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In this edition...
It's been a difficult week for the sector, with Chemgenex Pharmaceuticals and Antisense Therapeutics both reporting disappointing events. Chemgenex will need to develop a validated diagnostic for its oncology drug candidate before the FDA considers its compound for approval. And Teva has cancelled its MS program with Antisense Therapeutics.

We also look at Biotron, which will start a Phase II study in HCV and we consider the competitive landscape in that area.

The Editors
Companies Covered: ANP, BIT, CXS

	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 - Current)	65.0%
Cumulative Gain	**220%**
Av Annual Gain (9 yrs)	**20.3%**

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Chemgenex Pharmaceuticals – More Uncertainty Emerges

The FDA Oncology Drug Advisory Committee (ODAC) panel met last Monday to advise the FDA on Chemgenex Pharmaceutical's (CXS $0.43) new drug application for Omapro, an oncology drug candidate developed to treat a subset of patients with chronic myeloid leukemia (CML) who have failed treatment with the very successful Gleevec drug and have the T315I mutation. For these patients there are no other treatment options.

The panel did not reach a position where it could vote on the risk/benefit profile of the drug due to an unexpected obstacle. That obstacle is that there is no validated diagnostic test available to measure this mutation. Chemgenex is arguing that there is no commercially validated test available because its drug to treat CML with this mutation has yet to reach the market.

The panel voted 7-1 in favour of a validated test to detect this mutation being reviewed by the FDA prior to considering Omapro for approval. The panel did not vote on whether or not it should approve the drug candidate.

Another issue raised in an FDA review document just prior to the ODAC meeting was a safety issue relating to vial size, with Omapro developed in a 5mg vial for single use by the patient, however the average dose was 2.4mg, bringing with it the potential of overdose and the environmental impact of disposing of any unused drug. This is another issue the company will need to address.

We understand Chemgenex has maintained samples from patients in its trial which may allow retrospective testing with a standardised test. In the company's pivotal study, a pcr-based test was used at the University of Texas and a hplc test from a German university were used to pick up the mutation. Another concern that the FDA has is that 35% of patients enrolled in the study did not have central laboratory confirmation of the mutation at the time of enrolment. Developing a commercially validated test should not be onerously difficult for the company however this will delay a subsequent review of Omapro.

Other concerns raised by FDA

Other concerns raised by the FDA in its review document that was to be considered by the ODAC panel was: the "small and incomplete efficacy trial", the "uncertainty in response determination and duration", and the "uncertain clinical meaningfulness of response rates".

Chemgenex will meet with the FDA next month to review the diagnostic strategy for Omapro.

With the delayed launch of Omapro in the US, the concern is that additional funds may be required before the product is approved in the US. At the end of last year, Chemgenex had

Teva Hands Back ATL1102 to Antisense

In a second bit of bad news for the sector this week, Antisense Therapeutics (ANP: 2.6 cents) had its development program and licensing agreement with **Teva Pharmaceutical Industries** in Israel cancelled.

In February 2008, Antisense Therapeutics signed a licensing deal for its multiple sclerosis drug candidate, ATL1102. Antisense Therapeutics received a US$2 million upfront payment and has received US$6 million to date as part of the licensing deal.

In June 2008, Antisense Therapeutics reported positive Phase II trial results, where cumulative new brain lesions were reduced 54% over placebo at 12 weeks (p=0.01). The trial involved 77 patients. The result was also very encouraging because it was almost identical to the reduction achieved by the drug Tysabri in earlier Phase II trials.

Both Tysabri and ATL1102 inhibit the same target, VLA-4, which has proven to reduce the movement of white blood cells in areas of inflammation, in this case in the CNS. Whilst inhibiting the same target, the compounds work differently with Tysabri being an antibody and ATL1102 being an antisense drug (oligonucleotide). Tysabri now generates over US$1 billion in revenue a year for Biogen-Idec. The down side with this drug is that in less than one in a thousand patients, a deadly brain infection can occur, although that risk is considered acceptable by the FDA given the nature of the disease.

Pharma Hands Back Program

This is not the first time a major pharmaceutical company has handed back a drug candidate to an Australian biotech and it should not automatically be considered the end of a candidate's development program. In 2004, **Allergan** handed back the rights to skin cancer treatment drug candidate PEP005 to Peplin. Last year Peplin was sold to **Leo Pharma** in Denmark for US$287 million for rights to that compound.

Antisense Therapeutics received a one page letter from Teva stating that one of the long-term toxicology studies may need to be repeated lengthening the time to market for the program.

In 2004, Amrad also received a one page letter from its partner **Serono**, when Serono handed back rights to one of Amrad's drug candidates, Emfilermin for the treatment of infertility. The compound had previously generated very promising results in a Phase I/II trial in 17 women. Rights to the compound were returned when efficacy studies could not be repeated. Of interest to conspiracy theorists, both Teva and Serona had existing billion dollar products on the market in the same respective areas involved in the collaborations.

Antisense Therapeutics is considering its options with ATL1102. These potentially include finding a new partner, raising funds to conduct a dose ranging Phase II study, or to discard the program.

Isis Pharmaceuticals, which has almost US$600 million in cash and is moving ahead exceptionally well with stunning Phase III trial results with mipomersen for the reduction of LDL-cholesterol (28% reduction compared with 5% reduction in the placebo group over 26 weeks, with all patients on maximum statin dosage). This compound has been licensed to **Genzyme**. Isis may be in a position to provide some support in the future development of ATL1102. Isis is entitled to 33% of any funds Antisense Therapeutics receives from the commercialisation of ATL1102.

Antisense Therapeutics has lost around two years patent life protection on ATL1102 through its Teva partnership (due to two years Teva has taken to evaluate this compound). The patents on ATL1102 run out in 2018/2019 with further patents on the drug chemistry potentially extending protection out to 2023.

Summary

Moving forward, Antisense Therapeutics needs to decide on the future of its ATL1102 MS program, raise further funds (the company had $2.7 million in cash at the end of last year), and move its ATL1103 program into the clinic, which has the potential to become a very valuable asset. ATL is capitalised at $15 million.

Bioshares recommendation: **Speculative Hold Class B**

Bioshares

– Chemgenex...from page 1

$18.7 million in cash. This funding requirement may also depend on whether the company receives approval to sell the drug in Europe, with a decision we expect within seven months. Last December, Chemgenex licensed European rights (and the Middle East and parts of Africa) to Omapro in a deal worth up to $136 million, including a $17.8 million upfront payment already received. How the EMA will respond to the FDA concerns is another unknown, however the issue surrounding the validated diagnostic could be resolved by the time the EMA votes on the marketing application of Omapro.

Chemgenex has major institutional shareholders in **Orbis Capital**, **GBS Venture Partners** and **Alta Partners**. Whether the venture groups have the capacity and willingness to continue funding Chemgenex is unknown, although Orbis Capital has already increased its stake from 10% to 13% on Tuesday. If further funds are required, which is now likely, it may see major shareholders take a greater role in direction of the company.

Summary

The uncertainties for Chemgenex continue to grow as does the risk profile of this investment. The concerns raised by the FDA in its initial briefing document (see *Bioshares* 347S) not only remain but have expanded. We maintain our previous guidance, that investors wait until FDA (or EMA) approval is received before considering investing at current prices. With the potential for further capital raisings now, there may be further downward pricing pressure on this stock.

Chemgenex is capitalised at $122 million.

Bioshares recommendation: **Sell** (review on FDA/EMA approval)

Biotron's HCV Program Moves Forward

Biotron (BIT: 9.4 cents) has one of the sector's lowest profiles. However, the company has steadily moved its HCV candidate, BIT225, through a Phase I /IIa trial, with a Phase IIb trial set to commence in the very near term. BIT225 is a p7 ion channel inhibitor and looks to be the first in a new class of HCV drugs. The p7 ion channel is vital to cell replication and production. BIT225 is also being developed as an HIV treatment.

Biotron's Phase II trial will enrol 24 patients. Subjects will treated over 28 days in combination with standard of care treatments, interferon and ribavarin. Dosing will be twice daily although actual dose or doses to be evaluated are to be advised. The trial is expected to take about six months to complete.

Patients will be screened for the HCV Genotype 1 and for any previous treatment for HCV (i.e. to qualify they must be treatment naïve). Patients positive for HCV Genotype 1 generally respond poorly to interferon and ribavirin treatment.

Biotron has selected an Argentine CRO, **Aclires**, to recruit patients for the trial. Aclires also manages trials in Thailand. Recruitment for HCV patients is extremely competitive. If the trial was conducted in Australia, the trial could take two years to compete. Currently, there are 35 HCV trials listed in Australia. Australia is a popular clinical trials region because drug sponsors are not required to submit full toxicology packages when they wish to conduct combination therapy trials. Almost all HCV trials at the Phase II level or higher are designed as combination trials with the primary drug candidate administered alongside the standard of care.

Although Biotron can expect faster recruitment using sites in Argentina (or Thailand), one drawback is that it must fund the cost of the co-administered standard of care treatments.

Potential Merits of BIT225

The appeal of BIT225 is that it is an orally available drug. Of greater appeal is that its novel mechanism of action may see it gain a foothold as and when other drugs begin to experience resistance. There are very few other small molecule drugs in development that aim to disrupt HCV infection in novel ways, in contrast to the many drugs in development that are designed as protease or polymerase inhibitors. This position should be a competitive advantage to BIT225.

According to the WHO, an estimated 170 million are infected with HCV and it remains a disease that is poorly served by current medicines, with an estimated 10% of those receiving standard of care medicines (interferon and ribavirin) achieving a successful treatment outcome, with about 50% of patients receiving a sustained benefit. The disease progresses to liver failure and liver cancer and is consequently an onerous health burden.

Competition

There is a significant pipeline of compounds (and several vaccines) in development to treat HCV. Our table (see next page), drawn from the NIH Clinical Trials register, does not include every product in development, shows that almost 3,500 HCV patients are or will be enrolled in Phase II trials, with many of the trials being combination therapy trials in treatment naïve subjects.

An issue for protease inhibitors in late stage development (i.e. telaprevir and boceprevir) are their daily dosing demands and side effect profile. Boceprevir requires 12 tablets per day (800mg three times a day) although telaprevir is a 6 tablets per day regime. These regimes may prove onerous especially if their side effect profile is less than attractive. There are reports of up to 20% drop-outs in trials of these drug candidates.

More competition can be expected from the new polymerase inhibitors that are in the pipeline, although drugs in this class are still some years away from reaching the market. Competition is less likely to come from therapies that must be injected, unless they can offer compelling benefits.

Funding

Biotron held cash of $99,000 at December 31, 2009. However, since then the company received $2.1 million from an options issue conducted in December. The issue was oversubscribed. The options, with an exercise date of December 31, 2010, have an exercise price of $0.10. If shareholders exercise their option before the end of March they are entitled to a free additional $0.20 option for every option exercised (a piggyback option). If all options were exercised, the company could raise $11.4 million.

Deal Potential

Biotron could be in a position to license BIT225 for HCV later this year or more likely in 2011. **Vertex Pharmaceuticals** licensed VX-950 (telaprevir) to **Johnson & Johnson** on the back of Phase II studies for an up-front of US$165 million in 2006. **Intermune** licensed a pre-clinical NS3-4A protease inhibitor to **Roche** for a US$60 million up-front payment in 2006, and also in the same year at the preclinical stage was **Enanta's** licensing of protease inhibitors to Abbott for a US$57 million up-front payment. In 2006, **Biota Holdings** formed a preclinical HCV collaboration with **Boehringer Ingelheim** worth up to US$102 million. That collaboration is continuing although has yet to move into the clinic. And in 2008, the ex-management team from **Benitec**, who licensed the Benitec technology for an HCV application into **Tacere Therapeutics**, signed a deal with Pfizer worth up to US$145 million for a preclinical program including significant development funding for their RNAi program.

Summary

With the advance of BIT225 into a Phase II HCV trial, the stock is now in a zone of potential value creation, with trial results potentially available before year's end. The fundamental test for BIT225 is if it can deliver a sustained decrease in viral load with a favourable side effect profile.

Biotron is capitalised at $10.8 million and on a fully diluted basis is capitalised at $21.5 million.

Bioshares recommendation: **Speculative Buy Class B**

Bioshares

Current Open or Planned Hepatitis C Clinical Trials

- Registered with clinicaltrials.gov - Excludes Interferon or Ribavarin derivatives as primary agents

Company	Intervention	Target/Mechanism	ROA	Subjects	Comm.	Compl.	Comb.	Treat-ment Naïve	HCV Gen 1
Phase I	**Open**								
Merck	Vaniprevir (MK7009)	NS3/4a protease inhibitor	Oral	18	Apr-10	Oct-10			
Okairos	Ad6NSMut/ADCh3NSMut	Vaccine AdV Vectors	Injection-IM	50	Jul-07	Dec-10			
Idera Pharm.	IMO-2125	Synthetic DNA agonist of TLR9	SC	40	Sep-07	May-10		No	
Bristol Myers Squibb	BMS-824393	?	Oral	40	Oct-09	Jul-10		Yes	Yes
Transgene	TG4040	MVA-HCV (Vaccine)	Injection-	42	Dec-06	Dec-10		Yes	Yes
Idera Pharm.	IMO-2125 (with ribavarin	Synthetic DNA agonist of TLR9	Injection-SC	50	Sep-09	Jan-11		Yes	
Eiger Biopharm.	clemizole hydrochloride	NS4B-RNA binding inhibitor	Oral (2/day)	12	Jul-09	Dec-09		Yes	
AstraZeneca	AZD7295	NS5a inhibitor	Oral	35	Nov-08	Mar-10			
Cytheris SA	CYT107	Glyco-r-hll-7	IV?	15	Jan-09	Jun-11		No	Yes
Cytheris SA	CYT107	Glyco-r-hll-7	IV?	15	Jan-09	Dec-10		No	Yes
Santaris Pharma AS	SPC3649	Antisense miR-122 agonist	IV/SC	30	Sep-09	Aug-10			
Abbott	ABT-072	Polymerase inhibitor	Oral	24	Mar-10	May-10			
Merck	Vaniprevir (MK7009)	NS3/4a protease inhibitor	Oral	60	Jul-09	Mar-10			
Phase I/II	**Open**								
Curetech/Teva Pharm.	CT-011	PD-1 antibody	IV	20	Sep-09	Sep-10			Yes
Can-Fite BioPharma	CF-102	A3 adenosine R agonist	Oral	32	Jul-09	Jul-10			Yes
Phytohealth	PHN121	Complex botantical mixture (5)	Oral	18	Sep-09	Jan-12		No	Yes
Vertex Pharm./ViroChem Pharma	VCH-222	NS5B polymerase inhibitor	Oral	75	Apr-09	Jun-10		Yes	Yes
Cytheris SA	CYT107	Glyco-r-hll-7	IV?	18	Jul-08	Jun-11		No	Yes
Phase II	**Open**								
Abbott	ABT-450/ABT-072/ABT-333	Protease Inhibitor/Polymerase inhibitors	Oral	75	Feb-10	Nov-11	Yes		
MIGENIX	Celgosivir	a-glucosidase I inhibitor	Oral	50	Jun-06	Dec-08	Yes	Yes	
SciClone Pharm.	SCV-07	Dipeptide	Oral/SC ?	40	Jan-09	Jan-11	Yes	No	Yes
Novelos	NOV-205	hepatoprotective agent	SC	40	Mar-10	Oct-11		No	
Vertex Pharm./Tibotec	Telaprevir	Protease inhibitor	Oral 3/day	68	Oct-09	Jun-12	Yes	Yes	
Bristol Myers Squibb	BMS-790052/BMS-650032	NS5Apolymerase inhibitor/protease inhib.	Oral 1/day; Oral 2/day	50	Dec-09	Mar-13	Yes		Yes
Roche	RO5190591	Protease inhibitor	Oral 2/day	210	Aug-09	Aug-11	Yes	Yes	
Roche	RO5190591	Protease inhibitor	Oral 2/day	160	Feb-10	Sep-12	Yes	Yes	1 or 4
Vertex Pharm.	Telaprevir and VX-222	Protease inhibitor/NS5a Polymerase inhibitor	Oral 2/day	150	Apr-10	Mar-13	Yes	Yes	
Merck	Vaniprevir (MK7009)	NS3/4a protease inhibitor	Oral 2/day	160	Dec-09	Jun-13	Yes	No	
Schering Plough	Boceprevir	Protease Inhibitor	Oral 3/day	99	Nov-09	Apr-12	Yes	Yes	Yes
Boehringer Ingelheim	BI201335	Protease Inhibitor	Oral	22	Jul-99	Oct-11	Yes	Yes	
Pfizer	Filibuvir (PF-00868554)	NS5A inhibitor	Oral 2/day	40	Aug-08	Apr-10	Yes	Yes	Yes
Bristol Myers Squibb	BMS-790052/BMS-650032	NS5A inhibitor/protease inhib.	Oral 1/day ?	40	Mar-10	Oct-12	Yes		Yes
Novartis	NIM811	(Methyl. Cyclosporin) Cyclophilin inhibitor	Oral 2/day	250	Sep-09	Jul-13	Yes	No	
Merck	Vaniprevir (MK7009)	NS3/4a protease inhibitor	Oral 2/day	530	Aug-10	Jun-13	Yes	Yes	
Pfizer	Filibuvir (PF-00868554)	Non-nucleoside inhibitor	Oral 2/day	288	Nov-09	Nov-12	Yes	Yes	Yes
Idenix	IDX184	Polymerase inhibitor	Oral	80	Nov-09	Mar-10	Yes	Yes	Yes

NB: This table does not include every HCV drug in development

– Cont'd over

Bioshares Model Portfolio (26 March 2010)

Company	Price (current)	Price added to portfolio	Date added
Tissue Therapies	$0.22	$0.21	January 2010
Biodiem	$0.19	$0.15	October 2009
QRxPharma	$0.90	$0.25	December 2008
Hexima	$0.40	$0.60	October 2008
Atcor Medical	$0.14	$0.10	October 2008
CathRx	$0.17	$0.70	October 2008
Impedimed	$0.81	$0.70	August 2008
Mesoblast	$2.14	$1.25	August 2008
Circadian Technologies	$0.74	$1.03	February 2008
Patrys	$0.14	$0.50	December 2007
Bionomics	$0.34	$0.42	December 2007
Cogstate	$0.29	$0.13	November 2007
Sirtex Medical	$6.00	$3.90	October 2007
Clinuvel Pharmaceuticals	$0.25	$0.66	September 2007
Starpharma Holdings	$0.69	$0.37	August 2007
Pharmaxis	$2.62	$3.15	August 2007
Universal Biosensors	$1.70	$1.23	June 2007
Probiotec	$1.66	$1.12	February 2007
Acrux	$2.26	$0.83	November 2004
Alchemia	$0.61	$0.67	May 2004

Portfolio Changes – 26 March 2010

IN:
No changes.

OUT:
No changes.

Current Open or Planned Hepatitis C Clinical Trials

- Registered with clinicaltrials.gov - Excludes Interferon or Ribavarin derivatives as primary agents

Company	Intervention	Target/Mechanism	ROA	Subjects	Comm.	Compl.	Comb.	Treat-ment Naïve	HCV Gen 1
Transgene	TG4040	MVA-HCV (Vaccine)	Injection-SC	140	May-10	Jan-13	Yes	Yes	Yes
Roche	RO5024048	Polymerase inhibitor	Oral 2/day	400	Apr-09	Jul-11	Yes	Yes	1 and 4
Bristol Myers Squibb	BMS-650032	Protease Inhibitor	Oral/ 2 day	348	Feb-10	Jan-13	Yes	Yes	1 and 4
Conatus Pharm.	CTS-1027	MMP inhibition	Oral 2/day	60	Jan-10	Jan-12	Yes		Yes
Bristol Myers Squibb	BMS-790052	NS5a polymerase inhibitor	Oral	40	Dec-09	Jan-12	Yes	Part	Yes
Bristol Myers Squibb	BMS-790052	NS5a polymerase inhibitor	Oral	40	Dec-09	Jan-12	Yes	Part	Yes
Pharmasset	PSI-7977	Polymerase inhibitor	Oral	60	Jan-10	Nov-11	Yes	Yes	
Gilead Sciences	GS-9256/GS-9190	NS3 Protease Inhibitor/Polymerase inhibitor	Oral 2/day	30	Feb-10	Dec-11	Yes	Yes	
Phase III	**Open**								
Schering Plough	Remicade (Infliximab)	TNF-alpha blocker	IV	96	Jul-05	Jun-11	Yes	Yes	Yes
Schering Plough	Boceprevir/erythropoietin	Protease inhibitor	Oral 3/day	660	Dec-09	Nov-11	Yes	Yes	Yes
Tibotec/Vertex Pharm.	Telaprevir (VX-950)	Protease inhibitor	Oral 3/day	120	Mar-10	Mar-12	Yes	No	

How Bioshares Rates Stocks

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

Group A

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

Buy	CMP is 20% < Fair Value
Accumulate	CMP is 10% < Fair Value
Hold	Value = CMP
Lighten	CMP is 10% > Fair Value
Sell	CMP is 20% > Fair Value

(CMP–Current Market Price)

Group B

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

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

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

Speculative Buy – Class C
These stocks generally have one product in development and lack many external validation features.

Speculative Hold – Class A or B or C

Sell

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