EDISON

# Bionomics

Re-initiation of coverage

## Novel mechanisms in drug discovery

Pharma & biotech

**We are re-initiating coverage on Bionomics, a pharmaceutical company developing drugs for neuropsychiatric indications and oncology. It has leveraged its ionX and MultiCore development platforms to identify BNC210, a drug with a novel anxiolytic mechanism currently in Phase IIb for post-traumatic stress disorder (PTSD). It has also leveraged this platform with partner Merck to target cognitive dysfunction associated with Alzheimer's disease, in a deal worth US$506m in milestones plus royalties. We re-initiate with a valuation of A$418.7m or A$0.87 per share.**

| Year end | Revenue (A$m) | PBT* (A$m) | EPS* (A$) | DPS (A$) | P/E (x) | Yield (%) |
|---|---|---|---|---|---|---|
| 06/16 | 8.1 | (16.7) | (0.04) | 0.00 | N/A | N/A |
| 06/17 | 18.6 | (4.4) | (0.01) | 0.00 | N/A | N/A |
| 06/18e | 17.5 | (7.2) | (0.01) | 0.00 | N/A | N/A |
| 06/19e | 5.1 | (28.4) | (0.05) | 0.00 | N/A | N/A |

Note: *PBT and EPS are normalised, excluding amortisation of acquired intangibles, exceptional items and share-based payments.

## Finding new targets to reduce anxiety

BNC210 is a negative allosteric modulator of the α7 nicotinic acetylcholine receptor, a protein in the brain implicated in the response to stress that has been previously unexplored for its therapeutic potential. In earlier exploratory studies the compound supressed activation of regions of the brain associated with anxiety and reduced the intensity of panic, suggesting a novel anxiolytic activity. It is currently being investigated for PTSD in a Phase IIb study expected to have data in H218.

## Merck collaboration: In early clinical stages

The company signed a collaboration agreement with Merck in 2014 to develop small molecules for the treatment of cognitive dysfunction and received US$20m upfront. In February 2017, it announced that the first molecule from this programme had entered Phase I for Alzheimer's-associated cognitive dysfunction triggering a US$10m milestone. Few other details are available, but the company would be entitled to an additional US$476m in milestones, as well as royalties on sales, if the programme progresses. Additionally, Merck took a 4.5% equity stake in Bionomics in 2015. We find both of these to be encouraging validations of the platform.

## BNC101: Targeting a known cancer stem cell marker

The company is testing BNC101 in Phase I for colorectal cancer. The drug targets LGR5, a protein found on the surface of cancer stem cells in the gut that is associated with poor prognosis. It is being tested as a monotherapy and with chemotherapy. The company intends to find a partner for further development.

## Valuation: A$418.7m or A$0.87 per basic share

We arrive at an initial valuation of A$418.7m or A$0.87 per basic share based on a risk-adjusted NPV analysis. Clinical risk predominates (30% probability of success for BNC210 in PTSD, 10% for BNC101 in CRC) due to the unexplored nature of these targets. The company ended H118 (31 December) with A$32.0m in cash and A$20.1m in debt, providing a runway through clinical readouts in CY18.

**10 April 2018**

| | |
|---|---|
| **Price** | **A$0.56** |
| **Market cap** | **A$270m** |
| | A$1.25/US$ |
| Net cash (A$m) at 31 December 2017 | 11.9 |
| Shares in issue | 481.5m |
| Free float | 84% |
| Code | BNO |
| Primary exchange | ASX |
| Secondary exchange | OTCQX |

### Share price performance


| % | 1m | 3m | 12m |
|---|---|---|---|
| Abs | 16.5 | 46.8 | 61.4 |
| Rel (local) | 19.7 | 55.1 | 61.4 |
| 52-week high/low | A$0.59 | A$0.32 | |

### Business description

Bionomics is a clinical-stage pharmaceutical company with two small molecule discovery platforms: ionX for ion channel targets and MultiCore chemistry for rapid candidate identification. The company is testing BNC210 in Phase IIb for post-traumatic stress disorder (PTSD) and had a programme licensed to Merck in Phase I for royalties and US$506m in upfronts and milestones.

### Next events

| | |
|---|---|
| BNC101 CRC Phase I complete | H118 |
| Merck collab. Phase I complete | H118 |
| BNC210 PTSD Phase II complete | H218 |

### Analysts


Nathaniel Calloway +1 646 653 7036

Maxim Jacobs +1 646 653 7027

healthcare@edisongroup.com

Edison profile page

# Investment summary

## Company description: Breaking new ground

Bionomics is a pharmaceutical company developing small molecules and biologics for neuropsychiatric disorders and cancer. The company's lead programme is BNC210, an oral, small molecule modulator of the α7 nicotinic acetylcholine receptor with a novel anxiolytic mechanism of action, which is in Phase IIb for post-traumatic stress disorder (PTSD). The compound previously showed inhibition of fMRI activity in the brains of patients exposed to anxiety-generating stimuli in Phase II. Results of the Phase IIb are expected in H218. The company is also developing BNC101, a monoclonal antibody targeting the LGR5 protein, a marker of cancer stem cells, in colorectal cancer (CRC). This programme is in Phase I with results expected in H118. Additionally, the company has two development platforms, ionX and MultiCore, which it has leveraged into a development partnership with Merck worth US$506m in upfronts and milestones in addition to royalties. The first molecule from the collaboration entered Phase I clinical testing in February 2017, triggering a US$10m milestone, and we expect the trial to be complete in H118.

## Valuation: A$418.7m or A$0.87 per basic share

We arrive at an initial valuation of A$418.7m or A$0.87 per basic share based on a risk-adjusted NPV analysis. The majority of this value is driven by BNC210 with a valuation of A$329.7m. We assign a 30% probability of success for the PTSD programme because the molecule appears to be active and have anxiolytic activity, but has not been tested using an approvable functional endpoint. We currently only value BNC210 in PTSD, but if the compound is successful in its ongoing trial, we may include additional indications such as generalized anxiety disorder in our valuation. We also include BNC101 in the valuation (A$75.6m) with a 10% probability of success to reflect the high risks associated with investing in a drug with a previously untested mechanism of action. The remainder of our valuation reflects the potential milestones from the Merck collaboration, as well as revenue from the company's wholly owned contract research organization (CRO) businesses.

## Financials: A$32.0m in cash and A$20.1m in debt

The company's expenses are largely driven by its R&D activities, which totalled A$24.2m in FY17. The company ended H118 (31 December) with A$32.0m in cash and A$20.1m in debt, the latter mostly at 8.9%. We expect this cash to provide a runway through the near-term clinical readouts, and we expect the company to seek partners for its products to offset future financing needs. However, in the interim we record the financing shortfall to develop these products as A$35m in illustrative debt in FY20 before reaching profitability in 2022.

## Sensitivities: The risks of innovation

There are risks associated with Bionomics' business, although these are by and large typical for a clinical-stage drug company. The company is developing drugs with new mechanisms of action, which by its very nature carries significant risk. There are data to support these mechanisms, but it still remains to be seen how these drugs will perform against their target indications. In particular, PTSD has historically been a hard-to-treat disorder, which does not respond well to available anxiolytic drugs, although the hope is that the novel mechanism will avoid the sedating and memory impairing effects that limit their efficacy. Additionally, the cancer stem cell hypothesis on which the mechanism of BNC101 rests has not been successfully targeted in the clinic to date. In addition to clinical risks, the company intends to out-license these assets, which carries the associated partnering risks. We expect the company to use partnering to meet its future financing needs, but if it is unable to find satisfactory arrangements, it may have to resort to dilutive sources of funding.

## Company description: Leading discovery in ion channel biology

Bionomics was publicly listed in 1999, and has a history of both internal development and in-licensing of assets. In addition to its research activities, the company wholly owns two contract research organizations (CROs), Neurofit and Prestwick Chemical, both of which generate revenue.

The company's focus is on the development of drugs targeting ion channels. These proteins are important for a wide area of biology and are implicated in virtually every disease space. However, the company has a strategic focus on developing novel treatments for neuropsychiatric disorders. The main function of these channels is to allow ions such as sodium and potassium (among others) into and out of cells and across intracellular membranes. This process is so central to biology that it is present in all forms of life and in every cell in the body. However, the ubiquity of ion channels is only understated by their diversity. There are hundreds of genes in the genome devoted to ion channels, many of which code ion channel subunits that interact in various combinations to form thousands of potential channels. These proteins are important to a wide array of physiological functions such as metabolism, neurotransmission, cell signalling and immunology. Therefore the opportunity to develop drugs targeting ion channels is immense. Historically, a large number of drugs for neurological and neuropsychiatric disorders (as well as neurotoxins) target ion channels because their function is central to the transmission of information along neurons.

The company has developed the ionX drug discovery platform to identify novel candidates that target ligand and voltage-gated ion channels. The platform uses proprietary *in vitro* and *in vivo* models to rapidly screen potential drug candidates for ion channel activity. Additionally, the company has developed the MultiCore platform to produce diverse libraries of targeted small molecule drugs. MultiCore combines *in silico* drug design with synthetic techniques to rapidly diversify chemical species into targeted libraries of drugs.

The company's lead compound is BNC210, a novel small molecule modulator of the α7 nicotinic acetylcholine receptor with a novel anxiolytic mechanism. It is being developed in a Phase IIb for PTSD. The company has also developed two compounds, BNC101 and BNC105, with potential efficacy in oncology. Oncology is outside of the company's core focus on leveraging its ion channel development platform, and it intends to partner these assets for further development. BNC101 is an anti-LGR5 antibody in Phase I for colon cancer targeting cancer stem cells with a novel mechanism of action. BNC105 is a vascular disrupting agent that previously failed to meet its primary endpoints in a Phase II study in renal cell carcinoma, and is not included in this report. However, it is in investigator-sponsored trials for chronic lymphocytic leukaemia and melanoma (in combination with Keytruda). Additionally, Novartis is financing a biomarker study using samples collected during the previous trial. Finally, the company has a collaboration with Merck using an undisclosed compound identified with ionX for the treatment of cognitive impairment associated with Alzheimer's, and a Phase I trial was initiated in February 2017.

**Exhibit 1: Bionomics development programmes**

| Programme | Phase | Partner | Target | Indication |
|---|---|---|---|---|
| BNC210 | Phase IIb | N/A | α7 nicotinic acetylcholine receptor | PTSD |
| BNC101 | Phase I | N/A | LGR5 | colon cancer |
| BNC105 | Phase II | Novartis | Vascular disrupting agent | CLL and melanoma |
| Undisclosed | Phase I | Merck | Undisclosed | cognitive disorder |

Source: Bionomics

## BNC210

BNC210 is a negative allosteric modulator of the α7 nicotinic acetylcholine receptor. The drug was previously licensed by Ironwood Pharmaceuticals in 2012, which took the programme through Phase I, but in 2014 this agreement was mutually terminated (although Ironwood retains single-digit royalty rights). The drug is currently in a Phase IIb for PTSD, although if this trial is successful, the drug may be applicable to a broader set of anxiety-centered disorders such as generalized anxiety disorder (GAD), panic disorder (PD), and anxiety secondary to other psychiatric disorders. The molecule was previously investigated in an exploratory Phase IIa trial for GAD. We expect the drug to be protected via composition of matter patents in the US and Europe until approximately FY33, assuming full patent term extensions.

Nicotinic acetylcholine receptors are ligand-gated ion channels opened by the neurotransmitter acetylcholine and so named because they are activated by the nicotine found in tobacco. Each channel is composed of five subunits, and there are 16 different subunits that are variously combined in a multitude of combinations. However, the α7 nicotinic acetylcholine receptor is composed solely of five α7 subunits. The α7 receptor is found in the brain and widely expressed across different structures, and is one of the major subtypes associated with the cognitive effects of nicotine (although other forms have been implicated in the addictive aspects of the drug).

One of the highest concentrations of acetylcholine-releasing neurons (the cholinergic system) in the brain is in the basal forebrain. Of particular importance for anxiety is a region of the basal forebrain called the nucleus accumbens, associated with motivation, arousal and focus. However, the neurons of the basal forebrain project into many parts of the brain and have direct impacts on functions such as perception, memory and cognition. One region where these neurons project is the amygdala, a region important for developing emotional memories, which has been widely studied for its role in fear-based conditioning. The α7 receptor is found on excitatory (glutamatergic) neurons of the amygdala.[1] A reasonable hypothesis behind the anxiolytic activity of drugs inhibiting this receptor such as BNC210 is that the α7 receptor serves as a bridge between the cognitive state of arousal and the negative hyper-stimulatory effects of anxiety. This notion is supported by the fact that nicotine exposure strongly desensitises many acetylcholine receptor subtypes on inhibitory neurons but the excitatory α7 receptor remains intact,[2] potentially leading to overstimulation and the anxiety associated with nicotine withdrawal. Other anxiolytic drugs such as benzodiazepines work by directly engaging the inhibitory (GABAergic) nervous system which, as the name would suggest, supresses neural hyperactivity, but the entire central nervous system is depressed leading to drowsiness, cognitive impairment and loss of co-ordination.

Additionally, the α7 receptor is present in the hippocampal formation on both excitatory and inhibitory neurons. The hippocampus is the region of the brain important for narrative memory. The chronic activation of the cholinergic system by nicotine from smoking is known to increase the concentration of nicotinic receptors in the dentate gyrus,[3] part of the hippocampal formation. There is evidence to suggest that activity in the hippocampus is associated with anxiety-related behaviours.[4]

---

[1] Gotti C, et al. (2006) Brain nicotinic acetylcholine receptors: native subtypes and their relevance. *Trends in Pharmacol Sci* 27, 482-491.

[2] Fenster CP, et al. (1997) Influence of Subunit Composition on Desensitization of Neuronal Acetylcholine Receptors at Low Concentrations of Nicotine. *J Neurosci* 17, 5747-5759.

[3] Perry DC, et al. (1999) Increased Nicotinic Receptors in Brains from Smokers: Membrane Binding and Autoradiography Studies. *J Pharmcol Exp Therapeutics* 289, 1545-1552.

[4] Bannerman DM, et al. (2004) Regional dissociations within the hippocampus—memory and anxiety. *Nerosci Biobeavioral Rev* 28, 273-283.

As a negative allosteric modulator, BNC210 reduces the ion flux through the α7 receptor without preventing ligand binding and activation. This in effect reduces the intensity of these cholinergic signals without preventing their transmission. The trade-off with negative allosteric modulation in comparison to antagonism is that modulators are less potent, but that many unwanted side effects can potentially be avoided by not completely inhibiting the pathway.

## Post-traumatic stress disorder (PTSD)

PTSD is a disorder that occurs in patients following a traumatic experience, in which intrusive thoughts or feelings interfere with daily life for more than a month following the event. PTSD is classified in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) as a trauma- and stressor-related disorder, a shift from previous classifications that labelled PTSD as an anxiety disorder. This highlights the fact that although anxiety is a significant component of the disorder, the differential etiology of PTSD necessitates unique treatment protocols. According to the DSM-5, to be diagnosed with PTSD sufferers have to exhibit symptoms across four categories: intrusions, avoidance, mood and cognition and arousal (see Exhibit 2).

**Exhibit 2: Diagnostic criteria for PTSD**

| Intrusions (1+ symptoms present) | Avoidance (1+ symptoms present) | Mood & cognition (2+ symptoms present) | Arousal (2+ symptoms present) |
|---|---|---|---|
| Recurring nightmares, flashbacks | Avoid people, places, things | Alterations in cognition (negative) | Exaggerated startle response |
| Intrusive memories (images) | Avoid thoughts/conversations | Alterations in mood (negative) | "On guard" all the time |
| Physiological and psychological reactions to reminders | | Loss of interest | Irritability or angry outbursts |
| | | Social withdrawal | Difficult sleeping, concentrating |

Source: DSM-5

PTSD is a common disorder: The National Comorbidity Survey Replication study found that 3.5% of participants in the US had experienced the symptoms of PTSD in the previous year, and the lifetime prevalence was 6.8% (based on DSM-4 criteria). The disorder is more common in women by a wide margin, with a lifetime prevalence of 9.7% compared to 3.6% in men. However, the disorder is frequently underdiagnosed and undertreated. One study found that approximately half of PTSD patients are missed in a routine clinical setting, even when clinicians were provided with PTSD screening materials.[5] Other research on Afghanistan war veterans found that only 48% of those diagnosed with PTSD received any mental health service and only 24% were treated with psychiatric medication.[6]

There are a number of shortcomings associated with available treatments for PTSD. There are currently only two products approved for the disorder: paroxetine and sertraline, both SSRIs with the associated side effects and only modest effect size. Based on the Cohen's d statistic, where 0.2 is considered a small effect size, 0.5 is considered moderate and 0.8 is considered large,[7] both approved therapies have only small to moderate impacts (see Exhibit 3). Among other pharmacological therapies, some of which are used off-label after SSRI failure, meaningful effect sizes were generally seen only in small trials (the effect size for topiramate is heavily skewed by a 67-patient trial in Iran where the drug was tested as adjunct therapy rather than monotherapy for PTSD). Psychotherapies of various forms appear to be the only type of therapy today with consistent results; however, there is the issue of compliance as psychotherapies require frequent office visits.

[5] Zimmerman M and Mattia JI (1999) Is posttraumatic stress disorder underdiagnosed in routine clinical settings? *J Nerv Ment Dis* 187, 420-428.

[6] Hoge CW, et al. (2014) PTSD Treatment for Soldiers After Combat Deployment: Low Utilization of Mental Health Care and Reasons for Dropout. *Psych Serv* 65, 997-1004.

[7] Cohen J, Psychological Bulletin, 0033-2909, July 1, 1992.

**Exhibit 3: Effect size for various PTSD therapies**

| Class | Drug | Sample size | Effect size (Cohen's d) |
|---|---|---|---|
| SSRI | Paroxetine | 1,070 | 0.42 |
| | Sertraline | 1,123 | 0.26 |
| | Fluoxetine | 889 | 0.31 |
| | Citalopram | 35 | -0.34 |
| SNRI | Venlafaxine | 687 | 0.12 |
| TCA | Amitriptyline | 33 | 0.9 |
| | Imipramine | 41 | 0.24 |
| MAOI | Brofaromine | 48 | 0.58 |
| | Phenelzine | 37 | 1.06 |
| Anti-psychotic | Olanzapine | 34 | 0.14 |
| | Risperidone | 419 | 0.26 |
| Anti-convulsant | Topiramate | 142 | 0.96 |
| | Divalproex | 85 | 0.06 |
| | Tiagabine | 232 | 0.02 |
| Other pharmacological therapy | Prazosin | 50 | 0.4 |
| | Bupropion | 30 | -0.23 |
| | Mirtazapine | 29 | 0.27 |
| Psychotherapy | Cognitive processing therapy | 299 | 1.4 |
| | Cognitive therapy | 221 | 1.22 |
| | Cognitive behaviour therapy – exposure | 387 | 1.27 |
| | Cognitive behaviour therapy – exposure | 825 | 1.09 |
| | Eye movement desensitisation and reprocessing | 117 | 1.08 |
| | Narrative Exposure Therapy | 227 | 1.25 |

Source: UK NICE National Clinical Practice Guidelines, US Department of Health and Human Services Agency for Healthcare Research and Quality

Interestingly, although widely deployed as anxiolytics, benzodiazepines are contraindicated for PTSD. A meta-analysis published in 2015 of 18 clinical trials and over 5,000 patients found that not only were benzodiazepines ineffective at treating PTSD, they also resulted in worse overall symptoms, worse outcomes to psychotherapy, and an increased risk of developing PTSD if administered immediately following trauma.[8] The side effects of benzodiazepines such as sedation and memory impairment are implicated in interfering with patient progress. Benzodiazepines indiscriminately inhibit neural pathways, including those that are already depressed in PTSD patients. These functions are central to the patient's ability to adapt to the trauma. Moreover the drugs carry addition risks associated with cognitive impairment and severe withdrawal symptoms.

## Phase IIb trial design

Bionomics initiated a Phase IIb study of PTSD in June 2016. The study is a double-blind, randomized, placebo-controlled trial with a target enrolment of 192 PTSD patients. Three doses of BNC210 (150mg, 300mg, 600mg) are being compared against placebo over 12 weeks of twice-daily treatment. The primary endpoint of the study is improvement in Clinician-Administered PTSD Scale for DSM-5 (CAPS-5). CAPS-5 is a battery of 30 questions designed to determine whether the patient meets the criteria for PTSD as defined under the DSM-5 ranked on a scale of zero to four for severity and frequency. Improvement in CAPS-5 is the FDA-approvable endpoint for PTSD.

The trial will also measure the impact of the drug on anxiety using the Hamilton Anxiety Rating Scale (HAM-A), and on depression using Montgomery-Asberg Depression Rating Scale (MADRS) as secondary endpoints. This should provide insight into any other potential indications for which the drug could be useful. The company has announced that it expects to have top-line data in H218.

[8] Guina J, et al. (2015) Benzodiazepines for PTSD: A Systematic Review and Meta-Analysis. *J Psych Pract* 21, 281-303.

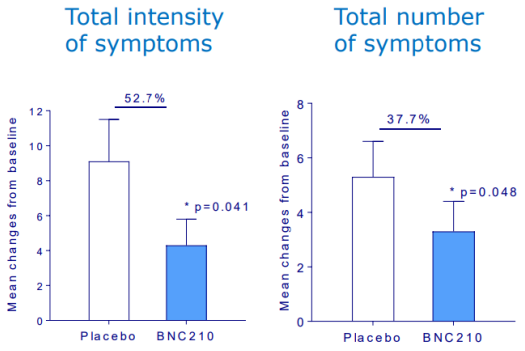
# Previous clinical results

## Induced panic Phase I

BNC210 was used in a Phase I clinical trial to reverse the symptoms of chemically induced panic in healthy volunteers. Panic is a feature of many anxiety-related disorders, including PTSD, and this study serves as an initial readout of the drug's anxiolytic activity in humans.

The trial was randomized, double blind, with a crossover design. Patients first received 2,000mg of BNC210 or placebo. Seven hours later panic was induced by the injection of CCK-4, a hormone than can induce severe anxiety. Panic was successfully induced in 15 of the patients, who were then evaluated for symptoms, and it was found that BNC210 successfully reduced both the number and severity of panic-related symptoms (p=0.041 and p=0.048, Exhibit 4). Additionally, data from the broader safety set of patients (n=59, including those that did not panic) showed a significant reduction in the serum concentration of the stress-related hormones adrenocorticotropic hormone and cortisol following CCK-4 (p=0.04). The results from this trial are important because they provided the first basis for the claims that BNC210 has anxiolytic properties in humans.

**Exhibit 4: BNC210 reduces intensity and number of panic symptoms.**




Source: Bionomics. Note: Panic scored on Panic Symptom Scale.

## Generalized anxiety disorder (GAD) Phase IIa

BNC210 previously underwent a Phase IIa trial for GAD. GAD is defined in the DSM-5 as excessive anxiety or worry about a variety of topics that occurs more often than not for at least six months.[9] The disorder must interfere with daily life functions and have three or more of the following manifestations (one for children): restlessness, fatigue, difficulty concentrating, irritability, muscle tension, sleep disturbance. The symptoms of GAD are similar to PTSD, as both disorders have elements of anxiety and unease. However, as a rule GAD is easier to treat pharmacologically than PTSD. There are many drugs that are considered effective for GAD, including SNRIs such as duloxetine and SSRIs such as escitalopram. Benzodiazepines are not contraindicated for GAD as they are for PTSD, although they are limited to the second line typically due to side effects. Although there is room for improvement in the treatment of GAD, we assume that the shift in development to PTSD was made as it represents a greater unmet medical need and a less competitive environment.

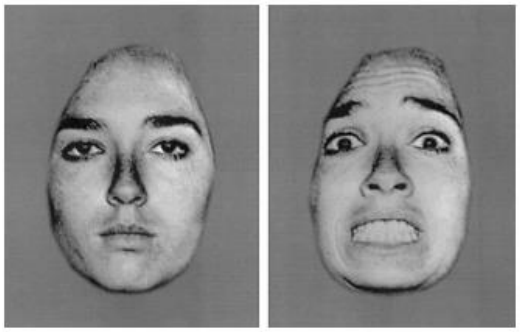
The GAD Phase IIa study enrolled 24 patients with a GAD diagnosis and examined two doses of BNC210 (300mg and 2,000mg) compared to lorazepam (1.5mg) and placebo in a double-blind, four-way crossover design. The primary endpoints of the study were to measure the change in cerebral perfusion and activation of the amygdala in response to the Emotional Faces Task. Cerebral perfusion, as measured by arterial spin labelling, was significantly changed at both doses ($p<0.05$), which indicates that the drug is potentially having an impact on cognition.

[9] American Psychiatric Association (2013) *Diagnostic and Statistical Manual of Mental Disorders* 5th ed. Arlington, VA, American Psychiatric Association.

In the emotional faces task, patients are presented with an image of a neutral face or a fearful face and asked to label its sex (Exhibit 5). Activity in the amygdala was measured using fMRI and compared between different face emotions. Activation of the amygdala is known to be associated with GAD and anxiolytic drugs are known to inhibit this activity.

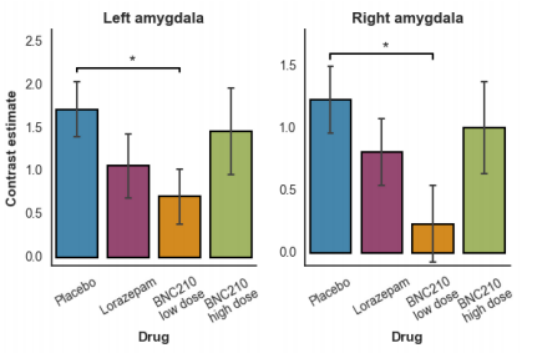
The study showed that the low dose of BNC210 significantly inhibited activation of the left and right amygdalae in response to the fearful faces (p=0.027, Exhibit 6). Interestingly, the higher dose of BN210 did not show a statistically significant effect on amygdala activation compared to placebo (p=0.33). Lorazepam trended towards lower activation, but did not reach statistical significance (p=0.086 and p=0.19 in left and right hemispheres respectively.

**Exhibit 5: Example of faces from emotional faces task**



Source: Bionomics

**Exhibit 6: Reduction in amygdala activation from low-dose BNC210**

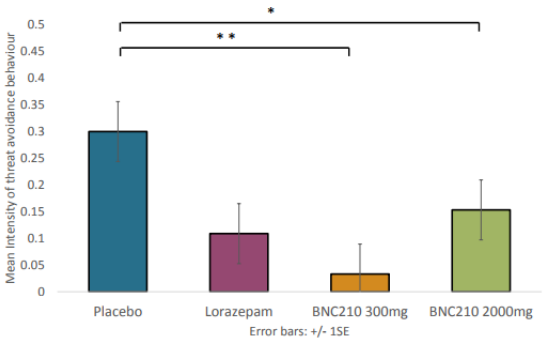



Source: Bionomics. Note: *p<0.05.

Additionally, the study investigated the connectivity between the left amygdala and the anterior cingulate cortex. The anterior cingulate cortex is a region of the brain associated with autonomic responses to emotion such as quickening heart rate and rise in blood pressure. The connection between these regions of the brain is elevated in patients with clinical anxiety.[10] The study found an almost complete depression in the connectivity to this region in response to fearful faces (p=0.04) at the low dose, with no change seen with placebo or lorazepam.

A secondary endpoint was the Joystick Operated Runway Task (JORT) designed to measure threat avoidance. In this test, patients played a simple Pac-Man style game in which they were being pursued. In half of the trials, an electric symbol was presented on the screen to indicate that they would be shocked if caught by the pursuer. The study found a significant reduction in the threat avoidance behaviour of these patients following both low (p=0.007) and high doses (p=0.033) of BNC210 (although it was more pronounced in the low dose).

**Exhibit 7: Threat avoidance behaviour in the JORT**




Source: Bionomics. Note: *p<0.05, **p<0.01.

[10] Robinson, O. J. et al. (2014) The dorsal medial prefrontal (anterior cingulate) cortex–amygdala aversive amplification circuit in unmedicated generalised and social anxiety disorders: an observational study. *Lancet Psychiatry* 1, 294–302.

This study provided several useful pieces of information. It established that regions of the brain that are involved in anxiety can be positively affected by BNC210, and it showed that the drug could then induce behaviour changes as demonstrated by the JORT. These results respectively provide a physiological and a functional basis to support the potential anxiolytic activity of BNC210. However, a key piece of information that was absent from the results was any direct assessment of the patient's anxiety symptoms. Drugs that have been approved for this indication have used semi-quantitative symptom ratings such as the HAM-A scale for approval and a majority of trials at this stage (Phase IIa) in GAD that we have been able to find have either an HAM-A assessment or some other symptom rating scale as the primary endpoint following a period of administration, and this type of assessment would not be appropriate in a single-dose study like this. The initial protocol for the trial did include a secondary endpoint of change in the affective self-report, a patient-reported measure of mood, but these results were never presented. We should note, though, that Bionomics' Phase IIa trial design is well founded and both Janssen and GSK have run small clinical trials using fMRI and the emotional faces test.

Another limitation of this study is that a clear dose response was not seen. The 2,000mg dose of BNC210, which showed efficacy in the Phase Ib induced panic study, showed very little effect. Bimodal dose response curves could signal issues with the pharmacology of the drug and these effects may become more pronounced with prolonged dosing. That said, U-shaped dose response curves have been observed in fMRI studies of widely used psychopharmacology drugs such as lithium[11] and amphetamine.[12] However, these have not limited the widespread use of the drugs. These hypothetical limitations to BNC210 do not necessarily preclude the utility or approvability of the drug.

## BNC101

BNC101 is a monoclonal antibody targeting the LGR5 protein (leucine-rich repeat-containing g-protein-coupled receptor 5). The drug was originally developed at Biogen and subsequently acquired by Bionomics in the 2012 acquisition of Biogen spin-out Eclipse Therapeutics. The company owes certain undisclosed earnouts on the programme associated with the merger. These earnouts are recorded as a A$14.6m contingent consideration liability on the balance sheet. The drug is currently in a Phase I trial for colorectal cancer. Bionomics stated that it is seeking a partner to further develop the drug as oncology is outside its core focus. Assuming full patent term extensions, we expect the product to have protective intellectual property until 2037.

The biology of LGR5 has only been investigated recently, as previously the function of the protein and its ligands were poorly understood. It was (along with LGR4) identified as an effector of the Wnt pathway, which is important for differentiation during fetal development. Wnt signalling has also been implicated in cancer, as many cancer phenotypes display "de-differentiation" in which cancer cells revert to more primordial forms. This process has particular importance to areas of research focusing on cancer stem cells, which are based on the premise that there is a subpopulation of cancer cells that drive propagation of the tumour. LGR5 has been identified as a marker for stem cells in the gut, and is overexpressed in colorectal cancer (CRC), among others.[13] Antibodies against LGR5 have been showed to identify what are believed to be cancer stem cells in CRC

[11] Hübers A, et al. (2014) Acute effects of lithium on excitability of human motor cortex. *Clin Neurophys* 125, 2240-2246.

[12] Tipper CM, at al. (2005) Processing efficiency of a verbal working memory system is modulated by amphetamine: an fMRI investigation. *Psychopharmacol (Berl)* 180, 634-643.

[13] Nakata S, et al. (2014) Emerging role for leucine-rich repeat-containing G-protein-coupled receptors LGR5 and LGR4 in cancer stem cells. *Cancer Manag Res* 6, 171-180.

tumours.[14] LGR5 is not essential to cancer survival and it has been demonstrated that LGR5+ cells can readily convert into LGR5- cells and remain viable.[15] However, there are strong negative correlations between LGR5 expression levels and survival,[16] and either the elimination of the LGR5+ cancer stem cells or conversion of these cells to LGR5- may result in patient benefits.

It should be noted that the research supporting LGR5's role in tumorigenesis is very preliminary, and there is little research available into this protein as a therapeutic drug target. BNC101 is the only drug targeting this protein in the clinic, to our knowledge. We only know of one preclinical development programme that targets LGR5 (MCLA-158 from Merus, although it also targets EGFR) and Genentech previously published the results of an anti-LGR5 antibody-drug conjugate in mouse models.[17] Moreover, there is a risk that BNC101 may be associated with significant adverse effects. LGR5 is expressed on healthy stem cells of the gut as well as other organs such as the ovaries, kidneys and hair, and targeting these tissues may cause undesirable effects.

## CRC market

Colorectal cancer (CRC) is one of the most common cancers worldwide, with approximately 1.36 million cases per year.[18] Incidence in the US and EU is similar at around 40 per 100,000 person-years. The prognosis of the disease is highly dependent upon the stage at which the cancer is detected, highlighting the need for improved CRC screening. According to the American Cancer Society, the five-year survival rate for patients who have their cancer detected in the localized stage is 90%, compared to just 14% when there are distant metastases.[19] Despite significant efforts to detect disease during early stages, approximately one-third of patients will be diagnosed with or develop metastatic disease.[20]

There are a range of treatments available to patients with advanced CRC. Regarding chemotherapy, leucovorin, 5-FU, platinum drugs, and nucleoside analogues are all used together in various combinations (for instance the FOLFIRI regimen: leucovorin, 5-FU, and irinotecan). Chemotherapy is frequently combined with targeted therapies, of which there are many, but dominated by VEGF inhibitors such as Avastin (bevacizumab, Roche), and EGFR inhibitors such as Erbitux (cetuximab, Eli Lilly).

There are over 300 ongoing clinical programmes targeting CRC across an array of mechanisms.[21] The general paradigm of CRC development is the continued shift into genetically defined cancer subsets. The PD-1 and PD-L1 inhibitors Keytruda (pembrolizumab, Merck) and Tecentriq (atezolizumab, Roche) are in Phase III and Imfinzi (durvalumab, AstraZeneca) is in Phase II. Measurements of PD-L1 expression in CRC vary but have been reported as high as 82%. Keytruda is currently available for CRC patients with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) forms of the disease following progression on fluoropyrimidine, oxaliplatin, and irinotecan. Array BioPharma is currently in testing for the combination therapy of MEK inhibitor,

[14] Kemper K, et al. (2012) Monoclonal Antibodies Against Lgr5 Identify Human Colorectal Cancer Stem Cells. *Stem Cells* 30, 2378-2386.

[15] Kobayashi S, et al. (2012) LGR5-Positive Colon Cancer Stem Cells Interconvert with Drug-Resistant LGR5-Negative cells and are Capable of Tumor Reconstitution. *Stem Cells* 30, 2631-2644.

[16] Wu XS, et al. (2012) Lgr5 is a potential marker of colorectal carcinoma stem cells that correlates with patient survival. *Wold J Surg Oncol* 10, 244.

[17] Junttila MR, et al. (2015) Targeting LGR5+ cells with an antibody-drug conjugate for the treatment of colon cancer. *Sci Trans Med* 7, 314ra186.

[18] International Agency for Research on Cancer.

[19] American Cancer Society (2017) *Colorectal Cancer Facts & Figures 2017-2019*.

[20] Grothey A, et al. (2016) Current Options for Third-Line Treatment of Metastatic Colorectal Cancer. *Clin Adv Hemeatol Oncol* 14, s3.

[21] EvaluatePharma.

encorafenib, a BRAF inhibitor and cetuximab, which has shown promising results in BRAF-mutated cancer (estimated at 10-15%). Similarly, Merck and Exelixis are developing the MEK inhibitor Cotellic (cobimetinib) in combination with the BRAF inhibitors Zelboraf (vemurafenib) in Phase III.

### Phase I clinical trial

BNC101 is currently in Phase I testing for patients with metastatic CRC. The trial is a dose-escalation study with a target enrolment of 21 patients, and in October 2017 the company announced that it was fully enrolled.

The clinical trial has two arms. The first arm is to investigate BNC101 as a monotherapy in patients who have had two prior lines of chemotherapy, and the second arm will examine the drug in combination with FOLFIRI in single refractory patients. The first arm of the study has been completed and identified 15mg/kg as the optimal dose for further studies. No dose-limiting toxicities or safety issues were reported.

In addition to dosing, the study will provide an array of biomarkers to investigate the mechanism of action of BNC101. These include both markers of immune system engagement as well as profiles of tissue from tumour biopsy. The company has already announced that these biopsy samples have revealed that the drug is performing as expected and is engaging LGR5 on colon cancer cells. Additionally, the drug modulated Wnt signalling as expected with effects on “cell adhesion pathway panels and in immuno-oncology associated gene groups”. The target completion date for the study is April 2018.

## Merck collaboration

Bionomics has a collaboration agreement with Merck, in which it has licensed its ionX and MultiCore development platforms for the discovery of drugs for cognitive dysfunction associated with diseases of the central nervous system. The company announced in February 2017 that Merck had advanced the first of these products to Phase I clinical trials for cognitive dysfunction associated with Alzheimer’s disease. Bionomics previously developed BNC375, a positive α7 nicotinic acetylcholine receptor modulator, for the same indication and the drug was licensed to Merck under this agreement. However, it is unclear whether this molecule, a derivative, or unrelated species is currently being progressed at Merck. The positive modulation of the cholinergic system makes sense in this context because nicotine is well known to enhance cognition, memory and to improve attention in patients with Alzheimer’s disease.[22] The specific modulation of the α7 receptor may preserve many of these effects and lesson the addictive potential of a drug compared to nicotine.

The total value of the deal is US$506m in upfront, research and milestone payments, as well as royalties on any drugs approved under the collaboration. The company received a US$20m upfront payment on signing the agreement and a US$10m milestone on initiation of the Phase I trial, as well as additional research support. Although the available details are scarce, this is a significant validation of the company’s development platform.

This is the second such collaboration Bionomics has had with Merck. Previously, it signed a similar agreement in 2013 to develop drugs for chronic and neuropathic pain. This previous deal was worth up to US$172m in upfronts and royalties.

Merck further signaled its confidence in the company when it took a 4.5% ownership stake in Bionomics in 2015.

[22] Warburton DM (1992) Nicotine as a cognitive enhancer. *Prog Neuropsychopharmacol Biol Psychiatry* 16, 181-191.

## Sensitivities

Bionomics is subject to the typical risks associated with clinical-stage pharmaceutical companies. There is significant clinical risk for both BNC210 and BNC101. BNC210 is being tested for PTSD, which is a difficult-to-treat disorder and has a different treatment profile in which currently available anxiolytics such as benzodiazepines are contraindicated. However, the limited efficacy of benzodiazepines is likely a result of its sedating and memory impairing side effects, and the novel mechanism of action of BNC210 may potentially circumvent these issues and mitigate these risks. This being said, the drug has no prior clinical exposure to PTSD. The Phase IIa GAD trial was supportive of anxiolytic activity, but was largely exploratory in nature. It is unclear why the compound showed a non-linear dose response in this trial, although this is not necessarily a limitation to its approvability if patients can be dosed stably over the longer term. If the drug is approved, there may be headwinds associated with targeting this market, because PTSD sufferers are both underdiagnosed and undertreated in practice.

We consider the BNC101 programme high risk because its anti-cancer mechanism of action has not been previously tested. There is encouraging basic research centering on LGR5 and its role in CRC, but this cannot forego the inherent risks of medical innovation. If successful, the drug could be an essential element of a new treatment paradigm. This being said, there is significant competition in the CRC market, ever increasing with a large number of ongoing clinical trials.

Finally, Bionomics carries the risks associated with being a pre-commercial company, as it will require additional financing to bring its drugs to market. We currently model the company needing A$35m in additional cash to reach sustained profitability in FY22, which we include as illustrative debt in FY20. We expect this need to be met wholly or in part through out-licensing its assets. There may be additional opportunities similar to the collaboration with Merck to license the company's ionX or MultiCore platforms. However, if the company is unable to secure a contract of significant enough size or if it fails to receive a milestone from the Merck collaboration, it may need to seek dilutive sources of funding.

## Valuation

We arrive at an initial valuation of A$418.7m or A$0.87 per basic share. Our valuation is based on a risk-adjusted NPV analysis using a 12.5% discount rate. Our model incorporates a series of assumptions regarding the products and markets, outlined in Exhibit 8. We model the full commercialisation of BNC210 for PTSD and BNC101 for CRC, even though there is a high probability of licensing these programmes, as this represents the value to a potential partner and we assume that any deals will be made on an NPV-neutral (or better) basis. Our pricing assumptions are made based on existing competitors, and adjusted for future price growth. BNC210 is priced at approximately the midrange for new branded neuropsychiatric medications (eg Fetzima US$2,500, Trintellix US$3,500, Rexulti US$8,500).[23] BN101 is priced in line with Ibrance (palbociclib, Pfizer). In both cases these prices are adjusted for future price growth. In addition, we model commercialisation in the US and Europe as the primary markets.

[23] WAC based on most recent data from EvaluatePharma

**Exhibit 8: Valuation assumptions**

| Programme | Development | Market | Pricing | Costs |
|---|---|---|---|---|
| BNC210 | 190 pts Phase II, 850 pts Phase III, modelled on Paxil approval. US20,000/pt | Diagnosed PTSD (50%), amenable to medication (25%), peak penetration of 5% | US$4,900/€3,700, 25% gross/net discount | 8% COGS (including Ironwood royalty), 10% cost of selling, US$5m overhead per region |
| BNC101 | 170 pts Phase II, 800 pts Phase III, based on Ibrance. US$50,000 per pt | Advanced disease (33%), 10% peak penetration | US$88,000/€54,000, 25% gross/net discount | 12% COGS (including Eclipse earnouts), 10% cost of selling, US$5m overhead per region |
| Merck collaboration | Phase I, II, III complete in FY18, FY20, FY23 | Unknown but associated with Alzheimer's | $340 total milestones, $140m development and regulatory, 5% royalty | None |
| CRO business | N/A | 2% growth y-o-y | N/A | 6% operating margin |

Source: Edison Investment research, Bionomics reports. Note: pts=patients

We assign a 30% probability of success to BNC210 in PTSD, which is average for drugs at this stage with supporting clinical data but without having previously met approvable endpoints. If the programme is successful in its ongoing Phase II PTSD trial, we expect this value to substantially increase (50-70%), and we may potentially add other indications such as GAD at that time. Our probability of success for BNC101 in CRC is 10%, because the drug and its mechanism of action are untested in the clinic.

We include the Merck collaboration in our valuation, although we do not have the details for the product. We include US$140m in clinical and regulatory milestones ($10m, $30m, $50m, $50m on Phase I, II, and III results and approval), and an additional US$200 in sales milestones post approval. The first of these milestones is currently included in FY18 on positive Phase I results, although this may change if the timing of the trial or the terms of the deal are different from our assumptions. We conservatively assign a 10% probability of success, based on the high risks of developing drugs for Alzheimer's and cognitive disorders. Although we do not have precise details on the target indication, we assume it will compete in a market similar to Aricept (donepezil, Eisai), which had sales of US$3.9bn before going generic. For the purposes of our model we conservatively assume a 5% royalty on peak sales of approximately A$1.8bn, and we expect to adjust this valuation as details from the programme are released.

**Exhibit 9: Valuation of Bionomics**

| Programme | Market | Prob. of success | Launch year | Peak sales (A$m) | Margin/ royalty | rNPV (A$m) |
|---|---|---|---|---|---|---|
| BNC210 | PTSD | 30% | 2022 | 916.3 | 54% | 329.7 |
| BNC101 | CRC | 10% | 2025 | 1103.3 | 55% | 75.6 |
| Merck collaboration milestones | Alzheimer's associated cognitive dysfunction | 10% | 2025 | 1821.0 | 5% | 16.2 |
| CRO business | | | | 6.6 | 4% | 1.2 |
| Unallocated costs | | | | | | (16.0) |
| Total | | | | | | $406.8 |
| Net cash and equivalents (H118) ($m) | | | | | | $11.9 |
| Total firm value ($m) | | | | | | $418.7 |
| Total shares (m) | | | | | | 481.5 |
| Value per share ($) | | | | | | $0.87 |
| Dilutive warrants and options (m) | | | | | | 52.34 |
| Total diluted shares | | | | | | 533.8 |
| Value per diluted share ($) | | | | | | 0.84 |

Source: Edison Investment research, Bionomics reports

# Financials

Bionomics has historically been a loss-making company, largely driven by research and development expenses. It reported A$24.2m in R&D expenses in FY17, A$11.8m in H118, and we expect this value to increase with the advancement of its clinical programmes. These costs are offset by two current revenue streams: the CRO business, which has a run rate of A$5-6m, and

milestones from the Merck collaboration. The most recent milestone was delivered in February 2017 for the initiation of a Phase I clinical trial associated with the programme. Additionally, we expect a portion of the company's R&D costs to be offset through the Australian Research and Development Tax Incentive programme, which can reimburse the company for up to 43.5% of R&D expenses. The company received A$6.8m from the programme for FY17.

Bionomics ended H118 with A$32.0m in cash and A$20.1m in debt. The largest portion of this debt is a bank loan at 8.9%, with payments starting in November 2018. We expect the company to meet the majority of its future financing needs through the licensing of its clinical assets and leveraging its development platforms. However, we currently record the shortfall in development expenses before profitability as A$35m in illustrative debt in FY20.

## Exhibit 10: Financial summary

| A$'000s | 2015 | 2016 | 2017 | 2018e | 2019e |
|---|---|---|---|---|---|
| 30-June | IFRS | IFRS | IFRS | IFRS | IFRS |
| **INCOME STATEMENT** | | | | | |
| Revenue | 6,827 | 8,143 | 18,606 | 17,500 | 5,100 |
| Cost of Sales | 0 | 0 | 0 | 0 | 0 |
| Gross Profit | 6,827 | 8,143 | 18,606 | 17,500 | 5,100 |
| EBITDA | (15,665) | (15,449) | (3,214) | (6,005) | (27,140) |
| Normalised operating profit | (16,176) | (16,071) | (3,671) | (6,461) | (27,596) |
| Amortisation of acquired intangibles | (1,203) | (1,316) | (1,286) | (1,286) | (1,286) |
| Exceptionals | 532 | 1,131 | 0 | 0 | 0 |
| Share-based payments | (515) | (400) | (504) | (504) | (504) |
| Reported operating profit | (17,362) | (16,656) | (5,461) | (8,251) | (29,386) |
| Net Interest | 85 | (668) | (766) | (694) | (842) |
| Joint ventures & associates (post tax) | 0 | 0 | 0 | 0 | 0 |
| Exceptionals | 0 | 0 | 0 | 0 | 0 |
| Profit Before Tax (norm) | (16,091) | (16,738) | (4,437) | (7,155) | (28,438) |
| Profit Before Tax (reported) | (17,277) | (17,324) | (6,227) | (8,945) | (30,228) |
| Reported tax | 328 | 732 | (523) | 1,920 | 1,277 |
| Profit After Tax (norm) | (15,786) | (16,031) | (4,810) | (5,619) | (27,237) |
| Profit After Tax (reported) | (16,949) | (16,592) | (6,750) | (7,025) | (28,951) |
| Minority interests | 0 | 0 | 0 | 0 | 0 |
| Other comprehensive income | 3,313 | 968 | (114) | 0 | 0 |
| Net income (normalised) | (12,473) | (15,063) | (4,924) | (5,619) | (27,237) |
| Net income (reported) | (13,637) | (15,624) | (6,864) | (7,025) | (28,951) |
| Basic average number of shares outstanding (m) | 418 | 457 | 481 | 505 | 531 |
| EPS - basic normalised (c) | (3.78) | (3.51) | (1.00) | (1.11) | (5.13) |
| EPS - diluted normalised (c) | (3.78) | (3.48) | (0.98) | (1.09) | (5.03) |
| EPS - basic reported (c) | (4.06) | (3.63) | (1.40) | (1.39) | (5.46) |
| Dividend (c) | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| **BALANCE SHEET** | | | | | |
| Fixed Assets | 31,251 | 31,723 | 29,597 | 28,096 | 26,676 |
| Intangible Assets | 27,416 | 28,504 | 26,595 | 25,229 | 23,943 |
| Tangible Assets | 3,451 | 2,835 | 2,618 | 2,484 | 2,350 |
| Investments & other | 384 | 384 | 384 | 384 | 384 |
| Current Assets | 37,881 | 58,086 | 54,478 | 50,410 | 22,899 |
| Stocks | 410 | 439 | 426 | 426 | 426 |
| Debtors | 9,069 | 11,003 | 9,893 | 9,758 | 9,825 |
| Cash & cash equivalents | 26,558 | 45,450 | 42,874 | 38,940 | 11,362 |
| Other | 1,844 | 1,194 | 1,286 | 1,286 | 1,286 |
| Current Liabilities | (13,706) | (11,386) | (13,889) | (6,885) | (8,431) |
| Creditors | (6,466) | (5,855) | (3,673) | (5,231) | (6,777) |
| Tax and social security | 0 | 0 | 0 | 0 | 0 |
| Short term borrowings | (5,460) | (2,732) | (8,496) | 0 | 0 |
| Other | (1,780) | (2,799) | (1,720) | (1,654) | (1,654) |
| Long Term Liabilities | (23,460) | (34,260) | (29,733) | (37,430) | (35,401) |
| Long term borrowings | (9,317) | (18,437) | (10,014) | (19,706) | (19,706) |
| Other long term liabilities | (14,143) | (15,824) | (19,719) | (17,724) | (15,695) |
| Net Assets | 31,966 | 44,163 | 40,454 | 34,191 | 5,744 |
| Minority interests | 0 | 0 | 0 | 0 | 0 |
| Shareholders' equity | 31,966 | 44,163 | 40,454 | 34,191 | 5,744 |
| **CASH FLOW** | | | | | |
| Op Cash Flow before WC and tax | (15,665) | (15,449) | (3,214) | (6,005) | (27,140) |
| Working capital | 17,290 | (327) | 51 | 1,408 | 2,145 |
| Exceptional & other | 3,310 | 417 | 1,723 | (1,674) | (3,375) |
| Tax | 0 | 0 | 0 | 0 | 0 |
| Net operating cash flow | 4,936 | (15,360) | (1,440) | (6,271) | (28,370) |
| Capex | (846) | (197) | (248) | (323) | (323) |
| Acquisitions/disposals | (391) | 69 | 0 | 0 | 0 |
| Net interest | 941 | 1,232 | 1,201 | 1,204 | 1,115 |
| Equity financing | 269 | 28,222 | 144 | 283 | 0 |
| Dividends | 0 | 0 | 0 | 0 | 0 |
| Other | 0 | 0 | 0 | 0 | 0 |
| Net Cash Flow | 4,908 | 13,967 | (342) | (5,106) | (27,578) |
| Opening net debt/(cash) | (6,856) | (11,781) | (24,281) | (24,364) | (19,234) |
| FX | 17 | (9) | (10) | (24) | 0 |
| Other non-cash movements | 0 | (1,457) | 435 | 0 | 0 |
| Closing net debt/(cash) | (11,781) | (24,281) | (24,364) | (19,234) | 8,344 |

Source: Company accounts, Edison Investment Research

| Contact details | Revenue by geography |
|---|---|
| 31 Dalgleish Street<br>Thebarton SA 5031<br>Australia<br>+618 8354 6100<br>www.bionomics.com.au | N/A |

**Management team**

| CEO & Managing Director: Deborah Rathjen | CFO: Steven Lydeamore |
|---|---|
| Dr Rathjen joined Bionomics in 2000 from Peptech, where she was general manager of business development and licensing. She was a co-inventor of Peptech's TNF technology and leader of the company's successful defence of its key TNF patents against a legal challenge by BASF. Dr Rathjen has significant experience in company building and financing, mergers and acquisitions, therapeutic product research and development, business development, and licensing and commercialisation. | Mr Lydeamore has senior executive experience spanning Asia Pacific, Europe, Latin America and North America in finance, business development, mergers and acquisitions, sales and marketing, manufacturing, and research and development. He worked in various finance roles for F.H. Faulding & Co in Australia over a 10-year period followed by four years in the US at Mayne Pharma (USA). For the 11 years prior to joining Bionomics, Mr Lydeamore worked for Aptex, the largest Canada-owned pharmaceutical company, most recently as president of Apobiologix. |
| **Chairman: Errol De Souza** | **Legal Counsel and Company Secretary: Jack Moschakis** |
| Dr De Souza is currently president and CEO of Neuropore Therapies and is the former president and CEO of US biotech companies Biodel (NASDAQ:BIOD), Archemix Corporation and Synaptic Pharmaceutical Corporation (NASDAQ:SNAP). He formerly held senior management positions at Aventis Pharmaceuticals (now Sanofi) and its predecessor Hoechst Marion Roussel Pharmaceuticals. Most recently, he was senior VP and site head of US drug innovation and approval (R&D) at Aventis. | Mr Moschakis has worked in senior legal/company secretary roles in the South Australian electricity industry for over 10 years and has expertise in energy law and energy-related commercial and contractual matters. His most recent position was at mining company, Rex Minerals, where he worked as a legal consultant. Prior to this, Mr Moschakis worked at Thomsons Lawyers, a top-tier Adelaide law firm that is now part of the national law firm, Thomson Geer, as an energy and infrastructure consultant. Mr Moschakis holds a Bachelor of Economics (Adel), Diploma in Law (NSW) and Graduate Diploma in Business Administration (Adel). |

| Principal shareholders | (%) |
|---|---|
| BVF Partners LP | 10.19 |
| Ausbil Investment Management | 6.99 |
| Private Portfolio Managers | 5.47 |
| Biotechnology VLU FD LP | 4.73 |
| CVC Ltd | 4.66 |
| Biotechnology VLU FD II LP | 3.06 |

**Companies named in this report**

Array (ARRY), AstraZeneca (AZN), Biogen (BIIB), Exelixis (EXEL), GlaxoSmithKline (GSK), Ironwood (IRWD), Janssen (JNJ), Merck (MRK), Merus (MRUS), Novartis (NVS), Roche (RHHBY)