

Bionomics (BNO)

RECOMMENDATIONS

| | |
|--------------|---------------|
| Rating | BUY ▲ |
| Risk | Speculative |
| Price Target | \$0.90 |
| Share Price | \$0.52 |

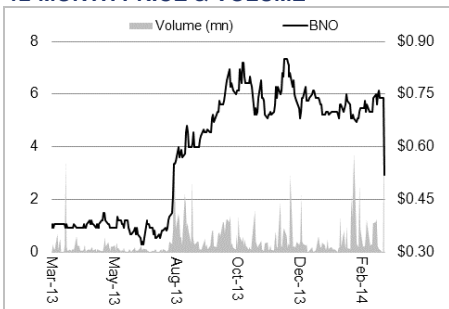
SNAPSHOT

| | |
|------------------|-------------|
| Monthly Turnover | \$8.0mn |
| Market Cap | \$309mn |
| Shares Issued | 417.3mn |
| 52-Week High | \$0.89 |
| 52-Week Low | \$0.32 |
| Sector | Health Care |

BUSINESS DESCRIPTION

Bionomics Limited (BNO) is an Australian biotechnology company focused on the discovery and development of therapeutics for cancer and diseases of the central nervous system. BNO has small molecule and antibody product development programs in the areas of cancer, anxiety, epilepsy and multiple sclerosis. BNO has commercial partnerships with a number of healthcare companies including Merck Serono, GenMab, Athena Diagnostics, LabCorp, Perkin Elmer, and Genetic Technologies Ltd.

12-MONTH PRICE & VOLUME



RESEARCH ANALYST

Stuart Roberts

+612 9250 8913 sroberts@baillieuholst.com.au

Disclosure

The author owns no shares in BNO.

COMPANY REPORT

Biomarkers show the way for BNC105

- Bionomics has what we consider to be favourable Phase II data from its BNC105 cancer drug in metastatic renal cell carcinoma.** In a 148 patient Phase II trial, where BNC105 was combined with Novartis' Afinitor, Progression Free Survival was 4.7 months for BNC105+Afinitor, versus 4.1 months for Afinitor only. The market didn't like this outcome because the comparison wasn't statistically significant, and roughly the same number of patients were Progression-Free at six months in each group. However, on a sub-group analysis, there was some very encouraging news to tell.
- The drug worked well in several patient subgroups.** Those patients with metastases to the liver enjoyed 6.6 months PFS with BNC105+Afinitor versus only 2.8 months for Afinitor. For those that had had a kidney removed, the comparable figures were 7.1 months and 4.1 months. And for patients with a particular kind of tumour pathology called 'Furhman Grade 2' PFS was 6.4 months vs 4.1 months. Future trials enriched for these patients can properly target BNC105 in metastatic renal cell carcinoma.
- The biomarker data is very encouraging.** Bionomics found in the trial that a bank of around seven biomarkers could predict with statistical significance, the level of PFS in the patients. This is important for future studies, because it can allow an 'adaptive design' clinical trial that recruits only patients with biomarkers predictive of efficacy. Adaptive design is set to become commonplace in late stage clinical trials as cancer drugs become more personalised.
- Bionomics has now entered the era of personalised medicine.** There are now a number of cancer drugs that are administered depending on biomarkers. The first great example of this was Herceptin, which only worked in HER2-positive breast cancer. It is now a US\$6.6bn blockbuster for Roche. Other recent drugs have included Roche's Zelboraf metastatic melanoma and Pfizer's Xalkori for non-small-cell lung cancer.
- \$0.90 price target maintained.** We value Bionomics on a probability-weighted DCF basis at \$0.91 base case and \$2.31 optimistic case. Our \$0.90 price target sits at the low point of this range. We anticipate Bionomics being re-rated by the market as the future clinical and commercial programme for BNC105 is unveiled – including (potentially) a licensing deal for BNC105 - and as BNC210 moves forward. We see today's fall in the share price as providing a good buying opportunity.

INVESTMENT SUMMARY

| Year End: 30 June | | 2012 (A) | 2013 (A) | 2014 (E) | 2015 (E) | 2016 (E) |
|-------------------|------|----------|----------|----------|----------|----------|
| Revenue | \$mn | 9 | 11 | 29 | 103 | 105 |
| EBITDA | \$mn | -3.6 | -9.3 | 6.7 | 77.4 | 79.3 |
| EBIT | \$mn | -4.3 | -10.5 | 5.5 | 76.2 | 78.1 |
| Reported Profit | \$mn | -3.1 | -10.0 | 6.3 | 74.7 | 58.0 |
| Adjusted Profit | \$mn | -3.1 | -10.0 | 6.3 | 74.7 | 58.0 |
| EPS (Reported) | ¢ | -0.9 | -2.3 | 1.5 | 17.5 | 13.6 |
| EPS (Adjusted) | ¢ | -0.9 | -2.3 | 1.5 | 17.5 | 13.6 |
| EPS Growth | % | N/A | N/A | N/A | N/A | -22.4 |
| PER (Reported) | x | N/A | N/A | 34.8 | 2.9 | 3.8 |
| PER (Adjusted) | x | N/A | N/A | 34.8 | 2.9 | 3.8 |
| Dividend | ¢ | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| Yield | % | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| Franking | % | 0 | 0 | 0 | 0 | 0 |

Financial summary

| | |
|-----------------------|----------------|
| Code | BNO |
| Analyst | Stuart Roberts |
| Date | 19 March, 2014 |
| Share price | \$0.52 |
| Market capitalisation | \$215m |
| Year end | 30 June |

| | |
|------------------|--------------------------|
| Rating | BUY |
| Price target | \$0.90 |
| Upside/downside | 74.8% |
| Valuation | \$0.909 / \$2.311 |
| Valuation method | Probability-weighted DCF |
| Risk | Speculative |

PROFIT AND LOSS (A\$m)

| Y/e June 30 (A\$m) | FY12A | FY13A | FY14E | FY15E | FY16E |
|-----------------------------|-----------|------------|----------|-----------|-----------|
| Revenue | 9 | 11 | 29 | 103 | 105 |
| EBITDA | -4 | -9 | 7 | 77 | 79 |
| D&A | -1 | -1 | -1 | -1 | -1 |
| EBIT | -4 | -11 | 5 | 76 | 78 |
| Net interest | 1 | 1 | 1 | 2 | 5 |
| Pre-tax profit | -3 | -10 | 6 | 78 | 83 |
| Tax | 0 | 0 | 0 | -4 | -25 |
| NPAT | -3 | -10 | 6 | 75 | 58 |
| Minority interests | 0 | 0 | 0 | 0 | 0 |
| Net profit after minorities | -3 | -10 | 6 | 75 | 58 |

BALANCE SHEET (A\$m)

| Y/e June 30 | FY12A | FY13A | FY14E | FY15E | FY16E |
|---------------------------------|------------|------------|------------|------------|------------|
| Cash | 17 | 22 | 21 | 63 | 80 |
| Current receivables | 0 | 1 | 1 | 1 | 1 |
| Inventories | 0 | 0 | 0 | 0 | 0 |
| Other current assets | 4 | 7 | 4 | 4 | 4 |
| Current assets | 22 | 31 | 26 | 67 | 84 |
| PPE | 1 | 1 | 1 | 1 | 1 |
| Intangible assets | 9 | 22 | 39 | 72 | 113 |
| Other non-current assets | 0 | 0 | 0 | 1 | 1 |
| Non-current assets | 9 | 23 | 40 | 74 | 115 |
| Total assets | 31 | 54 | 66 | 141 | 199 |
| Payables | 3 | 4 | 3 | 3 | 3 |
| Debt | 1 | 1 | 1 | 1 | 1 |
| Other liabilities | 1 | 7 | 12 | 12 | 12 |
| Total liabilities | 5 | 12 | 17 | 17 | 17 |
| Shareholders' equity | 26 | 41 | 49 | 124 | 183 |
| Minorities | 0 | 0 | 0 | 0 | 0 |
| Total shareholders funds | 26 | 41 | 49 | 124 | 183 |
| Total funds employed | 31 | 54 | 66 | 141 | 199 |
| W/A shares on issue | 345 | 374 | 417 | 418 | 420 |

CASH FLOW (A\$m)

| Y/e June 30 | FY12A | FY13A | FY14E | FY15E | FY16E |
|------------------------------|-----------|-----------|------------|------------|------------|
| NPAT plus discontinued ops. | -3 | -10 | 6 | 75 | 58 |
| Non-cash items | 0 | -5 | 1 | 1 | 1 |
| Working capital | 0 | 6 | 4 | 0 | 0 |
| Other operating cash flow | 0 | 0 | 0 | 0 | 0 |
| Operating cashflow | -3 | -9 | 12 | 76 | 59 |
| Capex | 6 | 0 | 0 | 0 | 0 |
| Investments | 0 | -1 | 0 | -1 | 0 |
| Other investing cash flow | 0 | 0 | -13 | -34 | -42 |
| Investing cashflow | 6 | -1 | -13 | -35 | -43 |
| Change in borrowings | -2 | 0 | 0 | 0 | 0 |
| Equity raised | 0 | 16 | 0 | 0 | 0 |
| Dividends paid | 0 | 0 | 0 | 0 | 0 |
| Other financing cash flow | 0 | 0 | 0 | 0 | 0 |
| Financing cashflow | -2 | 16 | 0 | 0 | 0 |
| Net change in cash | 1 | 5 | -1 | 42 | 17 |
| Cash at end of period | 17 | 22 | 21 | 63 | 80 |

EARNINGS (A\$m)

| Y/e June 30 | FY12A | FY13A | FY14E | FY15E | FY16E |
|------------------|-------|-------|-------|-------|-------|
| Net profit (\$m) | -3.1 | -10.0 | 6.3 | 74.7 | 58.0 |
| EPS (c) | -0.9 | -2.7 | 1.5 | 17.9 | 13.8 |
| EPS growth (%) | N/A | N/A | N/A | 1080% | -23% |
| P/E ratio (x) | -56.6 | -19.3 | 34.0 | 2.9 | 3.7 |
| CFPS (c) | -0.8 | -2.5 | 2.8 | 18.2 | 14.1 |
| Price/CF (x) | -61.4 | -20.5 | 18.7 | 2.8 | 3.6 |
| DPS (c) | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| Yield (%) | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% |
| Franking (%) | N/A | N/A | N/A | N/A | N/A |
| EV/EBITDA | -54.0 | -20.9 | 29.0 | 2.5 | 2.5 |
| EV/EBIT | -45.2 | -18.5 | 35.4 | 2.6 | 2.5 |

PROFITABILITY RATIOS

| Y/e June 30 | FY12A | FY13A | FY14E | FY15E | FY16E |
|----------------------------|---------------|---------------|--------------|--------------|--------------|
| EBITDA/revenue (%) | -40.5% | -83.0% | 23.5% | 75.4% | 75.5% |
| EBIT/revenue (%) | -48.3% | -94.2% | 19.3% | 74.2% | 74.4% |
| Return on assets (%) | -10.1% | -18.7% | 9.6% | 53.1% | 29.1% |
| Return on equity (%) | -12.1% | -24.2% | 12.9% | 60.2% | 31.8% |
| Return on funds empl'd (%) | -11.6% | -23.5% | 12.6% | 59.7% | 31.6% |
| Dividend cover (x) | N/A | N/A | 0% | 0% | 0% |
| Effective tax rate (%) | 5.8% | -0.4% | 0.0% | 4.5% | 30.0% |

LIQUIDITY AND LEVERAGE RATIOS

| Y/e June 30 | FY12A | FY13A | FY14E | FY15E | FY16E |
|----------------------------|---------------|---------------|---------------|---------------|---------------|
| Net debt/(cash) (\$m) | -16 | -21 | -20 | -62 | -79 |
| Net debt/equity (%) | -62.4% | -51.6% | -40.9% | -49.7% | -43.1% |
| Net interest cover (x) | N/A | N/A | N/A | N/A | N/A |
| Current ratio (x) | 4.9 | 5.1 | 4.8 | 12.5 | 15.6 |

INTERIMS

| Y/e June 30 (\$m) | 2H12A | 1H13A | 2H13A | 1H14F | 2H14F |
|-----------------------------|----------|-----------|-----------|-----------|-----------|
| Revenue | 7 | 4 | 7 | 5 | 24 |
| EBITDA | 0 | -3 | -6 | -6 | 13 |
| D&A | 0 | -1 | -1 | -1 | -1 |
| EBIT | 0 | -4 | -7 | -7 | 13 |
| Net interest | 0 | 0 | 0 | 0 | 1 |
| Pre-tax profit | 0 | -3 | -7 | -7 | 13 |
| Tax | 0 | 0 | 0 | 0 | 0 |
| NPAT | 0 | -3 | -7 | -7 | 13 |
| Minority interests | 0 | 0 | 0 | 0 | 0 |
| Net profit after minorities | 0 | -3 | -7 | -7 | 13 |

VALUATION

| | Base | Optim. |
|--------------------------------------|---------|--------|
| BNC210 (A\$m) | 125.6 | 232.1 |
| BNC105 (A\$m) | 115.2 | 272.4 |
| Other products A(\$m) | 121.0 | 502.6 |
| Total value for technology (A\$m) | 361.9 | 1007.1 |
| Value of tax losses | 21.8 | 21.8 |
| Underlying R&D cost | -9.6 | -9.6 |
| Cash now (A\$m) | 20.5 | 20.5 |
| Cash from options and casg to be rai | 23.9 | 23.9 |
| Total value (A\$m) | 418.5 | 1063.7 |
| Total diluted shares (million) | 460.2 | 460.2 |
| Value per share | \$0.91 | \$2.31 |
| Valuation midpoint | \$1.61 | |
| Share price now (A\$ per share) | \$0.515 | |
| Upside to midpoint | 212.7% | |

Biomarkers show the way for BNC105

- **BNC105 is a next-generation cancer drug.** Bionomics has been developing BNC105 since 2005 when it bought a privately-held Australian company called Iliad Pharmaceuticals. Iliad had been following through on evidence that a natural product called Combretastatin A4¹ was effective at inhibiting the polymerisation of tubulin, which is an important protein in tumour blood vessels. In 2006, BNC105 emerged from the Bionomics/Iliad drug discovery programme as a highly potent analogue of Combretastatin A4 and was taken into the clinic in 2008. Animal evidence from numerous studies since 2006 has shown that BNC105 is effective at cutting tumour vasculature as well as attacking cancer cells directly and triggering cancer cell apoptosis. BNC105 seems to be able to play a role in attacking all solid tumours. This ability points to a strong payoff. Phase II data from a trial of BNC105 in metastatic renal cell carcinoma released today has now pointed the way forward for the Bionomics' drug.
- **The drug didn't work for all patients, but it did seem to work for some important sub-groups.** Bionomics' trial, called 'Disruptor 1', recruited 148 patients who had failed Pfizer's Sutent or Amgen's Nexavar, and treated them with BNC105 plus Novartis' Afinitor² or with Afinitor alone. Progression Free Survival was 4.7 months for BNC105+Afinitor, versus 4.1 months for Afinitor only. This comparison wasn't statistically significant, and roughly the same number of patients was Progression-Free at six months in each group. We were surprised by this outcome because the interim data had suggested more survival with BNC105³. The market was clearly displeased with the Disruptor 1 top-line result. However on a sub-group analysis the trial had some encouraging news to tell.
- **Understanding the 'Bad News' from the top-line.** We theorise that Disruptor-1 mainly recruited 'sicker' patients because the median PFS for the control group was at least 16% lower than Novartis' prior clinical work with Afinitor would have predicted⁴. This potentially reduced the potential efficacy of BNC105 for the overall group. We argue however, that the sub-group and biomarker analyses need to be taken seriously.
- **The Good News Part 1 – BNC105 seemed to work well in several patient subgroups** that potentially covered half the patients in total:
 - For patients with a particular kind of tumour pathology called 'Fuhrman Grade 2', PFS was 6.4 months vs 4.1 months. Fuhrman is the standard grading schema for renal cell carcinoma, with four grades⁵ based on assessment of the uniformity of nuclear size, nuclear shape and nucleolar⁶ prominence⁷. Grade 1 has the best prognosis, Grade 4 the worst. 22% of the patients evaluated by Bionomics were Fuhrman Grade 2;
 - For Patients with metastases to the liver enjoyed 6.6 months PFS with BNC105+Afinitor versus only 2.8 months for Afinitor. 19% of the patients evaluated had liver metastases;
 - For Patients that had had a previous nephrectomy (ie: kidney removal) the comparable figures were 7.1 months and 4.1 months. 13% of the patients evaluated had had a nephrectomy;
 - Presumably some patients belonged in more than one of the subgroups described above. However added together these sub-groups could cover up to 54% of all the patients evaluated;
 - These subgroup analyses didn't have statistical significance because of the small sample sizes. However, combined with exciting biomarker data, they suggested that BNC105 remains a valuable drug.
- **The Good News Part 2 – BNC105's biomarker data is very encouraging.** Bionomics found in the trial that a bank of around seven biomarkers, mostly markers of inflammation⁸, could predict, with statistical significance the level of PFS in the patients. The p values here

BNC105 in metastatic renal cell carcinoma is now a biomarker story

¹ So called because it was obtained from the Bush Willow of South Africa (*Combretum cafrum*).

² See NCT01034631 at www.clinicaltrials.gov.

³ In November 2012 Bionomics reported that, of the first 12 patients in BNC105's Phase II trial in renal cell carcinoma (the dose escalation part up to 16 mg/m²), 7 had experienced stable disease and had received over 18 cycles of treatment. The '18 cycles' number is important because a cycle of treatment in the trial was 21 days, and a patient exited the trial after experiencing tumour progression. This meant that the seven patients experienced 12.4 months of Progression Free Survival (PFS).

⁴ That is, 4.1 months versus 4.9 months PFS for Afinitor as a monotherapy in Phase III when measured by independent central review and 5.5 months when measured by investigators (see Cancer. 2010 Sep 15;116(18):4256-65).

⁵ See Am J Surg Pathol. 1982 Oct;6(7):655-63.

⁶ The nucleolus is a small, round granular body composed of protein and RNA in the nucleus of a cell.

⁷ This is determined by looking at the cells under a microscope after hematoxylin and eosin (H&E) staining.

⁸ Such as interleukin-1 beta and alpha-2 macroglobulin.

ranged from 0.0136 up to 0.0348. This is important for future studies because it can allow an 'adaptive design' clinical trial that recruits only patients with biomarkers predictive of efficacy. No-one had ever gathered biomarker data for the trial of a Vascular Disrupting Agent before Bionomics.

- **The way forward for Bionomics.** Bionomics has suggested that a future clinical study of BNC105 – we presume another Phase II - would recruit and dose eligible patients but only retain those patients in the control arm whose biomarkers responded to the first cycle of treatment. This group would then be compared to a regular control arm in order to establish efficacy. The data from such a trial could then allow the most appropriate biomarkers to be pre-specified for recruitment into a Phase III. We believe that Big Pharma partners will be attracted to BNC105 coming out of this study based on the recent trend towards personalised medicine in cancer that has created drugs such as Zelboraf.
- **Bionomics has now entered the era of personalised medicine.** We argue that the subgroup and biomarker data needs to be taken seriously because cancer therapy has now moved past the era of 'all comers', where a drug or medical device will be suitable for all patients with a particular cancer. Basically, contemporary molecular biology has shown that every cancer is slightly different from every other, so that suitable therapies have to be personalised. The result can be quite lucrative even if a drug doesn't suite all comers:
 - Herceptin⁹, in 2013 a US\$6.6bn best-seller for Roche, only works for Her2-positive breast cancer, which is around 20% of all breast cancer. Trial Herceptin to 'all-comers' with breast cancer and you end up with survival data not unlike those which Bionomics has reported today.
 - Roche's Tarceva¹⁰, AstraZeneca's Iressa¹¹ and Boehringer Ingelheim's Gilotrif¹² only work in NSCLC patients who have tumours with EGFR mutations, which is around 10-15% of all patients. Tarceva was a US\$1.4bn drug in 2013 and Iressa had US\$647m in 2013 sales.
 - Roche's Zelboraf¹³ and GSK's Tafinlar¹⁴ for metastatic melanoma only work in patients that have the BRAF V600E mutation in their tumour, which is 40-50% of malignant melanoma.
 - GSK's Mekinist¹⁵, also for metastatic melanoma is approved in patients that have both BRAF V600E and BRAF V600K mutations.
 - Pfizer's Xalkori¹⁶ for non-small-cell lung cancer (LSCLC), and works for patients whose tumours carry the EML4-ALK fusion gene. That's a mere 3-7% of all NSCLC.
- **The regulators are already comfortable with clinical trials that have some 'adaptive design'.** The FDA regularly allows cancer trials with adaptive design in the form of an interim analysis that allows sample size re-estimation, such as:
 - Sunesis¹⁷ is in Phase III adaptive design study for its AML drug vosaroxin that allows an interim analysis of 'a broad range of clinically meaningful and statistically significant survival outcomes' and, if necessary, a trial enlargement.
 - The cancer immunotherapy company, Newlink Genetics¹⁸ is in a Phase IIb/III study in pancreatic cancer with adaptive design, where a Phase IIb will select the appropriate dose for NewLink's product and an interim analysis at Phase III will allow changed recruitment.

Herceptin is a US\$6.6bn pa personalised cancer medicine

⁹ Generic name trastuzumab, see www.herceptin.com. Herceptin gained FDA approval in September 1998.

¹⁰ Generic name erlotinib, see www.tarceva.com. Tarceva gained FDA approval in November 2004.

¹¹ Generic name gefitinib, see www.iressa.com. Iressa gained FDA approval in May 2003.

¹² Generic name afatinib, www.gilotrif.com. Gilotrif gained FDA approval in July 2013.

¹³ Generic name vemurafenib, see www.zelboraf.com. Zelboraf gained FDA approval in August 2011.

¹⁴ Generic name dabrafenib, see www.tafinlar.com. Tafinlar gained FDA approval in May 2013.

¹⁵ Generic name trametinib, see www.trametinib.com. Like Tafinlar, Mekinist also received FDA approval in May 2013.

¹⁶ Generic name crizotinib, see www.xalkori.com. Xalkori gained FDA approval in August 2011.

¹⁷ South San Francisco, Ca., Nasdaq: SNSS, www.sunesis.com.

¹⁸ Ames, Ia, Nasdaq: NLNK, www.linkp.com.

- **Adaptive design driven by biomarkers is here.** In recognition that personalised medicine is a way forward for development of new cancer therapies, the FDA and other agencies have, it would appear, become comfortable with adaptive design driven by biomarkers:
 - The I-SPY2 trial (Investigation of Serial Studies to Predict Your Therapeutic Response with Imaging And mOLecular Analysis 2)¹⁹ launched in 2010, is a classic case of adaptive design. This study, run by the Biomarkers Consortium²⁰, is exploring whether or not the addition of investigational drugs to standard chemotherapy is better than standard chemotherapy alone in locally advanced breast cancer before surgery. Women being recruited into this trial randomise to either the standard chemo arm or the standard chemo plus new drug arms. There are seven new drugs being tried out. As the investigators learn how different tumours respond to new drugs, women are assigned with higher probability to therapies that seem to be suitable for that subtype. A new drug then 'graduates' from the trial when there is a >85% probability that the drug would work for the relevant tumour subtype in a regular Phase III. A 2011 article in the *Journal of the American Medical Association* co-authored by the FDA's Dr Janet Woodcock²¹ discussed the use of the I-SPY 2 design as a basis for accelerated drug approvals²².
 - It is also worth noting the favourable outcome of the BATTLE trial (Biomarker-integrated Approaches of Targeted Therapy for Lung cancer Elimination)²³, in which 255 pre-treated lung cancer patients were randomised to various cancer drugs based on relevant molecular biomarkers. The favourable 46% 8-week disease control rate suggested that viability of biomarkers as treatment predictors.
- **Now that Bionomics can position its drug in renal cell carcinoma, it can also look at other drugs in this space.** In today's conference call, Bionomics indicated that it would look to see if BNC105 is synergistic with Roche's Avastin, as well as GSK's Votrient²⁴. Avastin gained FDA approval in metastatic renal cell carcinoma in August 2009, whilst Votrient gained approval in October 2009. Bionomics presented data at AACR last year showing that Votrient+BNC105 in rodent models doubled tumour growth inhibition compared to either drug alone²⁵. GSK enjoyed US\$518m in net sales of Votrient in 2013.
- **\$0.90 price target maintained.** We value Bionomics on a probability-weighted DCF basis at \$0.91 base case and \$2.31 optimistic case. Our \$0.90 price target sits at the low point of this range. We anticipate Bionomics to be re-rated by the market as the future clinical and commercial programme for BNC105 is unveiled – including (potentially) a licensing deal for BNC105 - and as BNC210 moves forward. We see today's fall in the share price as providing a good buying opportunity.

The I-SPY2 study has helped pave the way for what Bionomics may do with BNC105

BNC105 seems to work synergistically with GSK's Votrient

¹⁹ See www.ispy2.org.

²⁰ A public-private biomedical research partnership managed by the Foundation for the National Institutes of Health.

²¹ Director, Center for Drug Evaluation and Research.

²² See JAMA. 2011 Dec 21;306(23):2608-9.

²³ See Cancer Discov. 2011 Jun;1(1):44-53. Epub 2011 Jun 1.

²⁴ Generic name pazopanib.

²⁵ See Mol Cancer Ther 2013;12(11 Suppl):B67.

Bionomics (BNO) – Drug discovery powerhouse

- **Company description:** Bionomics is an Adelaide-based drug discovery company with two products in the clinic – BNC210, an anti-anxiety drug, and BNC105, a cancer drug which can disrupt the blood vessels feeding tumours. Both drugs have performed well in pre-clinical and clinical work. Bionomics licensed BNC210 to US biotech company, Ironwood Pharmaceuticals (Nasdaq IRWD) in January 2012 for a massive deal package worth US\$345m; the drug is now in Phase I. BNC105 has completed a Phase II trial in Renal Cell Carcinoma (RCC) and is in Phase II in ovarian cancer. The RCC trial read out data in March 2014 with favourable data for key subgroups. Behind BNC105 and BNC210 is an enviable pipeline of pre-clinical assets.
- **Bionomics' BNC210 may be the 'Next Big Thing' in anxiety.** The clinical data indicates that BNC210 can relieve anxiety quickly, without causing sedation or being addictive. There is also evidence that the drug can function as an anti-depressant. The market for anti-anxiety drugs is US\$5-12bn globally, driven by the ~3% of the population that suffers from Generalised Anxiety Disorder. The global market for anti-depressants is worth ~US\$20bn. We expect a steady flow of milestone income for Bionomics between now and its 2019 launch. We estimate that Bionomics will receive a mid-double digit royalty on Ironwood's sales. Ironwood has been a great partner to have for BNC210. It has already gained FDA approval for its first product - the constipation drug Linzess - and while it is now capitalised at US\$1.65bn²⁶, Ironwood is not so big that BNC210 would easily fall between the R&D cracks. We understand Ironwood has spent around US\$20m on BNC210 over the last two years.
- **BNC105 attacks cancer a number of ways.** BNC105 is a 'Pulsatile Activator of Tumour Hypoxia' (PATH) and employs three ways to attack solid tumours. The drug has been demonstrated in various animal models to be able to bust up the vasculature of tumours but whilst keeping healthy blood vessels intact. It is directly cytotoxic for cancer cells; it induces cancer cell killing via apoptosis. BNC105 seems to be effective in treating all solid tumours. In the Phase II trial in metastatic renal cell carcinoma the drug worked well in key subgroups. Future trials enriched for these patients can properly target BNC105 in metastatic renal cell carcinoma. Bionomics also found in the trial that a bank of around seven biomarkers could predict, with statistical significance, the level of PFS in the patients. This is important for future studies because it can allow an 'adaptive design' clinical trial that recruits only patients with biomarkers predictive of efficacy.
- **Bionomics is a cancer stem cell play.** In 2012 Bionomics acquired Eclipse Therapeutics, which was pre-clinical with a couple of antibodies targeted at cancer stem cells. The earliest of these antibodies, BNC101, enters the clinic next year. There is potential for Bionomics to attract the same investors that have appreciated Verastem et. al.
- **Bionomics is collaborating with Merck & Co. in the pain field.** In July 2013 Bionomics announced a collaboration with Merck looking for new pain drugs, and Bionomics is set to potentially receive US\$172m in option exercise fees as well as development and regulatory milestone payments. Neuropathic pain alone is a US\$2-3bn market inadequately served by existing drugs, mostly opioid in nature (and therefore potentially addictive).
- **Bionomics has multiple drug discovery platforms.** Bionomics' proprietary Multicore, Angene and ionX drug and target discovery platforms have provided the company with an engine for future growth. These platforms have helped create valuable pre-clinical programmes including the Kv1.3 programme, with potential for anti-inflammatory drugs, and the BNC375 programme for Alzheimer's and other CNS disorders.
- **Bionomics has good management.** We like the commercial approach that CEO, Dr Deborah Rathjen has inculcated at Bionomics. Since 2005, Dr Rathjen and her colleagues have transformed Bionomics and taken it way up the value curve.
- **We value Bionomics on a probability-weighted DCF basis at \$0.91 base case and \$2.31 optimistic case.** Our \$0.90 price target sits at the low point of this range. We anticipate Bionomics to be re-rated by the market as the future clinical and commercial programme for BNC105 is unveiled – including (potentially) a licensing deal for BNC105 - and as BNC210 moves forward. We see today's fall in the share price as providing a good buying opportunity.

Bionomics has a collaboration in the pain drug space with Merck & Co.

²⁶ 18 March 2014 close on Nasdaq.

Valuation methodology – how we get to 90 cents per share and beyond

- Our probability-weighted DCF of Bionomics was built as follows:
 - Our WACC was 16.9% (Speculative);
 - We modelled payoffs from BNC210 (anxiety, 32% probability of success), BNC105 (cancer, 32%), BNC101 (cancer, 21-38%), Nav1.7 (neuropathic pain, 21-38%), Kv1.3 (MS, 21-38%) and BNC375 (Alzheimer's, 11-19%);
 - We assume all products are licensed over the next six years for an average US\$40-70m upfront, US\$200-260m in milestones and 13-18% royalties; and
 - We assume average peak sales for a typical Bionomics licensed product of US\$2.1bn to US\$3bn.

Major shareholders

- Link Traders (Laurence Freedman, 9.6%);
- John Leaver (5.9%);
- Ausbil Dexia (5.8%);
- Australian National University (5.3%).

Key risks

- Scepticism around efficacy for BNC105 in RCC;
- Ironwood's commitment to BNC210;
- Funding risk.

This document has been prepared and issued by:

Baillieu Holst Ltd

ABN 74 006 519 393

Australian Financial Service Licence No. 245421

Participant of ASX Group

Participant of NSX Ltd

Analysts' stock ratings are defined as follows:

Buy: The stock's total return is expected to increase by at least 10-15 percent from the current share price over the next 12 months.

Hold: The stock's total return is expected to trade within a range of ± 10 -15 percent from the current share price over the next 12 months.

Sell: The stock's total return is expected to decrease by at least 10-15 percent from the current share price over the next 12 months.

Disclosure of potential interest and disclaimer:

Baillieu Holst Ltd (Baillieu Holst) and/or its associates may receive commissions, calculated at normal client rates, from transactions involving securities of the companies mentioned herein and may hold interests in securities of the companies mentioned herein from time to time. Your adviser will earn a commission of up to 50% of any brokerage resulting from any transactions you may undertake as a result of this advice.

When we provide advice to you, it is based on the information you have provided to us about your personal circumstances, financial objectives and needs. If you wish to rely on our advice, it is important that you inform us of any changes to your personal investment needs, objectives and financial circumstances.

If you do not provide us with the relevant information (including updated information) regarding your investment needs, objectives and financial circumstances, our advice may be based on inaccurate information, and you will need to consider whether the advice is suitable to you given your personal investment needs, objectives and financial circumstances. Please do not hesitate to contact our offices if you need to update your information held with us. Please be assured that we keep your information strictly confidential.

No representation, warranty or undertaking is given or made in relation to the accuracy of information contained in this advice, such advice being based solely on public information which has not been verified by Baillieu Holst Ltd.

Save for any statutory liability that cannot be excluded, Baillieu Holst Ltd and its employees and agents shall not be liable (whether in negligence or otherwise) for any error or inaccuracy in, or omission from, this advice or any resulting loss suffered by the recipient or any other person.

Past performance should not be taken as an indication or guarantee of future performance, and no representation or warranty, express or implied, is made regarding future performance. Information, opinions and estimates contained in this report reflect a judgment at its original date of publication and are subject to change without notice. The price, value of and income from any of the securities or financial instruments mentioned in this report can fall as well as rise. The value of securities and financial instruments is subject to exchange rate fluctuation that may have a positive or adverse effect on the price or income of such securities or financial instruments.

Baillieu Holst Ltd assumes no obligation to update this advice or correct any inaccuracy which may become apparent after it is given.

Baillieu Holst Ltd

ABN 74 006 519 393

Australian Financial Service Licence No. 245421

Participant of ASX Group

Participant of NSX Ltd

www.baillieuholst.com.au

Melbourne (Head Office)

Address Level 26, 360 Collins Street

Melbourne, VIC 3000 Australia

Postal PO Box 48, Collins Street West

Melbourne, VIC 8007 Australia

Phone +61 3 9602 9222

Facsimile +61 3 9602 2350

Email melbourne@baillieuholst.com.au

Bendigo Office

Address Cnr Bridge & Baxter Streets

Bendigo, VIC 3550 Australia

Postal PO Box 40

North Bendigo, VIC 3550 Australia

Phone +61 3 5443 7966

Facsimile +61 3 5442 4728

Email bendigo@baillieuholst.com.au

Geelong Office

Address 16 Aberdeen Street

Geelong West Vic 3218

Postal PO Box 364

Geelong Vic 3220 Australia

Phone +61 3 5229 4637

Facsimile +61 3 4229 4142

Email geelong@baillieuholst.com.au

Newcastle Office

Address Level 1, 120 Darby Street

Cooks Hill, NSW 2300 Australia

Postal PO Box 111

The Junction, NSW 2291 Australia

Phone +61 2 4925 2330

Facsimile +61 2 4929 1954

Email newcastle@baillieuholst.com.au

Perth Office

Address Level 10, 191 St Georges Terrace

Perth WA 6000 Australia

Postal PO Box 7662, Cloisters Square

Perth, WA 6850 Australia

Phone +61 8 6141 9450

Facsimile +61 8 6141 9499

Email perth@baillieuholst.com.au

Sydney Office

Address Level 18, 1 Alfred Street

Sydney, NSW 2000 Australia

Postal PO Box R1797

Royal Exchange, NSW 1225 Australia

Phone +61 2 9250 8900

Facsimile +61 2 9247 4092

Email sydney@baillieuholst.com.au