

### **A note from the editors**

Welcome to the 13th edition of *Bioshares* but also the first edition of *Bioshares* in its new format as an electronically delivered weekly report. We are continuing with the same numbering system because it's important to remember that *Bioshares* wasn't born yesterday. After 12 quarterly editions, *Bioshares* has achieved a solid reputation for providing independent investment advice for the Australian life sciences sector and has also given a context to drug and medical device development both in Australia and internationally.

The weekly format will allow subscribers to receive more timely investment research and our end of quarter reports will continue to provide you with sector progress summaries. We look forward to your feedback over the coming weeks and thank you for your continued support of this independent investment resource.

Mark Pachacz and David Blake

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# Bioshares

Number 13

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

### **Therapeutic Product Trials Update**

The number of therapeutic products undergoing clinical development by ASX-listed companies, as well as in partnership with other firms, has continued to expand since our survey was last presented to *Bioshares* in February 2002.

In this survey, other products, such as Agenix's Thromboview blood clot imaging agent, CSL's fibrin bandage and Biotron's cancer diagnostic have been included, to give an expanded picture of product development that requires safety and efficacy evaluation prior to regulatory approval.

A total of 26 products are undergoing, or are set to commence evaluation, in 35 clinical trials. Only one product, CSL's HPV vaccine, is at the Phase III level of evaluation which is being managed by Merck in the USA. Phase II data suggests that this vaccine is a very promising candidate for the prevention of cervical cancer caused by the human papilloma virus.

There are 21 Phase II trials underway or in planning, the largest number of Phase II trials on record, and there are 3 combination Phase I/II trials and 9 Phase I trials underway or in planning.

Overall fewer companies have partnered their compounds. Those that have include Amrad (Serono), CSL (Merck and the American Red Cross), Genesis R&D (SRI Pharma and Corixa) and Peplin (Allergan).

### **Disease Areas**

From a disease perspective 37% of trials are targeted towards various cancers. Inflammatory disorders, such as psoriasis, are the next most targeted area, amounting to 23% of trials underway or in planning.

### **Failures and inconclusive results**

The last twelve months has also seen a number of product failures. Amrad's drugs for hepatitis B (AM365) and for nerve damage (emfilermin) failed in Phase II trials. Gropep's diabetic neuropathy drug (PV705) failed to generate efficacy, but may be effective if a suitable transdermal drug delivery technology is found.

Bresagen had partnered E21R with British Biotech for evaluation in the treatment of acute myeloid leukemia. However, this arrangement was terminated prior to the commencement of clinical testing. More recently Virax's prima-and-boost HIV vaccine showed inconclu-

*continued on page 4*

**Bioshares is an independent report that services a niche investment market. It has been in publication for over three years and its survival relies on the support of subscribers. To ensure its successful continuation we ask that readers do not circulate this report.**

Table: Therapeutic Product Trials

Company/ Project	Phase	Status/Expected completion	Disease / Indication	Trial Locations	Patients Enrolled	Study Endpoints	Comments
<b>Agenix</b>							
Thrombocytopenia (imaging agent)	I	Commence March 2003 - complete Nov. 2003	Blood clots	Q-Pharm, Brisbane		Safety	
<b>Amrad</b>							
AM336	II	Expect to start Q1 2003	Chronic Pain			Safety and tolerability	Have commenced further to studies, prior to commencing PII
Emfilermin	II	To commence in 2003	Treatment of embryo implantation failure				
<b>Antisense Therapeutics</b>							
ATL1102	I	Commence Mar 2003	Multiple Sclerosis	Stamford Hospital, London	42 male volunteers	Safety and pharmacokinetics	Single escalating doses
<b>AustCancer</b>							
Pentrix	Ib/Ia	Completed Nov. 2002	p53 'positive' cancers	Sydney	5 completed the trial	Safety	Induced antibody and T-Cell response
Pentrix	Ib	TBA	p53 'positive' cancers	Melbourne			
<b>Biotron</b>							
CT-2	I	Commence Nov. 2002 -complete May 2003	Cancer diagnostic - colorectal	Prince of Wales, St George Hospitals Sydney	150 plus	Safety	
BIT009	I	Commence - First half 2003	HIV			Safety	
<b>Bresagen</b>							
E21R	I/II	Complete Dec. 2003	Rheumatoid Arthritis	Royal Adelaide Hospital	1 of 13	Clinical & surrogate response	
<b>CSL</b>							
HPV vaccine (Type 16)	II	Completed	Cervical cancer				100% efficacy
HPV vaccine (Type 16)	III	Underway	Cervical cancer				
Cervax16	I	Completed	Cervical and anal cancer				
ESO-1 vaccine	I	Completed	Melanoma				Phase II in planning
HCV	I	Underway	Hepatitis C				Second safety test planned for 2003
Fibrin bandage	I/II	Commence mid-2003	Traumatic bleeding				IND lodged
<b>Epitan</b>							
Melanotan; [Nle4,Phe7]-alpha MSH	Ib	Completed March 2002	Protection against UV-induced skin damage	CMAX, Royal Adelaide Hospital.	16 pts	(1) Pharmacokinetics and safety of 0.16mg/Kg/day dose over 10 days. (2) Skin melanin content	12 active and 4 placebo subjects. No serious adverse effects and increased skin melanin significantly increased in active group.
Melanotan; [Nle4,Phe7]-alpha MSH	II	Enrolling subjects/Aug 2003	Protection against UV-induced skin damage	Royal Prince Alfred Hospital, Sydney & Royal Adelaide Hospital.	10 out of 80	(1) skin melanin content (2) UV-induced erythema	Subjects given 3 x 10 daily aqueous injections over 3 months.
Melanotan; [Nle4,Phe7]-alpha MSH	Ib	Due to commence mid-2003 / Oct 2003	Protection against UV-induced skin damage	Q-Pharm, Brisbane	0 out of 24	(1) Pharmacokinetics & maximum tolerated dose (2)Skin melanin content	Dose escalation study of sustained-release (1 month) implant

Table: Therapeutic Product Trials (contd)

Company/ Project	Phase	Status/Expected completion	Disease / Indication	Trial Locations	Patients Enrolled	Study Endpoints	Comments
<b>Genesis R&amp;D</b>							
AVAC paediatric	I	Comp. March 2003	Atopic dermatitis	NZ	12 pts	Safety	Shown to be safe and well tolerated. Initial efficacy observed.
AVAC paediatric	II	Planned start Q3 2003	Atopic dermatitis	NZ	NA		
SRP299	II	Enrolling. Compl Q1 2004	Atopic dermatitis	UK	Target 120	Change in AD severity score	
PVAC	IIb	Enrolling. Compl Q1 2004	Psoriasis	USA	Target 240	> 75% reduction in PASI score at 24 weeks	
PVAC / UVB	II	Fully Enrolled. Compl mid 2003	Psoriasis	NZ	60 pts	% change in PASI score at 20 weeks	
<b>Gropep</b>							
PV701	1b	Completed Feb 2002	Oral Mucositis	Peter McCallum Cancer Institute		Safety, tolerability and preliminary efficacy	
PV702	II	Enrolment will be completed in 2002/03	Venous ulcers	Six Australian Study Centres	87 patients enrolled	Safety and efficacy	
<b>Meditech Research</b>							
HyFIVE	I/IIa	Completed	Metastatic colorectal cancer	Melbourne, Perth	13 pts	(A)Safety (B) Reduction in tumour volume/ Reduction in treatment toxicity	3 patients stable disease/ 9 patients progressive disease
HyDOX	I/IIa	Completed	Various cancers	RMH, Melbourne	16 pts	(A)Safety (B) Reduction in tumour volume/ Reduction in treatment toxicity	4 patients partial response/3 patients stable disease/ 9 patients
HyFIVE and HyCAMP	II	Commence H1 2003 / Complete 12-18 months	Colorectal cancer	RMH, Melbourne			Expects to improve patient tolerability
<b>Metabolic</b>							
AOD9604	IIa	Completed March 2003	Obesity	Adelaide	36 pts	Safety - multiple dose	Successfully completed
AOD9604	IIb	Commence mid-2003	Obesity	Four Australian sites	Target - 250 patients	Efficacy in generating weight loss	Pts dosed daily for three months
<b>Novogen</b>							
Phenoxodiol	I	Completed	Various cancers (excl leukemia)	Sydney			IV injection
Phenoxodiol	I	Completed	Various cancers (excl leukemia)	Sydney			IV injection
Phenoxodiol	I	Completed	Various cancers (excl leukemia)	Cleveland, Ohio	10 pts		IV injection
Phenoxodiol	II	Continuing	Leukemia	Royal North Shore			Continuous IV
Phenoxodiol	II	Continuing	Prostate Cancer	Melbourne			Oral
Phenoxodiol	II	Commenced Dec 2002	Ovarian cancer	Yale University	~40 pts	Tumor mass, tumor markers, 1 yr survival	IV injection, 2-ce weekly, over 12 weeks
NV-04	I	Commenced 2002	Actinic damage	Brisbane, Sydney			
NV-07 alpha	I	Commenced 2002	Cardiovascular	Melbourne		Safety and tolerability	
<b>Peplin</b>							
PEP005	II	In planning (but expected to run 2003-2004)	Non-melanoma skin cancers and Actinic Keratoses	In planning	In planning	In planning	To be conducted by Allergan, Inc. (licensee for the Americas) but expected to be for worldwide registrations
<b>Prana Biotechnology</b>							
PBT-1	II	Completed Jan 2002	Alzheimer's	Melbourne	36 pts	Efficacy	amyloid protein levels decreased; cognition deterioration slowed. Awaiting publication of results in peer reviewed journal. Had to resubmit after first attempt.

**Table: Therapeutic Product Trials (contd)**

Company/ Project	Phase	Status/Expected completion	Disease / Indication	Trial Locations	Patients Enrolled	Study Endpoints	Comments
<b>Prima Biomed</b>							
CancerVax	I	Completed Oct 2003	Cancer (Solid tumours)	Melbourne	10 pts	Safety.	Immune response observed. Study extended for follow up.
CancerVax	II	Planning underway -commence 2003	Cancer (Solid tumours)	Melbourne	50 pts	Efficacy	
<b>Progen</b>							
PI-88 + Docetaxel	I	Ongoing/End 03	All Tumours	Colorado, USA	up to 30 planned	Safety, Pharmacokinetics	Dose escalation component to determine MTD.
PI-88	I/II	Ph I: Qtr II 03 (ongoing) / Phase II: End 04	Melanoma	Colorado, USA	Phase I; 30 planned Phase II; 30 planned	Safety, Pharmacokinetics, Angiogenesis markers and clinical outcome	Ph I dose escalation component to determine MTD. Ph II fixed PI-88 dose from Ph I
PI-88	II	Qtr III 03 (ongoing)	Multiple Myeloma	Brisbane/Newcastle/Melbourne, Australia	27 planned	Safety, Angiogenesis markers and clinical outcome	
PI-166	I	Qtr I 04 (ongoing)	Hepatoma	Sydney, Australia	15-30 planned	Safety, Pharmacokinetics Tumour markers	Dose escalation component to determine optimal dose.
PI-88 + Docetaxel	II	Planning	Non Small Cell Lung Cancer	Colorado and potentially one other site, TBD.	TBA		Ph II PI-88 fixed dose from Ph I
<b>Psiron</b>							
Sorafin-AD	II-B	Commence July 2003	Atopic dermatitis	IDT			
Sorafin-P	II-B		Psoriasis	St Vincent's Sydney			
<b>Virax</b>							
VIR201	I/IIa	Reported Feb 2003	HIV	NCHECR Sydney and Melbourne	34 pts	Safety	Safety confirmed. Extension study continuing. No immune response elicited.
<b>VRI Biomedical</b>							
Lactobacillus acidophilus	II		Allergy		150 pts		

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sive results in a Phase I/II trial but the company will continue an extension study.

The sector can expect to experience further failures of drug candidates consistent with industry trends.

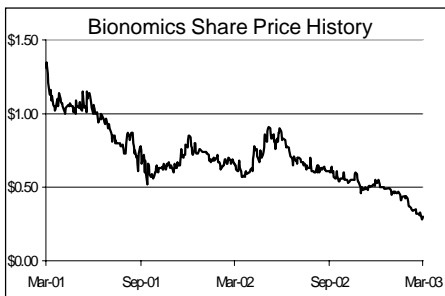
### Implications for investors

This survey is useful for investors from two angles. Firstly it allows identification of products that should produce reportable outcomes this year, although many companies do not specify expected completion or reporting dates for their trials. Products with declared conclusion dates include Agenix's Thromboview (Nov. 2003), Biotron's CT-2 test (May 2003) and Bresagen's E21R for arthritis (Dec. 2003). A number of other companies may report full or partial results in 2003, (eg Metabolic), however the survey indicates more reporting is likely to occur in 2004. The survey highlights the time consuming nature of clinical trials.

The second benefit of the survey is that it assesses the state of the pipeline in an aggregate sense, and investors can use the information to calculate potential capital requirements as well as strategic outcomes. Given that a greater number of results will be expected in 2004, then the likelihood of potential partnering ar-

rangements will also increase in that year.

The most surprising finding is the less than expected number of drugs or products in Phase I clinical trials. There is a great deal of activity at the pre-clinical level in companies such as Starpharma and in unlisted companies such as Cerylid, Xenome and Cytopia, and this activity would have been expected flow on into Phase I trials. However, financial pressure on the sector in 2002, such as the freezing of the Federal Government R&D Start grant program, coupled to a weakened capacity of companies to raise funds on the market, meant companies had to moderate their development projects. In addition, many companies experienced difficulties in their pre-clinical development programs.



### Consistency in communications is a challenge for Bionomics

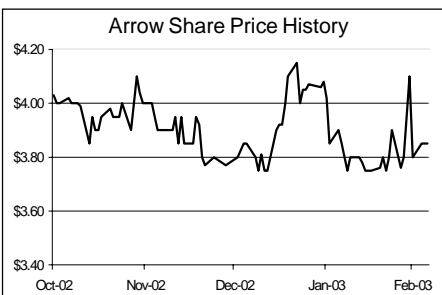
Bionomics (BNO; \$0.30) is one of three genomics companies listed on the ASX, the others being Autogen and Genesis R&D. Bionomics was first covered in Bioshares edition 12. Bionomics' share price has fallen 55% over the last year and is 67% down from its 52 week high. Genomics companies have been out of favour with investors, where prospects of sizable revenues are more distant compared to drug development companies.

A degree of Bionomics' share price slide can be attributed to events that have occurred this year; since December 31, 2002, the stock has fallen by 40%. On February 7, the company announced that its drug target validation program with Johnson and Johnson Research was to be wound up after 12 months of operation. Bionomics was expecting to extend and broaden the collaboration. Bionomics CEO, Dr Deborah Rathjen, said the collaboration was proceeding slightly ahead of schedule and on target and was "very surprised" by J&J Research's decision.

On February 25, the company's Chief Scientist Dr Tom Gonda resigned. The company intends to announce this event when it files its half-yearly report shortly. However, it is a point of argument that the filling or relieving of the position of a Chief Scientist is a material event warranting immediate disclosure.

The key issue for Bionomics is that it must be consistent in its announcement and reporting policy. On May 3 2001 it was "delighted" to announce the appointment of Dr Gonda to the position of Chief Scientist. It would be disappointing if the progress that company is making in the CNS area, in particular epilepsy, was jeopardised by sloppy communication with the market and a reluctance to be full and frank about important company matters. *Bioshares* retains its recommendation for Bionomics.

*Bioshares* Recommendation: **Speculative Buy Class B**



### Arrow Pharmaceuticals

Arrow Pharmaceuticals (AWP; \$3.85), a marketer and distributor of generic and private (non-PBS) pharmaceuticals, reported its first set of results as a listed company. The gross revenue increased by 70% in 2002 over the previous year to \$267 million, outperforming its prospectus forecast of \$250 million. The company's net profit result also outperformed forecasts, increasing to \$9 million (forecast \$8 million).

Arrow was one of the few companies in the sector to outperform expectations in 2002 and it highlights the low risk nature of its business. Arrow has only one serious competitor in Australia, Alphapharm, which has the lion's share of the generics business in Australia. By developing its own range of generic products (which are manufactured by Sigma), Arrow is able to increase its proportion of higher margin products, taking market share away from Alphapharm. With the Federal Government conscious of the need to restrict PBS expenditure and with \$800 million of generic pharmaceuticals to come off patent over the next seven years, Arrow should experience strong growth in the medium term. The company is currently trading on a PE of 25 and with an estimated net profit growth of 30% p.a. over the next three years, Bioshares maintains a Strong Buy recommendation on the stock.

*Bioshares* Recommendation: **Strong Buy**

**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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