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In this edition...
Universal Biosensors has been sold down in reaction to a recall by Lifescan of One Touch Verio blood glucose meters which use the strips manufactured by UBI. UBI collects a 1 cents a strip royalty from the strips Lifescan also manufactures and then sells. Is the selling an over-reaction? We think so, especially given positive progress with Siemens for a suite of POC products for prothrombin testing. Prana Biotech is a genuine stayer in the long distance challenge known as Alzheimer's Disease drug development. Sheer persistence means it has stayed alive to be around to benefit from recently written FDA guidance on AD drug development, which is expected to shorten the time and lower the cost of getting AD drugs to market.
Companies Covered: PBT, UBI, Verva Pharmaceuticals

	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 - May '13)	3.1%
Year 13 (May '13 - Current)	-1.9%
Cumulative Gain	**250%**
Av. annual gain (12 yrs)	**16.6%**

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Bioshares

7 June 2013
Edition 506

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

Universal Biosensors – An Outstanding Investment Proposition

Universal Biosensors (UBI: $0.65) has been sold down in recent weeks. News of a product recall by the company's partner Lifescan (Johnson and Johnson) has been partially to blame, as has a decision by Lifescan to manufacture more of the glucose strips developed by UBI at its own facility. However, UBI remains an outstanding investment proposition and any blips in quarterly service fees from Lifescan (around US 1 cent per strip sold, not made), may offer an even more attractive stock price for investors.

In the March quarter, UBI received service fees from Lifescan of $840,000 (annualised rate of $3.36 million). This is the key income stream for UBI, and is essentially a royalty income from any of the UBI developed glucose testing strips that Lifescan sells globally. If Lifescan was to eventually transition the 4.5 billion blood glucose test strips that it sells from the 'Ultra' version to the UBI designed 'Verio' system, then it would translate to around US$45 million in annual revenue to UBI. However, it should be noted that this figure is unlikely to ever be reached because Lifescan has an undisclosed buyout clause for this service fee entitlement.

Strip sales in the March quarter, excluding stocking volumes, increased by around $630,000 from the previous corresponding period. If that growth continues as a bare minimum, then in March next year the company should be receiving around $1.6 million ($6.4 million annualised), taking into account also the favourable currency movements in the Australian dollar.

In the March quarter, revenue that UBI receives from making the glucose strips decreased from $4.7 million in the December quarter to $3.7 million in the March quarter. The revenue fell because Lifescan is increasing the amount of strips it is making at its own facility in Scotland. The fall in revenue should not be a concern to investors. The highest margin revenue comes from the service fee (100%) with manufacturing delivering less than a 20% profit margin in our estimates. Our assumption is that Lifescan will want to

Cont'd on page 3

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2013 Speaker List

Ron Weinberger (CEO of **Nanosonics**)
Jackie Fairley (CEO of **Starpharma**)
Paul Wright (CEO of **Universal Biosensors**)
Brad O'Connor (CEO of **Cogstate**)
Steven Mercer (CEO of **Tissue Therapies**)
Neil Verdal-Austin (CFO of **Somnomed**)
Paul Ashton (CEO of **pSivida**)
Peter French (CEO, **Benitec Biopharma**)
Robert Crane (CFO of **GI Dynamics**)
Megan Baldwin (CEO of Opthea (subs. of **Circadian Tech.**))
Mike McCormick (CEO of **Osprey Medical**)
Julian Chick (COO of **Allied Healthcare Group**)
Neil Frazer (CEO of **Oncosil Medical** (from 1/7/2013))
Michelle Carr (CEO of **Telezon**)
Steve Gourlay (**GBS Venture Partners**)
Andrew Kelly (**BioPacificVentures**)
Graeme Wald (**Bioscience Managers**)
Rebecca Wilson (**Buchan Consulting**)
Tim Clark (**Piper Alderman**)
David Blake (**Bioshares**)
Steve Henry (CEO/CSO of **Kode Biotech**)
Mark Heffernan (CEO of **Nexvet**)
Rob Birrell (Founder of **Human Genetic Signatures**)
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– UBI cont'd

maintain a second facility for its strips to ensure product supply. And for that to occur, it will have to give UBI minimum volumes to justify keeping the facility operational. The costs also increase for Lifescan as volumes fall.

Product Recall

In March this year Lifescan announced a product recall of three of the OneTouchVerio glucose meters. The issue was that the meters did not issue an extremely high glucose level warning when glucose levels exceeded 10 times normal levels. The possibility of this occurring was remote according to Lifescan. However the meters needed to be replaced, which does not directly involve UBI.

In April this year, Abbott, which has 15% market share in the US, also recalled its glucose meter, the Freestyle Insulinx meter, with almost the same problem. Lifescan has 27% market share in the US.

UBI said there might be some impact on strip sales in the coming months but that it should not affect longer term sales. We do not view this as a serious issue for UBI.

UBI has no live development programs with Lifescan, although it still assists with manufacturing issues that Lifescan may have. Last month Lifescan received FDA approval for the OneTouch Verio Sync, which automatically sends data from the glucose meter to the iPad or iPhone.

Second Product Launch this Year

UBI is on track to see its second product launched in the market this year. That product is a PT-INR test to be used to calibrate warfarin dosage in patients. It will be launched by UBI's partner Siemens. UBI will share more in the upside with this product, having contributed to around 50% of the development costs over the last 12 months. The launch of this product will be a key driver for this stock in the next six months.

Under the Siemens collaboration there are two other coagulation testing products also in development. Feasibility of both of these products was achieved in mid-2012 with commercial development now in progress.

Under the Siemens collaboration, UBI stands to receive six milestone payments, of which two for US$1.5 million each have been received. We expect the remainder to be received next year with the two additional product launches in 2014.

One of the core strengths now of UBI is the new product development 'engine room', where a suite a new diagnostics can be rapidly brought to market. The PT-INR test, now called the 'Xprecia Stride Coagulation Analyzer', should be launched in only two years after the collaboration with Siemens was first formed in 2011. Siemens recently featured this product at a trade show in Italy, highlighting that it was the first product to be developed with its partner Universal Biosensors.

Cont'd over

Biotech Royalty Plays

	UBI	ACL	ACR
Most recent annualised income ($M)	$3.4	$7.8	$8.8
Market Cap ($M)	$113	$113	$620
Royalty income/Market cap (%)	3.0%	6.9%	1.4%
12 month (annualised) forecast ($M) e	$6.4	$12.2	$18.0
12 month royalty forecast/market cap (%)	5.5%	10.8%	2.9%
Comments	Strong growth anticipated, up to max US$45 million	Approaching peak royalties	Plus US$25 million milestone payment expected this financial year. Strong royalty growth expected

Universal Biosensors is one of several ASX listed biotechs which can be categorised as royalty plays. Two others listed in the table above are Alchemia and Acrux. One forthcoming royalty play is pSivida.

The table lists each company's royalty income annualised, this income expressed as percentage of its market capitalisation, a forecast of annualised earnings in 12 months time, which is also expressed as a percentage of current market capitalisation.

Alchemia has the highest percentage royalty income, forecast at 10.8% next year. However, we do not expect this income to show much additional growth. Conversely, we expect Universal Biosensors and Acrux to achieve significant continued growth in royalty income in the subsequent years.

– UBI cont'd

Siemens is a world leader in coagulation testing, but at the pathology lab level. It has had no previous expertise in coagulation point-of-care testing. It is one of the top two global, *in vitro* diagnostic groups.

Some buyers will be quick to transition to a point-of-care testing process, such as speciality coagulation clinics. However, larger groups such as hospitals will likely take longer to change operation protocols before a point-of-care test can replace central lab testing for setting warfarin dosage.

Unlike the deal with Lifescan, with Siemens the company will be the exclusive manufacturer of the strips. UBI will not receive a 'service fee' but will be effectively selling the strips to Siemens by receiving a manufacturing margin. We expect this margin will be significantly higher than that received for making the glucose strips for Lifescan. UBI will also share in some of the profits if sales exceed expectations.

We understand that the collaboration with Siemens is progressing very well. Our view is that this initial partnership has a good chance of being extended into developing further products based on the UBI diagnostic platform.

Third Market Opportunity

UBI is also developing a PT-INR test independent of Siemens for use outside of the hospital, clinic and pathology areas (professional use settings). UBI will look to sell a PT-INR test for use by general practitioners and at home by patients. The company will use distributors and we anticipate the product launch to occur in 2014. For this product, UBI will also be developing the meter, which in the previous collaborations has been done by Lifescan and Siemens.

Germany is a large market for at-home testing for PT-INR, where about 25% of patients self-test. The US is a less progressive market, where less than 10% of patients self-test.

UBI expects to sign its first distribution arrangement for this product this year. The strip design is complete and the meter is now being developed.

Threats to the PT-INR testing market

One of the threats to the PT-INR market is that warfarin may be replaced with other, new oral blood thinning products. These include Pradaxa and Xarelto, which are currently on the market. These products are and will take further market share away from warfarin. However, there are two factors that will support the continued use of warfarin, for at least the next 10 years.

The first is the cost of these new drugs, which as branded pharmaceuticals can be four times as much as the generic warfarin. The second is that the regular blood coagulation level testing required with warfarin usage allows the doctor to closely monitor the patient. With the new products this is not the case and so doctors may be more reticent to prescribe them.

Summary

UBI retained $20.2 million in cash at the end of March. One way to look at UBI is that if all other assets and costs are excluded other than the service revenue, then based on expected annualised quarterly numbers for March 2014, UBI should be generating 5.5% gross profit based on its market value of $113 million in 12 months time.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Verva Pharmaceuticals – Update for ChemGenex Legacy Shareholders

Verva Pharmaceuticals held its fifth AGM on May 31, 2013. Verva Pharmaceuticals was formed by the de-merger from ChemGenex Pharmaceuticals in 2007, to develop ChemGenex's metabolic diseases drug discovery assets. Since the de-merger, $7.25 million has been invested in the company, principally by local venture and private equity investors including Queensland Biocapital Fund (~34% holding), GBS Ventures (~27%) and Uniseed (12%). Legacy Chemgenex shareholders own approximately 15% of the company.

Verva's lead program is the compound VVP-808 (methazolamide) as an insulin sensitizer. VVP-808 is a repurposed molecule, Neptazan, which was approved 50 years ago for the treatment of glaucoma. The compound is an inhibitor of carbonic anhydrase, which represents a new target for intervening in Type 2 diabetes.

Insulin sensitizing drugs aim to make insulin sensitive cells more responsive.

The market for insulin sensitizing agents has opened up again following the advent of safety issues which emerged with Avandia (risk of heart attack) and Actos (risk of bladder cancer).

Phase IIa Results

Verva completed a Phase IIa trial of VVP808 in 2012; 37 patients completed the 24 week trial with VVP808 (40 mg twice a day) and 39 patients completed the trial on a placebo treatment. Trial subjects were also segmented further according to whether they received metformin or not (metformin naive). Metformin, an oral drug, is from a class of drugs known as biguanides, which reduce high blood sugar levels by decreasing liver generated sugar production. However, metformin's usefulness decreases over time and incurs a range of negative side effects.

The trial showed that VVP808 caused a -0.4% decrease in HbA_{1c} after 24 weeks of treatment, compared to the control arm. It also showed that 33% of patients in the treatment arm saw their HbA_{1c} levels fall under 6.5% at the end of 24 weeks compared to 8% at the commencement of treatment. The number for the placebo group with HbA_{1c} levels under 6.5% remained unchanged at 13% over the 24 week study period. [Measures of significance were not disclosed.]

Important New Data

Some new data made available at the AGM showed that VVP808 also instigated weight loss in VVP808 trial subjects, who lost nearly 2 kg more than the several hundred grams lost by the placebo group over the 24 week treatment period. [p=0.040]

At 24 weeks, VVP808 also sustained reduced liver enzyme levels, a -10.7 change in mean ALT levels from a base level of ~32 (U/L), compared to a -1.4 change for the placebo group from a base level of ~34. [p<0.0001]

The degree of the effect of VVP808 on weight reduction and liver enzymes came as something of surprise to the company. Studies in diabetic mice have showed that VVP808 can lower lipid levels and reverse fatty live disease (NAFLD/NASH). Together with data from the Phase II trial, it may mean that VVP808 could also be developed to treat fatty liver disease, a large market indication for which there are no effective therapeutics.

This new data has been made public following the filing of the patents 'Method of Weight Reduction' and 'Method of Improving Liver Function' in March this year. The company announced post-AGM on June 4 that's its foundation patent 'Insulin Sensitizers and Methods of Treatment' was granted in the USA. (USPTO Number 8,455,4320)

An expert panel that has reviewed the Phase IIa trial has recommended that a Phase IIb trial be conducted to evaluate the effect of VVP808 on patients with a baseline HbA_{1c} greater than 8% (the baseline in the Phase IIa trial was between 7% and 8%) and power the trial sufficiently to confirm the effect of change in body weight and in liver enzymes.

Commercial Objective

The current commercial goal for Verva Pharmaceuticals is to sell or licence its assets or sell the business by 2013 Q4 or 2014 Q1.

To make the company transaction-ready it must discover the physical target for VVP808 and screen its library of analogues against this protein target. This discovery process has commenced.

The rationale for the target screening program is that potential pharmaceutical acquirers or licencees would value a more secure IP position that comes from ownership of a novel target which serves as an insulin sensitizing agent, that can also generate weight loss, and that also serves as a target for agents which can reverse fatty liver disease, a condition where there is an unmet need.

Summary

Shareholders in Verva Pharmaceuticals who inherited the holding from an original holding in Chemgenex may now form the expectation that their investment has an increased chance of being crystalised in less than twelve months time.

Bioshares

Bioshares Model Portfolio (7 June 2013)

Company	Price (current)	Price added to portfolio	Date added
Atcor Medical	$0.072	$0.082	May 2013
Circadian Technologies	$0.270	$0.270	March 2013
Tissue Therapies	$0.150	$0.255	March 2013
Allied Healthcare	$0.044	$0.026	February 2013
Psivida	$3.49	$1.550	November 2012
Benitec	$0.012	$0.016	November 2012
Nanosonics	$0.540	$0.495	June 2012
QRxPharma	$1.17	$1.66	October 2011
Somnomed	$0.89	$0.94	January 2011
Cogstate	$0.330	$0.13	November 2007
Clinuvel Pharmaceuticals	$2.02	$6.60	September 2007
Universal Biosensors	$0.65	$1.23	June 2007

Portfolio Changes – 7 June 2013

IN:
No changes

OUT:
No changes

The FDA's New Guidance for Alzheimer's Disease Drug Developers

The FDA issued a new guidance document in February 2013 for the development of drugs for the treatment of Alzheimer's Disease. The guidance document indicated how drug developers may approach the development of drugs for treating Alzheimer's disease given the FDA's updated views on the current scientific landscape together with impediments which have held back the development of new Alzheimer's disease drugs.

The FDA has expanded its focus on issues relating to the development of drugs that can be administered in the earlier stages of the disease before dementia overt.

The FDA recognized in its document that well before overt dementia occurs, 'cognition becomes increasingly effected and relatively mild but detectable impairments in some functional abilities emerge as well'.

The FDA stated that while the use of both cognition and function as efficacy endpoints are desirable, the reality is that evidence of a delay in cognitive impairment 'may provide sufficient evidence of effectiveness'.

Composite Scale Tests for Prodromal AD

The FDA was of the view that composite scale tests which incorporate cognition and function, which have been validated in early stage patients, would be suitable assessment tools of prodromal AD (a state which precedes overt dementia). The FDA refers to the Clinical Dementia Rating - Sum of Boxes as an example of a suitable tool.

The adoption of a single composite efficacy score (cognition and function) would potentially make trials shorter and require fewer numbers to be enrolled.

Stepped Registration Process

One of the changes supported by the FDA was that drug developers could in the case of preclinical AD where 'only subtle cognitive deficits are present in the absence of any detectable functional impairment' file for marketing approval based on cognitive performance efficacy endpoints but, post approval, continue the clinical program to also demonstrate functional benefits. Such an approach could speed up the development process.

Time to Diagnosis

The FDA also discussed the value of a using a 'time to diagnosis of dementia' as an efficacy endpoint in subjects with early AD.

Biomarkers

On the matter of biomarkers, the FDA was of the view that no reliable bio-markers exist which could be used as primary endpoint measures but that it is open to their use in arguments in a secondary capacity.

Summary of the FDA's Position

The FDA has eased the hurdles and accelerated the process for AD drug developers by allowing for the use of cognition-only endpoints but coupled to a staged approval process and also by accepting a composite score measure to demonstrate efficacy.

Implications

For AD drug developers such as Prana Biotech (PBT: $0.245), which is currently conducting a Phase II imaging trial of PBT2 (a metal chelating compound) in 40 pro dromal AD patients, the implications are significant. Previously, the commercial prospects for PBT2 were weak, given the requirement for large Phase III trials targeting dementia and conducted over lengthy time periods (e.g 78 weeks), rather than preclinical or pro dromal AD.

Theoretically, and assuming positive Phase IIb results due later in 2013, Prana could contemplate commissioning a Phase III trial of PBT2 in pro dromal AD in 2014 and secure a trial outcome possibly 12 months later which could trigger a registration process with the FDA in 2015, based on showing a cognitive benefit alone. Such a development plan would require further funding. From an investment perspective, however, the licensing potential of PBT2 as an AD drug looks to have improved considerably.

Prana Biotech is capitalised at $93 million and held cash of $9.1 million at March 31, 2013.

Bioshares recommendation: **Speculative Buy Class B**

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, Impedimed, QRxPharma, LBT Innovations, Mesoblast, Tissue Therapies, Viralytics, Phosphagenics, Phylogica, Bluechiip, pSivida, Antisense Therapeutics, Benitec BioPharma, Allied Healthcare Group, Calzada, Bioniche, Atcor Medical, Invion, Circadian Technologies