

22 February 2010

## Bionomics

Year End	Revenue (A\$m)	PBT* (A\$m)	EPS* (c)	DPS (c)	PE (x)	Yield (%)
06/09	2.9	(7.8)	(3.2)	0.0	N/A	N/A
06/10e	3.5	(6.7)	(2.3)	0.0	N/A	N/A
06/11e	3.5	(6.9)	(2.2)	0.0	N/A	N/A
06/12e	3.5	(7.2)	(2.3)	0.0	N/A	N/A

Note: \*PBT and EPS are normalised, excluding goodwill amortisation and exceptional items; revenue is adjusted to exclude interest income, per IFRS. Excludes commercialisation revenue.

### Investment summary: VDA development plan

The investment case for Bionomics centres on its two lead candidates, BNC105, a vascular disrupting agent in Phase II studies for mesothelioma and kidney cancer, and BNC210, an anxiolytic/antidepressant compound in Phase Ib studies. Licensing deals for both compounds are possible on completion of the current studies and a deal for either or both – possible by 2012 – should generate Bionomics a significant economic return. Bionomics is funded to complete these studies and may seek to engage with potential partners based on interim data, due later this year.

#### BNC105: Phase II studies underway

BNC105 is a vascular disrupting agent differentiated by a dual mechanism of action with direct anti-tumour activity and a high level of selectivity for tumour vasculature. Phase II studies are targeting two orphan indications (renal cell carcinoma and mesothelioma) which have potential for fast-track registration. Studies should render interim results this year and final results in early 2012. Studies in other indications could be pursued by a partner.

#### BNC210: Anxiety is first target

BNC210 is an early clinical candidate with an attractive profile for the treatment of acute and chronic anxiety, including with co-morbid depression. Animal studies suggest BNC210 may offer a number of advantages over established treatments.

#### Financials

Following a A\$15m fundraising last year, Bionomics is funded to complete the ongoing Phase II studies of BNC105 and Phase I studies of BNC210.

#### Valuation: Risk-adjusted NPV of A\$175m

We are indicating a value of A\$175m based on a risk-adjusted net present value of key programmes. This is derived from our assessment of the potential economic reward and timelines associated with the successful development.

Price 0.30c  
Market Cap A\$95m

#### Share price graph



#### Share details

Code BNO/BMICY  
Listing ASX/NASDAQ  
Sector Biotech  
Shares in issue 318.1m

#### Price

52 week High 43c Low 17c

#### Balance Sheet as at 30 June 2010\*

Debt/Equity (%) N/A  
NAV per share (c) 8.2  
Net cash (A\$m) 10.1

\*Edison estimates.

#### Business

Bionomics is an Australian biotech company focused on developing small molecule products for cancer, anxiety, epilepsy and multiple sclerosis. Its lead programmes are a VDA and an anxiolytic compound.

#### Valuation

	2009	2010e	2011e
P/E relative	N/A	N/A	N/A
P/CF	N/A	N/A	N/A
EV/Sales	N/A	N/A	N/A
ROE	N/A	N/A	N/A

#### Revenues by geography

	UK	Europe	US	Other
0%		75%	5%	20%

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## Investment summary: Australian biotech

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### Company description: CNS/cancer expertise

Bionomics is an Australian biotech company focused on the development of products for the treatment of cancer and central nervous system disease. The company was founded in 1999 and initially conducted research into the genetics of epilepsy, angiogenesis and breast cancer and later evolved into a drug development business. It now has two proprietary compounds in clinical trials: BNC105, a tumour vascular disrupting agent (in Phase II for mesothelioma and kidney cancer) and BNC210 (in Phase I for anxiety). The company is based in Thebarton, a suburb of Adelaide, and has a CRO subsidiary in Illkirch, near Strasbourg, France. Bionomics has completed two acquisitions to date: in January 2005 it acquired Neurofit Preclinical Research, a French CRO specialising in neurology (€1.25m in cash and shares) and in May 2005 it acquired Iliad Chemicals, a Melbourne-based firm with chemistry expertise (40.9m shares, with potential milestone payment of a further 13.6m shares). Bionomics has been listed on the ASX since 1999 (it also has ADRs listed on NASDAQ) and has raised A\$75m in equity funding to date and has 34 employees.

### Valuation

We are indicating a value of A\$175m based on a risk-adjusted net present value of the key programmes, based on our assessment of the risks, potential economic rewards and timelines associated with successful development. The valuation largely excludes the value of milestones (including those potentially receivable from Merck Serono in relation to the Kv1.3 programme) or from potential licensing agreements for BNC105 and BNC210.

### Sensitivities

Bionomics's business is subject to the usual risks associated with biotech companies, including the possibility of unfavourable outcomes in clinical trials, success of competitors and commercial decisions by partners and potential partners. Furthermore, there is significant risk associated with a single product, since BNC105 contributes the bulk of our valuation. We have ascribed a low probability to BNC210 because of its earlier stage of development, so there is considerable upside associated with success in partnering this product. As with many biotech firms, funding is also a sensitivity, although following a successful capital raise in Q409 Bionomics has funding for the next two years (indeed it has committed not to raise further funds for this period, unless there is a change of business strategy).

### Financials

The company's year-end is 30 June and it reports semi-annually in accordance with stockmarket requirements of the Australian equivalents to IFRS (AIFRS). Under Australian accounting standards, interest income is treated as a revenue item. For greater comparability, we have adjusted the revenue to exclude this, while including grant income. Interest income is shown as a separate line item on the income P&L account, while reported pre-tax profit is equivalent to that shown by the company. The company has projected expenditures such that cash at 30 June 2011 would be A\$6.4m (Edison model A\$6.7m).

## Company description: Australian cancer/CNS play

The investment case for Bionomics rests largely on the outcome of studies with its two lead compounds: BNC105, the vascular disrupting agent (VDA), which is in Phase II studies for mesothelioma and metastatic renal cell carcinoma; and BNC 210, which is in development for anxiety/depression and is entering a second Phase I trial. In both cases, the outcome of these studies is expected to form the basis for attracting a commercial partner. The value of such arrangements is difficult to predict, but could in both cases deliver a substantial economic return to Bionomics if successful, in our view.

Bionomics has other early stage compounds in its R&D pipeline, including a programme that is partnered with Merck Serono. With the exception of the partnered Kv1.3 programme, all of Bionomics products are wholly owned. Bionomics's R&D activities are driven by three proprietary technology platforms: Angene, an angiogenesis target and drug discovery platform; MultiCore, a proprietary, diversity orientated chemistry platform for the discovery of small molecule drugs; and ionX, a set of novel technologies for the identification of drugs targeting ion channels for diseases of the central nervous system. The R&D pipeline is summarised in Exhibit 1.

**Exhibit 1: Bionomics R&D summary**

Programme	Indication	
BNC105	Mesothelioma/ metastatic renal cell carcinoma (Phase II)	60-pt Phase II trial in second-line mesothelioma (interim results: H111, final H112). A 152-pt Phase II study in progressive metastatic renal cell carcinoma, either in combination with or following Afinitor (everolimus) in patients who have disease progression following treatment with a tyrosine kinase inhibitor (interim results H210, final results: June 2012).
BNC210	Anxiety and depression. Phase Ib	Phase Ib study in healthy volunteers planned for Q110. The first Phase I trial showed the drug to be safe and well tolerated and able to achieve plasma levels equivalent to those required for anxiolytic activity in rodents. Preclinical data shows that in animals BNC210 is able to reduce anxiety without drowsiness, impairment of memory or motor function. BNC210 has been shown to be fast-acting and effective with a single daily dose. Other animal studies have shown that BNC210 affects regions of the brain involved in anxiety and have provided biomarkers for evaluation in the clinical setting.
Kv1.3 inhibitors	Multiple sclerosis/other autoimmune conditions/preclinical	Partnership with <b>Merck Serono (Merck KGaA)</b> . Upfront payment of US\$2m received and up to US\$47m per compound based on successful development and commercialisation plus undisclosed royalties. R&D funding. Merck Serono will be able to select compounds for development and will fund all development activities, including clinical development.
BN 069	Angiogenesis/ preclinical	Programme to develop small molecule inhibitors for novel target (p73 RhoGAP) for inhibiting angiogenic processes. BNO69 is over-expressed in endothelial cells. Xenograft models treated with BNO69 gene-silencing molecules showed a >75% reduction in size vs untreated tumours in experiments conducted over 31 days.
GABA <sub>A</sub> agonists	Epilepsy/discovery	This discovery programme utilises Bionomics's ionX platform incorporating gene mutations observed in patients with epilepsy.

Source: Edison Investment Research

### BNC105: VDA with dual mechanism advantage

BNC105 is a novel small molecule vascular targeting agent (VDA), which acts via tubulin polymerisation inhibition. It is one of a small number of molecules in this exciting potential new class of cancer drug, which is characterised by disruption (ie shutting down) of the blood vessels that supply tumours, thereby starving them of oxygen and nutrients. VDAs are expected to be used in conjunction with classical or targeted chemotherapy to improve the anti-tumour effect.

BNC105 has shown effectiveness in animal models of: head and neck, brain, prostate, breast, colon and lung cancers. Bionomics has completed the Phase I studies and has recently embarked on a Phase II programme in mesothelioma and metastatic renal cell carcinoma (mRCC), two orphan indications.

The mesothelioma study will evaluate BNC105 as a single agent in second line treatment after failure of pemetrexed/cisplatin, while the mRCC study, which is being conducted in the US, will investigate BNC105 in combination with or following Afinitor in patients metastatic RCC following treatment with tyrosine kinase inhibitors. In the mesothelioma study BNC105 will be administered at a dose of 16mg/m<sup>2</sup> on days one and eight of a 21-day cycle. The mRCC study has a Phase I portion designed to determine the maximum tolerated dose of BNC105 in combination with Afinitor to a maximum dose of 12.6mg/m<sup>2</sup>, with BNC105 administered on days one and eight of a 21 day cycle. In both studies BNC105 will be administered IV over 10 minutes.

Bionomics has identified the indications to be pursued on the basis that they should provide data quickly and have potential for fast-track to registration, while not positioning BNC105 as a direct competitor to any of the other VDAs currently in development. The indications are profiled in Exhibit 2.

#### Exhibit 2: BNC105: target indication profile

	<b>Mesothelioma</b>	<b>Metastatic renal cell carcinoma (mRCC)</b>
<b>Description</b>	Cancer of the mesothelium (the membrane that forms the lining of several body cavities). Most commonly affects the pleura (the outer lining of the lungs and internal chest wall). Usually diagnosed at a late stage of the disease (life expectancy is only 6-12 months from diagnosis).	Metastasised form of kidney cancer arising in the lining of the proximal convoluted tubules. Patients are usually diagnosed with non-metastatic RCC and standard treatment is nephrectomy (surgical removal of the kidney) but the disease usually becomes metastatic after a period of several years.
<b>Incidence</b>	Incidence varies depending on prior occupational exposure to asbestos. In the US, c 2,200 new cases are reported per year. In Europe the incidence is about 5,000 cases per year.	Some 210,000 new cases of kidney cancer are diagnosed worldwide each year, accounting for c 2% of all cancers. Some 55,000 cases/year are reported in the US and 63,000 in the EU. RCC accounts for c 90% of all kidney cancers. Five year survival rate in metastatic disease <2%.
<b>Current treatments</b>	Surgery and radiotherapy are used but are usually as a palliative treatment. Alimpta (pemetrexed, Lilly) is approved for malignant pleural mesothelioma in combination with cisplatin. No other drugs are indicated for first or second line use.	Standard treatment for mRCC is immunotherapy (IL-2 or IFN-alpha) in combination with a TKI. Four TKIs are approved: Sutent (sunitinib, Pfizer), Nexavar (sorafenib, Bayer), Afinitor (everolimus, Novartis) and Torisel (temsirolimus, Pfizer). Afinitor is the only one indicated for second line use. Avastin (bevacizumab, Roche) is approved in combination with IFN-alfa.
<b>Competing development programmes</b>	Zolanza (vorinostat, Merck & Co, Phase III), Milataxel (Taxolog, Phase II), Recentin (cedirinib, AstraZeneca, Phase I/II) and CBP501 (CanBas, Phase I/II). Various investigator-sponsored studies with single agent and combinations of bortezomib, oxaliplatin, bevacizumab, imatinib and gemcitabine.	Pazopanib (GSK, Phase III), axitinib (Pfizer, Phase III). Various combinations of approved products. A number of agents are in Phase I/II studies as single agents or in combination with approved therapies including TKI258 (Novartis); panobinostat (Novartis), aflibercept (Sanofi-Aventis), AMG386 (Amgen) and Revlimid (lenalidomide, Celgene).
<b>Bionomics study</b>	60-pt Phase II study in pts unresponsive to pemetrexed + cisplatin. The primary endpoint is response rate (modified RECIST) and secondary endpoints are PFS; six-month PFS; time to treatment failure; overall survival; symptom control – quality of life and lung function. Conducted in collaboration with the Australasian Lung Cancer Trials Group and Australian National Health and Medical Research Council Clinical Trials Centre.	152-pt Phase II study of BNC105 + everolimus (Afinitor) in second line mRCC and BNC105 alone in patients progressing on everolimus. Patients will be randomized 1:1 to the two arms of the study. The primary endpoint: six month PFS; secondary endpoints are response rate on BNC105+ everolimus vs everolimus alone; PFS with BNC105 alone; adverse events of everolimus and BNC105 in combination or sequential regimen, overall survival and correlation of PFS with biomarkers. Conducted in the US by Hoosier Oncology Group, a US CRO.
<b>Results</b>	An interim analysis will be performed after the first 24 patients have been enrolled (results due H111) with final results in 2012.	Interim results are expected at the end of 2010, with final trial data out in 2012.
<b>Notes</b>	The lack of existing treatments allows single agent utility to be examined. There is a possibility that strong interim data would allow resizing study to provide pivotal data. Pemetrexed was approved based on a single study in 456 patients which showed median survival of 12.8m vs 9m for cisplatin alone.	This design provides the opportunity to evaluate BNC105 as monotherapy albeit in third-line setting. There is some evidence of synergistic action with an mTOR inhibitor as deregulated mTOR-HIF signalling seems to protect RCC from the VDA action. mRCC is a highly vascularised and therefore likely to be a good target for a VDA (a mRCC patient in Phase I studies showed a clinical response).

Source: Edison Investment Research

Data was reported at ASCO last year from Phase I studies of BNC105 in nine patients (seven male and two female, median age 60 years) with advanced solid tumours. This study had dose escalations in from 2.1mg/m<sup>2</sup> to 18.9mg/m<sup>2</sup> and a single patient was treated at each of the dose levels 2.1 and 4.2mg/m<sup>2</sup>. At 8.4mg/m<sup>2</sup>, one patient experienced Grade 2 mucositis. This observation led to the '3+3' design switch where three patients were enrolled at each subsequent dose escalation to check for adverse side effects. No dose limiting toxicities were observed at 12.6mg/m<sup>2</sup>.

At doses of 8.4mg/m<sup>2</sup> and above, DCE-MRI images indicate changes in tumour blood flow within 3-6 and 24 hours following BNC105 treatment. Drug levels achieved in patients correlated with drug exposure required for activity in preclinical experiments. Two out of nine treated patients had stable disease in this initial analysis and received additional cycles of treatment. One patient with mesothelioma treated with 8.4mg/m<sup>2</sup> had stable disease up to week 22 of treatment. A second patient suffering from renal cell cancer (treated at the 12.6mg/m<sup>2</sup> dose level) had stable disease for nine weeks.

## Competitive position

BNC105 is one of perhaps seven VDAs currently in active development. VDAs are considered to have significant commercial potential in the treatment of cancer, especially as their mechanism makes them likely to be applicable to a wide variety of solid tumour types. The excitement surrounding VDAs is the potential ability to target existing as well as newly formed vasculature supplying tumours, in contrast to anti-angiogenic agents such as Avastin (bevacizumab, Roche)<sup>1</sup>, which can only inhibit the growth and formation of new blood vessels around tumours.

The lead product in the class is Novartis/Antisoma's ASA404 (vadimezan), which is in Phase III studies for non-small cell lung cancer (both first and second line) in combination with chemotherapy. ASA404 has been studied to date in non-small cell lung cancer (where it showed evidence of activity in both squamous and non-squamous disease), hormone-refractory prostate cancer and ovarian cancer (which showed poor results).

BNC105 has a number of potential advantages in comparison with existing agents. Preclinical studies have demonstrated a high level of selectivity for activated endothelium for BNC105 over other agents. It has a higher therapeutic index<sup>2</sup> than combrestatin and is not affected by the P-glycoprotein multidrug resistance mechanism. Preclinical studies suggest BNC105 can inhibit tumour growth as a single agent, which has not been seen with other comparable VDAs.

Competing VDAs are shown in Exhibit 3.

<sup>1</sup>Avastin, a monoclonal antibody against VEGF-A, is approved for metastatic colorectal, non-squamous non-small cell lung and breast cancers and glioblastoma multiforme. It is also in development for multiple indications including non-metastatic breast cancer, renal cell carcinoma, ovarian cancer, castration-resistant prostate cancer, non-metastatic unresectable liver cancer and metastatic or unresectable locally advanced pancreatic cancer.

<sup>2</sup> BNC105 exhibits single agent efficacy with 20% tumour clearance rate in preclinical models with no effects on normal blood vessels giving rise to an increased therapeutic window. It has a >10 fold therapeutic window compared to combrestatin in cancer patients

**Exhibit 3: Competitive landscape in tumour-vascular disrupting agents**

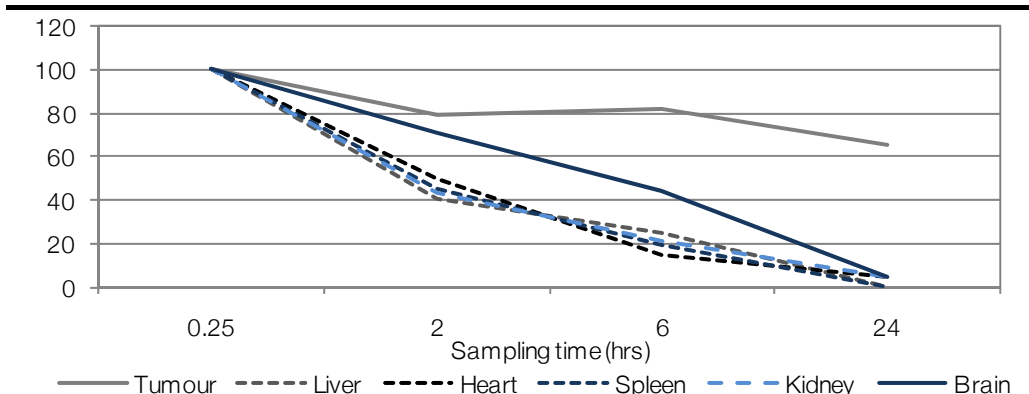
Product	Company	Development stage/notes
ASA404/ AS1404 (DMXAA/ vadimezan)	Novartis/ Antisoma	Phase III studies are underway in first-line non-small cell lung cancer in combination with carboplatin and paclitaxel (results: late 2010/early 2011) and in second line NSCLC in combination with docetaxel (results: H1 2011). A Phase II study is underway in small cell lung cancer and one is planned in HER-2 negative metastatic breast cancer; both are in combination with carboplatin/paclitaxel chemotherapy. Regulatory filings for NSCLC are planned in 2011 and launch in 2012. Novartis holds worldwide rights under a development and commercialisation deal valued at US\$890m, which comprised US\$75m upfront with US\$355m in milestones in development/approval milestones, and US\$325m in sales milestones.
AVE8062	Sanofi- Aventis	300-pt Phase II/III in advanced-stage soft tissue sarcoma after failure of anthracycline and ifosfamide (results: Oct 2011). 85-pt Phase I in combination with platinum-taxane doublet in advanced solid tumours (results: May 2010).
Zybrestat (fosbretabulin/ combretastatin/ CA4P)	OXIGENE	60-pt Phase II (FALCON) study with carboplatin, paclitaxel and bevacicumab in chemotherapy-naïve NSCLC (results: March 2010); Phase II/III (FACT) study with carboplatin/paclitaxel in anaplastic thyroid cancer (results: Dec 2010) and 40-pt Phase II (FAVOR) study against vasculopathy of the retina. Positive interim results seen in investigator-sponsored open-label Phase II study in platinum-resistant ovarian cancer, in combination with carboplatin and paclitaxel.
NPI-2358	Nereus Pharma	174-pt Phase I/II (ADVANCE) in combination with docetaxel in advanced NSCLC (results: November 2010).
Azixa (MPC- 6827)	Myriad Pharma	68-pt Phase I/II in recurrent glioblastoma multiforme (results: Jan 2011) and 30-pt Phase I/II in combination with carboplatin in recurrent/relapsed GBM (results: Oct 2009). 22-pt Phase I/II study with temozolomide in metastatic melanoma (results due shortly). Licensed from EpiCept.
CYT997	YM Biosciences	35-pt Phase II study in combination with carboplatin and etoposide in relapsed GBM (results: Feb 2010).
crinobulin	EpiCept	33-pt Phase I in advanced cancer completed. Phase Ib with other chemotherapy planned.
ABT-751/ E-7010	Abbott/ Eisai	88-pt Phase II studies in refractory neuroblastoma (results: Jan 2012) and 35-pt Phase I/II in relapsed/paediatric ALL (results: June 2009). 165-pt Phase II study in combination with pemetrexed in advanced NSCLC did not show efficacy. Phase II studies in NSCLC in combination with taxotere and refractory haematological malignancies terminated.

Source: Edison Investment Research

BNC105's dual mode of action and direct cytotoxic effect should potentiate effectiveness of existing anticancer therapy (radiation treatment, cytotoxic chemotherapy and biological agents). Pharmacokinetic studies suggest BNC105 is retained within tumours, possibly due to the rapid vascular disruption; this is shown in Exhibit 4.

**Exhibit 4: Retention of BNC105 within tumours vs other organs**

Note: Vertical scale shows % of BNC105 tissue distribution in the tumour and other organs, expressed as a percentage of the amount seen in the tumour at 25 minutes post administration.



Source: Bionomics

## BNC210 – novel agent for anxiety

BNC210 is a novel small molecule with an undisclosed novel mechanism of action and potential activity in anxiety, both acute and chronic (generalised anxiety disorder) with co-morbid depression. It may also have potential in depression. Bionomics is about to start a Phase Ib study in healthy volunteers, the results of which should be available at the end of this year. A Phase Ia study, also conducted in healthy volunteers, was completed last year. The first part of this trial showed BNC210 to be safe and well tolerated in healthy male volunteers at plasma levels equivalent to those where anxiolytic activity was seen in rodents. BNC210 was taken at single doses up to and including 1,200mg with no clinically significant adverse events reported. The next stage will evaluate a higher dose level in healthy volunteers, and for the first time will examine potential effects of BNC210 on neuroendocrine markers.

Preclinical studies showed BNC210 was able to reduce anxiety without drowsiness or impairment of memory or motor function. The drug was also fast-acting and effective with a single daily dose. Other animal studies involving the use of EEG recordings have shown that BNC210 affects regions of the brain involved in anxiety and have provided potential biomarkers for evaluation in the clinical setting. This should allow a better evaluation of the side effect profile, including whether there is any sedative effects.

BNC210 has shown effectiveness in animal models of stress-induced anxiety reducing anxiety levels to pre-stress or baseline levels. Studies have not shown any evidence of dependence<sup>3</sup> following cessation of treatment. BNC210 has shown activity in a rat model of depression following both acute treatment and daily dosing for 14 days.<sup>4</sup> Withdrawal of BNC210 treatment following 14-day repeat dosing does not result in adverse physical events usually seen following withdrawal of opioids, benzodiazepines or SSRIs.

The activity profile seen with BNC210 in these preclinical tests expands its therapeutic utility and Bionomics believes BNC210 offers competitive advantages over existing anxiety and depression treatments, including speed of onset (of action), lack of sedation, memory and motor impairment and risk of habituation.

Current anxiety treatments, such as benzodiazepines and selective serotonin reuptake inhibitors, have various side effects associated with their use. Benzodiazepines offer acute relief from anxiety but have sedative, cognitive and motor impairing side effects. In addition, their protracted use can result in tolerance and addiction. SSRIs exhibit slow onset of action and are associated with side effects such as early agitation, gastric disturbances, sexual dysfunction and weight gain (Exhibit 5).

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<sup>3</sup> Abrupt cessation of treatment in rats dosed repeatedly with BNC210 for a period of 14 days at 0, 10, 30 and 100mg/kg/day did not produce changes in rat body temperature, weight gain or food consumption for the duration of the post-treatment period (five days).

<sup>4</sup> BNC210 exhibits antidepressant activity in the rat forced swim test, which was comparable to imipramine (active control). The antidepressant effect increased markedly following 14-days repeated administration, which was also seen with known antidepressants.

**Exhibit 5: Current anxiety treatments**

Class/drug examples	Positives	Negatives	Notes
Benzodiazapines (alprazolam, bromazepam, clazepam, lorazepam, diazepam)	Rapid acting. Suitable for acute anxiety.	Sedation. Memory impairment/confusion. Reduced muscle coordination/balance.	Suitable only for short-term use because of risk of tolerance and habit formation. Generally recommended only for second line use.
Selective serotonin re-uptake inhibitors (paroxetine, escitalopram, sertraline, fluvoxamine)	Lack of sedation or cognitive impairment.	Slow onset of action (several weeks). Sexual dysfunction/weight gain. Discontinuation syndrome.	Various drug-drug interactions (contraindicated with MAOIs). Approved for panic, social anxiety and generalised anxiety in adults (paroxetine is contraindicated for children).
Azapirone (buspirone)	Lack of addiction/dependence/tolerance issues. Not sedative.	Slow onset of action.	Suitable for chronic use.
Serotonin, norepinephrine reuptake inhibitor (duloxetine, venlafaxine)	Lack of addiction/dependence/tolerance issues.	Withdrawal symptoms (venlafaxine).	Venlafaxine is contraindicated in children and adolescents because of risk of suicidal ideation.

Source: Edison Investment Research, literature sources

The anxiety market is in our view mature and, with many of the leading products off patent, has seen relatively little development activity in recent years. As a consequence there are fewer competing development agents. Competing programmes in later stage development for anxiety are shown in Exhibit 6.

**Exhibit 6: Competing developments in anxiety (Phase II or later)**

Class	Company	Mechanism	Notes
Lu AA21004	Lundbeck/ Takeda	5-HT <sub>3</sub> antagonist, 5-HT <sub>1a</sub> agonist and 5-HT enhancer	457-pt Phase III completed (no results published). 300-pt Phase II in relapse prevention (fully recruited, results: April 2010). Three Phase III studies completed for depression; two did not reach significance, a third trial showed mixed results. Further dose ranging studies expected.
AZD2327	AstraZeneca	Selective, high affinity enkephalinergic agonist	96-pt Phase II study for anxious major depression (results: August 2011). 80-pt Phase II in anxious major depressive disorder (results: Feb 2010).
GSK561679	GSK	CRFR1 antagonist	150-pt Phase II in women with post-traumatic stress disorder (results: Dec 2012).
orvepitant	GSK	NK1 antagonist	Phase II for PTSD.
ABIO 08/01	Abiogen	N/A	Phase II (no details disclosed).

Source: Edison Investment Research

**Kv1.3 inhibitors – deal with Merck KGaA/Merck Serono**

Bionomics has a programme to develop a number of orally-available inhibitors of the Kv1.3 potassium ion channel<sup>5</sup> as potential anti-inflammatory agents. A number of other companies are looking at this target, although Bionomics's programme appears to be one of the most advanced. The programme is subject to a partnership with Merck KGaA, which was signed in 2008 and under the agreement Bionomics receives R&D funding. Merck Serono will be able to select compounds for development and will fund all development activities, including clinical development and Bionomics will receive up to US\$47m in milestones per compound based on successful development and commercialisation plus undisclosed royalties.

Bionomics has identified compounds with high potency (as low 5nM), high specificity (c 25-fold or greater selectivity for related ion channels such as Kv1.1 or Kv1.5 and at least 100-fold selectivity over the hERG channel, indicating that the risk of cardiovascular toxicities is low). Efficacy has been shown in animal models of inflammatory disorders such as Delayed Type Hypersensitivity (DTH) and Experimental Autoimmune Encephalomyelitis (EAE), a model of multiple sclerosis.

<sup>5</sup> Kv1.3 is a key regulator of the effector-memory T-Cells of the immune system that are key mediators of inflammatory diseases. Kv1.3 is an interesting target as it is expressed in a limited range of tissues.

## Sensitivities

Bionomics's business is subject to the usual risks associated with biotech companies, including the possibility of unfavourable outcomes in clinical trials, success of competitors and commercial decisions by partners and potential partners.

The ability to partner BNC105 and/or BNC210 is crucial to the investment case and is therefore a key sensitivity. While BNC105 is likely to be, in our view, a very attractive asset, BNC210 addresses a market that has seen less innovation and may be considered by major pharmaceutical companies to be well-served by existing treatments (despite their limitations) and is now largely generic. The compound is nonetheless attractive, although its early stage of development may place greater uncertainty over the ability of Bionomics to partner BNC210 on attractive economic terms. As with many biotech firms, funding is a sensitivity, although following its recent capital raise Bionomics has funding for the next two years.

## Valuation

We are indicating a value of A\$175m, based on the risk-adjusted NPV of the key R&D assets, namely BNC105, BNC210 and the Kv1.3 programme, which compares with Bionomics's current enterprise value of A\$85m. The probability of securing a development/commercial partner and the potential commercial terms of any such licensing arrangement (in terms of upfront, milestones and royalties) and peak sales are difficult to estimate. This is especially true for BNC210, because the anxiety market is now largely generic and has seen little in the way of new innovations in drug development. The inputs used in Edison's valuation model are shown in Exhibit 7.

### Exhibit 7: Edison valuation model inputs

Note: Valuation uses net cash as of 30 December, not balance sheet cash.

Product	Indication	Status	Probability of success	Est launch	Est peak market	Potential market value	Est maximum royalty	Est peak sales
BNC105	mesothelioma	Phase II	30%	2013	25%	\$750m	18%	\$278m
BNC105	mRCC	Phase II	30%	2013	10%	\$1,500m	18%	\$281m
BNC105	other solid tumours	Phase I	15%	2014	5%	\$5,000m	18%	\$468m
BNC210	anxiety	Phase I	15%	2014	5%	\$5,000m	12%	\$487m
Kv-1.3	MS/other autoimmune	Preclinical	5%	2015	5%	\$10,000m	12%	\$900m
<b>Total rNPV</b>			<b>A\$165m</b>					
<b>Current net cash</b>			<b>A\$10m</b>					
<b>Total valuation</b>			<b>A\$175m</b>					

Source: Edison Investment Research

A partnership for BNC105 could generate substantial economic return. Antisoma's VDA ASA404 was partnered with Novartis, when in Phase II, in 2007, in a deal with a value of up to US\$890m including a US\$75m upfront and double digit royalties. Recent licensing deals of cancer products are listed in Exhibit 8 to provide an indication of the value that may be achieved in a licensing deal for BNC105.

**Exhibit 8: Recent cancer licensing deals**

Drug/licensee	Licensor	Development status	Notes
belinostat TopoTarget (Feb 2010).	Spectrum Pharma	Pivotal Phase II/III trial in peripheral T-cell lymphoma; Phase II for cancer of unknown primary. Various other (NCI-sponsored) studies.	Deal covering North America and Indian rights with a right of first offer for China, provides a US\$30m upfront and US\$320m in (mostly sales) milestones, double digit royalties and c US\$4m in shares. Future development costs split (70%:30%).
OGX-011/ Oncogenix (Dec 2009)	Teva	Phase II in prostate cancer. Two Phase III trials planned for 2010: in first and second-line metastatic CRPC and one in 2011 in NSCLC.	Global licensing deal provides US\$20m upfront, US\$10m equity investment (at premium), with up to US\$370m in milestones (including regulatory and sales) and tiered royalties on sales (mid-teens to mid-twenties). Teva will also make a US\$30m prepayment for development costs and is responsible for all commercialisation and development expenses.
Omacetaxine/ Chemgenex (Dec 2009)	Hospira	Phase III completed in CML T315I BCR-ABL mutation. Phase II/III in CML.	Deal for Europe, Middle East and Africa provides €11.1m upfront and milestones of up to €74.1m and royalties on sales.
CP-4126/ Clavis (Nov 2009)	Clovis Oncology	Phase II in pancreatic cancer.	Deal covering North/South America and Europe provides US\$15m upfront and up to US\$365m in milestones (development, regulatory & sales) plus tiered double-digit royalties.
INCB18424 & INCB28060/ Incyte (Nov 2009)	Novartis	Phase III in myelofibrosis (INCB18424); Phase I in solid cancers (INCB28060).	Deal covers INCB18424 (JAK1/2 inhibitor), worldwide ex-US and INCB28060 (cMET inhibitor) worldwide. Upfront of \$210m and up to c US\$1.1bn in milestones (development and sales) and tiered, double-digit royalties on INCB18424 sales (undisclosed royalties on INCB28060 sales).
Alpharadin/ Algeta (Sept 2009)	Bayer Schering	Phase III in prostate cancer bone metastases	Global licensing deal with upfront of \$61m, \$740m of development and regulatory milestones and tiered royalties on net sales (high teens, rising to in excess of 20%).
XL147 and XL765/ Exelixis (May 2009)	Sanofi- Aventis	Phase I in solid tumours (both products). XL-147 now in Phase II.	Worldwide license to XL147 and XL765 provides an upfront of US\$140m, research funding of US\$21m over a three years, development, regulatory and commercial milestones of US\$1bn and royalties on sales.
ARQ 197 Arqule (Nov 2008)	Daiichi Sankyo:	Phase II in solid tumours (NSCLC, c-Met sarcomas, pancreatic cancer, HCC, germ cell tumours and CRC).	Worldwide (ex-Asia) licensing deal with a US\$60m upfront and undisclosed, significant development and sales milestone payments plus royalties on sales. Costs of Phase II and Phase III studies will be shared (funded by milestones and royalties).

Source: Edison Investment Research

## Financials

Bionomics's year-end is 30 June and the company reports semi-annually, in accordance with stockmarket requirements, to the Australian equivalents to IFRS (AIFRS). Under Australian accounting standards, interest income is treated as a revenue item. For greater international comparability, we have adjusted the revenue to exclude this while including grant income. Interest income is therefore shown in our model as a separate line item on the income P&L account. Reported pre-tax profit is equivalent to that shown by the company.

Bionomics generates revenue from licence fees and payments from Merck Serono as well contract research services from Neurofit. Bionomics reported cash of A\$16m as of 30 December 2009 (A\$13m net of long-term liabilities). We have modelled R&D expenditure of A\$8m per year for FY09/10 and the subsequent two years. In connection with the A\$15m fund-raising last year, Bionomics projected income (based on contracted R&D and Neurofit revenue) of A\$7.1m. It estimates the cost of the BNC105 programme at just under A\$14m (kidney cancer study: A\$8.1m, mesothelioma A\$5.5m) and BNC210 Phase Ib trials (A\$3.6m). Its projected cash as of 30 June 2011 is A\$6.4m (Edison model A\$6.7m).

Our model is shown in Exhibit 9.

**Exhibit 9: Financial results and forecasts**

Note: Reported revenue is adjusted to exclude interest income, in line with IFRS, which is shown separately in income statement. Revenue also includes grant income. No assumption of potential licensing deals is anticipated in the model.

Year end 31 December	A\$'000s	2007	2008	2009	2010e	2011e	2012e
		IFRS	IFRS	IFRS	IFRS	IFRS	IFRS
<b>PROFIT &amp; LOSS</b>							
<b>Revenue</b>		<b>3,089</b>	<b>6,513</b>	<b>2,926</b>	<b>3,540</b>	<b>3,540</b>	<b>3,543</b>
Cost of sales		(145)	(213)	(338)	0	0	0
Gross profit		2,944	6,300	2,588	3,540	3,540	3,543
<b>EBITDA</b>		<b>(6,672)</b>	<b>(4,058)</b>	<b>(7,023)</b>	<b>(6,396)</b>	<b>(6,488)</b>	<b>(6,583)</b>
<b>Operating profit (before GW and except.)</b>		<b>(7,198)</b>	<b>(4,661)</b>	<b>(7,555)</b>	<b>(6,926)</b>	<b>(7,018)</b>	<b>(7,112)</b>
Intangible amortisation		(446)	(479)	(502)	(500)	(500)	(499)
Exceptionals		0	0	0	0	0	0
Share-based payments		(286)	(258)	(242)	(242)	(242)	(241)
<b>Operating profit</b>		<b>(7,930)</b>	<b>(5,398)</b>	<b>(8,298)</b>	<b>(7,668)</b>	<b>(7,760)</b>	<b>(7,852)</b>
Net interest		(305)	(313)	(283)	250	150	(100)
<b>Profit before tax (norm)</b>		<b>(7,503)</b>	<b>(4,975)</b>	<b>(7,838)</b>	<b>(6,676)</b>	<b>(6,868)</b>	<b>(7,212)</b>
<b>Profit before tax (FRS 3)</b>		<b>(8,235)</b>	<b>(5,712)</b>	<b>(8,581)</b>	<b>(7,418)</b>	<b>(7,610)</b>	<b>(7,952)</b>
Tax		2,449	359	37	0	0	0
<b>Profit after tax (norm)</b>		<b>(5,054)</b>	<b>(4,616)</b>	<b>(7,801)</b>	<b>(6,676)</b>	<b>(6,868)</b>	<b>(7,212)</b>
<b>Profit after tax (FRS 3)</b>		<b>(5,786)</b>	<b>(5,353)</b>	<b>(8,545)</b>	<b>(7,418)</b>	<b>(7,610)</b>	<b>(7,952)</b>
Average number of shares outstanding (m)		180.4	225.3	243.0	286.0	318.1	318.1
EPS - normalised (c)		(2.8)	(2.0)	(3.2)	(2.3)	(2.2)	(2.3)
EPS - FRS 3 (c)		(3.2)	(2.4)	(3.5)	(2.6)	(2.4)	(2.5)
Dividend per share (c)		0.0	0.0	0.0	0.0	0.0	0.0
Gross margin (%)		95.3	96.7	88.5	100.0	100.0	100.0
EBITDA margin (%)		N/A	N/A	N/A	N/A	N/A	N/A
Operating margin (before GW and except.) (%)		N/A	N/A	N/A	N/A	N/A	N/A
<b>BALANCE SHEET</b>							
<b>Fixed assets</b>		<b>16,866</b>	<b>19,457</b>	<b>18,837</b>	<b>17,914</b>	<b>16,991</b>	<b>15,963</b>
Intangible assets		8,238	10,839	10,458	9,958	9,458	8,959
Tangible assets		8,628	8,618	8,379	7,956	7,533	7,004
Investments		0	0	0	0	0	0
<b>Current assets</b>		<b>13,954</b>	<b>8,856</b>	<b>5,888</b>	<b>14,794</b>	<b>8,049</b>	<b>1,368</b>
Stocks		99	79	122	148	148	148
Debtors		339	2,315	775	938	938	939
Cash		12,820	6,280	4,757	13,475	6,731	49
Other		696	182	232	232	232	232
<b>Current liabilities</b>		<b>(3,613)</b>	<b>(3,051)</b>	<b>(2,791)</b>	<b>(3,110)</b>	<b>(3,110)</b>	<b>(3,111)</b>
Creditors		(2,597)	(2,109)	(1,626)	(1,945)	(1,945)	(1,947)
Other current liabilities		(110)	(241)	(109)	(109)	(109)	(109)
Short-term borrowings		(542)	(672)	(629)	(629)	(629)	(629)
<b>Long-term liabilities</b>		<b>(4,860)</b>	<b>(3,955)</b>	<b>(3,850)</b>	<b>(3,489)</b>	<b>(3,189)</b>	<b>(3,189)</b>
Long-term borrowings		(3,877)	(3,536)	(3,165)	(2,803)	(2,503)	(2,503)
Other long-term liabilities		0	(50)	(50)	(50)	(50)	(50)
<b>Net assets</b>		<b>22,347</b>	<b>21,307</b>	<b>18,083</b>	<b>26,110</b>	<b>18,742</b>	<b>11,031</b>
<b>CASH FLOW</b>							
<b>Operating cash flow</b>		<b>(6,533)</b>	<b>(6,512)</b>	<b>(4,986)</b>	<b>(6,266)</b>	<b>(6,488)</b>	<b>(6,582)</b>
Net interest		232	569	287	250	150	(100)
Tax		0	0	0	0	0	0
Capex		(135)	(386)	(107)	(107)	(107)	0
Payment of deferred consideration		0	0	0	0	0	0
Capitalisation of development costs		0	0	0	0	0	0
Expenditure on intangibles		0	0	(4)	0	0	0
Acquisitions/disposals		0	0	0	0	0	0
Financing		14,487	103	3,739	15,203	0	0
Dividends		0	0	0	0	0	0
Net cash flow		8,050	(6,226)	(1,070)	9,080	(6,445)	(6,682)
<b>Opening net debt/(cash)</b>		<b>(356)</b>	<b>(8,401)</b>	<b>(2,173)</b>	<b>(1,063)</b>	<b>(10,143)</b>	<b>(3,699)</b>
HP finance leases initiated		0	0	0	0	0	0
Other		(5)	(4)	(39)	0	0	0
<b>Closing net debt/(cash)</b>		<b>(8,401)</b>	<b>(2,172)</b>	<b>(1,063)</b>	<b>(10,143)</b>	<b>(3,699)</b>	<b>2,983</b>

Source: Edison Investment Research

Growth	Profitability	Balance sheet strength	Sensitivities evaluation	
N/A	N/A		Litigation/regulatory	●
			Pensions	○
			Currency	◐
			Stock overhang	○
			Interest rates	◐
			Oil/commodity prices	○

Growth metrics	%	Profitability metrics	%	Balance sheet metrics		Company details	
EPS CAGR 07-11e	N/A	ROCE 10e	N/A	Gearing 10e	N/A	Address:	
EPS CAGR 09-11e	N/A	Avg ROCE 07-11e	N/A	Interest cover 10e	N/A	31 Dalgleish Street, Thebarton SA 5031 Australia	
EBITDA CAGR 07-11e	N/A	ROE 10e	N/A	CA/CL 10e	2.6	Phone	+618 8354 6100
EBITDA CAGR 09-11e	N/A	Gross margin 10e	100	Stock turn 10e	15.3	Fax	+618 8354 6199
Sales CAGR 07-11e	N/A	Operating margin 10e	N/A	Debtor days 10e	96.7	www.bionomics.com.au	
Sales CAGR 09-11e	N/A	Gr mgn / Op mgn 10e	N/A	Creditor days 10e	189		

Principal shareholders		%	Management team	
Start-Up Australia Ventures		27.8	<b>CEO: Dr Deborah Rathjen</b>	
Link Traders (Aust)		9.4	Appointed in June 2000. Formerly, general manager, business development and licensing at Peptech and co-inventor Peptech's TNF technology licensed to J&J and Abbott. Holds BSc in biological sciences from Flinders University and PhD in Biology from Macquarie University. Also chairman of the AusBiotech Board.	
The Australian National University Investment Section		7.4		
Welas		4.6		
Phillip Asset Management		4.3		
National Nominees		4.2		
			Appointed CFO and company secretary in December 2009 (not a board director). 25 years in various management positions spanning commercial, financial and treasury roles in public companies involved in various industries including grain, rural services, retail and food.	
Forthcoming announcements/catalysts	Date *		<b>Chairman: Christopher Fullerton</b>	
BNC210 Phase Ia results	Q1 2010		Managing director of Mandalay Capital. Former chairman of Cordlife and of Health Communication Network and director of Global Health, The Environmental Group, Standard Chartered Australia, Alliance Properties and Federal Airports.	
BNC105 presentations at ASCO/AACR	Q2 2010			
BNC210 Phase Ib trial initiation	Q2 2010			
BNC210 Phase Ib trial completed	Q2 2010			
AGM	November 2010			
Note: * = estimated				

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