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In this edition...
Consolidation in the biotech sector is in full swing however for investors it highlights one important point: biotech investments are offering very good value for medium to longer term investors ahead of an anticipated turnaround in the sector in 2007.

We update readers on developments at Bionomics, Phylogica and Agenix. And David Blake and Andrew Nash provide a retrospective look at Zenyth Therapeutics (formerly Amrad Corporation) as the end of an era draws near for one of Australia's earliest biotechs.

The editors

Companies covered: AGX, BNO, PYC, ZTL

	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 (from 5 May '06)	-17.5%
Cumulative Gain	**129%**
Average Annual Gain	**21.0%**

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Bioshares

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

Consolidation Signals Value for Biotech Investors

The biotech sector is the middle of a downturn making positive investment returns very difficult to achieve in the short term. However as prices slide in the sector, value opportunities for medium to longer term investors are continuing to become more favourable.

Most recently this week, **Merck KgaA** in Germany has bid US$13.3 billion for Switzerland's biotech group **Serono**. Serono sells the Multiple Sclerosis drug Rebif. The bid represents 22.6 times Serono's operating profit last year. **Zenyth Therapeutics** (Amrad) investors will remember Serono for handing back the failed fertility treatment drug Emfilermin in 2004.

The clearest indicator of this value proposition locally is the spate of M&A deals that have occurred this year. Since January 2006, eight Australian life science companies have been acquired or bid for, representing a total deal value of over $3.4 billion.

Consolidation within the sector had been long anticipated and slow to eventuate. With low share prices and an increased competition for investor attention within the sector, M&A activity should continue until the sector rebounds, which we anticipate will occur in 2007 in sync with the four year global biotech investment cycle.

The largest acquisition put forth has been by US-based **Hospira**, which has bid over $2.6 billion for **Mayne Pharma**. It follows on from the company's earlier bid last month for biopharmaceutical manufacturing group **Bresagen**. **Vision Systems** has received a second bid recently, this time from the US diagnostic screening group **Cytyc Corporation**, offering $497 million for the company.

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Acquisitions in Australian Life Sciences Sector in 2006

Company	Acquirer	Date announced	Status	Acquisition Price
Scigen	Bioton (Poland)	January	Acquired 90.5%	$51 million
Meditech Research	Alchemia	March	Completed	$16.9 million*
Zenyth Therapeutics	CSL	July	In progress	$108 million
Bresagen	Hospira (USA)	August	In progress	$21 million
Gropep	Novozymes (Denmark)	August	In progress	$96 million
Vision Systems	Cytyc Corporation (USA)	September	Tender offer submitted	$497 million
Mayne Pharma	Hospira (USA)	September	In progress	$2,628 million
Avantogen	Chopin Opus One LP	September	Conditional offer submitted	$5.5 million
			total	**$3,423 million**

** Price at time acquisition announced*

Stock Updates

Phylogica Expands Fragment Libraries

Phylogica (PYC: 39.5 cents) has recently completed an expansion of its core technology, its protein fragment libraries. For the company and its 14 scientists, it's a major achievement, with the four-fold library expansion process taking almost one year to achieve.

The implication for the company is that it has an improved diversity of protein fragments, labeled Phylomers by the company, which will improve the quality of drug candidates that can be delivered against drug targets for in-house development and with external collaborations including with **Johnson & Johnson.**

Phylogica began constructing its libraries of protein fragments in 1998. Its source was 19 of the then available 25 ancient bacterial genome sequences. As the number of available ancient bacterial genomes, which date back as far as 3 billion years, have increased to approximately 100, Phylogica has modified and expanded its Phylomer libraries to protein fragments from 25 of the most diverse bacterial genomes, yielding the company now seven libraries with about 260 million diverse Phylomer peptides. An advantage of working with protein fragments from these origins is their superior stable properties that have the potential to deliver improved drug candidates.

The full spectrum of protein shapes or fold

Phylogica's point of difference with other antibody and peptide library companies is that it concentrates on establishing libraries of protein fragments that encompass the full spectrum of protein shapes or folds, estimated to be approximately 3000 different folds. This is the core of its technology platform. Its other proprietary technologies include the ability to express this diverse array of Phylomers in an unbiased manner. The third arm to its technology platform is protein extraction methods the company has developed to isolate these protein fragments. Phylogica is also working to present these proteins in an array on a protein chip to allow more efficient screening of Phylomer peptides against drug targets.

In last week's edition of *Bioshares*, Dr Merilyn Sleigh from **Evogenix** looked at some of the successful antibody library companies that have been created, including **Cambridge Antibody Technology**, which earlier this year was acquired by AstraZeneca for US$1.4 billion. Phylogica's approach differs to the antibody library companies in that its protein fragment library does not concentrate on one class of fold - the antibody variable region - but seeks to provide the full library of protein folds with many permutations for commercial drug screening.

Phylogica has recently announced a capital raising for up to $3.75 million. It had $2.6 million in cash at the end of June this year and is capitalised at $43 million.

Bioshares recommendation: **Speculative Buy Class A**

Bioshares

Agenix's Thromboview Program Awaits Partner

Agenix (AGX: 15 cents) has been clearing its decks this year as it has been continuing licensing discussions for its core technology asset of Thromboview. In April this year the company sold its animal health business for $10 million. In June, the company sold and leased back its head office facilities for $5.1 million. Aside from Thromboview, this leaves the company with its human diagnostic business, which is now up for sale as well. That business generates free cash flow of about $2.5 million and a sale price of around $12 million might be achieved. The company has $8.6 million in cash with no debt following the sale of its property assets.

Thromboview is a novel technology that allows imaging of blood clots within the body. Recruitment of patients in clinical trials has now ceased and the company is seeking to partner development of the technology with a large imaging group. It's unlikely Agenix will begin Phase II trials in detecting pulmonary emboli (PEs) without a partner although clinical trial design and regulatory submissions will continue.

Agenix has significantly reduced its burn rate to $400,000 a month, with clinical trials effectively halted while a partnership agreement for Thromboview is negotiated. The company is investigating the use of the Thromboview humanised antibody with another imaging modality, Positron Emission Tomography or PET, for the detection of arterial (rather than venous) based blood clots. This program is being externally conducted and funded by the **Australian Nuclear Science and Technology Organisation**.

With the continuation of the Thromboview program now dependent on the company finding a development partner, the future of this technology is less secure. Although the technology appears to offer advantages over existing imaging products for

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M&A in the sector follows on from the $800 million acquisition last year of **Arrow Pharmaceuticals** by **Sigma**. Of the eight M&A deals announced this year, five were for cash generating businesses, suggesting that companies with products on or near the market with depressed share prices will continue to be targeted for acquisition.

One unusual bid announced this week was for Avantogen by a company controlled by Avantogen's Chairman, Richard Opara. The bid made was for 2 cents a share, which is peculiar given the stock last traded at 5.1 cents.

Bioshares

the detection of PEs, and we believe the company may still be successful in finding a development partner, the uncertain position of this program has resulted us downgrading this stock and removing it from our portfolio.

Bioshares recommendation: **Lighten**

Bionomics Raises $5M and Maintains Programs on Track

In these difficult market conditions for biotech companies, Bionomics (BNO: 16.5 cents) has shown that its drug candidate-focused business plan has helped the company secure additional funding this week with $5 million being raised though a private placement. An added positive sign for the company was that it was able to secure two new institutional investors in this current funding round.

Bionomics is capitalised now at $32 million and had $4.7 million in cash at the end of June this year excluding the $5 million just raised. In the last 12 months, it generated revenue of $2.2 million from the company's two diagnostic products on the market li**censed to LabCorp** and from out-licensing of anti-angiogenesis targets to **Genmab** earlier this year.

The company's lead compound, BNC105, originated through the **Iliad Chemicals** acquisition and is progressing well with clinical trial approval expected to be received towards the end of 2007. This drug is a vascular disrupting agent (VDA) that seeks to block the blood supply to solid tumours. By applying the 'Multicore' technology developed by Illiad, Bionomics has produced a significantly enhanced VDA analogue of an existing VDA drug (Combretastatin A-4) currently in Phase III trials with **Oxigene**. In preclinical models, Bionomics has shown this compound can achieve substantially better outcomes in driving tumour regression than Combretastatin A-4.

The Multiple Sclerosis program, also accessed through the Iliad acquisition, is expected to move into the clinic in early 2009. The company has developed synthetic analogues of existing natural compounds that bind to the Kv1.3 ion channel. The compounds work by arresting the inflammation process in the body by inhibiting memory T-cells that attack oligodendrocytes that make and protect the myelin sheath in the central nervous system, resulting in the progression of MS. Positive animal studies were recently presented by the company showing that the compounds were very selective for this ion channel. Other potential advantages of this program is the oral delivery of an MS drug. The compounds may also have an application in treating other inflammatory diseases such as rheumatoid arthritis.

Following BNC105, the company's epilepsy program is expected to move into the clinic in the first half of 2008 and its anxiety program is expected to begin clinical testing in late 2008. By early 2009, the company anticipates that it will have its four leading programs in clinical trials although the aim is to have at least one of these programs licensed to partners. Licensing processes for all four programs are now in progress.

The acquisition last year of Iliad Chemicals by Bionomics is bearing fruit as evidenced by the company's ability to progress its preclinical therapeutic programs. Combining Bionomics' genomics platform with the Iliad Multicore drug optimisation technology and new drug synthesis capabilities has transformed Bionomics into a company with a valuable engine room for drug discovery and lead candidate selection.

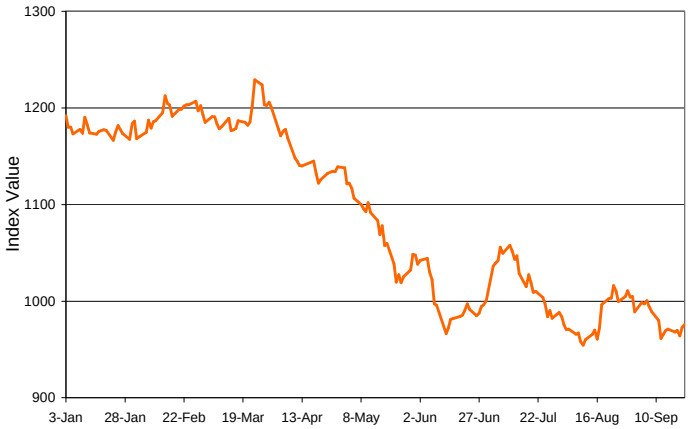
Bioshares recommendation: **Speculative Buy Class A**

Bioshares Model Portfolio (22 September 2006)

Company	Price (current)	Price added to portfolio
Acrux	$0.75	$0.83
Alchemia	$0.63	$0.67
Avexa	$0.235	$0.15
Bionomics	$0.17	$0.210
Biosignal	$0.18	$0.22
Cytopia	$0.665	$0.46
Chemgenex Pharma.	$0.47	$0.38
Evogenix	$0.420	$0.47
Optiscan Imaging	$0.450	$0.35
Mesoblast	$1.180	$1.27
Neuren Pharmaceuticals	$0.40	$0.70
Pharmaxis	$1.88	$1.90
Prima Biomed	$0.059	$0.09
Sirtex Medical	$2.35	$1.95
Sunshine Heart	$0.16	$0.19

Portfolio changes:
Agenix has been removed from the portfolio

The Bioshares 20 Index



The Bioshares 20 Index

Change from Dec 30, 2005	**-20.2%**
Change from June 30, 2006	**-2.4%**
Change - week ago	**0.5%**

Nasdaq Biotech Index

Change from Dec 30, 2005	**-6.9%**
Change from June 30, 2006	**-0.9%**
Change - week ago	**-1.6%**

Amrad I – A Business Model Perspective

Evolution of the Amrad Business Model – 10 Years as a Listed Biotech

Andrew Nash – Chief Executive Officer, Zenyth Therapeutics

At a recent breakfast meeting on September 5, 2006 the BioMelbourne Network featured three presentations focusing on the history and performance of Amrad. Two of those speakers, Dr Andrew Nash and Bioshares Co-editor, David Blake provide in the following pages written versions of those presentations

Amrad was established as a private venture in 1986 by a consortium that included the Victorian State government and some of Australia's best known medical research institutes. Against a backdrop of perceived "missed-opportunities" the Company's objective was to provide a vehicle for the commercialisation of Australia's highly rated medical research output. Twenty years later and with the company about to be acquired, albeit in another guise, there is an opportunity to review the evolution of the business model and to reflect on both its contribution to the local sector and the lessons to be learned.

The model

At the time of its debut on the ASX in 1996 Amrad had been at the forefront of the Australian biotechnology sector for some 10 years. The mission statement as espoused in the 1997 Annual Report remained simple and entirely consistent with the original objective:

"To be a successful internationally recognized pharmaceutical company commercializing Australian biomedical research with a portfolio of innovative products selling in world markets".

Underpinning this ambitious mission statement, however, was a business model that was rather more complex. With perhaps a view towards long-term sustainability a number of "profit-making" business units were established to support ongoing core R&D activity: Amrad Pharmaceuticals, a joint venture with Merck Sharp & Dohme, Australia (55% Amrad) was established to market in-licensed pharmaceuticals within the Australian environment; Amrad Biotech was established to market reagents and equipment to the medical research sector and; Amrad Discovery Technologies (ADT) had developed a unique library of natural product extracts and was to screen the library on a fee-for-service basis. Further adding to this list, in 1998 Amrad acquired a Sydney based point-of-care diagnostics business and established Amrad ICT. At this point in time Amrad employed in excess of 300 staff across 3 sites in Melbourne and one in Sydney.

With respect to "core" R&D activity, a perceived key strategic advantage for Amrad at the time of listing was preferential access to the research output and commercial opportunities arising from some of Australia's most esteemed research organizations. Included amongst the list of 11 "Member Institutes" were, **The Walter and Eliza Hall Institute** and **The Howard Florey Institute** in Melbourne, **The Queensland Institute for Medical Research** in Brisbane and **The Centenary Institute** in Sydney (see Table 1 for complete list). In return for this "preferential access" to their healthcare and biotechnology projects the Member Institutes received the benefits of assistance with protection and commercialization of their intellectual property and participated in any upside through ownership in Amrad - at the time of listing Member Institutes collectively held approximately 10% of Amrad's issued share capital. While each of the Member Institutes clearly excelled in its particular field of interest, these interests and the associated research activities were diverse and in reality the only theme common to all was a broad interest in human health.

Table 1. Amrad Member Institutes at the time of ASX listing in 1996

Institute	Location
The Walter and Eliza Hall Institute for Medical Research	Melbourne
Royal Children's Hospital Research Foundation	Melbourne
Murdoch Institute for Research into Birth Defects	Melbourne
The Macfarlane Burnet Centre for Medical Research	Melbourne
Howard Florey Institute for Experimental Physiol. & Medicine	Melbourne
Centenary Institute for Cancer Medicine and Cell Biology	Sydney
The Heart Research Institute	Sydney
Queensland Institute of Medical Research	Brisbane
Australian Institute of Marine Science	Townsville
Menzies School of Health Research	Darwin
The Immunogenetics Research Foundation	Perth

This diversity in the interests and research activities of the Member Institutes was to a large extent reflected in the Amrad R&D portfolio. Between 1996 and 2004 Amrad progressed, either alone or in partnership, six projects (five compounds) into clinical studies (see Table 2) for indications ranging from neuropathy and pain through to infertility and infectious disease. Amongst the variety of therapeutic strategies and/or compounds were a protein-based growth factor, a small peptide, an attenuated viral vaccine, a traditional small molecule and an injectable anaesthetic. Preclinical projects included therapeutic antibodies for inflammation and oncology, a growth factor with potential application in cardiovascular disease and small molecule drugs for infectious diseases, stroke and pain. Of the clinical programs four failed due to lack of efficacy, one failed as a result of unexpected adverse events and another was halted due to lack of a genuine commercial opportunity. In contrast, many of the preclinical programs continue to progress towards the clinic but in the context of either Zenyth or Avexa rather than Amrad (discussed further below).

Problems with the model

With the benefit of hindsight, and in the context of a sector that is now considerably more mature, the fundamental problems for both the Amrad business and R&D models are readily apparent

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– both were overly complex and both lacked a discernable focus.

Business model

The research and development of new therapeutics is a drawn-out, expensive, high-risk process and there is no guarantee of success. In this context the notion of profitable business units supporting core research and development activity must have been appealing. Unfortunately, while all of the business units could be more-or-less grouped within the "healthcare sector" they were, in reality, diverse in nature. Furthermore, while there were a number of precedents pointing to the potential success of businesses such as Amrad Pharmaceuticals and Amrad Biotech this was not the case, either locally or internationally, in respect of the high throughput screening-based ADT business. This diversity in business activity and the lack of precedent would stretch the expertise of any Management team and / or Board of Directors. While this diversity created issues from an operational perspective the complex nature of the model also proved difficult for the market to deal with. On what aspect of the business did the market focus its attention - were the revenues and margins of the business units more relevant than the progress of R&D projects? This created a situation where any perceived failures, even those of limited significance, would inevitably out-compete successes for influence over the stock price.

R&D model

As was the case with the business model, the notion of preferential access to the output of many of Australia's leading research institutions must have been an attractive one. In reality however it seems likely that the diverse interests of the research institutes, combined with an expectation of commercialization by Amrad, was a major factor driving the development of Amrad's complex R&D portfolio. Indeed a direct link between the diversity of interest, an Amrad mission statement that referred to "innovative products in world markets" rather than specific therapeutic indications and/or therapeutic strategies and the nature of the R&D portfolio is clearly plausible. By any standards, the notion that a relatively small R&D group within a newly listed company would have the expertise and resources to deal with the breadth of therapeutic indications and drug development strategies encompassed within the Amrad R&D portfolio was extremely ambitious. Perhaps at that time the complex nature of the R&D portfolio was viewed as an approach to risk mitigation - more projects, more technologies, more shots on goal. In hindsight it is easier to argue that this approach increased rather than mitigated risk.

Table 2. Amrad clinical programs, 1996-2004

Candidate ID.	Therapeutic indication	Therapeutic strategy/compound
AM424	chemotherapy induced peripheral neuropathy	protein growth factor – Leukemia Inhibitory Factor,
AM94	prevention of postnatal rotavirus infection	attenuated viral vaccine
AM149	injectable anaesthetic	novel propofol formulation
AM365	hepatitis B	nucleoside analogue
AM336	opioid resistant chronic pain	conotoxin
AM424*	infertility	LIF as described above

* Phase II studies conducted by Serono under license agreement with Amrad

A further important point to make is that while the Member Institutes were able to provide Amrad with access to exciting new intellectual property, they were rarely in a position to offer ready-to-go drug candidates. As a result Amrad was getting access to very early stage projects, and it was essential that Amrad develop the capacity to translate basic research into clinical candidates. While this was achieved with a considerable degree of success, it required a significant commitment of resources by way of time, cash and management. In addition, with such early projects many were destined to fail to produce drug candidates within a suitable time frame.

As noted above, these comments in respect of the original Amrad business model and approach to research and development are made with the benefit of hindsight and in the context of a more mature sector. In 1987 when Amrad was established, and indeed in 1996 when it listed on the ASX, there were very few examples worldwide (and none in Australia) demonstrating exactly how to create and grow a successful biotechnology company. While therapeutic focus and specialisation in a particular drug discovery platform now appear key to the success of any new biotech, this was not the case 20 or even 10 years ago. Furthermore, it would be inappropriate not to acknowledge that the original business model did result in some outstanding successes. While success in the clinic may have been elusive for Amrad there were many ground breaking partnering deals that pushed projects forward as well as providing very significant revenues for both Amrad and for the Member Institutes from where the intellectual property originated. Our ongoing deal with Merck to develop an antibody against the IL-13R for the treatment of asthma is but one example. To date Amrad (and more recently Zenyth) has received preclinical milestone payments in excess of US$16.5m with a significant proportion flowing back through to WEHI. While this deal has been highlighted, it should not be forgotten that during its history Amrad has had significant deals with **Merck**, **Chugai**, **Baxter**, **RPR**, **GSK** and **Serono**, and that Zenyth continues a joint collaboration with **Cambridge Antibody Technology**.

Deconstructing the model - the road to commercial focus

What was once Amrad is now represented on the ASX by Zenyth Therapeutics and Avexa. In contrast to Amrad, both Zenyth and Avexa readily demonstrate all the characteristics we have come

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to associate with small biotechnology companies - they have a clear therapeutic focus, employ clearly defined and consistent drug discovery strategies and, perhaps to the chagrin of many, burn a significant amount of shareholder dollars in the process. Amrad appears to have arrived at this point through a combination of both circumstance and strategic decision making. Taking a purely chronological perspective - the Amrad Biotech business was sold to **Chemicon** in December of 1999 and in that same month Amrad Discovery Technologies was spun-out as a private venture, originally operating under the name of **Exgenics** and subsequently as **Cerylid Biosciences**. In February of 2000 the Amrad ICT business was sold/written off and in September of 2000 Merck, Sharp and Dohme acquired Amrad's 55% stake in the Amrad Pharmaceuticals joint venture.

As a result of these transactions, by 2001 Amrad's activities were restricted to research and development, and the Company's operations had contracted to a single site with employee numbers down from a peak of over 300 to around 50-60. However, while the business model had become significantly less complex, the R&D portfolio still retained many of its original characteristics - research activities were spread across a variety of therapeutic indications (inflammation, cancer, infectious and neurological diseases) and there was no consistent approach to drug discovery. To further refine and focus R&D activity Amrad's anti-infectives projects were packaged into Avexa, and was spun-out of Amrad as a new ASX listed entity in September 2004. The remaining neurology projects were out-licensed to start-up venture CNSBio in June of 2005 and this left Amrad with a focused portfolio of high-value therapeutic antibody projects targeting inflammatory and oncology indications, and the core internal R&D expertise required to progress these projects. To reflect these profound changes in both the business and R&D models Amrad, changed its name to Zenyth Therapeutics in December 2005.

The point of the process outlined above is that it has given both Zenyth and Avexa the opportunity to succeed and, importantly, expanded the opportunity for shareholders to receive a return on their investment. Both companies have a clear focus, they know exactly where to continue to develop their expertise and they know where to spend their resources in order to obtain the maximum benefit. Importantly, both companies can succinctly describe their business to the market. It is interesting to contrast Zenyth's stated objective with the Amrad mission statement noted above - there are some similarities but also some profound differences.

"Zenyth's objective is to be a leader in the development and commercialization of antibody-based therapeutics for the treatment of inflammation and cancer".

For Zenyth and its shareholders recognition of the value in Zenyth has come early, with the recent announcement of the acquisition of Zenyth by Australia's most successful biotechnology company, **CSL**.

Perspective from David Blake follows on next page 7

Amrad II – The Bioshares Investment Perspective

Fig 1. Zenyth (Amrad) Sales 1987-2006

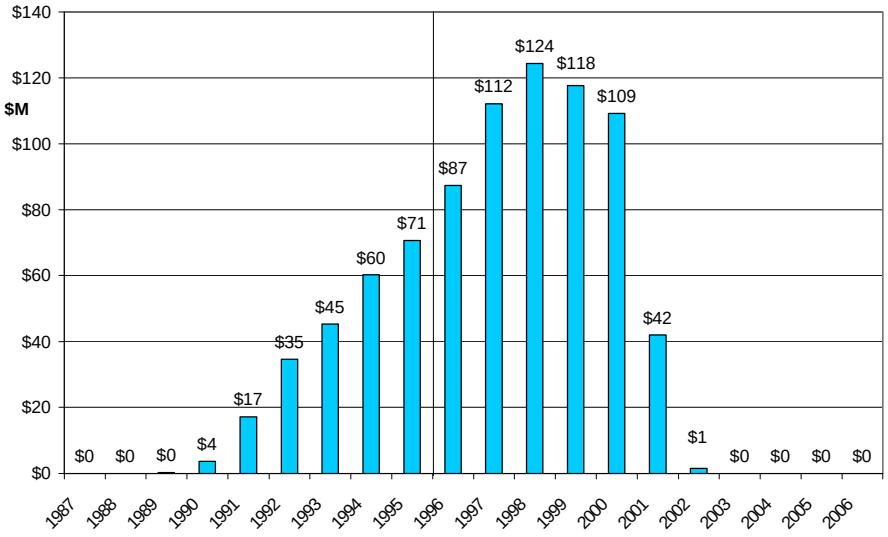


Fig 2. Zenyth (Amrad) Other Revenue1987-2006

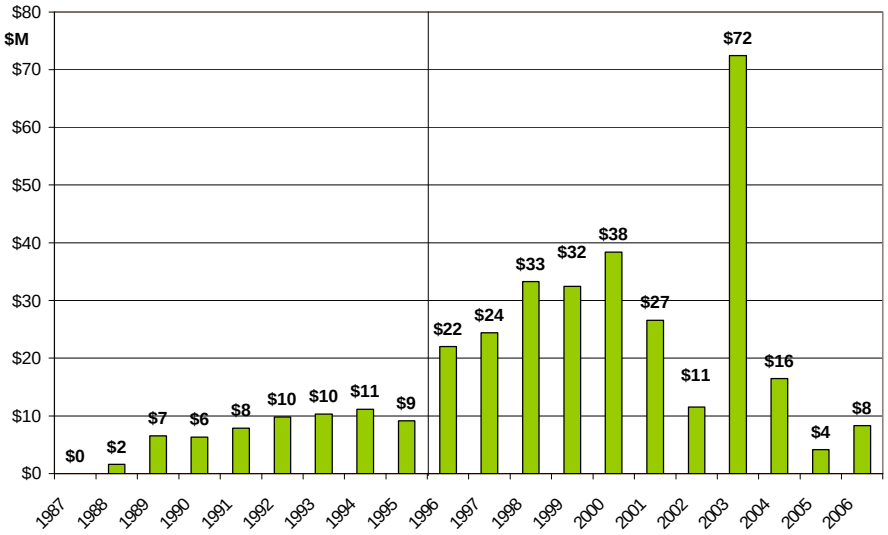
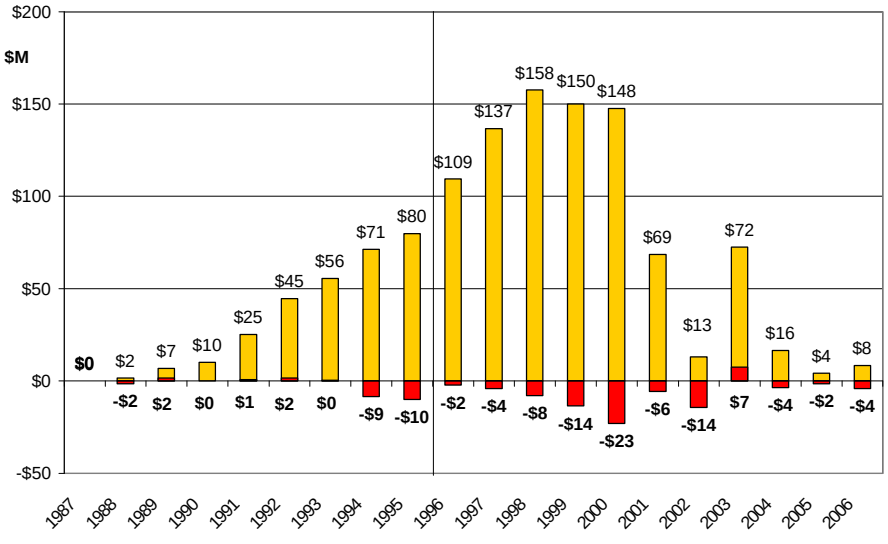


Fig 3. Zenyth (Amrad) Total Revenue and Proft/Loss 1987-2006



Zenyth Therapeutics, formerly Amrad Corporation, was incorporated in July 1986. The firm is currently subject to a merger by schemes of arrangement with **CSL**. If the court approves the schemes and the required shareholder approval is obtained, an important chapter in the history of Victorian, and Australian, biotech will close. The company listed on the ASX in 1996, spending half of its time as a private company and the remainder as public listed entity. The objective of the company has always been to develop and commercilise Australian medical discoveries.

There are several ways to appraise Amrad from an investment perspective. What, if any, sales and revenues did the company generate over the last 20 years? Was the company profitable? Did Amrad pay any dividends to investors? Did Amrad investors achieve any capital return on their investments?

Sales and Revenues

For a number of years Amrad conducted several trading businesses including Amrad Pharmaceuticals, of which it owned 55% and **Merck** Australian subsidiary **Merck Sharpe & Dohme** (MS&D) owned 45%. Amrad Pharmaceuticals was established in 1988. Amrad's 55% stake was sold back to MS&D in October, 2000. Other businesses operated by Amrad included Amrad Biotech, a reagents business and Amrad ICT, a diagnostics business.

Amrad recorded sales of $3.7 million in FY1990. Subsequently, sales posted healthy gains each year, peaking at $124.4 million in FY1998.

Three Amrad trading businesses and a fourth natural products screening operation were divested between December 1999 and October 2000. Sales from four months' trading by the pharmaceuticls business were reflected in Amrad's FY2001 accounts, but from thereafter, the company effectively recorded nil sales.

Amrad has been successful at building revenues from other sources. To date, the company has received $91 million in license

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fee and royalty income, $66 million in interest and investment income, $28 million in government grants and $92 million from the sale of businesses, land or property.

Profitability

Amrad has been profitable in only four of the last twenty years. It has accumulated losses of $87 million. The most profitable year occured in FY2003, when a net profit of $7.4 million was reported. The profit was driven by the sale of land and buildings in Richmond, where Amrad has been located, for $47 million.

Dividends

Amrad has not paid an dividends to shareholders of the listed vehicle. However, it paid dividends totalling $11 million to an equity partner in its subsidiary operation, Amrad Pharmaceuticals, over a period of six years.

Capital Return

By and large, investors who subscribed for shares when Amrad made its initial public offering in 1996, will have recorded a significant loss on that $1.95 per share investment. Only for several days did the the Amrad stock price exceed the IPO price of $1.96 in August 1997. From late 1997 through to 2000, the Amrad share price declined steadily, reaching a low of 35 cents in May 2000. The low point occurred during the period in which Amrad sold its trading businesses, but following the decision to cease development of two drug candidates. These were AM149, an injectable anaesthetic, and AM94 a vaccine for rotovirus.

The stock recovered for a period in 2000, weakened in 2001, and began a recovery that saw the stock peak at $1.10 in early 2002, near to the time that a $15 million capital raising took place. Once again the stock slumped during 2001 as two more clinical programs were halted. A trough in the Amrad share price was broken when the sale of Amrad's property interest took place in May 2003, and also several months later when a change in management occurred.

Since mid-2002, the stock has traded around 50 cents. However, with the announcement of the proposed acquisition by CSL, with a bid valuing Amrad (now Zenyth) and its shareholding in Avexa at 86 cents per share, investors who entered in the stock from July 2002 onwards are looking at approximate capital gains of between 70% and 150%. This excludes shares allotted in Avexa (on the basis of one Avexa share for every two Amrad shares) following its demerger from Amrad in September 2004.

Perhaps the single most successful investor in Amrad has been the State Government of Victoria, which provided initial seed capital of $14 million. Following Amrad's IPO in 1996, the Victorian Government received $20 million through a buyback of 10.2 million shares. The Victorian government also received a $5.2 million payment from Amrad for land where the company was located in Richmond. Its current shareholding in Amrad is worth $17 million, and its shareholding in Avexa is worth $2.3 million, both of which it has effectively held on a cost-free basis since Amrad's listing in 1996.

Return on Funds Invested

Prior to 1996, investors provided Amrad with funds of least $60 million. At its IPO, $70 million in shareholder funds were committed. Another $15 million was invested through a placement in 2001. Amrad's

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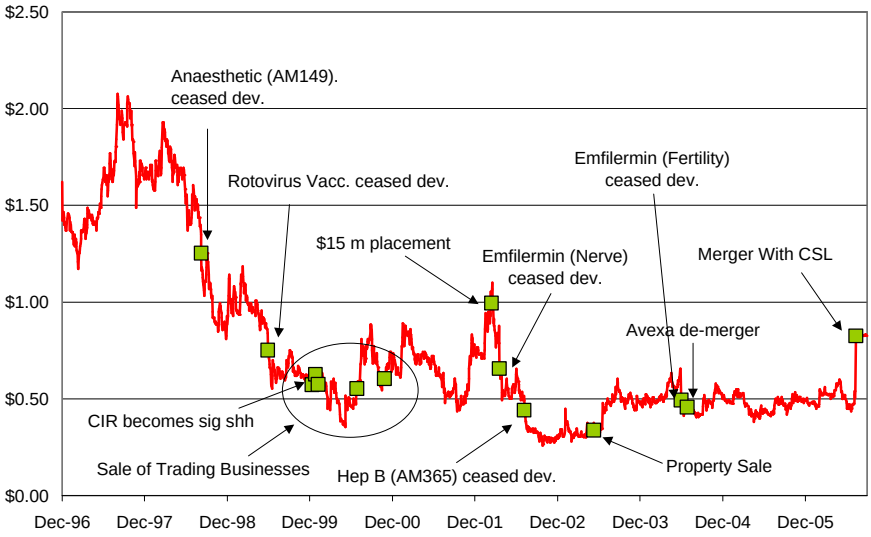
Table 1. Zenyth (Amrad) Summary of Income 1987-2006

		Amrad - Public Listed		
			Diversified Business	Focused R&D
	Total 87-06 ($M)	Total 96-06 ($M)	Total 96-01 ($M)	Total 02-06 ($M)
Income				
Sales	$826	$594	$593	$1
Lic. Fee and Roy. Income	$91	$86	$45	$41
Interest and Inv. Income	$66	$39	$24	$16
Government Grants	$28	$24	$21	$4
Sale of business, land or property	$92	$92	$36	$55
Total Revenue	$1,179	$884	$770	$114
Total Revenue less Sales	*$352*	*$290*	*$177*	*$113*
Profit/Loss	-$87	-$71	-$54	-$17
R&D Expense	-$237	-$192	-$128	-$65

Fig 4. Zenyth (Amrad) Share Price History



valuation at listing (excluding the State Government buyback and cash assets of $90 million) was $127 million. Its current approximate valuation based on the takeover offer but excluding cash assets is $60 million. Total R&D expenditure for the period 1987-2006 was $237 million, of which $192 million was expended in the period post-listing.

(Some) Investment Lessons from Amrad

Amrad now serves as a case study for what not do in commercialising medical discoveries. The first observation is that investment markets and analysts encounter difficulty in evaluating and valuing diversified operations and even diversified development companies. The lesson then is that biotech companies that are clearly focused on a disease or product area are more likely to gain stronger investor support and interest. The Avexa demerger proves that the spinning out of a business that is more keenly focused on one technology class (small molecule drugs) targeting a set of associated diseases (infectious diseases such as HIV and HBV) can be rapidly beneficial to shareholders.

Table 2. Zenyth (Amrad) Cash Flows 1996-2006

Amrad/Zenyth Cash Flow Statements	**1996-2001** $M	**2002-2006** $M
Cash Flows Operating Activities		
Receipts	735	60
Net Cash Operational	**-$48.1**	**-$34.7**
Cash Flows Investing		
Net cash Investing	**-$37.6**	**$41.4**
Financing		
Issue of Shares	**$70.5**	**$14.9**
Pmt for buy back of shares	**-$20.0**	**$0.0**
Share issue costs	**-$5.1**	**$0.0**
Cash transferred to funds under management	**-$79.0**	**-$25.9**
Cash drawn down from funds under management	**$106.7**	**$25.1**
Cash drawn down from borrowings	**$26.8**	**$0.0**
Repayment of borrowings	**-$7.1**	**-$20.3**
Cash outlay on share buy back	**$0.0**	**-$3.4**
Outside eq.int. in div. paid by a controlled equity	**-$10.1**	**$0.0**
Net cash provided by financing	**$82.6**	**-$9.6**
Increase in cash held	**-$3.1**	**-$2.9**
Cash Beginning	**$6.2**	**$3.1**
Cash End	**$3.1**	**$0.2**

To date, nothing from Amrad's R&D pipeline has been commercialised, and no commercial returns have resulted from the $237 million expended. This is despite the successful progress being made so far in two current drug development collaborations with **Merck** and **Cambridge Antibody Technology**. Perhaps twenty or more projects have been cancelled over twenty years, with the actual figure likely to be much higher. In other words, Amrad is a lesson in the reality of failure in medical product development. The lesson for investors is that biotech companies need to learn to set reasonable expectations of failure, not unreasonable expectations of success. And Amrad also illustrates the point that translating a researcher's medical invention into a product is a challenging task, indeed a very challenging task.

One interesting aspect of Amrad's financing history is that even for a company endowed with property assets and a pool of funds under management (see Table 2), such resources do not mitigate against the actual risk of technical failure. Since 1996, Amrad has drawn down $132 million from funds under management. Access to a large pool of funds may mitigate against dilutionary effects that the necessary and numerous fund raising rounds often entail. However, biotech investors seem to prefer, by and large, to adopt portfolio management techniques to manage company and technical risk, rather than place that management of risk in the hands of company managers.

(Some) Other Outcomes

When Amrad was founded in 1986, there were next to no providers of venture capital for life science start-ups. Amrad, along with pioneering companies such as Agen Biomedical (now Agenix) (founded 1984), Biota Holdings (1984), Circadian Technologies (1984), Peptech, (1986), Virax Holdings (1986), Medical Innovations (now Ventracor) (1986), had to develop and test business models that were unknown and develop financing strategies and mechanisms that were also novel.

Today, the capital markets within Australia for medical product development opportunities are, by comparison with 1986, deeper, more extensive and better informed. In addition the ability of Australian biotech inventors and entrepreneurs to access international funding sources has increased markedly.

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

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