

3 March 2010

## Bionomics

Year End	Revenue (A\$m)	PBT* (A\$m)	EPS* (c)	DPS (c)	P/E (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: BNC210 Phase I data

Final data from an escalating single-dose Phase Ia study of the anxiety/depression compound BNC210 in healthy volunteers show the drug to be well tolerated at potentially therapeutic doses. Evidence of anxiolytic activity was seen through a lowering of plasma cortisol levels. A Phase Ib study is planned this year. The investment case for Bionomics rests on the twin pillars of BNC210 and BNC105, a vascular disrupting agent in Phase II studies for mesothelioma and kidney cancer. Licensing deals for both compounds are possible on completion of the current studies.

#### BNC210 data

Final results from a Phase Ia study of BNC210 show the compound to be well tolerated at up to and beyond potentially therapeutic doses and provided some evidence of activity in terms of plasma cortisol levels. A Phase Ib study is expected to be conducted this year, after which Bionomics plans to seek a licensing partner(s) for further development and commercialisation.

#### BNC105: Phase II studies underway

Bionomics is developing BNC105 for renal cell carcinoma and mesothelioma, both orphan indications with the potential for fast-track registration. Studies should render interim results this year with final results in early 2012.

#### Financials

Bionomics is currently funded to complete the planned repeat Phase I studies of BNC210 and the two Phase II studies of BNC105.

#### 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 (BNC105) and an anxiolytic compound (BNC210).

#### 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%

#### Analyst

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## Update: Encouraging early clinical data for BNC210

Final results from a Phase Ia study of Bionomics' anxiety/depression compound BNC210 in healthy volunteers show the compound to be well tolerated at potentially therapeutic doses and provided the first evidence of activity in terms of a reduction in plasma cortisol levels. A Phase Ib study is expected to be conducted this year, after which Bionomics plans to seek a licensing partner(s) for further development and commercialisation.

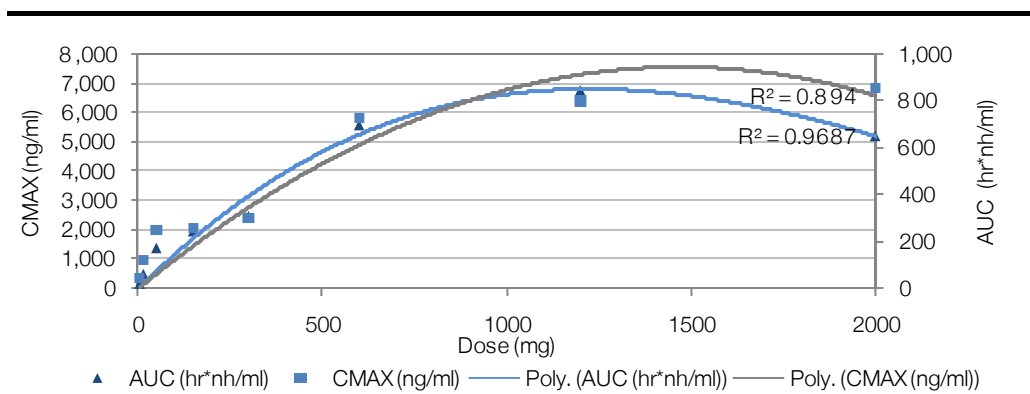
BNC210 is a novel small molecule with an undisclosed novel mechanism of action and potential activity in anxiety, both acute and chronic (generalised anxiety disorder) and with co-morbid depression (it may also have potential in depression).

Bionomics conducted a two-part, escalating single-dose Phase Ia study in healthy volunteers. The first part, which reported in October last year, showed BNC210 to be safe and well tolerated in healthy male volunteers at plasma levels equivalent (and higher than) 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 most common reported side-effects which are possibly related to the drug were fatigue and headache, in all cases mild). In this double blind study, there were eight cohorts, each of four subjects (three of which were randomised to BNC210 and one placebo). The drug was administered as an oral (10-20mL) liquid suspension.

The second stage of this study evaluated doses up to 2,000mg. PK data showing  $C_{MAX}$  and AUC (area under the curve) for various doses are shown in Exhibit 1. These data indicate an absorption plateau at between 600-1,200mg.

### Exhibit 1: BNC210 drug exposure following oral administration in healthy volunteers

Note: Data points shown. Trend lines (polynomial) have been superimposed by Edison.

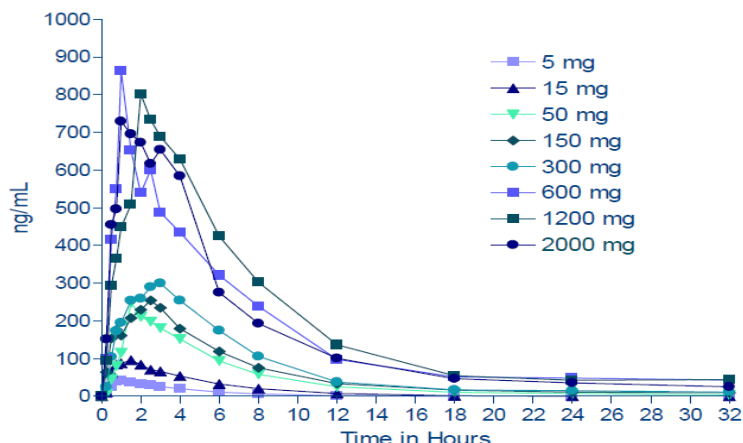


Source: Bionomics, Edison Investment Research

PK profiles for each dose cohort are shown in Exhibit 2 below. These data suggest that BNC210 is fast-acting and potentially effective with a single daily dose, while rapidly cleared. The data would suggest a dose of 300-600mg might be optimum, in our view.

**Exhibit 2: BNC210 plasma pharmacokinetics in healthy volunteers**

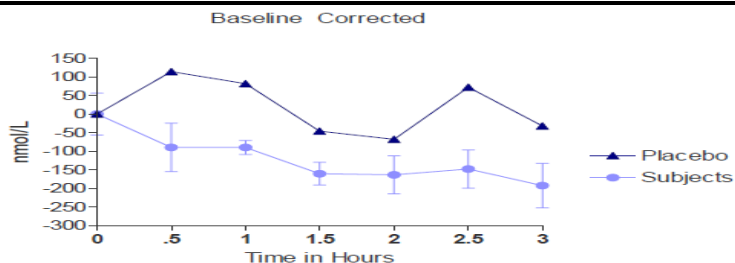
Note: PK profiles of different doses.



Source: Bionomics

The study also examined potential effects of BNC210 on neuroendocrine markers, particularly plasma cortisol levels. Cortisol was lower in subjects receiving BNC210 and as anxiety and stress lead to an elevation of cortisol, this change is consistent with anxiolytic activity. The lead investigator of the study commented that this finding, which he stated requires confirmation, may enable cortisol and potentially other neuroendocrine hormones to be used as biomarkers for BNC210 activity. Cortisol levels in healthy volunteers dosed with 2,000mg of BNC210 are shown in Exhibit 3.

**Exhibit 3: Plasma cortisol levels**



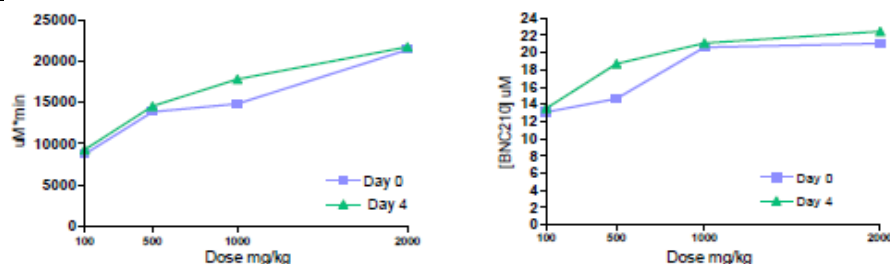
Source: Bionomics

**Preclinical safety data**

The plasma levels of BNC210 achieved in the Phase Ia study were well above those that would be expected to produce an anxiolytic effect in animal models – the minimum dose of BNC210 that consistently produced an anxiolytic effect in the rat model was 0.1-1mg/kg (equivalent to 7-70mg for a 70kg human). Preclinical safety studies in rat and dogs also indicate that BNC210 is safe and tolerable at oral doses up to 2,000mg/kg.

PK studies in rats showing C<sub>MAX</sub> and area under the curve (AUC) for various doses are shown in Exhibit 4 overleaf. These data indicate exposure increases only slightly between the 1,000mg/kg and 2,000mg/kg doses, and given the minimum dose required for anxiolytic effect in rats and mice is 0.1mg/kg, this represents a therapeutic window of 10,000x.

**Exhibit 4: Rat AUC and C<sub>MAX</sub>**



Source: Bionomics

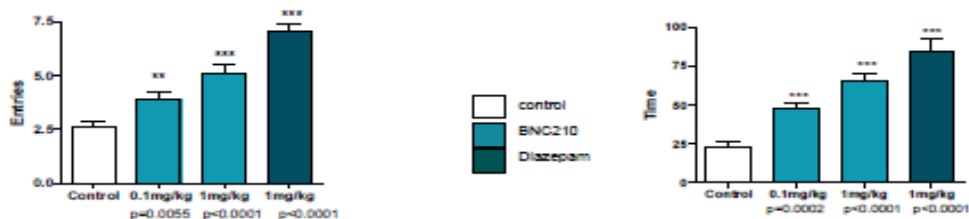
Other studies have found no evidence of dependence following cessation of treatment. Withdrawal of BNC210 treatment following 14-day repeat dosing does not result in adverse physical events. Abrupt cessation of treatment in rats dosed repeatedly with BNC210 for a period of 14 days at 0mg, 10mg, 30mg 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).

**Preclinical efficacy data**

Various preclinical studies have shown BNC210 to be able to reduce anxiety without drowsiness or impairment of memory or motor function. Data from the rat elevated plus maze model is shown in Exhibits 5 and 6. The number of entries into and time spent on the open arms of the maze was significantly increased by both doses.

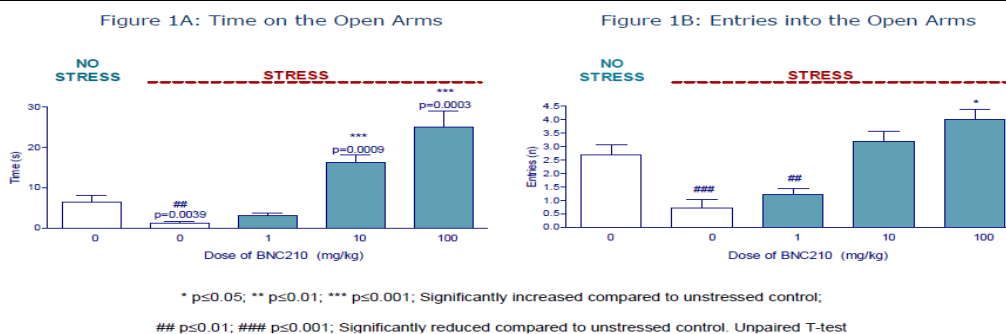
**Exhibit 5: Rat elevated plus maze**

Note: Data represents mean ± SEM. n=10 rats, p values calculated using Fisher’s protected least significant difference test.



Source: Bionomics

**Exhibit 6: Pre-stressed rats in elevated plus maze**



\* p<0.05; \*\* p<0.01; \*\*\* p<0.001; Significantly increased compared to unstressed control;  
 ## p<0.01; ### p<0.001; Significantly reduced compared to unstressed control. Unpaired T-test

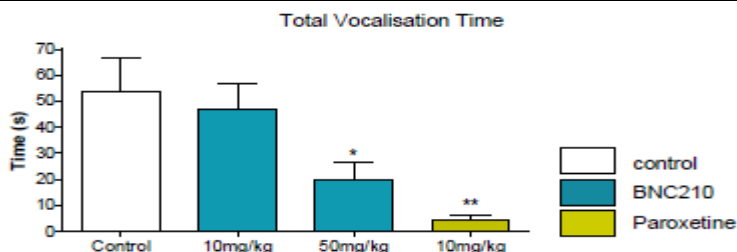
Source: Bionomics

Single doses of BNC210 at 1mg, 10mg and 100 mg/kg reversed the swim stress-induced reduction in entries into and time spent on the open arms. The activity was dose dependent with the 100mg/kg dose producing the largest benefit.

BNC210 has shown activity in the guinea pig anxiety model at 50mg/kg. The profile of BNC210 in this model shows good correlation with paroxetine, a non sedating anti-anxiety compound used as an active control (Exhibit 7).

**Exhibit 7: Guinea pig isolation induced vocalisations**

Note: Data represents mean ±SEM. n=10 guinea pig pups, \*p<0.05, \*\*p<0.01, Fishers Protected Least Significant Difference test. \* Significant reduction in total vocalisation time

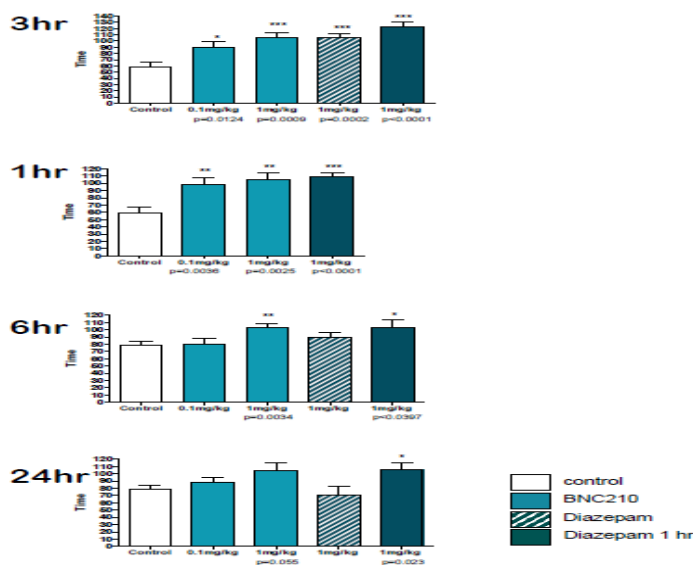


Source: Bionomics

Data from BNC210 in the mouse light dark box model are shown in Exhibit 8. At the six-hour time point, mice treated with 1mg/kg of BNC210 still spent significantly more time in the lit area whereas the diazepam treated mice (1mg/kg; PO) were similar to control animals.

**Exhibit 8: BNC210 vs diazepam in the mouse light dark box**

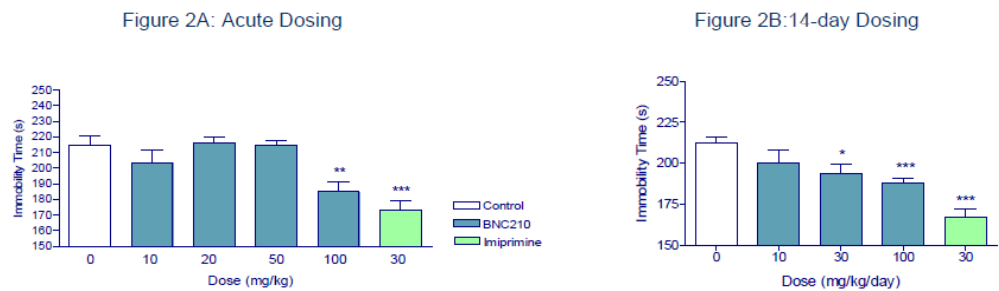
Note: Data represents mean ± SEM. n=10 mice, p values calculated using Fisher's protected least significant difference test. BNC210 and diazepam were assessed at 1, 3, 6 and 24 hours in the light dark box.



Source: Bionomics

**Depression**

BNC210 has shown activity comparable to imipramine in a rat forced swim model of depression following both acute treatment and daily dosing for 14 days. BNC210 reduced immobility time compared to vehicle at the 100mg/kg dose, although the lower doses of BNC210 were not active. Chronic administration of BNC210 for 14 days at 10mg, 30mg and 100mg/kg/day resulted in a half log increase in potency with the dose of 30mg/kg also causing a significant reduction in immobility time. Results are shown in Exhibit 9.

**Exhibit 9: Rat forced swim model**

Source: Bionomics

**Other R&D programmes**

BNC210 is one of Bionomics' two clinical stage development programmes. Its other programme is BNC105, a vascular disrupting agent (VDA) that is in Phase II studies for mesothelioma and metastatic renal cell carcinoma. The R&D pipeline is summarised in Exhibit 10.

**Exhibit 10: Bionomics R&D summary**

Programme	Indication	Notes
BNC105	Mesothelioma/ metastatic renal cell carcinoma (Phase II)	60-pt Phase II study in pts unresponsive to pemetrexed + cisplatin (interim results: H111, final H112). 152-pt Phase II study of BNC105 + everolimus (Afinitor) in second line mRCC and BNC105 alone in patients progressing on everolimus (interim results H210, final results: June 2012).
BNC210	Anxiety and depression. Phase Ib	Phase Ib study in healthy volunteers planned. 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.
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. 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.
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' ionX platform incorporating gene mutations observed in patients with epilepsy.

Source: Edison Investment Research

## Valuation

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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' current enterprise value of A\$85m.

## Sensitivities

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Bionomics' 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. This risk has in our view been mitigated to an extent by the Phase Ia data. As with many biotech firms, funding is a sensitivity, although following its recent capital raise, Bionomics has funding for the next two years.

## Financials

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Bionomics' 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. Our model is shown in Exhibit 11.

**Exhibit 11: 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.

	A\$'000s	2007	2008	2009	2010e	2011e	2012e
Year end 31 December		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)	(602)	(600)	(600)	(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)	(572)	(529)	(529)	(529)	(529)
<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

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