

# Bone Medical Limited

ASX: BNE

Bloomberg: BNE AU

Reuters: BNE.AX

18 October 2004

\$0.60

COMM\*

## Using new oral delivery technologies to target osteoporosis and rheumatoid arthritis

# of Shares:	54M	Market Cap:	\$32.5M	Current Price	\$0.60
% All Ords:	0.0%	% Sector:	0.1%	12 Month Target:	Na

FIGURE 1: SHAREPRICE CHART



TABLE 1: EARNINGS SUMMARY

Yr to Jun	2003A	2004A	2005F	2006F
NPAT Rep (\$M)	0.0	0.0	(4.7)	13.1
NPAT <sup>1</sup> Adj (\$M)	0.0	0.0	(4.7)	13.1
EPS (c)	0.0	0.0	(7.0)	17.4
DPS (c)	0.0	0.0	0.0	0.0
P/E (x)	0.0	0.0	(8.6)	3.4
Yield (%)	0.0	0.0	0.0	0.0
Franking (%)	0	0	0	0
EPS growth (%)	n/a	n/a	n/a	n/a

<sup>1</sup> Profit & EPS adjusted for options, goodwill, notional earnings and non recurring items.

### Event

We initiate coverage of recently listed biotechnology company, Bone Medical Ltd ("BNE").

### Implications

BNE has one lead osteoporosis product, Oral Calcitonin, undergoing a series of phase II trials, a second lead osteoporosis product, Oral PTH, commencing phase I trials and a third lead product, a TNF regulator for rheumatoid arthritis and other auto-immune diseases in pre-clinical testing. BNE also has an earlier stage R&D pipeline. We like the company's three lead products, each of which address large global markets in which a safer or easier way to take treatments should be well taken up. We also like the company's prospects of securing significant licensing deals in the next 12 - 18 months.

BNE's CEO, Dr Jim Phillips, is an experienced and senior pharmaceutical executive having worked at Novartis and Johnson & Johnson. BNE's cash reserves are sufficient to fund around 15-20 months at expected cash burn rates. BNE's corporate relationships are complex and the company is about 75% controlled by a trust associated with the ex-CEO of Cortecs, Mr Glen Travers. Several related party transactions exist. Our risk-adjusted DCF valuation uses a 22% discount rate and values BNE at \$42.3M or \$0.78 per share.

### Investment Opinion

The research on this company has been commissioned and as such Aegis has received a fee for its initiation and ongoing research coverage. We believe it is inappropriate and misleading to provide a recommendation, investment opinion and/or share price target. However, we provide a valuation and earnings forecasts, as well as other relevant information to assist investors to form a view on the investment prospects of this company.

# Bone Medical

Recommendation<sup>1</sup>: COMM\*

12M Target: \$NaN

Company risk<sup>2</sup>: n/a

Share Price risk<sup>2</sup>: n/a

Ethical rating<sup>3</sup>: n/a

Year end Jun. All figures in A\$M

Profit & loss summary					Ratio analysis				
	2003A	2004A	2005F	2006F		2003A	2004A	2005F	2006F
<b>Operating revenue</b>	<b>0.0</b>	<b>0.0</b>	<b>0.0</b>	<b>23.7</b>	Revenue growth (%)	0.0	0.0	0.0	0.0
Invest & other income	0.0	0.0	(4.8)	0.0	EBITDA growth (%)	n/a	n/a	n/a	n/a
<b>EBITDA</b>	<b>0.0</b>	<b>0.0</b>	<b>(4.8)</b>	<b>12.8</b>	EPS growth (%)	n/a	n/a	n/a	n/a
Depreciation/Amort	0.0	0.0	0.0	0.0	EBITDA/Sales margin (%)	0.0	0.0	0.0	53.9
<b>EBIT</b>	<b>0.0</b>	<b>0.0</b>	<b>(4.8)</b>	<b>12.8</b>	EBIT/Sales margin (%)	0.0	0.0	0.0	53.9
Net Interest	0.0	0.0	0.1	0.3	Tax rate (%)	0.0	0.0	0.0	0.0
<b>Pre-tax profit</b>	<b>0.0</b>	<b>0.0</b>	<b>(4.7)</b>	<b>13.1</b>	Net debt/equity (%)	0.0	(13.6)	4.6	(37.5)
Tax expense	0.0	0.0	0.0	0.0	Net debt/net debt + equity (%)	0.0	(15.8)	4.4	(60.0)
Minorities/Assoc./Prefs	0.0	0.0	0.0	0.0	Net interest cover (x)	n/a	n/a	n/a	n/a
<b>NPAT</b>	<b>0.0</b>	<b>0.0</b>	<b>(4.7)</b>	<b>13.1</b>	Payout ratio (%)	0.0	0.0	0.0	0.0
Non recurring items	0.0	0.0	0.0	0.0	Capex to deprec'n (%)	0.0	0.0	0.0	0.0
<b>Reported profit</b>	<b>0.0</b>	<b>0.0</b>	<b>(4.7)</b>	<b>13.1</b>	NTA per share (\$)	0.00	0.16	(0.02)	0.22
NPAT add Goodwill & Pref	0.0	0.0	0.0	0.0	ROA (%)	0.0	0.0	(21.3)	49.9
<b>Adjusted profit</b>	<b>0.0</b>	<b>0.0</b>	<b>(4.7)</b>	<b>13.1</b>	ROE (%)	n/a	0.0	(21.7)	50.4
Cashflow summary					Multiple analysis				
	2003A	2004A	2005F	2006F		2003A	2004A	2005F	2006F
<b>EBITDA</b>	<b>0.0</b>	<b>0.0</b>	<b>(4.8)</b>	<b>12.8</b>	Market cap (\$M)		32.5		
Working capital changes	0.0	0.0	0.6	0.0	Net debt (\$M)		(3.3)		
Interest and tax	0.0	0.0	0.1	0.3	Peripheral assets (\$M)		(0.0)		
Other operating items	0.0	0.0	0.0	0.0	<b>Enterprise value (\$M)</b>		<b>29.2</b>		
<b>Operating cashflow</b>	<b>0.0</b>	<b>0.0</b>	<b>(4.2)</b>	<b>13.1</b>	<b>EV/EBIT (x)</b>	<b>0.0</b>	<b>0.0</b>	<b>(6.1)</b>	<b>2.3</b>
Required capex	0.0	0.0	0.0	0.0	<b>EV/EBITDA (x)</b>	<b>0.0</b>	<b>0.0</b>	<b>(6.1)</b>	<b>2.3</b>
<b>Maintainable cashflow</b>	<b>0.0</b>	<b>0.0</b>	<b>(4.2)</b>	<b>13.1</b>	EV/EBITDA rel All Ind (x)	n/a	n/a	n/a	n/a
Dividends	0.0	0.0	0.0	0.0	<b>P/E (x)</b>	<b>0.0</b>	<b>0.0</b>	<b>(8.6)</b>	<b>3.4</b>
Acq/Disp	0.0	0.0	0.0	0.0	P/E rel All Ind (x)	n/a	n/a	n/a	n/a
Other investing items	0.0	0.0	0.0	0.0	P/E rel All Ind ex banks (x)	n/a	n/a	n/a	n/a
<b>Free cashflow</b>	<b>0.0</b>	<b>0.0</b>	<b>(4.2)</b>	<b>13.1</b>	P/E rel sector (x)	n/a	n/a	n/a	n/a
Equity	0.0	0.0	0.0	0.0	Assumptions				
Debt inc/(red'n)	0.0	0.0	4.2	(13.1)	GDP growth (%)	2.93	3.73	3.41	3.20
Balance sheet					Interest Rates (%)	4.79	5.36	5.50	5.50
	2003A	2004A	2005F	2006F	Inflation (%)	3.09	2.30	2.04	2.65
Cash & deposits	0.0	3.3	0.0	12.2					
Inventories	0.0	0.0	0.0	0.0					
Trade debtors	0.0	0.9	0.0	0.0					
Other curr assets	0.0	0.0	0.0	0.0					
<b>Total current assets</b>	<b>0.0</b>	<b>4.2</b>	<b>0.0</b>	<b>12.2</b>					
Prop., plant & equip.	0.0	0.0	0.0	0.0					
Non-curr intangibles	0.0	20.4	20.4	20.4					
Non-curr investments	0.0	0.0	0.0	0.0					
Other non-curr assets	0.0	0.0	0.0	0.0					
<b>Total assets</b>	<b>0.0</b>	<b>24.6</b>	<b>20.4</b>	<b>32.5</b>					
Trade creditors	0.0	0.4	0.0	0.0					
Curr borrowings	0.0	0.0	0.0	0.0					
Other curr liabilities	0.0	0.0	0.0	0.0					
<b>Total current liab.</b>	<b>0.0</b>	<b>0.4</b>	<b>0.0</b>	<b>0.0</b>					
Borrowings	0.0	0.0	0.9	0.0					
Other non-curr liabilities	0.0	0.0	0.0	0.0					
<b>Total liabilities</b>	<b>0.0</b>	<b>0.4</b>	<b>0.9</b>	<b>0.0</b>					
Minorities/Convertibles	0.0	0.1	0.1	0.1					
<b>Shareholders equity</b>	<b>0.0</b>	<b>24.2</b>	<b>19.5</b>	<b>32.5</b>					

**Notes:** 1. The recommendation system rates stocks on a 12 month, absolute basis based on the total return (capital and dividends). BUY denotes an expectation of 15% or more total return; SELL 5% or less; HOLD within the range of 5-15%. ACCEPT OFFER relates to a situation where there is a public offer for shares and our view is to accept that offer. COMM means this research has been commissioned and Aegis has received a fee for publication and therefore it contains no recommendation.

2. The risk ratings are on a 12 month perspective, where five stars denotes low risk and one star denotes high risk. Company risk takes into account expected financial, strategic and execution risks associated with the company. Share price risk is a measure of the expected volatility of the price and other trading factors.

3. The Ethical rating rates a company on an ethical investment basis where five stars denote very good and one star a poor rating. The score is based on four key factors: areas of operating, environmental, corporate governance and social factors. For more information see [www.aer.com.au](http://www.aer.com.au)



## Key Points

- BNE was created through the backdoor listing in Aug-04 of a UK company, Bone Ltd, which holds the exclusive right to commercialise certain drug development technologies for use in bone and joint disorders.
- BNE's lead drug is oral Calcitonin, used for osteoporosis. It has successfully completed a phase I/IIA trial and will soon commence a phase II trial. Calcitonin has long been used in injectable and nasal spray formulations and the oral delivery enhancers are also in common use, so BNE may not be required by the FDA to do a pivotal phase III trial. If this were the case, the oral Calcitonin drug may be approved for market release as early as the beginning of CY07.
- The oral Calcitonin market is large (US\$700M globally) but relatively static. Nevertheless, we consider it likely that a successful Phase II trial would result in a substantial licensing deal during the second half of CY05.
- BNE's second lead drug is Oral Parathyroid Hormone (PTH), which is also used for osteoporosis and is due to commence a phase I trial shortly. The oral PTH drug candidate will most likely need to pass through the full FDA approval process. We place a market launch for oral PTH around the second half of CY09.
- PTH is a relatively new drug which is projected to enjoy rapid growth for many years. We consider a licensing deal for oral PTH most likely in early CY06 subject to successful phase I and II clinical trials.
- BNE also has an earlier stage R&D pipeline which includes pre-clinical TNF regulator compounds (for Rheumatoid Arthritis) and the search for new bone formation regulators.
- BNE has a little over A\$4M in cash, representing about 5 quarters' cash at the current burn rate.
- BNE's CEO, Dr Jim Phillips, has a strong pharmaceutical background, having been at both Novartis and Johnson & Johnson in Europe. He has had experience with clinical trials, regulatory affairs and licensing negotiation. He also has extensive industry networks and a deep knowledge of the Calcitonin and PTH markets.
- BNE's licensing rights relate to intellectual property developed by a scientist at a company called Proxima Concepts Ltd ("Proxima Concepts"). Proxima Concepts is controlled by a discretionary trust associated with Mr Glen Travers, who was previously Executive Chairman of Cortecs plc. Although Mr Travers was responsible for building up the international pharmaceutical foundations of Cortecs, he was dismissed amidst controversial circumstances and the company subsequently suffered sharp falls in financial performance and shareholder value.
- BNE is obligated to pay Proxima Concepts, which owns about 74% of BNE, around A\$2.5M for rights to the IP by Jan-06 and around A\$3.5M over three years for provision of the CEO, access to laboratory facilities and contract research services, including the services of Chief Scientist, Dr Roger New.
- If BNE is unable to make the IP payments within the required time, then Proxima Concepts can terminate BNE's rights to use the IP.
- BNE faces a risk that it may run out of cash if it does not raise secondary capital or complete a licensing deal in CY05.
- We view BNE's Calcitonin and PTH products favourably, and consider prospects for successful licensing deals good, but we note that BNE carries risks in relation to its corporate structure, related party payment obligations and 15 - 20 months of cash reserves. Trading in the stock has been very thin and the current lack of liquidity adds to investor risk.
- **Our risk-adjusted DCF valuation for BNE is \$42.3M or \$0.78 per share**, based on 55.2M shares (including 1M in-the-money options). We have used a discount rate of 22%.
- The valuation is highly sensitive to the underlying assumptions regarding discount rate, size of upfront and milestone payments, royalty rates, timing of market launch of each product, probability weightings used to risk-adjust each product and revenue growth rates.

## Company Overview

- Bone Medical Limited ("BNE") was formed in Aug-04 by the backdoor listing of a British company holding valuable biotechnology assets into an ASX-listed vehicle called Revenir Ltd.
- The independent experts' report, prepared by PKF Corporate Advisory, determined that the backdoor listing transaction was done on "fair and reasonable" terms to the existing Revenir shareholders, and provided a mid-point valuation of Bone Ltd of A\$51.9M, which is equivalent to an undiluted value of A\$0.96 per share.
- Australia was selected as the ideal place for BNE's domicile primarily because the cost of conducting research and clinical trials is far lower than in either of the other two major biotechnology centres, the US and the UK.
- A secondary benefit of listing on the ASX for BNE is that the Australian capital market seems to be more receptive than US or UK markets to companies that seek capital in small tranches.

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- In brief, BNE's key assets are the exclusive, perpetual, worldwide rights to three platform technologies for use in all musculo-skeletal indications.
- These technologies were developed by an internationally respected medical scientist, Dr Roger New, who has a track record of creating research that is later licensed by big pharma and turned into high-sales products.
- The technologies are owned by subsidiaries of UK company Proxima Concepts.
- The three platform technologies licensed by BNE are:
  - "Axxess" - an oral peptide delivery technology that facilitates the absorption of peptides and short proteins
  - "Mozaic" - a drug discovery technology that identifies new molecular structures capable of binding to cell receptors and regulating the activity of those cells
  - "Vaccine" - an oral vaccine delivery technology that allows certain vaccines that could previously only be given by injection to be taken by mouth in a combination which also stimulates the immunity response.
- BNE has specific projects related to each of these technologies underway.

## Background to the licensor of BNE's technology, Proxima Concepts, and to BNE's UK predecessor (Bone Ltd).

- Proxima Concepts was formed in 2000 by Dr Roger New, a scientist who was previously Head of Research at Cortecs plc, and Glen Travers, who was previously the CEO and Chairman of Cortecs plc.
- Proxima Concepts was created as an R&D vehicle for the Axxess, Mozaic and Vaccine drug discovery and delivery technologies that have been under development by Dr New since 1999.
- Proxima Concepts developed several projects that applied these technologies to musculo-skeletal disorders, and then set up Bone Ltd in Nov-02 as the vehicle to commercialise these projects. Bone Ltd was granted the exclusive right for use of the three technologies for all musculo-skeletal indications.
- In Jan-04, Bone Ltd secured A\$1M of seed money to advance its development projects and in particular to commence a phase I/IIA human clinical study for its lead project BN002 oral Calcitonin.
- One of Bone Ltd's seed investors was the Chairman of ASX-listed Revenir, which had recently sold its operating businesses and was seeking a new business opportunity.
- Bone Ltd was backdoor listed into Revenir in parallel with modest capital raising, enabling Bone Ltd to access funding from the public capital markets.

## Technology

BNE's licensed technologies cover three distinct platforms.

### 1. Axxess Oral Delivery Technology

- The oral delivery technology uses aromatic alcohols to enhance the absorption of some small proteins ("peptides"), which are normally broken down in the gut or not absorbed.
- Aromatic alcohols have long been used in oral drug formulations, but not as absorption enhancers. Their long accepted use means that they do not need to go through regulatory approval processes.
- Importantly, the combination of Axxess's aromatic alcohol enhancer with an active peptide agent does not involve a chemical interaction between these compounds and so does not result in a New Chemical Entity (i.e a novel drug).
- Therefore, if a particular peptide already has approval for use in an injected form, then the enhancer-peptide combination may not have to go through the full clinical trial pathway of new drugs. Instead, a much shorter clinical path may be sufficient. The new combination must be shown to have "bioequivalence" (i.e. results in similar therapeutic blood levels) with the existing injectable peptide.

### 2. Mozaic Drug Discovery Technology

- The drug discovery technology involves adding little fatty strands to a solution of amino acids, the building blocks of peptides and proteins. The fatty tails attach to the amino acids creating millions of comet-like objects. When these comets are put into a water-based solution, the fatty tails hide from the water by clumping together in the centre of a circle, partly shielded by the amino acids around the outside. This structure is called a micelle.
- Each solution of amino acids yields millions of micelles with different amino acid sequences. The next step is to see if any of the micelles will bind to receptors on the surfaces of different cells.

- Binding micelles are separated from the others and then they are observed to see if any of them turn any therapeutically useful cell processes on or off.
- If so, they are isolated, identified and then reconstructed to confirm the activity observed. Once one of these micelles has been made in the lab, its level of activity is confirmed again, before being put into pre-clinical trials.

### 3. Vaxcine Oral Vaccine Technology

- The oral vaccine technology encloses an immune stimulating antigen, the vaccine part, in a capsule. The encapsulated antigen is then added to an oil. This combination is absorbed well by immune cells called Peyer's Patches that line the surface of the gut.
- Once absorbed into the Peyer's Patches, the antigen stimulates an immune response in these cells, which in turn become capable of attacking any similar antigens which try to gain entry into the gut cells in the future.
- Importantly, the encapsulating substance and the oils have been in use in other ways for many years and are all registered for use orally.
- Again, as this platform technology does not create "New Chemical Entities, a simple and relatively brief regulatory approval process can generally be followed.

## Intellectual Property Protections

- Patent coverage for the three technologies licensed by BNE relates to six families of patents, three for Axxess, two for Vaxcine and one for Mozaic.
- The three Axxess patent families were filed in the UK between 2000 and 2003, and so if granted, protection would last until 2020 – 2023. Proxima Concepts' subsidiary, Axxess Ltd, has already applied for one of the patents in the US and plans to seek coverage for each of the three patents in all other major territories as well.
- The two Vaxcine patent families were first filed in the UK in 1994. One of the Vaxcine patents was granted in both Europe and the US, but the US patent was later "abandoned". The other patent was granted in the US but the European application was "abandoned". We understand from BNE that Dr New acquired the rights to the 1994 patents and subsequently assigned these rights to Proxima Concepts' subsidiary, Vaxcine Ltd. According to BNE's CEO, updated Vaxcine patents are in the process of being filed in the major jurisdictions.
- The Mozaic patent family was filed in the UK in 1998 and if granted in the next year or so, protection would be obtained until around 2018. Applications have been made for this patent family in major jurisdictions also. We also understand from BNE that Dr New acquired the rights to the Mozaic patents and subsequently assigned these rights to another Proxima Concepts' subsidiary, Mozaic Discovery Ltd.
- BNE's rights to the Axxess, Vaxcine and Mozaic patents are established by the License Agreements, which are discussed below.
- We have not investigated the Proxima Concepts' subsidiaries rights to the titles of these three patent families, which are obviously critical to BNE's business model.

## Project Pipeline

BNE has licensed the right to apply each of the three technologies to musculo-skeletal diseases, as well as the following specific projects already commenced by the original British commercialisation vehicle, Bone Ltd.

### 1) Oral Calcitonin (BN002)

- Normal bone is kept healthy when the actions of one type of bone cell, osteoblasts, which act to build new bone, are in balance with the actions of another type of bone cell, osteoclasts, which act to break down old bone.
- In some diseases, like osteoporosis, an imbalance between these two cell types occurs, and more bone is broken down by the osteoclasts than can be remade by the osteoblasts. This results in thin and fragile bones which break easily.
- Calcitonin is a natural human peptide hormone that reduces the activity of osteoclast cells, thereby slowing the rate of bone breakdown. Calcitonin is also effective at lowering high levels of calcium in the blood, which occurs in certain diseases.
- As the calcitonin found in salmon is far more potent than human calcitonin, the salmon form is normally used as a therapeutic agent. Salmon calcitonin has traditionally been given by injection, although recently a nasal spray has also been launched onto the market. There are no oral forms available.
- BNE has used the Axxess oral delivery technology to develop an oral form of salmon calcitonin (BN002).

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- In mid-September, BNE announced successful results of a Phase I/IIA trial of BN002 conducted in the UK showing bioequivalence to the nasal form of calcitonin. The trial showed that BNE's orally delivered calcitonin was effectively absorbed and was biologically active, significantly reducing bone breakdown in trial patients.
- BNE is now preparing to conduct a definitive Phase II trial to determine optimal dosage and formulation, and to further document the efficacy of the oral calcitonin product.
- The successful Phase I/IIA trial provided clear validation that the Axxcess technology works. This is particularly important as Axxcess is also the basis of BNE's Parathyroid Hormone project.

## 2. Oral Parathyroid Hormone (BN003)

- Parathyroid Hormone (PTH) is a natural human protein hormone that acts on the other side of the osteoblast-osteoclast balance equation to calcitonin by increasing the number and activity of osteoblasts, thereby causing new bone to form.
- PTH has been shown to be more effective than any other therapy for osteoporosis, and is capable of reducing vertebral fractures by up to 90% and reducing fractures of other bones by 50%. The first PTH treatment was only approved in 2002, so BNE's product will need to undergo the full clinical trial path for regulatory approval, including a pivotal Phase III trial, although briefer phase I development may be possible than the usual 12 months required.
- PTH therapy is currently only available by injection and has a number of significant drawbacks. The injections are clinic based, so patient compliance is a major issue. It is expensive and also can cause some serious side effects, like dangerously high blood calcium levels.
- Regulatory authorities have recommended that the length of treatment be limited to 12 – 24 months. Unfortunately, there does not appear to be any sound evidence that the new bone remains once the injections are stopped.
- BNE has used the Axxcess technology to develop an oral form of PTH, which may allow more flexibility in use than the injections.
- One of the major pharmaceutical companies has funded and conducted pre-clinical studies of BNE's oral PTH candidate in rhesus monkeys. These animals are very expensive experimental subjects, suggesting a serious interest by the pharmaceutical company in assessing the effectiveness of BNE's oral PTH product.
- The pre-clinical studies were successful and showed that oral PTH tablets were effective in raising blood levels of PTH and calcium.
- BNE is now preparing to undertake phase I human trials with the oral PTH during the last quarter of calendar 2004. These studies will also allow assessment of the efficacy of the product.

## 3. TNF Regulators (BN006)

- Tumour Necrosis Factor (TNF) is well recognised as a causative factor in Rheumatoid Arthritis (RA) and certain other auto-immune diseases. In RA, TNF causes inflammation of the tissue lining joints, resulting in pain, swelling and, over time, degeneration of the joints.
- BNE has used the Mozaic technology to identify several micelle structures effective in reducing the secretion of TNF. The amino acid sequence and structure of this micelle has been engineered into a library of multiple peptide strands which have been shown to retain the activity of the micelle. The library represents a new class of potentially therapeutic anti-TNF peptides.
- BNE has now completed in-vitro tests with BN006 peptides in preparation for initiating pre-clinical animal studies for safety and efficacy.
- In late Sep-04, BNE announced that the BN006 peptides from this new class had successfully demonstrated the ability to restore TNF production to normal levels in macrophage cells that produce TNF.
- BNE's anti-TNF peptides are unique molecules, which means that it will need to pass through the full clinical testing pathway required by the FDA and other regulatory agencies for new drugs. However, if they do succeed in clinical trials, then the opportunity for an orally effective anti-TNF agent is very large.

## 4. Bone Cell Regulators (BN005 and BN008)

- BNE is also using the Mozaic technology to develop new peptide entities designed to regulate (turn on or turn off) the cells that build new bone (osteoblasts).
- Early studies have shown indirect evidence that signalling pathways are being triggered by certain micelles formed using Mozaic. Later this year, BNE plans to start trying to identify micelles capable of regulating the cells that break down bone (osteoclasts).
- The BN005 and BN008 projects are at very early stages of development.



## 5. Joint Protection and Collagen Tolerance Programme (BN007)

- Type II Collagen is believed to be one of several proteins targeted by the body's own antibodies in Rheumatoid Arthritis (RA).
- BNE would like to apply the Vaxcine technology to immunomodulate certain mediators to prevent Type II Collagen autoimmune reactions in RA.
- BNE is seeking an academic partner to work on this project with it.
- Pre-clinical animal studies are set to commence this year.

## Markets and Competition

Musculoskeletal disorders are very prevalent. BNE is targeting two of the most common bone and joint diseases, Osteoporosis and Rheumatoid Arthritis.

### 1) Osteoporosis

#### The osteoporosis market is very large and growing

- Osteoporosis is estimated to affect about a third of women between 60 and 70 years old, and two-thirds of women over 80 years. The lifetime risk for fractures caused by osteoporosis is between 30% – 40% for women, and about 13% for men. Aging of populations worldwide is driving growth in the occurrence of osteoporosis.

#### Calcitonin plays a minority role among osteoporosis treatment options

- Treatments for osteoporosis are designed to strengthen bones, reduce bone breakdown and prevent fractures.
- Several different types of therapeutic agents are used to treat osteoporosis including estrogens (in post-menopausal women), bisphosphonates, calcitonin and PTH.
- The use of estrogens has become controversial since the 2003 WHI study which showed a higher incidence of stroke, heart disease and breast cancer in women on estrogen as post-menopausal hormone replacement therapy.
- The bisphosphonates form a relatively new class of drug which inhibits osteoclasts, stops bone breakdown, increases bone density and reduces fractures. Bisphosphonates can be taken orally. In some people, bisphosphonates cause oesophageal irritation and may even cause oesophageal ulcers, but this is uncommon.
- Calcitonin is a less effective osteoporosis treatment than either the estrogens or the bisphosphonates, causing a lesser increase in bone density than these drugs.
- Calcitonin is also used to treat several other uncommon disorders, including Paget's Disease and hypercalcemia.

#### Nevertheless, the global market for calcitonins is significant, around US\$700M

- Calcitonin sales in the US in 2002 were approximately US\$375M, compared with US\$2.2B for the market leading bisphosphonate product, Fosamax.
- US calcitonin sales are estimated to grow modestly to US\$430M in 2006, but it should be recalled that there are no approved oral Calcitonins on the market as yet.
- Worldwide calcitonin is currently estimated to generate US\$700M in sales. Estimates of growth in calcitonin sales vary between about 3% per year to a gradual decline as newer treatment modalities come onto the market.

#### An oral calcitonin would rapidly replace injectable forms

- While an oral product would not change the low growth rate of calcitonins, we expect that patient and doctor preference for an oral formulation would cause relatively rapid cannibalisation of existing injectable calcitonins.
- These form by far the largest share of the calcitonin market.
- A nasal spray calcitonin product (developed by Novartis) was approved by the FDA in 1995 and has now obtained about 50% market share.
- Although substitution of nasal spray product by an oral form would be less complete than for the injectables, the user population is elderly and we expect many to prefer the familiarity of tablets rather than having to use a nasal spray.

## **Novartis and Nobex are developing competing oral calcitonin products...slowly**

- Novartis and Emisphere started to collaborate on using Emisphere's oral delivery technology in 1997 to develop an oral calcitonin product. The product completed a Phase I trial in 1999. In 2000, Novartis licensed the right to commercialise this oral calcitonin and took responsibility for progressing the product through FDA approval. A Phase IIA trial was completed in early 2003. However, little information on further progress on the oral calcitonin project is available and it appears to be fairly low on Novartis's research priorities.
- Private American pharmaceutical Nobex is also developing an oral calcitonin product, which was previously partnered with Elan. A Phase 1 trial was initiated in early 2002, but Elan may have withdrawn involvement following its crisis in 2002. Little information is available on this project which may be in limbo until Nobex signs a replacement partner.
- Importantly, the Novartis and Elan projects both use proprietary synthetic molecules to enhance oral absorption and so the calcitonin product is likely to be considered by the FDA a New Chemical Entity, requiring both to complete full-scale phase 3 trials. BNE's oral calcitonin project has a potentially more rapid path to FDA approval as it does not fall in the New Chemical Entity category.

## **PTH is a new treatment option but the focus of considerable research**

- Eli Lilly launched the first PTH treatment in 2002. It is an injectable PTH fragment used for severe cases of osteoporosis due to its expense and the fact that it can cause high calcium levels in the blood in some patients. Low blood pressure is another PTH side effect.
- Two more injectable PTH products are in Phase III trials.

## **Eli Lilly and Glaxo Smith Kline are also developing oral PTH products**

- Eli Lilly is working with Inhale Therapeutics to develop an inhaled version of PTH. Lilly has also partnered with Emisphere to develop an oral form.
- GSK has partnered with another oral delivery technology specialist, Unigene, on an oral PTH product, which will soon enter Phase I trials.

## **The PTH market is predicted to grow rapidly**

- In 2003, the US market for Lilly's injectable PTH was US\$95M. Datamonitor projects this market to grow to US\$1.5B by 2011, an annual growth rate of 41%, driven particularly by the availability of oral PTH formulations.

## **New drug classes are also being developed for osteoporosis, but remain several years from market**

- Novartis has two new drugs in its R&D pipeline directed at improving treatment effectiveness in osteoporosis.
- GSK is also developing a new drug class aimed at osteoporosis, but a lead compound has not yet been identified putting a market launch at least 5 – 7 years away.

## **2) TNF Regulators for Rheumatoid Arthritis and other Auto-Immune diseases**

### **Anti-TNF products treating Rheumatoid Arthritis have become major blockbuster drugs in the past five years**

- Anti-TNF antibody products were first approved for use against Rheumatoid Arthritis (RA) a few years ago, and approvals are now occurring for other auto-immune diseases such as Crohn's Disease.
- RA is said to affect about 2.5M people in the US and over 9M globally. More than 50% of patients are over 65 years old, and so aging demographics is predicted to cause a progressive increase in the incidence of the disease.
- Each of the three approved anti-TNF products currently on the market have grown to be billion-dollar drugs within a short space of time (Amgen's Enbrel, Centocor's Remicade and Abbott's Humira). Sales growth of each product is predicted to continue at double digit rates until at least 2010.
- The total RA treatment market in the US is forecast to grow to US\$7.3B in 2010.

### **However competitors are rushing into the anti-TNF space...**

- Many companies are currently developing novel approaches to treating RA, including a number of attempts to develop effective antibody fragments that can be delivered more conveniently than the current injectable formulations.
- For example Pfizer has developed an antibody fragment with Celltech which is due to launch in 2005 assuming a smooth path through regulatory approvals.

## **BNE has identified two lead compounds, and these are now in pre-clinical testing**

- BNE has undertaken and successfully completed preclinical bench tests on the lead compounds that were identified using the Mozaic technology.
- BNE's peptide agents target TNF earlier in the pathway than existing antibody treatments, and if effective as an oral agent, could potentially become a standard first-line treatment, replacing the injectable antibodies currently used.
- The next step is to move the compounds into pre-clinical animal tests for safety and efficacy. This work is being done in collaboration with the Institute of Bone and Joint Research, headed by Professor Philip Sambrook in Sydney.
- Assuming pre-clinical testing is successful, entry into clinical trials is likely to be around 12 months away.

## **3) Collagen Tolerance generation for Rheumatoid Arthritis**

### **This novel approach to treating Rheumatoid Arthritis is in very early stages**

- BNE is seeking to design a vaccine that will prevent the body's immune system from attacking a common joint target in Rheumatoid Arthritis, Type II Collagen.
- No such vaccine has been successfully developed to date.
- No information on potential market size or competitors with similar products under development is available.

## **Commercialisation Strategy**

### **BNE is seeking to generate early cash flow through its Calcitonin and PTH projects**

- The oral Calcitonin project is expected to complete a series of Phase II trials by end FY05 and a successful trial result seems likely as the recent Phase I/IIA trial showed that BNE's orally delivered Calcitonin was biologically active.
- Further successful Phase II trials are likely to secure a licensing deal with a major pharmaceutical company in late FY05 or during FY06, and start generating licensing and milestone fees.
- The oral PTH project is due to complete a Phase I trial by the end of 1H FY05, and if successful, should complete a Phase II trial during 1H FY06.
- Under such circumstances, we expect to see a pharma licensing deal during FY06.

### **We expect BNE to raise new capital or complete a licensing deal to fund its R&D pipeline later in FY05 or during 1H FY06**

- We estimate that BNE has around 15 months cash at its current burn rate (or around 20 months if cashflow constraints entitle outgoings to related parties to be accrued) but more cash will be needed to accelerate development of its TNF regulator and bone cell regulator projects.
- BNE also plans to develop a novel combination Calcitonin/PTH product which will need further cash.
- A licensing deal should allow BNE to raise more capital at a much higher valuation than its recent listing valuation.
- The need to raise further capital would be avoided if sufficient upfront and milestone payments were obtained from a pharmaceutical licensor.

## **Partnerships and Collaborations**

### **BNE's pre-clinical work on two lead compounds has been in collaboration with a large pharma company**

- BNE has been undertaking pre-clinical work on the two lead compounds, in collaboration with a major pharmaceutical company, under a confidential agreement.
- The existing collaborative relationship and interest in the lead compounds at the pre-clinical stage heightens the chances of a commercial partnership developing.

### **BNE's first research collaboration has been struck with the prestigious Institute of Bone and Joint Research (IBJR) at Sydney's Royal North Shore Hospital**

- In early Sep-04, BNE signed a Collaborative Testing Agreement with the IBJR to progress the TNF regulation project (BN006) through pre-clinical testing.
- The IBJR is devoted to musculo-skeletal diseases and is led by Professor Philip Sambrook, the Florence and Cope Professor of Rheumatology at the University of Sydney who is also a member of the editorial boards of several respected journals, including Osteoporosis International and Journal of Rheumatology. Professor Sambrook also serves on the Asia Pacific League of Associations for Rheumatology.

## Management and Board

### Dr Jim Phillips, CEO

- Dr Phillips is a medical doctor with business and clinical development experience gained at Novartis and Johnson and Johnson. He has had roles as a medical director as well as head of business development & licensing for Europe. He has also spent several years working on e-business initiatives at these pharmaceuticals. Dr Phillips also engineered an MBO of healthcare information technology from J & J which was later sold in a trade sale.
- Dr Phillips was CEO of UK-based Bone Ltd before it backdoor listed into Revenir to form Bone Medical (BNE). As Bone Ltd's CEO, Dr Phillips was employed by Proxima Concepts. As BNE's CEO, continues to be paid by Proxima Concepts, with BNE paying for his services via the Laboratory and Management Services Agreement with PLMS.
- Dr Phillips is also currently the Managing Director of another Proxima Concepts subsidiary, Diabetology Ltd, formed to commercialise an oral insulin product. Dr Phillips spends over 90% of his time on BNE and will fully focus executive energy on BNE when a new MD of Diabetology is appointed.

### Mr John Fitzgerald, COO

- Mr Fitzgerald has worked for over ten years in the pharmaceutical and biomedical industries in product management, intellectual property, business development and marketing. He has significant work experience in the area of musculo-skeletal disorders. He has worked in the Australian offices of Proctor & Gamble Pharmaceuticals and Knoll BASF Pharma (Australia). Most recently, he spent three years at VRI Biomedical. He is a full time employee at BNE.

### Dr Roger New, Chief Scientist

- Dr New is a founder and key shareholder of Proxima Concepts and also the inventor of these technologies. Prior to Proxima Concepts, Dr New spent 7 years working at Cortecs, including as Director of Research. Dr New is a recognised authority on liposomes and has had multiple patents granted. Dr New devotes much of his time to researching the core platform technologies at Proxima Concepts.
- Dr New is employed by Proxima Concepts and his services are covered by BNE's Laboratory and Management Services Agreement with Proxima Concepts (which also covers two other research scientists).

### CFO and other management roles

- BNE obtains the services normally provided by the CFO and company secretary from a third party, Bluewater Capital, which had a pre-existing corporate advisory services agreement with UK-based Bone Ltd dating back to Jan-04, prior to the backdoor listing transaction. Provided BNE has secured such services at competitive rates, this should be an economical approach to use during pre-clinical research phases. Dedicated in-house resources may become warranted as more of the research pipeline moves into clinical trials and the company grows.

### The Board comprises six Directors, including three pre-existing Revenir Directors

- Mr Michael Perrott, Chairman, who has been involved in construction, contracting, mining and land development industries and who holds several other board positions.
- Mr Ross Kestel, who is an accountant and has been a director of an accounting firm since 1980.
- Mr Richard Basham, who is also an accountant, is a former managing partner of Grant Thornton and who specialises in corporate advisory work in resources and biotechnology.

### One of BNE's Directors was a senior executive in the pharmaceutical industry

- Mr Chris Bilkey is an independent director who spent his career in international pharmaceutical companies. He previously held senior roles at Pharmacia, including VP Global Women's Health Care and VP Country Operations.

### Two of BNE's Directors are related to Proxima Concepts

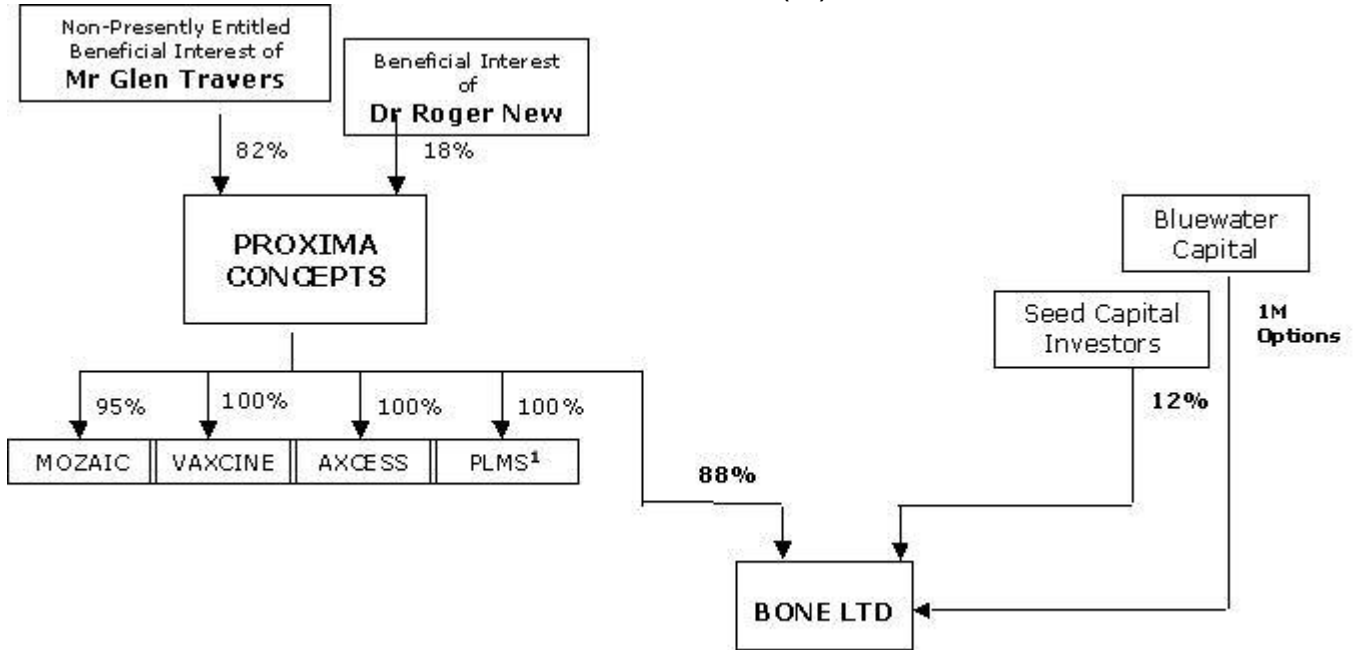
- Mr Glen Travers is a non-presently entitled beneficiary of the trust that owns 82% of Proxima Concepts, which in turn owns about 74% of BNE. Mr Travers therefore appears to effectively control about 61% of BNE, and this level of control will increase slightly with future conversions of preference shares on issue (unless diluted by future capital raisings).
- Mr Travers was previously CEO and Chairman of Cortecs plc. He was responsible for developing Cortecs into an emerging pharmaceutical company but departed amidst turbulent circumstances in mid-1998, and the company subsequently suffered sharp falls in financial performance and shareholder value.
- Although Mr Travers appears to control a majority stake in BNE, he has not used that control to fill the Board with related party directors. On the contrary, a majority of the board are independent non-executive directors.
- Dr Phillips, CEO of BNE, is a Board member, and he is also related to Proxima Concepts by virtue of his work as a contractor to that company or one of its subsidiaries.

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## Corporate Structure

- BNE's key asset, aside from its cash balance, is its 80% shareholding in the company Bone Ltd, which holds an exclusive license to commercialise Proxima Concepts' three platform technologies in the field of musculo-skeletal disorders.
- The figures below shows the structure of the group of companies related to Proxima Concepts before and after the backdoor listing of Bone LTD into Revenir to create BNE.

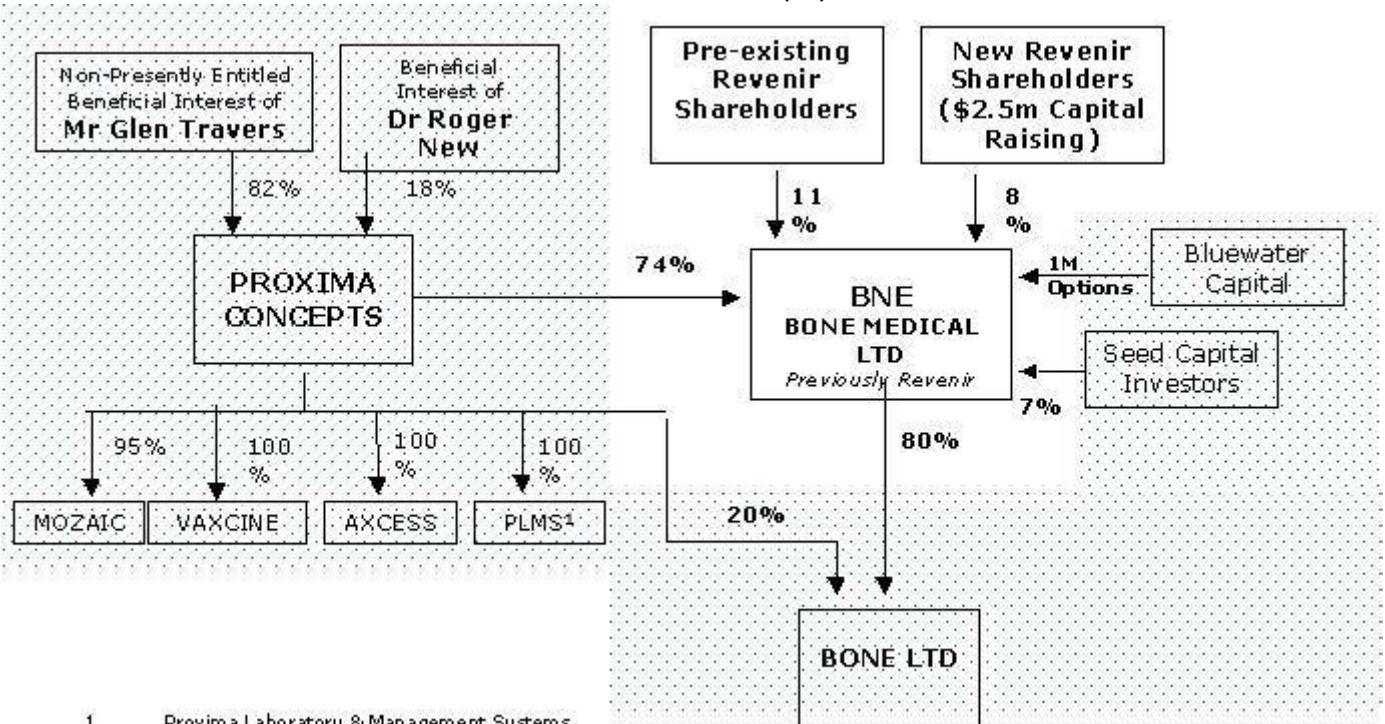
FIGURE 2: CORPORATE STRUCTURE OF PROXIMA CONCEPTS AND BONE (UK) PRIOR TO BACKDOOR LISTING



1. Proxima Laboratory & Management Systems

Source: Company/Aegis Equities

FIGURE 3: CORPORATE STRUCTURE OF PROXIMA CONCEPTS AND BONE (UK) AFTER BACKDOOR LISTING



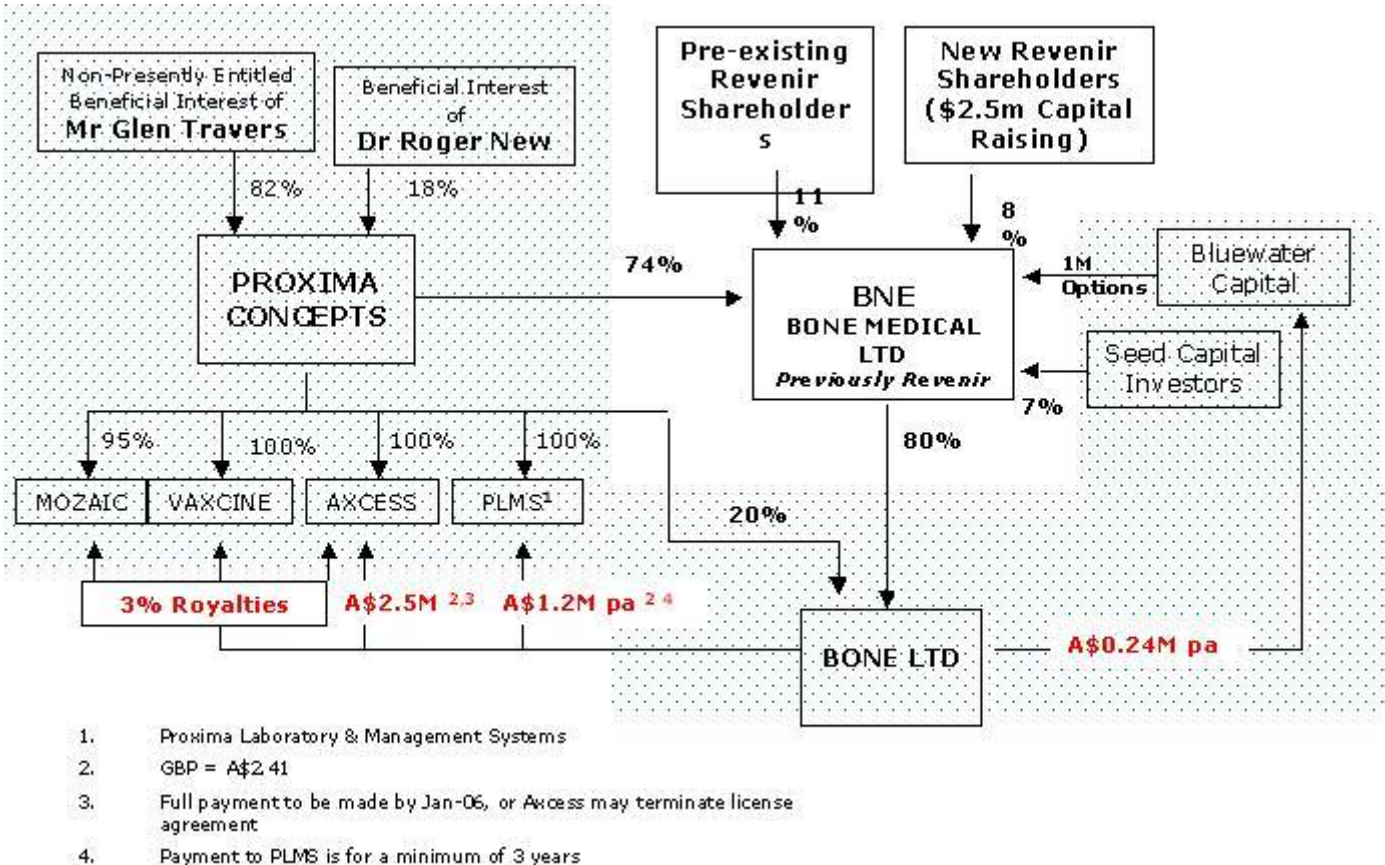
1. Proxima Laboratory & Management Systems

Source: Company/Aegis Equities

## Related Party Transactions and Significant Contracts

- As part of the deal to backdoor list Bone Ltd into Revenir to create BNE, Bone Ltd entered into certain contracts with subsidiaries of Proxima Concepts, and with Bone Ltd's provider of corporate advisory services, Bluewater Capital, which have a material effect on BNE's cashflows and/or risks. We will not cover all of the significant contracts surrounding the transaction here, but rather highlight the importance of certain key ones.
- The figure below outlines the money flows that Bone Ltd is contracted to pay to members of the Proxima Concepts' group of companies, as well as to Bluewater Capital.

FIGURE 4: RELATED PARTY TRANSACTIONS



Source: Company/Aegis Equities

### 1. The Intellectual Property License Agreements with Proxima Concepts

- The three license agreements require BNE to “pay a 3% royalty of revenue from sales of Products” to the Proxima Concepts' subsidiaries that hold the intellectual property being used by BNE to develop its research pipeline.
- Of note, the royalty is payable to the subsidiaries on any licensing fees and milestone payments received by BNE from a pharma licensee, as well as on royalties received by BNE from a pharma licensee on product sales.
- 3% of BNE's license-related receipts appears a modest price for BNE to pay, but is compensated for by the large “front-end” payments payable to the Access Ltd subsidiary under the agreement that follows.
- Proxima Concepts' subsidiaries did not warrant that any of their patents were valid, creating some patent risk for BNE.

### 2. Additional lump sum license payments to the Access Ltd subsidiary

- BNE is required to pay two lump sum payments totalling GBP1.03M (about A\$2.5M) to Access Ltd, one of Proxima Concepts' IP subsidiaries, on achievement of certain capital raising and/or sales triggers.
- Significantly, if any of this amount remains unpaid by early Jan-06, then Access may immediately terminate its license agreement, which would leave BNE unable to commercialise its oral Calcitonin and PTH candidates.
- As BNE's existing cash is due to run out by Dec-05 (or around Jun-06 if payments to related parties need to be accrued), BNE must raise more cash before then or receive a large up front payment from a pharmaceutical company or it may lose one of the licenses on which part of its core business is based.

### 3. The Laboratory Facility and Management Agreement with Proxima Concepts

- BNE is required to pay PLMS (wholly-owned by Proxima Concepts) a minimum of GBP0.48M per year (about A\$1.2M), for a minimum of three years with 12 months notice to cancel, for Proxima Concepts to provide management and laboratory services.
- This amount covers contract fees payable to BNE's CEO, Dr Jim Phillips, the research services of Dr Roger New, two PhD scientists and a lab technician, and includes product formulation work, manufacturing of substances for the clinical trials, identification of new lead compounds and access to the necessary laboratory equipment.
- The monthly amount accrues unless cashflow is sufficient for payment. This provides BNE with the possibility of stretching out cash reserves to some extent, but if no amount is paid to PMLS in a 6 month period, then Proxima Concepts may terminate the agreement (which might create a business continuity risk for BNE).
- BNE's obligation to pay Proxima Concepts at least A\$1.2M a year for 3 years under this agreement adds an inflexibility to the expense side of BNE's P & L not commonly seen in biotechnology companies which are yet to generate revenues. While Proxima Concepts' three primary researchers may have unique skills, the size of this annual budget highlights Australian cost advantages when compared with UK-Based resources.

### 4. The Bluewater Corporate Services Agreement

- Bluewater Capital provided corporate advisory services to Bone Ltd before it was backdoor listed into Revenir to become BNE and one of Bluewater Capital's directors was also a director of Bone Ltd.
- In addition to 1M options issued to Bluewater Capital for services provided prior to Bone Ltd's backdoor listing into Revenir, Bone Ltd pays Bluewater Capital A\$240,000 per year, or A\$20,000 per month (up from A\$12,000 per month prior to the recent fundraising) to provide corporate advisory services including accounting and management reporting services, provision of an Australian-based CFO, preparation of annual reports and tax returns and company secretarial support.
- In due course, we might expect internal provision of these services with ad hoc engagement of specialist skills to be potentially more cost-effective than a fixed price outsourcing arrangement.

## Key Risks

As a biotechnology company seeking to commercialise pharmaceutical products, BNE faces several significant risks, including:

- **Lack of cash** – BNE is currently forecast to have sufficient cash to last until the end of CY05 or the first half of CY06, so unexpected delays in signing licensing deals may cause cash strains during the second half of next year. Delays in securing a licensing partner would negatively affect market sentiment and lower the likely price at which further capital can be raised.
- **Trial delays or failures** – Trial delays and failures commonly occur in drug development companies. We consider the risk of failure to be lower than normal for BNE's oral Calcitonin product due to the active ingredient's long presence on the market in injectable and nasal spray forms, as well as the fact that BNE has already completed a phase I/IIA trial demonstrating that the product is orally absorbed. The oral PTH product is earlier stage but the active ingredient is also a long-used therapeutic agent so the risk is considerably lower than for a new compound. The other products in BNE's R&D pipeline are New Chemical Entities in pre-clinical or earlier stages, and so are considered to carry normal development risks.
- **Regulatory delays or rejections** – The regulatory approval process is complex, fastidious and time-consuming. Delays are common and rejections may occur even with successful trial results. BNE is seeking FDA agreement to accept a Bioequivalence Registration of the oral Calcitonin product, which would avoid the need to conduct a phase III trial. We consider this a likely outcome and so consider regulatory risks reduced for this product. Oral PTH is unlikely to have this option and so faces normal regulatory risks.
- **Licensing delays or failures** – Licensing negotiations with big pharma may be notoriously drawn-out and may become a key risk to BNE's cash balance, which in turn may weaken BNE's ability to execute a deal on the most favourable terms. A significant licensing deal with an up front component signed in the first half of CY05 would substantially reduce BNE's risk profile. BNE has been in discussions with potential partners for up to 18 months.
- **Well-resourced competitors** – BNE's major competitors for oral Calcitonin and oral PTH products are major pharmaceuticals with very deep pockets. These companies can make life difficult for biotechnology minnows, particularly through intellectual property suits. Stronger resources also make it easier to accelerate clinical trials. Until BNE signs a major pharma partner for each of its two lead products, it will remain exposed to such competitive risks.

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- **Intellectual property risks** - Competitors may challenge a biotechnology company's patents even without merit to the action simply to tie up the smaller rival's limited resources. BNE also faces the risk that a genuine infringement claim may be made against Proxima Concepts or BNE itself. BNE's other key risk is loss of right to use Proxima Concepts' intellectual property due to termination of a license agreement for non-payment of a due amount.
- **Key person risks** – As inventor of the licensed patents and BNE's Chief Scientist, we consider Dr New a key person and his loss may adversely impact BNE's ability to commercialise some or all of its R & D pipeline. However, know-how associated with the Oral Calcitonin and Oral PTH compounds is well documented and reproducible. Also, Dr New works with 2 PhD's who have been trained by him, so we consider this key person risk reasonably mitigated.
- **Control and liquidity risks** - With a 75% shareholder on BNE's register, there can be no control premium built into BNE's share price. This also reduces stock liquidity and BNE's stock has been highly illiquid to date. Together, these factors may reduce BNE's appeal to prospective investors and therefore adversely affect future capital raising ability.
- **Market risks** – BNE is exposed to the general market risks faced by all listed companies. However, BNE is also exposed to the highly volatile market sentiment that characterises the biotechnology sector. This may make it more difficult for BNE to raise capital as and when it is needed in the future.
- **Foreign exchange risks** – Pharmaceutical license and royalty fees are typically paid in US\$, so BNE will face currency risks as and when revenues eventuate.
- **Related party contract risks** – As Proxima Concepts controls 74% of BNE (following granting of the A class Preference Shares), Proxima Concepts is in a position to control the granting of additional related party contracts between BNE and Proxima Concepts or the amendment of existing related party contracts between BNE and Proxima Concepts. Proxima Concepts has not used its majority shareholding to influence the company to this point.

## Financials

### Revenues, Expenses and Profitability

- BNE has no revenues, with revenue potential during CY05 from up front payments if a licensing partner is secured for either the company's two lead products. We expect the oral Calcitonin product to be the earliest licensing candidate.
- The company's cash burn rate is around A\$0.75M per quarter so we expect the company to have around five quarters of cash reserves.
- However with the 3 month cashflow clause in all contracts the company can reduce outgoings to A\$0.3M per quarter leaving around seven quarters of cash reserves.
- The following table shows our risk-adjusted forecasts for BNE's revenues, expenses and EBITDA out to FY10.

**TABLE 2: RISK ADJUSTED POST-TAX CASHFLOW FORECAST TO FY10**

A\$M	FY05 F	FY06 F	FY07 F	FY08 F	FY09 F	FY10 F
<b>Revenues</b> <sup>1,2</sup>						
Calcitonin	0.0	22.4	13.0	10.7	12.3	13.5
PTH	0.0	6.1	4.9	2.4	4.9	9.5
TNF	0.0	0.0	0.0	2.0	1.6	0.8
<b>Total</b>	<b>0.0</b>	<b>28.6</b>	<b>17.9</b>	<b>15.2</b>	<b>18.8</b>	<b>23.8</b>
<b>Expenses</b> <sup>1</sup>	<b>-5.3</b>	<b>-12.6</b>	<b>-9.4</b>	<b>-5.6</b>	<b>-6.2</b>	<b>-6.5</b>
<b>EBITDA</b>	<b>-5.3</b>	<b>16.0</b>	<b>8.6</b>	<b>9.5</b>	<b>12.7</b>	<b>17.3</b>
Working capital changes plus capex	0.0	0.0	-0.7	-0.6	-0.8	-1.0
Tax <sup>3</sup>	0.0	-3.2	-2.6	-2.9	-3.8	-5.2
<b>Post-tax cashflow</b>	<b>-5.3</b>	<b>12.8</b>	<b>5.3</b>	<b>6.1</b>	<b>8.1</b>	<b>11.2</b>

1. Revenues and expenses have been risk-adjusted by applying probability weightings to raw forecasts

2. Revenues include up-front and milestone payments, as well as ongoing royalty revenues

3. Assumes accrued tax losses used prior to tax becoming payable

Source: Company/Aegis Equities

### Balance Sheet

- The company has no debt and as at 1/9/04 had cash assets of around A\$4.5M, which is also likely to represent BNE's approximate net tangible asset position.



## Valuation

### Valuation Approach

- A Discounted Cash Flow methodology has been used to value BNE based on forecast revenues generated by license fees, milestone payments and royalties paid by partners on BNE's three lead drug candidates.
- Early preclinical R & D projects were excluded from the valuation model due to the conservative approach taken in developing the valuation. These projects include potential upside to our valuation model.
- The lack of earnings history clearly makes BNE an unsuitable candidate for valuation by a capitalization of earnings methodology.

### Key Assumptions

In view of the early stage nature of the company, many significant assumptions have been made in arriving at the valuation range. Major assumptions include the following:

- **Products included in forecasts** – revenue forecasts have been included for Calcitonin, PTH and TNF regulator drug candidates
- **Excluded Products** - Revenue forecasts have not been made for the following projects due to their early stage, lack of significant R & D resources and poor potential revenue visibility:
  - Combination Calcitonin-PTH product, Osteoclast and Osteoblast regulators, Collagen Tolerance project.
- **Growth period** – cash flow forecasts commence in FY05 and cease after 2020, around when we estimate that the primary Axxess patent will expire. We acknowledge the potential for this and other patents to be extended beyond this date, but consider any "terminal value" accruing from BNE's licensing rights to be unquantifiable upside.
- **Discount Rate** – a discount rate of 22% has been used. We typically use a discount rate of 20% - 22% for similar stage biotechnology companies.
- **License and milestone fees** –
  - **Oral Calcitonin:** We assume that BNE will succeed in signing a major pharma partner for oral Calcitonin early in FY06. Oral Calcitonin is assumed to generate US\$10M as a sign on licensing fee and aggregate milestone payments of US\$20M. All cash flows relating to an Oral Calcitonin have been risk-adjusted by applying a 50% probability of occurrence to reflect regulatory approval uncertainty given the product's current stage of trials.
  - **Oral PTH:** We assume that BNE will sign a major pharma partner for oral PTH during 2H of FY06. We believe oral PTH has a larger market potential than Oral Calcitonin and is assumed to attract an up-front licensing fee of US\$10M, followed by aggregate milestone payments of US\$20M. All cash flows relating to an Oral PTH have been risk-adjusted by applying a 30% probability of occurrence to reflect regulatory approval uncertainty given the product's current stage of trials.
  - **Oral TNF Regulator:** We assume that BNE will sign a major pharma partner for an oral TNF regulator product in early FY08. We view the potential market for a successful anti-TNF product as larger than for the PTH product. We assume an up-front licensing fee of US\$10M, followed by aggregate milestone payments of US\$20M. All cash flows relating to an Oral TNF regulator have been risk-adjusted by applying a 10% probability of occurrence, due to the novel nature of the science and the pre-clinical stage of research.
- **Royalty rates and timing** –
  - **Oral Calcitonin:** A royalty rate of 12% of forecast sales has been applied to oral Calcitonin and royalties are assumed to first flow for this product in 2H FY07.
  - **Oral PTH:** A royalty rate of 12% of forecast sales has also been applied to oral PTH and royalties have been assumed to commence in the beginning of FY10 for this product.
  - **Oral TNF Regulator:** For a TNF regulator product, we have assumed a 12% royalty rate with revenues first being generated in the 2H of FY11.
- **Exchange Rate** – The A\$:US\$ exchange rate is assumed to be \$0.70, and the GBP:A\$ rate is assumed to be 2.41.
- **Income Tax** – A tax rate of 30% has been applied.
- **Minority Interest** – The valuation has been conducted on the basis that Proxima Concepts retains a 20% interest in Bone Ltd, and therefore BNE's valuation represents approximately 80% of the total value generated by the licensed Intellectual Property.

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## Valuation

Based on these assumptions, we derive a valuation for BNE as follows:

**TABLE 3: DILUTED RISK-ADJUSTED DCF VALUATION OF BNE**

Risk-adjusted NPV of Bone Ltd's discounted cash flows		\$ 52.9 M
BNE's shareholding in Bone Ltd		80 %
<b>Risk-adjusted NPV of BNE's interest in Bone Ltd</b>		<b>\$ 42.3 M</b>
Diluted number of shares in BNE (1,2,3)		55.2 M
<b>Fully diluted risk-adjusted value of BNE (1,2,3)</b>	<b>\$/Share</b>	<b>\$ 0.78</b>

1. Includes conversion of 1M Options (exercisable at \$0.50) issued to Bluewater Capital and payment of \$0.5M to BNE for option exercise.
2. Does NOT include 10M B Class Pref shares which require BNE's market cap to be over A\$80M, (or \$1.48 per share) for issue
3. Does NOT include 10M C Class Pref shares which require a product approval in Europe or the US for issue

Source: Company/Aegis Equities

## Sensitivity Analysis

- Our valuation is highly sensitive to many underlying assumptions, particularly discount rate, size of upfront and milestone payments, royalty rates, timing of market launch of each product, probability weightings used to risk-adjust each product and revenue growth rates.
- In the tables below, we demonstrate the impact on our valuation of incremental changes in each of the major underlying assumptions, while holding all other variables constant.
- Table 4 shows that a 1% change in the discount rate used in the valuation model has a moderately significant impact (approximately 5%-6%) on the value of BNE shares.
- Table 4 also shows that a 1% change in the royalty rate used in the valuation model has a more significant impact (approximately 8%-9%) on the value of BNE shares. A US\$5M variation in the size of the combined upfront and milestone payments assumed to be achieved for each product has a similar impact on value as the 1% changes in royalty rates.

**TABLE 4: SENSITIVITY ANALYSIS FOR DISCOUNT RATE, ROYALTY RATES AND UPFRONT/MILESTONE PAYMENTS**

	Discount Rate / WACC		Royalty Rates		Total Upfront plus Milestone Payments	
	19.0%	\$ 0.93	9.0%	\$ 0.58	US\$15M	\$ 0.59
	20.0%	\$ 0.88	10.0%	\$ 0.64	US\$20M	\$ 0.65
	21.0%	\$ 0.82	11.0%	\$ 0.71	US\$25M	\$ 0.71
<b>DCF assumption</b>	<b>22.0%</b>	<b>\$ 0.78</b>	<b>12.0%</b>	<b>\$ 0.78</b>	<b>US\$30M</b>	<b>\$ 0.78</b>
	23.0%	\$ 0.73	13.0%	\$ 0.84	US\$35M	\$ 0.84
	24.0%	\$ 0.69	14.0%	\$ 0.91	US\$40M	\$ 0.90
	25.0%	\$ 0.65	15.0%	\$ 0.98	US\$45M	\$ 0.96

Source: Company/Aegis Equities



# Bone Medical

- Table 5 below shows that a 5% change in the probabilities assigned to risk-adjust the revenues assumed to be earned by each product also has a significant impact on the value of BNE shares. The PTH product is the most sensitive to changes in probability weightings closely followed by the Calcitonin product.
- Changes to probability weightings for the TNF regulator product have much less impact on the value of BNE shares due to the long lead time before this product is due to reach market.

**TABLE 5: SENSITIVITY ANALYSIS OF PROBABILITY WEIGHTINGS USED TO RISK-ADJUST PRODUCT REVENUES**

	Risk adjustment for Oral Calcitonin product		Risk adjustment for Oral PTH product		Risk adjustment for TNF Regulator product	
	35%	\$ 0.58	15%	\$ 0.56		
	40%	\$ 0.65	20%	\$ 0.63	0%	\$ 0.69
	45%	\$ 0.71	25%	\$ 0.70	5%	\$ 0.73
<b>DCF assumption</b>	<b>50%</b>	<b>\$ 0.78</b>	<b>30%</b>	<b>\$ 0.78</b>	<b>10%</b>	<b>\$ 0.78</b>
	55%	\$ 0.84	35%	\$ 0.85	15%	\$ 0.82
	60%	\$ 0.91	40%	\$ 0.92	20%	\$ 0.86
	65%	\$ 0.97	45%	\$ 0.99	25%	\$ 0.90

Source: Company/Aegis Equities

- Table 6 below shows that the value of BNE shares is similarly affected by a 2% change to the assumed compound annual growth rate (CAGR) of royalty revenues to 2020 on either Oral Calcitonin or Oral PTH.
- Due to the significantly longer lead time before the TNF Regulator product will be in the market, a 10% change in the CAGR of royalty revenues causes a similar impact on BNE share value as caused by the 2% change for Calcitonin and PTH.
- Table 7 below shows that a one year delay in launching the Oral Calcitonin product would have the largest impact on the value of BNE shares, while a one year delay in launching the Oral TNF Regulator product would have the least impact.

**TABLE 6: SENSITIVITY OF VALUATION TO CHANGES IN CAGR OF ROYALTY REVENUES EARNED FOR EACH PRODUCT**

Product	Base year <sup>1</sup>	Base year royalty <sup>2</sup>	CAGR	Valuation
Oral Calcitonin	FY08	A\$10.7M	4.9%	\$ 0.75
<b>Oral Calcitonin<sup>3</sup></b>	<b>FY08</b>	<b>A\$10.7M</b>	<b>6.9%</b>	<b>\$ 0.78</b>
Oral Calcitonin	FY08	A\$10.7M	8.9%	\$ 0.81
Oral PTH	FY09	A\$9.5M	10.2%	\$ 0.75
<b>Oral PTH<sup>3</sup></b>	<b>FY09</b>	<b>A\$9.5M</b>	<b>12.2%</b>	<b>\$ 0.78</b>
Oral PTH	FY09	A\$9.5M	14.2%	\$ 0.82
Oral TNF Regulators	FY12	A\$1.9M	15.4%	\$ 0.75
<b>Oral TNF Regulators<sup>3</sup></b>	<b>FY12</b>	<b>A\$1.9M</b>	<b>25.4%</b>	<b>\$ 0.78</b>
Oral TNF Regulators	FY12	A\$1.9M	35.4%	\$ 0.82

1. The Base Year is the year in which the first full year of sales takes place for each product

2. The Base Year Royalty is the risk-adjusted royalty earned by BNE on the first full year of sales of a product

3. DCF Assumptions

Source: Company/Aegis Equities

**TABLE 7: IMPACT OF A 1 YEAR DELAY IN THE LAUNCH OF EACH PRODUCT ON THE VALUATION**

Product launch delay	Valuation
<b>No Delay<sup>1</sup></b>	<b>\$ 0.78</b>
Impact of 1 year delay in launching:	
Oral Calcitonin	\$ 0.64
Oral PTH	\$ 0.68
Oral TNF Regulator	\$ 0.76

1. DCF Assumption

Source: Company/Aegis Equities





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