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In this edition...
Antisense Therapeutics has reported positive results from its Phase I trial of ATL1103, which it hopes to progress as a treatment for the growth disorder of acromegaly. Immuron has signed a distribution partner for Travelan in Canada and Latin America and also gained valuable funding in the process. Although the pSivida partnered product Illuvien was rejected by the FDA, its platform of drug delivery technologies provide upside for the stock. Cogstate is on track to post healthy profits this half. And Phylogica believes its next partnering deal is not far away.
The Editors
Companies Covered: ANP, CGS, IMC, PVA, PYC

	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 - May'11)	45.4%
Year 11 now commenced	-26.0%
Cumulative Gain	**211%**
Av. annual gain (10 yrs)	**21.2%**

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Bioshares

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

Positive Phase I Trial Results for Antisense Therapeutics' Acromegaly Drug Candidate

Antisense Therapeutics (ANP: 2.9 cents) has delivered some positive results in its Phase I trial with its lead drug candidate, ATL1103. This antisense drug was designed to block growth hormone receptor expression and as a direct result reduce IGF-1 levels in the blood. This trial showed just that and importantly, so far, the side effect profile looks good.

Increased IGF-1 levels are associated diseases such as acromegaly, diabetic neuropathy and some types of cancer.

Results – Safety

The main endpoint for this trial was to examine the safety profile of this drug. The trial involved 36 healthy volunteers. Doses from 75mg up to 400mg were explored as a once off dose, then eight volunteers received six doses of 250mg over three weeks.

All adverse events were mild to moderate, with the most common adverse event being an injection site reaction however these effects reduced with subsequent injections. One patient recorded an increased level of the liver enzyme ALT, however this was only temporary and reduced to normal as the dosing part of the study continued.

Results – Efficacy

Although the trial was designed to evaluate safety, given the nature of this program, efficacy is also very straightforward to monitor. One of the main endpoints in this trial were IGF-1 levels, which is also serves as a biomarker. The mean reduction in IGF-1 levels reached 7% at 21 days, and was maintained for the next week, falling to a 1% reduction at day 35 (two weeks after dosing had stopped).

At day 28, there was a 19% reduction in GHBP (growth hormone binding protein) levels which is an indication that growth hormone receptor level expression is being blocked. This is precisely what ATL1103 is supposed to do, which confirms its mechanism of action.

There was a very clear response in increasing reductions of IGF-1 levels as the volunteers received more (subcutaneous) injections of ATL1103.

Discussion

Antisense Therapeutics has achieved sufficient information that warrants moving this program into a Phase II trial. The safety profile appears good, however the question that still needs to be answered is can this drug candidate reduce IGF-1 levels by 30% (a 7% reduction was achieved in this trial) whilst maintaining a favourable safety profile.

The attraction of this program is that the drug appears to be working, and that there is very good clarity available for measuring efficacy because IGF-1 is both the biomarker

– Antisense Therapeutics cont'd

and the endpoint (as opposed to for instance Alzheimer's disease where the biomarker might be beta amyloid levels in the brain but the endpoint is improvement in cognition or delaying cognitive decline).

What the company will likely explore in the Phase II trial is the effect on IGF-1 when ANP1103 is taken for 12 weeks (not three weeks as in this trial) and potentially higher doses, up to 400mg.

ATL1103 displayed similar side effects to other second generation drugs, the main one being injection site reactions, and other antisense drugs in development. The cholesterol lowering drug candidate Mipomersen has been dosed at 400mg per week and antisense drug candidates for cancer have been dosed at 600-700mg per week.

The company believes there may also be an increased (percentage) fall in IGF-1 in patients over volunteers because of their higher levels of the growth hormone receptor and of circulating IGF-1.

Antisense drugs accumulate in the liver, the site of the growth hormone receptor and where IGF-1 is produced, so there should be a cumulating effect of the drug until a steady state level of ATL1103 is attained in the liver.

Market

The market for this drug is as a superior alternative to the drug Somavert. Somavert is expensive, being a pegylated peptide and costing between $60,000-$90,000 a year, depending on dose. It also needs to be injected daily and needs to be reconstituted daily. It has been shown to cause an increase in growth hormone levels and has shown to increase liver enzymes.

The potential market size for ATL1103 we estimate at between $450-$600 million a year.

Summary

The Phase I clinical trial has presented a positive result for Antisense Therapeutics. However, the results do not show the 30% reduction in IGF-1 levels to deliver adequate therapeuty. However, there is a liklihood that this might be achieved with prolonged dosing, with a higher dose or with both.

Antisense is capitalised at $28 million and had $1.4 million at the end of September. It will need to raise funds to progress this program unless it seeks to partner the program.

The stock has had a strong run in recent weeks on high turnover. *Bioshares* recommends to **Take Profits** for short term investors and places a **Speculative Buy Class C** for longer term investors.

Bioshares

Phylogica – Looking to Sign its Fourth Pharma Deal

Phylogica (PYC: 5.7 cents) is still working towards its fourth pharmaceutical discovery deal. The company had previously set a target for the end of this year to complete three more deals. The timeline has been extended to the end of this financial year although the company is looking to close one of those three deals by year end if all goes well.

Dealing with pharmaceutical companies can be a drawn-out process. As indicted last week, the cost-cutting and re-prioritisation underway across this industry is stretching out negotiation periods. Whilst Phylogica will not meet its target this calendar year, it's refreshing to see companies, particular biotech companies, setting distinct targets by which investors can judge their progress.

The three deals the company expected to sign this year are still progressing. A lot of the interest at the moment - around half - in the Phylogica technology is around the use of the company's Phylomers (peptides) as a way of delivery other drugs into cells or across the blood-brain-barrier. That Phylogica's peptide library is derived from ancient genomes of bacteria perhaps explains some of their natural properties in penetrating cells.

Progress on Existing Collaborations

Cell penetration is the focus of Phylogica's Roche collaboration. Phylogica has built up eight series of cell penetrating Phylomers, of which one of these series Roche has an option on. Roche is currently conducting its own work on this series of Phylomers, seeking to mimic the results of Phylogica's work in its own labs. Roche has until the end of the first quarter of 2012 to exercise its rights on these compounds.

Phylogica also has collaborations with Pfizer and MedImmune (AstraZeneca). Its Pfizer collaboration involves the use of Phylomers to improve the characteristics of vaccines.

The MedImmune agreement has advanced to the final stages with Phylogica having received payments of US$1.5 million to date. This collaboration is based around finding a novel approach to treating the pseudomonas bacterial infection. In bio-dollars, this deal is worth up to US$98 million in milestone payments.

Deal Flow Payments to Increase

Payments from partners should start to increase in size as Phylogica is moving further along the value chain. Whilst it is working towards signing deals with new partners and further new and larger deals with exiting partners, progressing existing deals will start to bring in larger payments. If Roche decides to progress its collaboration and exercise its option, then Phylogica may receive one of its largest payments to date. Discovery and preclinical milestone payments will also kick in as these collaborations move forward.

Building Competitive Tension

With multiple partners, Phylogica is also in a very good position to build competitive tension, and this is what will likely drive an acquisition of the company, if it can continue to hit its collaboration milestones.

Progress Towards Cash Sustainability

Phylogica's model is not to move to profitability immediately, but to cash sustainability, where its increasing revenue from collaborations can be used to build the business. The company currently

Cont'd over

Immuron Secures Travelan Licensee for Selected Territories

Immuron (IMC:$0.046) has used the services of US corporate advisory firm Roberts Mitani to secure a licensing and distribution deal with Canadian specialty pharmaceutical firm Paladin Labs.

The deal grants Paladin the rights to Immuron's Travelan product for Canada, Latin America and Sub-Saharan Africa. Paladin also gained an option to rights to IMM-255, a product in development for the treatment of influenza, for those same territories. Paladin will pay Immuron an up-front fee of C$500,000 and with potential sales related milestone payments of up to C$115 million.

Travelan is an over-the-counter product for the prevention of travellers diarrhea.

Paladin is capitalised at C$728 million. It recorded revenues Of C$127 million and posted a net profit of $29.8 million in 2010. Paladin has in-licensed products in the areas of urology, endocrinology, womens health, pain and dermatology. Travelan complements the Paladin's suite of OTC products.

Importantly for Immuron, Paladin has provided Immuron with up to C$1.5 million of funds in the form of a secured convertible debenture. This is significant for Immuron, given that its rights issue completed early in November raised $0.53 million. The rights issue received little support with a participation rate of 12%.

Investors should keep in mind that Immuron maintains control over the manufacture of Travelan, which is derived from colostrum collected from immunised dairy cattle at sites in Victoria. Other licensing and distribution deals for Travelan concerning Europe, the US and Japan, are be expected to follow in 2012.

IMM-124E – IND for NASH

Immuron submitted an Investigational New drug (IND) application to the FDA in early November for IMM-124E for NASH (a liver disease). The company has yet to be advised by the FDA of the status of its application, where a consent is usually advised by way of a lapse of a 30 day period without questions from the regulator.

Challenges

Immuron is moving to a new phase in its corporate life which involves over-seeing the manufacturing and sale, through distributors, of Travelan to global markets and the clinical development of new products for influenza and NASH. A timely consideration for the board would be to review its capabilities to support the current direction of the business, with skills in the area of international pharmaceutical sales and marketing potential a desirable addition.

Project funding remains a key issue for Immuron, as it looks to obtain approximately $5 million to support the Phase IIb development of IMM-124E under a US IND protocol. What the company needs to do is to re-build its share register with institutional investors with an appreciation of the commercial prospects for Immuron's NASH and influenza products.

Acrux's Other Dividend

One the consequences of the move by Acrux to reduce its headcount over past few months is that it has made available staff for employment by other Australian biotechs. In the case of Immuron, the company has picked up the services of a Acrux's former Vice President of Business Development, Dr Nina Webster, a highly experienced licensing executive. This is an extremely positive move for Immuron as it vigourously moves ahead with its Travelan licensing program

Summary

As with Mesoblast, Phosphagenics, Tissue Therapies and most recently articulated by Biota, Immuron is aiming to capture manufacturing margins from the sale of its products. There is now a clear investment thematic for investors to follow with this group of companies who are seeking to substantially improve returns to shareholders.

Immuron's main challenge is now the funding the NASH Phase IIb program. If successful with funding, Immuron may be a stock to follow in 2012, with licensing deals, product sales and clinical programs driving valuation.

Immuron is capitalised at $15.7 million. We estimate that following the Paladin deal it has access to cash of $2 million.

Bioshares recommendation: **Speculative Buy Class B**

Bioshares

– Phylogica cont'd

has 25 staff with 20 scientists. It expects to increase its scientific head count by three and will shortly be adding new robotic systems to increase its screening output capacity.

The company's broker, RBS Morgans is forecasting $5 million in revenue for this financial year, which is a reasonable target. The company has an annual burn rate for $6 million and we believe the company should move into cash sustainability in the next financial year. However this is all based on new deal flow and progressing existing programs.

Summary

The pressure the pharmaceutical industry is under is likely increasing the difficulty in securing early stage collaborative deals. However Phylogica has certainly spiked the interest of the drug development industry with its ability to transport other drugs across cells using its Phylomer compounds. Its programs appear to being going well. And with its fourth deal with a top 10 pharmaceutical company hopefully not too far away, the interest in this company should continue to grow.

Phylogica is capitalised $23 million. It had $3.2 million at the end of September.

Bioshares recommendation: **Speculative Buy Class A**
(Note, at the time of publication, Phylogica had gone into a trading halt due to a pending capital raising.)

Bioshares

pSivida – Will an EU Approval Offset FDA Rejection for Illuvien?

pSivida ($1.27) suffered a major setback in November when licensee Alimera Sciences received its second Complete Response letter from the FDA for application for Iluvien, a sustained release product for the treatment of Diabetic Macular Edema (DME). The first Complete Response letter (CRL) was received in December 2010 and in that letter the FDA said the Iluvien was not approvable until data became available from the completion of its FAME study (at 36 months). Alimera had made a subsmission based on 24 months of data.

A CRL sets out a drug candidate's approvability status.

The FDA said that it was unable to approve the Iluvien NDA because "the NDA did not provide sufficient data to support that ILUVIEN is safe and effective in the treatment of patients with DME", with risks not offsetting the benefits. The FDA's view was that the risks of adverse events in the study were significant. The FDA also said that Alimera would need to conduct two further studies to demonstrate that Iluvien was safe and effective.

DME initially presents as blurring in the middle of the central field of vision, ultimately leading to blindness. The condition is caused by leaky blood vessels in the central section of the rentina (otherwise known as the macula). Alimera estimates the annual incidence of DME in the US to be 340,000.

There are no drug therapies approved by the FDA to treat DME. Current standard of care is laser photocoagulation and the off-label use of cortico-steroids and anti-VEGF agents such as Lucentis and Avastin.

Iluvien is a sustained release formulation of the cortico-steroid fluocinolone acetonide, designed to be released over 36 months.

Iluvien Side Effects

	Trials A&B Combined			
IOP Increase	Control N=185	ILUVIEN N=375	Control N=185	ILUVIEN N=375
	As of Month 24 Database Lock		*As of Trial Completion*	
	Percentage of Subjects Responding			
IOP >30 mmHg	2.7%	16.3%	4.3%	18.4%
Patients requiring One or More IOP Lowering Surgeries	0.5%	3.7%	0.5%	4.8%
Cataract (Phakic Patients at Baseline Only)	Control N=121	ILUVIEN N=235	Control N=121	ILUVIEN N=235
	As of Month 24 Database Lock		*As of Trial Completion*	
	Percentage of Subjects Responding			
Cataract Formation	46.3%	80.0%	50.4%	81.7%
Cataract Surgery	23.1%	74.9%	27.3%	80.0%

Source: Alimera Sciences - Presentation
Cowen and Company 31st Annual Health Care Conference, March 8, 2011

What were the FDA's Concerns?

The FDA was concerned that the benefits of Iluvien did not outweigh the risks.

On the risk side:

Combined trials data showed in the low dose treatment group that at the 24 month database lock point, 2.7% of control subjects had experienced intro-ocular pressure of greater than 30 mm of mercury, compared to 16.3% of Iluvien subjects. At the completion of the 36 month period, 4.3% of control subjects had experienced intro-ocular pressure of greater than 30 mm of mercury, compared to 18.4% of Iluvien subjects.

The percentage of patients over the 36 month period requiring surgery to lower IOP was 0.5% compared to 4.8% in the Iluvien group.

For subjects with no history of cataract surgery, over the 36 month trial, 80% required cataract surgery compared to 27.3% in the control arm.

On the benefit side:

Iluvien was shown in two Phase III studies (collectively known as the FAME study) to provide 28.7% of patients greater than 15 letters increase in visual acuity versus a 18.9% for the control group (p=0.029), thus meeting the trials efficacy endpoint.

The FDA looks to have adopted a very conservative position in its current rejection of the Iluvien application. This is possibly influenced by the large size of the DME patient pool. In contrast, the uveitis patient pool, for which pSivida's Retisert (licensed to Bausch & Lomb) was approved in 2005, is one fifth the size of the DME pool and its also qualified as an Orphan Drug.

Retisert is also a formulation of fluocinolone acetonide. In it clinical trials, approximately 50% of patients experienced intra-ocular pressure of greater than 30 mm HG and and approximately 30% of patients required surgery.

European Approval Process

Alimera is continuing with the European approval process for Illuvien with a primary decision expected early in 2012 and various member state approvals following over the course of the year. pSivida entitlements under an EU approval are the same as for the US, which is that pSivida is entitled to 20% of profits and if Illuvien is licensed to another company, the 20% of royalty income and 33% any other non-royalty income.

Implications for pSivida

The FDA has at best paused Alimera's attempt to market Iluvien. Alimera will seek to understand more precisely the reasons for its rejection.

Both Alimera and pSivida were disappointed by the FDA CRL, with Alimera expressing frustration in a conference call that its discussions with retinal specialists did not discover any risk-benefit concerns of the type that appear to have inlfluenced the FDA's decision.

Cont'd over

Bioshares Model Portfolio (9 December 2011)

Company	Price (current)	Price added to portfolio	Date added
QRxPharma	$1.39	$1.66	October 2011
Mayne Pharma Group	$0.450	$0.435	September 2011
Genetic Technologies	$0.12	$0.18	August 2011
Acrux	$2.87	$3.37	June 2011
Bioniche	$0.69	$1.35	March 2011
Somnomed	$1.01	$0.94	January 2011
Phylogica	$0.057	$0.053	September 2010
Biota Holdings	$0.78	$1.09	May 2010
Tissue Therapies	$0.41	$0.21	January 2010
Atcor Medical	$0.08	$0.10	October 2008
Impedimed	$0.56	$0.70	August 2008
Bionomics	$0.54	$0.42	December 2007
Cogstate	$0.24	$0.13	November 2007
Sirtex Medical	$4.32	$3.90	October 2007
Clinuvel Pharmaceuticals	$1.51	$6.60	September 2007
Pharmaxis	$1.07	$3.15	August 2007
Universal Biosensors	$0.72	$1.23	June 2007
Alchemia	$0.300	$0.67	May 2004

Portfolio Changes – 9 December 2011

IN:
No changes

OUT:
No Changes

Cogstate – A Strong First Half Anticipated

Cogstate (CGS: 24 cents) is having an exceptionally strong first half, its best yet on record. It has historically built its business specialising in providing cognitive assessment in the clinical trials of drug candidates in the areas of Alzheimer's disease and schizophrenia. While its market in Alzheimer's drug testing has always been strong, there was a fall off in schizophrenia in the last two years. That has now changed.

This year data has been reported in two Phase IIb studies and one Phase III study where its test was used as a primary endpoint and a secondary endpoint respectively. All of these studies delivered a positive outcome. This is a very noteworthy achievement, given the difficulty the pharmaceutical industry has had in bringing therapeutics to market for this disorder.

In a press release, Cogstate's CSO Dr Paul Maruff said "The positive results from these two Phase IIb studies and the Phase III study makes me optimistic that cognitive impairment in schizophrenia is a treatable condition."

Earlier this month the company signed another Phase IIb trial in schizophrenia worth US$0.73 million, and last month it signed two trials for the treatment of depression worth US$3.5 million. As of 8 December, Cogstate had secured $9.27 million in revenue for this financial year in only the first five months. This is a 27% increase over the full 12 months of the previous financial year.

We expect the company will move into profitability this financial year. Cogstate is capitalised at $18 million. It had $3.2 million in cash at the end of September.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

– pSivida cont'd

However, while there is a cloud over the Iluvien product in the US, the upside for pSivida is that the trial clearly demonstrated the drug release properties of its Medidur technology, encouraging an un-named company to sign an evaluation agreement with pSivida in November.

Summary

We suggest that pSivida shares have been oversold following the receipt by Alimera of its CLR from the FDA and irrespective of a favourable European regulatory decision for Iluvien. Apart from the Illuvien indications licensed to Alimera, pSivida retains the rights to Illuvien for treating uveitis, a condition for which a regulator could arguably tolerate a more severe risk-benefit profile than for DME. pSivida also has other technologies, including Tethadur, as well as R&D relationships with Pfizer for Durasert (for the drug latanoprost) and more recently with an unnamed company.

pSivida is capitalised at $26 million and retained cash of US$9.8 million at September 30, 2011.

Bioshares recommendation: **Speculative Buy Class B**

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

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