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In this edition...
Almost ten years ago, TNF-alpha blocker inventor and biotech entrepreneur Dr Roger Aston was joined on the board of Australian Cancer Technologies (ACT) by healthcare entrepreneur Paul Hopper. ACT (ASX ticker ACU) was unsuccessful in developing a difficult to understand cancer vaccine, Pentrix. Other business plans also failed; the name changed to Avantogen, then Acuvax. The leadership of the company transitioned to Dr Leonard Firestone, to Dr Richard Opara and then to Dr William Ardrey IV. Now Aston and Hopper are back planning to use the ACU shell as a home for a novel vaccine therapy from Vienna that could compete with Roche's breast and stomach cancer drug Herceptin. Its an interesting play that has some attractive features for investors to note.
Companies Covered: ACU (Biolife), PBT, NEU, SPL

	Bioshares Portfolio
Year 1 (May '01 - May '02)	21.2%
Year 2 (May '02 - May '03)	-9.4%
Year 3 (May '03 - May '04)	70.6%
Year 4 (May '04 - May '05)	-16.3%
Year 5 (May '05 - May '06)	77.8%
Year 6 (May '06 - May '07)	17.4%
Year 7 (May '07 - May '08)	-36%
Year 8 (May '08 - May '09)	-7.4%
Year 9 (May '09 - May '10)	50.2%
Year 10 (May '10 - May'11)	45.4%
Year 11 (May '11 - May '12)	-18.0%
Year 12 (May '12 - current)	3.5%
Cumulative Gain	**257%**
Av. annual gain (11 yrs)	**17.8%**

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Bioshares

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Entrepreneurs Return with Biolife Cancer Vaccine Play

Biotech entrepreneurs Paul Hopper and Roger Aston are looking to raise $5 million through the shell of Acuvax (ACU: $0.001), which will be renamed Biolife Science Ltd. The capital raising is being managed by Patersons Securities.

Biolife intends to acquired a vaccine (HER-Vaxx) from a research group at the Medical University of Vienna. The technology is currently under a deed of assignment to a company named Biolife Science Qld Ltd, which is to be vended into Acuvax.

The vaccine is a potential competitor to Roche's HER2 antibody, Herceptin (trastusumab). Herceptin generated sales for Roche of CHF 5.9 billion in 2012. In the US, a course of treatment with the drug costs about US$54,000 for 52 weeks of treatment.

Herceptin is approved for treating late stage HER2-positive breast cancer and HER2-positive stomach cancer.

HER2 is a member of a receptor found on cells which are over expressed (meaning there are many more than normal) on cancer cells. It is estimated that about 20% of people with stomach cancer test positive for HER2 and 25% of people with breast cancer test positive for HER2.

Issues for Herceptin

Since approval in the US in 1998, Herceptin has become a commercially successful monoclonal antibody drug. However, its cost is an issue for patients and payors in some parts of the world. Herceptin also has Black Box label warnings regarding cardiovascular and pulmonary toxicity and infusion reactions.

Patents covering Herceptin expire in Europe in 2014 and in the US in 2019. While biosimilar pathways differ between the US and Europe, the likelihood or a biosimilar emerging in Europe is high and its impact on Roche's Herceptin European revenues is could be material. In 2012, sales of Herceptin in Europe accounted for 33% of total global sales of the drug.

An implication is that a new patent-protected therapy that could compete on price and performance with Herceptin and biosimilars-of-Herceptin is likely to gain the interest of Roche, if the therapy shows promise in advanced clinical studies.

HER-Vaxx – Design and Mode of Action

Biolife's HER-Vaxx vaccine is designed to stimulate a patient's own immune system to generate antibodies to the HER2 receptor. This is in contrast to Herceptin, which is a monoclonal antibody manufactured in a bioreactor, and which after formulation as a drug, is delivered by IV infusion into a patient.

Biolife's HER-Vaxx vaccine is constructed from three small fragments (peptides), termed P4, P6 and P7, of the larger HER2 receptor (a protein). These peptides have been engineered to sit on the outside of a virosome (a sphere shaped vessel very similar to the outershell of a virus). One advantage of a virosome is that its of a size and shape that is more readily recognised by the immune system.

The use of virosomes as a transportation vehicle means the peptides can be positioned facing the right way and distributed uniformly across the spheroid shape of the virosome.

The selection of three peptides (which are antigens as seen by the immune system) is designed to elicit a stronger or broader response by immune system. The vaccine approach also means that a longer lasting response can be generated against HER2 expressing cells.

The approach may not mean that all tumour cells are completely eradicated but it offers the potential to stabilize the disease and therefore extend life. In some cases, the approach may mean that the immune system is supported to help achieve disease remission. In a Phase I study of HER-Vaxx, 50% of patients were reported as achieving stable disease.

Merits of the Approach

Potential merits of the vaccine approach include a superior dosing regime and less onerous rout of administration.

While it has yet to be determined, HER-Vaxx may be administered anywhere between one and four times for a course of treatment in contrast to 18 30-90 minute IV infusions over 52 weeks required for Herceptin. (Another unknown is whether booster doses after the main phase of treatment will be required for HER-Vaax.)

HER-Vaxx is injected rather than delivered by IV infusion, with injections saving time and money at the point of treatment.

It is likely that the COGS of HER-Vaxx will be much lower than for a Herceptin and its potential biosimilars. This may increase the global market opportunity for the therapy.

Phase II Trial Planned [Under FDA IND]

Biolife is planning to conduct a Phase II trial of HER-Vaxx in 78 patients with relapsed metastatic gastric cancer who test positive for HER2 over-expression. The trial would involved HER-Vaxx being administered in combination with chemotherapy (5FU and cisplatin). The combination of the subject group (relapsed metastatic gastric cancer) and chemotherapy will mean the vaccines will be tested in difficult circumstances, which is however, par for the course with immunotherapies.

The immune systems of patients with advanced cancers and those who also have been treated previously with other drug therapies are typically stressed. Another factor that is likely to have an impact on the success of the trial is the timing of the administration of the vaccine, so that timing is optimised to work with and for the effector arm of the immune system.

The trial will first enrol 10 patients to evaluate dosing, which will be followed by the enrolment of 34 patients in the treatment arm and 34 patients in the control (chemotherapy) arm.

The trial would commence in 2014 Q3 and will allow 12 months for recruitment. HER-Vaxx will be administered at Day 1, Day 14, Day 42 and Day 98, followed by booster shots every six weeks thereafter for up to 52 weeks.

The trial is estimated to cost $2.5 million, with cost advantages obtained from running the trial in countries in Eastern Europe.

Biolife is aiming to file an IND with the FDA in 2013 Q4.

Meeting on March 22, 2013

A meeting of the shareholders of Acuvax will be held on March 22, 2013, to approve the acquisition of Biolife Science Ltd, to approve a 1:200 share consolidation, to approve the issue of up to 25 million placement shares, the issue of shares issued in respect of the acquisition and to change the name of the company to Biolife Science Ltd. Post- placement, share issue for the acquisition and reconstruction there will be 76.4 million shares on issue.

Deal Terms

Biolife has acquired the HER-Vaxx vaccine technology from an Austrian company associated with the inventors, Bio Life Science Forschungs-Und Entwicklungsges M.B.H.

Biolife (formerly Acuvax), the Australian entity, will pay $700,000 in addition to the payment of an 18% royalty from income it receives from the drug, to the founding scientists.

Biolife will also pay 20 million shares (post consolidation) and 20 million shares (post consolidation) based on performance milestones.

Patents

Biolife has two patent families that cover its vaccine technology. In Australia, two patents have been granted to Bio Life Science Forschungs-Und Entwicklungsges M.B.H. The patents expire in 2022 and 2027.

It is also acquiring a manufacturing patent from the manufacturer of the vaccine, Pevion of Switzerland, for CHF 200,000. Pevion will also be entitled to a 2% net royalty.

Investment Analysis

Biolife is a simple proposition for investors looking for a relatively short term proof-of-concept play, which if successful would see the company acquired by companies such as GlaxoSmithKline or Roche. We estimate results from the trial, assuming a 2014 Q4 start for the main body of the trial and favourable rates of recruitment, to become available at the earliest in 2017.

Clinical studies beyond the proof-of-concept stage will be very expensive and time consuming. An optimal outcome would be the sale of the whole company after proof-of-concept is achieved.

Cont'd on page 4

Companies With Pivotal Events Ahead – Part 3

Starpharma – Phase II Results Imminent

Starpharma Holdings (SPL: $1.19) has completed a Phase II trial of Vivagel for the *prevention of recurrence* of bacterial vaginosis (BV) which has involved 205 women.

The trial completed recruitment at the end of June in 2012. Women were treated for 16 weeks on alternate days to prevent the recurrence of the condition. The trial was completed last year and results are due to be released by the end of this month (in two weeks).

Last year the company completed two Phase III trials looking at using Vivagel to not prevent but to treat BV. While the trials demonstrated success at the end of treatment, they did not demonstrate success at two-to-three weeks after treatment had stopped, defined as a 'clinical cure'. The results were confounding with the efficacy lower than that seen in the previous Phase II study, and the patients in the placebo group having actually improved after treatment stopped. At some sites there was a very high efficacy in the placebo groups.

The endpoint should be easier for Starpharma to achieve in the current Phase II *prevention* study, because the endpoint is not clinical cure in the weeks after treatment, but at the end of treatment.

The market for prevention of BV is estimated by Starpharma at three times that of the treatment market.

A positive outcome in this trial has the potential only for a small share price gain, given that Phase III trials will still be required. A negative result can potentially cause a reasonable fall in the share price.

Starpharma is capitalised at $338 million and had $33.1 million at the end of last year.

This stock offering high risk but low short-term returns as it approaches this clinical milestone. Investors would be better placed by not being exposed to the stock.

Bioshares recommendation: **Sell**

Prana Biotechnology – Alzheimer's and Huntington's Phase II Data in H2

Prana Biotechnology (PBT: $0.22) has two major inflection points before the end of this year. The company has two Phase II trials to treat two differential neurological conditions. One is in Alzheimer's disease and the second is in Huntington's disease. Both are testing the same compound, PBT2.

The Alzheimer's disease trial has recruited 40 patients with early stage disease. The last patient was enrolled in November last year and patients are treated for 12 months.

This trial will use some interesting endpoints. There will be the standard NTB test for cognition and an MRI to measure brain volume. But for possibly the first time in a clinical trial, believes CEO Geoffrey Kempler, the company will used a novel imaging technology to screen patients to look at the distribution of amyloid plaques in the brain using the approved PIB imaging test. Patients were imaged before treatment and are also imaged during treatment.

Prana had achieved some success in a Phase II a study previously. This current trial is not large because of funding restraints. However it will be a critical milestone to see if the compound should be progressed further. News that the FDA is lowering the bar for Alzheimer's disease therapeutics is a positive for the company. To complete commercial development of this project, the company will need to find a partner. Positive results in this trial may facilitate that.

The second trial, in Huntington's disease, has recruited around 100 patients. Recruitment was completed in December last year and patients are treated for six months. Results are expected in October this year. The trial is being conducted at 20 sites in Australia and the US.

The drug candidate, PBT2, is believed to be neuroprotective and neurorestorative. In a Huntington's disease animal model, the drug candidate was shown to improve motor function, increase life span and reduce brain degeneration.

With the commercialisation of PBT2 for the treatment of Huntington's disease, the company believes it can be in control of its own destiny and bring the drug to market on its own. There is only one drug on the market to treat Huntington's disease, and that drug was approved only the back of two small clinical studies (in 24 and 50 patients).

That drug, tetrabenazine, has some serious side effects and works on motor function and control, but not cognition. Prana believes that its drug might work on both.

If this Phase II trial is successful, the company plans to conduct a single 'confirmatory trial', targeting approval in just four years time.

Prana is approaching some binary events in the second half of this year. Success in either Phase II study has the potential for substantial price gains in the stock, particularly in the Huntington's disease application. A negative result in both trials is likely to have a similar effect on its stock price in the opposite direction.

This is a high risk/high return stock. We rate the changes of success as low-moderate given the difficult disease classes.

Prana is capitalised at $76 million. It had $8.8 million at the end of December.

Bioshares recommendation: **Speculative Hold Class B**

Cont'd over

Bioshares Model Portfolio (15 March 2013)

Company	Price (current)	Price added to portfolio	Date added
Circadian Technologies	$0.280	$0.270	March 2013
Tissue Therapies	$0.245	$0.255	March 2013
Allied Healthcare	$0.031	$0.026	February 2013
Psivida	$2.00	$1.550	November 2012
Benitec	$0.012	$0.016	November 2012
Nanosonics	$0.490	$0.495	June 2012
QRxPharma	$1.13	$1.66	October 2011
Somnomed	$1.08	$0.94	January 2011
Cogstate	$0.440	$0.13	November 2007
Clinuvel Pharmaceuticals	$2.60	$6.60	September 2007
Universal Biosensors	$0.78	$1.23	June 2007

Portfolio Changes – 15 March 2013

IN:
No changes.

OUT:
No changes.

Neuren Pharmaceuticals – TBI and Retts Recruitment Challenges

Neuren Pharmaceuticals (NEU: $0.034) is running a number of clinical studies in the treatment of brain injuries. The lead study is with NNZ-2566 for the treatment of traumatic brain injury (TBI).

This study is being funded by the US Army and is being conducted in the US. The company has completed the first two cohorts of the trial, involving 60 patients. The third cohort will recruit 200 patients. That trial has been slow to recruit because of the difficulty in getting consent following an emergency brain injury.

The company is now seeking to complete recruitment by the end of this year. The primary endpoints are adverse events before discharge or 30 days after randomisation in the trial, and also serious adverse events in the three months after treatment. This should see results become available around mid 2014 on the current schedule.

The company has added more sites to speed up recruitment and also has been implanting what is called an Exemption from Informed Consent, which will allow it to implement treatment without consent.

In December last year the company received the go ahead from the FDA to conduct a Phase II study in people with Rett Syndrome, which is a rare neurological disorder. An oral version of NNZ-2566 is being explored to see if the compound can restore neuronal function. The company believes there is considerable pathological overlap between Rett Syndrome and TBI.

This will be a 60 patient study. It is expected to take a year to complete with recruitment now open. The trial will involve a placebo arm. The Rett Syndrome Foundation will help fund the trial with a grant of US$600,000. If this trial is successful, the company believes it can move into a pivotal study in adults and children that will allow it to file the drug candidate for approval.

Neuren is also seeking to start a Phase II trial with an oral version of NNZ-2566 in the treatment of concussion. This study is also supported by the US Army by way of a US$3.8 million in funding for this trial and the development of an oral version of NNZ-2566.

The treatment and prevention of brain injury presents an enormously high technical challenge. Running trials in traumatic brain injury is difficult because of the challenge of recruitment. The potential reward is high, however the road is litter with failures. Neuren has built up enormous levels of preclinical data that supports clinical evaluation of NNZ-2566.

The challenge for 2013 will be recruitment into clinical studies in TBI, Rett Syndrome and concussion. Progress can be measured this year with the rate of recruitment into these three trials. Next year will be a pivotal year for the company with results from three clinical studies.

Neuren is capitalised at $40 million. It had NZ$6.5 million in cash at the end of last year. In January this year it appointed Richard Treagus as Executive Chairman, presumably to help accelerate commercial development.

Bioshares recommendation: **Sell**

Bioshares

– Biolife cont'd

Summary

Biolife's attractions include decreased risk that comes from targeting a highly validated cancer target with a large and proven sales record, and a potentially cheaper technology from a COGS perspective.

The cost to test the investment proposition is very low and the route to a commercial outcome (trade sale) is clear cut.

Clinical trial and technology risks still exist and should not be treated trivially. The time to pay-off is more than three years away in our estimate. However, the risk-reward payoff could be very attractive if the Phase II trial yields strong results.

Bioshares recommendation: **Vote in Favour of Resolutions [If passed – 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

Corporate Subscribers: Pharmaxis, Starpharma Holdings, Cogstate, Bionomics, Biota Holdings, Impedimed, QRxPharma, LBT Innovations, Mesoblast, Tissue Therapies, Viralytics, Phosphagenics, Immuron, Phylogica, Bluechiip, pSivida, Antisense Therapeutics, Benitec BioPharma, Allied Healthcare Group, Calzada, Bioniche, Atcor Medical, Invion, Circadian Technologies