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In this edition...
Each year, Steve Burrill provides his State-of-the-Industry address at the international BIO conference, held in Atlanta earlier this month. In a jam-packed 90 minute address, Burrill gives his outspoken and forward-looking views on the state of the biotech industry, covering all aspects of biotech commercialisation. And according to Burrill, we are moving into a major sea change for the industry, with a very different future to that seen with biotech in the past. The good old days are well and truly over!

And we also provide coverage on two AGMs held this week, on Phosphagenics and private company Verva Pharmaceuticals.

The Editors
Companies Covered: ACL, BTA, POH, Verva Pharmacueticals, BIO coverage

	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)	10.1%
Cumulative Gain	**114%**
Av Annual Gain (8 yrs)	**14.7%**

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

Burrill's BIO 2009 Biotech State-of-the-Industry Address

Steve Burrill, CEO of US biotech investment bank **Burrill & Co**., delivered his annual State-of-the-Industry address at the BIO conference held recently in Atlanta. Burrill said that the industry was experiencing a major sea change that should see the delivery of a better and stronger biotech industry.

Companies seeking to create the next Amgen, Genentech or Genzyme will fail suggested Burrill. Over the last 40 years capital has been cheap and available. However, both Sell and Buy sides have been permanently restructured. Venture capitalists' appetite for risk has decreased dramatically, with VCs looking to support existing investments with an investment focus on existing portfolio companies. Access to capital for micro-cap stocks (less than US$1 billion) has dramatically decreased and Big Pharma is happy to wait for prices to get cheaper before they invest.

Creativity has now become an absolute requirement according to Burrill. The biotech industry will survive, however it needs to become more creative. [Note - in the context of this talk 'biotech' refers to both small and large medical innovation companies, in contrast to 'pharma' which is a reference to large multinational drug development and marketing firms.]

Pharma Model a Dinosaur

The top five pharmaceutical companies have lost 20% of their value over the last five months, while biotechs have appreciated by 18% over the same time. Genentech is now worth more than Pfizer, Amgen is worth more than Bristol-Myers Squibb, and Gilead is worth more than Eli Lilly. Astoundingly, over the last eight years, the top 10 Pharma companies' aggregate value has fallen by US$712 billion! Pharma continues to lay musical chairs with M&A although the Pharma model has now become outdated, a dinosaur, argued Burrill. The pharmaceutical industry will continue to see more consolidation and biogenerics are inevitable he said.

Interesting Facts on US biotech

Burrill pointed to some interesting facts about the biotech sector in the US. Of the 324 listed biotechs, 43 have a market capitalisation over US$1 billion, and 42% of all biotechs listed in the US have less than 12 months cash. There are 60 biotechs trading below their cash backing and there has only been one IPO since the start of 2008, which has since been delisted. This is in stark contrast to 2000, when 66 companies listed, raising US$6.6 billion. Of the listed companies, 53% are now worth less than US$100 million, and over 100 companies have announced restructuring plans in the last few months to cut costs.

In Burrill's opinion, 2008 was not altogether a bad year for (follow-on) financings, with US$10 billion raised through financings in 2008, although most was for later stage companies.

Cont'd over

From page 1

Significant M&A deals

Some of the more significant M&A deals completed over 2008/2009 included:

- Pfizer/Wyeth (US$68 billion)
- Roche/Genentech (US46 billion)
- Merck/Schering Plough (US$41 billion)
- Novartis/Alcon (US$10.4 billion)
- Takeda/Millennium (US$8.4 billion)
- Invitrogen/Applied Biosystems (US$6.7 billion)
- Eli Lilly/Imclone (US$6.2 billion)
- GSK/Stiefel Laboratories (US$3.6 billion)
- Celgene/Pharmion (US$2.7 billion)
- Roche/Ventana (US$3.4 billion)
- King/Alpharma (US$1.6 billion)
- Gilead/CV Therapeutics (US$1.4 billion)

The pharmaceutical industry has been one of the hottest areas for consolidation, after the finance industry, in the last 12 months, and Burrill suggested we are not done yet. He noted Japanese firms will be very active in the M&A space.

Overall

Overall, VCs and angel investors have been hesitant to invest in 2009. The business models are changing and there has been more of a focus on financing specific projects to a crucial stage where evidence that a project works can be shown. However even with the difficult times, strangely the rate of biotech start-ups around the world are increasing. The bottom line according to Burrill was that it's a fabulous time to be an investor, but not such a good time to be a biotech company.

Healthcare Reform

Healthcare reform underway in the US means there will be changes in who pays for healthcare and how it is paid for. However, this won't have a major impact on what biotech does. Burrill expects the US Congress will give Medicare more power to negotiate with drug companies, which will make things more difficult for the pharmaceutical/biotech industry. Burrill said that a sea change is underway in the heathcare sector – the Pharma model is broken, the population is aging, Pharma blockbusters are coming off patent, and the funding channel (capital markets) for innovation is broken. And by 2016, the Medicare system will be bankrupt.

Burrill's Prediction: A 2020 Wellness System

According to Burrill, although some think 60% of the US healthcare budget is spent of pharmaceuticals, this figure is actually less than 10%. Most healthcare costs are absorbed late, at the chronic disease level, when the likelihood of reversing disease is low. Sounding like Peter Farrell from **Resmed**, Burrill lamented that we have been operating in a 'sickcare' system for over 2000 years, not one aimed at preventing disease, a true healthcare system, when disease progression has a higher chance of reversal. Burrill's predicted that by 2020, this system will radically change. "You will walk into WalMart with your information on a chip, you will get analysed, and you will get your medicine on your way out."

Burrill said that around 55% of people want to communicate via email with their doctors, 57% want to make doctors appointments via email and 57% want to buy prescriptions via email. Walmart initially didn't have the system right. But we will rapidly move to a patient-centric, digital world. The next few years will see a rapid change from sickness to wellness care he said. "We are spending more on fitness coaches than on doctors."

Companion Diagnostics To Become Value Drivers

According to Burrill, companion diagnostics will become primary value drivers (another reason *Bioshares* readers should be looking at **Universal Biosensors**) and low margin generic therapeutics (an area in which China and India will dominate) will become the companion product. Pharma has in the past divested diagnostic assets, now they are looking to regain them (eg **Roche/Ventana** merger). The future may yet see iPods or Blackberries accepting blood samples for diagnostics and home monitoring.

Most companion diagnostics are developed independent of Big Pharma, and Big Pharma is looking to diagnostic developers to support their therapeutics.

At the moment the focus is on late stage detection and intervention, where there are no incentives for the medical profession to deliver wellness care, and where treatment consists of fragmented multiple reimbursements for treatments rather than an integrated, forward looking wellness system. In the US chronic diseases such as diabetes and congestive heart failure account for 75% of total medical costs.

Healthcare is moving towards personalisation, prediction, prevention (or pre-emption) and patient responsibility. "Consumers are becoming an important factor in the healthcare equation", said Burrill. However, Burrill believes the US will be a late adopter of a wellness care system.

The China Factor

China will become an increasingly dominant player in world healthcare. In a few years time, the entire US population will match the number of people in China over the age of 65. Healthcare spending in the US will reach 22% of GDP. The US currently spends more than any other nation per capita on healthcare yet has the sixth best healthcare system.

In 2005, the US accounted for 21% of world GDP. This is forecast to fall to 15% by 2035, at which time China is expected to contribute 27% of global GDP. Seven of the 10 highest economic developments to come from China will be in healthcare. Currently China is the sixth largest market for pharmaceuticals, although will become the third highest by 2013.

Big New Markets

Big new markets according to Burrill will be: Alzheimer's disease, memory loss, obesity and diabetes, anti-aging, anti-infectives, and in wellness. Medical tourism is booming and is expected to increase in value from US$60 billion in 2008 to over US$100 billion in 2010. In the US, a hip replacement procedure costs US$43,000. However this procedure can be conducted for as little as US$5000 in India or US$12,000 in Thailand.

Cont'd on page 4

AGM Reports – Phosphagenics and Verva Pharmaceuticals

By coincidence, the AGMs of two companies with a financial year ending December 31, 2008, **Phosphagenics** and **Verva Pharmaceuticals** were held on Friday, several hours apart in the same building in Melbourne. *Bioshares* attended both events.

While commenting on private company AGMs and their affairs is something we do less of in the pages of *Bioshares*, we thought it worth our while to report on Verva Pharmaceuticals because a significant number of investors hold shares in that company as a consequence of its de-merger from ASX-listed **ChemGenex Pharmaceuticals**.

Phosphagenics

Drug delivery company Phosphagenics (POH: $0.14) is developing a suite of dermal and transdermal drug products based on its novel alpha-tocopheryl phosphate and di-alpha-tocopheryl phosphate technology, which is also known as phosphorylated Vitamin E. Phosphagenics is evaluating the incorporation of its technology in various trans-dermal delivery systems, including vesicular, micro-emulsion, liquid, patch (both reservoir and matrix) and spray.

A Year of Consolidation

The chairman of Phosphagenics, Andrew Vizard, described 2008 as a year of consolidation, but highlighted the strong financial position at the end of the year, with the company holding $12.9 million in cash.

The company undertook a share placement in early 2008 to raise $9.1 million, even though financial markets were deteriorating. It now can be said that Phosphagenics acted with a commendable degree of foresight, after having made the assessment in late 2007 that market conditions would worsen over 2008.

Phosphagenics' consolidation activities included the relocation of four Melbourne-based sites into the one location at Clayton, the management of staff numbers through natural attrition and the focusing of its product pipeline towards products that have a shorter time to market.

Following the retirement of Michael Preston, the company also strengthened the board with the appointment of Michael Ashton, who has previously worked for **Merck**, **Pfizer**, **Faulding** and also as the CEO of **Skypharma**.

In 2007, the company demonstrated that it could deliver both small or large molecules using its proprietary technology for localised or systemic administration. However, the company has decided to concentrate on localised applications e.g. the delivery of retinoic acid for the treatment of acne or lidocaine as a topical anaesthetic. Phosphagenics completed Phase I trials for diclofenac, lidocaine and retinoic acid during 2008, but has to repeat the diclofenac (a non-steroidal anti-inflammatory) study at a future point. Phase II studies for lidocaine and retinoic acid are being prepared.

The company continues to develop two systemic applications, for insulin delivery and oxycodone (for pain). The next step for the insulin program will be for a Phase IIb study conducted under an FDA Investigational New Drug Application (IND) filing. A Phase I study of a gel formulation of oxycodone is in development.

The company's objectives over the next twelve months also include filing INDs for an oxycodone product and a lidocaine product. Achieving all three IND filings would in our estimate represent significant progress for the company.

The company has learnt from its insulin studies to date that patients do not prefer the gel formulation of insulin, which impacts on basel (background) insulin levels. They are more interested in a patch that can meet basel insulin requirements for up to 7-8 hours.

The personal care market remains an important commercialisation opportunity for the company. Phosphagenics is developing the Total E range of skin care products, including an anti-aging face cream, concentrated anti-oxidant serum, an after-sun care product and an after shave skin balm. The company expects to launch its skin-care products in Q4 2009 or Q1 2010.

One interesting question posed by a shareholder at the AGM was why the company has not performed as well as rival drug delivery company **Acrux**. Acrux shares have increased by 21% over the last twelve months whereas Phosphagenics shares have increased by 16%. Phosphagenics is capitalised at $93 million whereas Acrux is capitalised at $193 million.

While many factors contribute to the difference in market valuations of these two companies, a point of distinction is that one of Acrux's products has achieved marketing status in the USA and a second product is well on the way to completing a Phase III study. In other words, Acrux is much further down the commercialisation path than Phosphagenics.

The major weakness with Phosphagenics has been a deficiency in in-house drug delivery product development expertise, i.e personnel with a demonstrated ability to refine product development concepts into products seen as providing clear benefits to patients.

Bioshares recommendation: **Speculative Hold Class B**

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Verva Pharmaceuticals

Verva Pharmaceuticals came into existence as a result of the demerger (November 2007) of **ChemGenex Pharmaceuticals'** metabolic diseases drug research program and the consequent merger with the privately held obesity drug discovery company **Adipogen** (December 2007).

Prior to the collapse in the local and international stockmarkets in 2008, the board and management of Verva had planned on an IPO for the company, but these plans were shelved. Attempts to raise funds from others sources also met without success, including from potential licensees of the company's lead product VVP808, an insulin sensitising agent.

Cont'd over

Burrill cont'd

In 2008, 750,000 Americans went overseas for an operation. In 2010, six million people are expected to travel overseas for surgery.

Summary

Burrill said the good old days for biotech are gone forever and it's time for survival mode. Expect many acquisitions, with it being a buyers market. There will be significantly stronger demand for medicines relating to aging, with the US population over 65 due to increase by 50% by 2020.

Companion diagnostic tests have surged in the last few years. Biomarkers are booming globally according to Burrill and this is where all the action will be in all stages of drug development.

For investors this will be the best year ever for buying opportunities although Burrill warned there will be bankruptcies. Companies will need to conserve cash, concentrating on the programs that will deliver the most value and placing the other programs on hold. Companies may need to become creative with their financing, perhaps focusing on the valuable parts of the business and doing creative deals with major pharmaceutical companies.

With 75% of the healthcare budget spent on chronic diseases, there needs to be sea change that involves moving from treating sickness to promoting wellness.

A parting comment from Burrill was that the word dilution needs to be removed from investors vocabulary, although he also said that "we will come through these turbulent times and be better for it!"

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Verva cont'd

These potential partners found the compound to be interesting but called for proof of concept data (i.e. Phase II) to be provided. Potential partners were also interested in understanding the mechanism of action of VVP808.

An additional factor that has dampened specialist investor interest in diabetes drug programs is that the FDA has raised the safety bar for new and emerging candidates, especially in regard to cardiovascular safety following issues with **GlaxoSmithKline's** Avandia.

To fund the necessary Phase II trial and mechanism of action studies, several existing investors have provided funding of $2 million, through the issue of Class A redeemable preference shares. This share issue was approved at the AGM and is in effect a re-capitalisation of the company.

VVP808 History

VVP808 was discovered through the metabolic drug screening program developed by ChemGenex Pharmaceuticals. It is a known pharmaceutical product with a 40 year history of use in the US, Canada and Argentina. It is indicated as a systemically administered treatment for glaucoma.

VVP808 has certain enzymatic inhibitory properties but Verva has also determined that these are not related to its insulin sensitising properties. This mechanism of action has yet to be established, and when that is determined significant value could be created because it will reveal a new target for drugs to treat diabetes.

VVP808 Phase I/II Trial

Verva Pharmaceuticals plans to conduct a relatively straightforward two arm 60 patient Phase II trial. The trial will be conducted under the CTN scheme by Dr Geoff Nicholson at Barwon Health. The treatment arm would receive 40mg twice a day over 24 weeks. The dose could reduce to 30mg if acidosis occurred in greater than 10% of patients.

Trial endpoints will include safety and efficacy, including HbA1c (0.5%), fasting blood glucose, post prandial glucose, weight loss and improved lipid profile.

What is important to note is that the dose of 40mg is less than the currently approved dose/s of 50mg-100mg either twice a day or three times a day. Should a clinical program establish efficacy at or below 40mg twice a day, then a barrier to entry against possible generic competitors could be established.

Apart from the long history of use and a known safety profile, what also makes VVP808 an attractive drug development candidates is that it has a low cost-of-goods advantage. Avandia sells for about $6 a tablet, whereas VVP808 sells for 40 cents. However, if developed as a sustained release, once-a-day tablet, the price of VVP808 could increase to $1 or $2.

VVP808 (in its approved form) is only available in North America (and Argentina). This means that Verva, or its partners have a first to market opportunity in the rest of the world.

Although it might appear that Verva's re-purposing of a known compound presents competitive problems, in fact there are several barriers to competition that can be built up from development of different dosage forms and from beachhead access in territories where the drug has no approval history at all.

Summary

With funding approved shareholders, Verva can now concentrate on completing the Phase II trial of VVP808. The company expects to start manufacturing drug material this quarter and to initiate the study in Q4 2010. It also expects to complete mechanism of action studies in H1 2010 and to finalise data from the Phase II trial in Q2 or Q3 2010.

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Alchemia Update

It's not all smooth sailing for the most serious threat to Alchemia's drug, generic fondaparinux. Xarelto, an oral anticoagulant drug developed by **Bayer**, did not receive immediate approval from the FDA this week. The FDA would like to examine further data from the recently completed Atlas study, and may even want to see more data from an ongoing study looking at the effects of higher doses of Xarelto.

Xarelto has the potential to significantly disrupt the US$5 billion anticoagulant market, because it is an effective oral drug compared to injectable drugs such as Lovenox (the market leader) and fondaprinux, which is sold by GlaxoSmithKline and the only generic is expected to be released by Alchemia (Dr Reddy's) in early 2009.

According to **Cowen & Co** analyst Sara Michelmore (*Wall Street Journal Health Blog* May 28, 2009), there are "lingering concerns" about liver toxicity for Xarelto, which is slowing up approval by the FDA. Approval may now not come until late 2009 or 2010 in the US. The drug is approved for use in Europe and Canada. The longer Xarelto stays off the market and the more concerns about toxicity that emerge, the better the outcome for the other players in this market, including Alchemia.

Bioshares recommendation: **Speculative Buy Class A**

Biota Update

As the swine flu A/H1N1 outbreak continues to spread across the globe unabated, governments continue to utilise and expand their antiviral stockpiles of Tamiflu and Relenza. This week the Australian Government placed an additional order for 1.6 million Relenza courses, which will generate an additional royalty to Biota Holdings of $4.3 million.

To clarify a previous point on the patent life of Relenza, patents begin to expire in smaller countries in Europe in mid 2011. In the USA the core patent around Relenza expires in mid 2013 and in the major countries of Europe the patents expire in 2014.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares Model Portfolio (31 May 2009)

Company	Price (current)	Price added to portfolio	Date added
ASDM	$0.33	$0.30	December 2008
QRxPharma	$0.41	$0.25	December 2008
Hexima	$0.42	$0.60	October 2008
Atcor Medical	$0.20	$0.10	October 2008
CathRx	$0.55	$0.70	October 2008
Impedimed	$0.80	$0.70	August 2008
Mesoblast	$0.73	$1.25	August 2008
Cellestis	$2.92	$2.27	April 2008
IDT	$1.56	$1.90	March 2008
Circadian Technologies	$0.76	$1.03	February 2008
Patrys	$0.07	$0.50	December 2007
Bionomics	$0.26	$0.42	December 2007
Cogstate	$0.24	$0.13	November 2007
Sirtex Medical	$3.01	$3.90	October 2007
Clinuvel Pharmaceuticals	$0.36	$0.66	September 2007
Starpharma Holdings	$0.34	$0.37	August 2007
Pharmaxis	$2.60	$3.15	August 2007
Universal Biosensors	$1.15	$1.23	June 2007
Biota Holdings	$1.41	$1.55	March 2007
Probiotec	$1.75	$1.12	February 2007
Peplin Inc	$0.69	$0.83	January 2007
Arana Therapeutics	$1.40	$1.31	October 2006
Chemgenex Pharma.	$0.53	$0.38	June 2006
Cytopia	$0.09	$0.46	June 2005
Acrux	$1.21	$0.83	November 2004
Alchemia	$0.37	$0.67	May 2004

Portfolio Changes – 29 May 2009

IN:
No changes

OUT:
No changes

How Bioshares Rates Stocks

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

Group A

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

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

(CMP–Current Market Price)

Group B

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

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

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

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

Speculative Hold – Class A or B or C

Sell

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