting being unimpressed by either of the options presented (or not presented). Calzada's statement after the EGM is of interest. "Calzada's focus is on ensuring that the new board of Avexa is working in the best interests of all shareholders to protect and enhance shareholder value." No doubt Calzada will be keeping a very close eye on any new expenditures at Avexa. It is seeking board representation at Avexa.

Avexa is capitalised at $31 million and is expected to have had at least $23 million at 30 June this year (or 2.7 cents per share cash).

Bioshares recommendation: **Avoid**

Bioshares

– Atcor Medical..from page 2

Summary

Atcor Medical is capitalised at $14 million. The company is making steady yet incremental progress towards its goal of getting the use of its Sphygmocor systems by primary care physicians reimbursed in the US on a national basis. The recent Michigan decisions represent signalling events to other insurance providers of the medical value of non-invasive central pressure testing.

At its current share price, essentially no value is being ascribed to the primary care market that Atcor is seeking to access in the US. However, the closer the company gets to achieving a unique CPT code as published by the American Medical Association (expected as soon as November 2010), and equally important increased coverage by CMS and private health insurers, then the stock should begin to reflect these commercial opportunities.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

– Biotron...from page 2

Biotron's main challenge is to complete its HCV Phase II trial on time and on budget. Should the results be positive it is unlikely that a partnering deal would be concluded soon after. Such deals can take, in our estimation, anywhere from six to 12 months to complete. It would be a sensible move for the company to place itself on a comfortable financial footing prior to partnering BIT225 as a potential HCV therapy.

Biotron is capitalised at $7 million and held cash of $2.4 million at March 31, 2010.

Bioshares recommendation: **Speculative Buy Class B**

Bioshares

Alchemia's Drug Nears Approval as Competitor Surfaces

A second generic drug developer has surfaced as a competitor to Alchemia (ACL: $0.40) for generic fondaparinux. The branded drug Arixtra is sold by **GlaxoSmithKline**. Alchemia believed it was the only group developing a generic version of Arixtra. Its view was based on the extreme level of difficulty in making the drug. Alchemia's core technology simplifies this process by about half although it remains a very challenging task to make the drug.

This week **Apicore** from India announced it had succeeded in making the drug and had submitted a Drug Master File (DMF) with the FDA. The DMF specifies the manufacturing process and provides complete information on finished drug product, including stability, purity and impurity profile. The DMF filing allows the company to protect its intellectual property from other groups including its partner.

Comments

There was always the possibility that other generic groups would attempt to enter this market. The difficulty in manufacturing the drug was expected to limit and slow the potential competitors in coming to market with their own generic versions, which has been the case. Apicore is the first competitor to announce its plans to compete in this market and there may in fact be others.

In Alchemia's advantage, it should enjoy at least two and a half years of selling the only generic to Arixtra in the US. Arixtra sales in the US are currently tracking at US$244 million a year. It is not an insignificant market and the news of other competitors validates the market.

Our estimate is that Alchemia should be able to generate a profit before tax of around $40 million a year whilst there are no other generic competitors on the market. Alchemia and its partner **Dr Reddy's** are still awaiting news from the FDA on the approval of their generic, which has now been under review for 14 months by the FDA.

Approval Imminent?

In 2007, the FDA stated that its intention was to approve first generics within six months. Between 2006-2009, the overall approval times have ballooned out by 10 months (according to **RBS Morgans** research) with the FDA recently stating there is a backlog of around 2,000 applications. This is likely being driven by surge in low cost generic manufacturers coming from India and China (and the added extra time required to evaluate those manufacturing sites) and an increase in the number of drugs coming off patent.

With an FDA intention to approve first generics within six months and a 10 month increase in overall approval time for generics, Alchemia shareholders might expect an FDA decision within 16 months of acceptance of its ANDA submission. This would place an amended expected approval date, if there are no further questions from the FDA, by early September 2010.

Competitor Background

The competitive threat from Apicore needs be assessed. Apicore is a relatively new company. It started operations in the US in 2005 and in India in 2006. It currently has 50 employees however it has only filed eight DMFs. The company says it has partnered with a major generic pharmaceutical company, in 2007, to develop generic fondaparinux, which is the same year Alchemia partnered with Dr Reddy's, also in India.

What has surprised Alchemia and its investors is that another group has been able to manufacture the drug so quickly. CEO of Alchemia Pete Smith does not think it is using the Alchemia technology, but if it, is Alchemia will be able to tell through a number of ways, including specific impurity levels in the finished drug which differ to the Arixtra manufacturing process.

It took Sanofi 10 years to work out how to make Arixtra, which was what delayed the drug getting to market. It is unclear where the Arixtra drug is currently being manufactured for GlaxoSmithKline, using a ~50 step process compared to ~25 steps using Alchemia's technology.

The Apicore 12 acre site in India – it is located several hundred kilometers away from the Dr Reddy's site – appears to be more of an R&D facility at the moment. It's facility will likely need to be scaled up to commercial production size. One of the peculiar aspects is why Apicore is publicizing its DMF submission when it remains a private company and generic companies prefer to divulge as little information as possible to their competitors. As indicated above, the filing of the DMF may be a way for the company to protect its manufacturing IP from its generic partner.

The next step is for Apicore's partner to file an ANDA, which from there will take at least 27 months to get the generic approved by the FDA at current review timelines.

Profit impact for Alchemia

With Alchemia/Dr Reddy's supplying the only generic to Arixtra, our conservative estimate is that pricing will drop by 20% and the company will gain 40% market shares. At a 60% profit share, Alchemia should receive around $38 million a year. With a second generic on the market in the US, we expect Alchemia's market share would drop to 30% and pricing would fall by 50% from current levels. This estimate this would drop profit share to between $15-$18 million a year.

Summary

Another generic competitor emerging is surprising. That competitor will likely be at least three years behind Alchemia and potentially five years, depending on how long it takes to achieve scale up.

This means Alchemia should enjoy close to a $40 million revenue stream for at least three years, but may then drop to as low as $15 million with the entry of the second generic.

Following the approval of Alchemia's product by the FDA, we expect in the next 60 days, Alchemia will then be in a position to launch its Phase III program for HA Irinotecan.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares Model Portfolio (9 July 2010)

Company	Price (current)	Price added to portfolio	Date added
Sunshine Heart	$0.035	$0.036	June 2010
Biota Holdings	$0.96	$1.09	May 2010
Tissue Therapies	$0.20	$0.21	January 2010
QRxPharma	$1.10	$0.25	December 2008
Hexima	$0.21	$0.60	October 2008
Atcor Medical	$0.14	$0.10	October 2008
CathRx	$0.26	$0.70	October 2008
Impedimed	$0.56	$0.70	August 2008
Mesoblast	$1.77	$1.25	August 2008
Circadian Technologies	$0.60	$1.03	February 2008
Patrys	$0.11	$0.50	December 2007
Bionomics	$0.29	$0.42	December 2007
Cogstate	$0.25	$0.13	November 2007
Sirtex Medical	$5.15	$3.90	October 2007
Clinuvel Pharmaceuticals	$0.24	$0.66	September 2007
Starpharma Holdings	$0.51	$0.37	August 2007
Pharmaxis	$2.05	$3.15	August 2007
Universal Biosensors	$1.40	$1.23	June 2007
Probiotec	$1.33	$1.12	February 2007
Acrux	$1.80	$0.83	November 2004
Alchemia	$0.40	$0.67	May 2004

Portfolio Changes – 9 July 2010

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

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

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