EDISON

Bionomics

Clinical update

Phase IIa in agitation of the elderly initiated

Pharma & biotech

Bionomics announced on 23 May 2018 it has initiated a Phase IIa study of its α7 nicotinic receptor inhibitor for the treatment of agitation in the elderly in a hospital setting. Agitation is a common problem (13-24%) in patients with dementia, and we expect the trial to focus primarily on this population. It will enrol a target of 40 patients across Australia and is expected to provide top-line data in calendar Q119.

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	(7.1)	(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.

Significant need with poor options

Agitation in patients with Alzheimer's disease and other forms of dementia is a significant burden on the healthcare system because of the increased needs of these patients. One study estimated costs of £29,000 to £57,000 per affected patient per year in the UK. Moreover, pharmacologic treatment options are limited to benzodiazepines; these are sedating and anti-psychotics, which have a black-box warning for increased mortality in these patients.

Novel mechanism may provide a solution

BNC210 holds the potential for being a non-sedating anxiolytic, thereby potentially enabling it to be used in patients with agitation both in the acute and chronic setting. The company previously presented data from its Phase II anxiety study showing that the drug inhibited the activation of the amygdalae, a region of the brain rich in α7 receptor and associated with fear and emotional responses, which points to the potential utility of this drug for the treatment of agitation.

Posttraumatic stress disorder fully enrolled

In April 2018 the company announced that its Phase IIb study of BNC210 in posttraumatic stress disorder (PTSD) was fully enrolled and on schedule to report top-line results in calendar H218. The trial has 193 patients being observed over 12 weeks, with the primary outcome as improvement in the functional PTSD symptom rating, Clinician-Administered PTSD Scale for DSM-5 (CAPS-5).

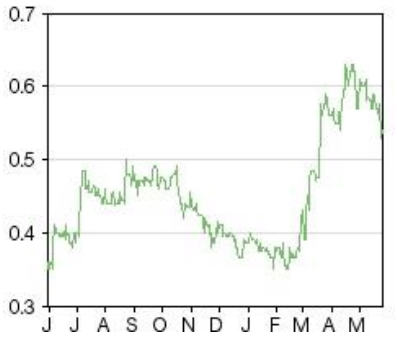
Valuation: Increased to A$492m or A$1.02

We have increased our valuation of Bionomics to A$492m or A$1.02 per basic share from A$418.7m or A$0.87 per basic share. This increase is largely driven by the inclusion of the agitation indication in our models (A$47.6m) with a 20% probability of success. Additionally the increase is driven by rolling forward our NPVs to the most recent period. The company ended fiscal Q318 with A$32.3m in cash and A$19.4m in debt.

29 May 2018

Price	**A$0.54**
Market cap	**A$261m**
	A$1.25/US$
Net cash (A$m) at 31 March 2018	12.9
Shares in issue	482.8m
Free float	83%
Code	BNO
Primary exchange	ASX
Secondary exchange	OTCQX

Share price performance



%	1m	3m	12m
Abs	(5.3)	25.6	56.5
Rel (local)	(6.4)	25.7	48.3
52-week high/low		A$0.6	A$0.3

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 and Phase IIa for agitation. It also had a programme licensed to Merck in Phase I for royalties and US$506m in upfronts and milestones.

Next events

Merck collab. Phase I complete	H118
BNC210 PTSD Phase II complete	H218

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Edison profile page

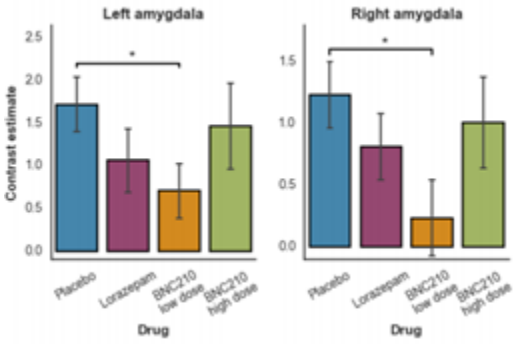
Expanding BNC210 into agitation

On 23 May 2018 Bionomics announced that it had initiated a clinical study of BNC210 for the treatment of agitation in the elderly in a hospital setting. Agitation is a common neuropsychiatric symptom typically associated with dementia. Agitation in this population represents a significant burden on the healthcare system. There are 1.4 million patients in nursing home care in the US, of which approximately 80% have dementia of some form (predominantly Alzheimer's disease). One report estimated the prevalence of agitation at between 13% and 24% at any given time in dementia patients.[1] A study examining the costs of agitation in British Alzheimer's disease patients found costs of £29,000 to £57,000 per affected patient per year in the form of increased health and social care costs.[2]

Unfortunately, there are limited options for the treatment of dementia-related agitation. There are no approved medications for this indication. Benzodiazepines can be used for the short-term alleviation of symptoms but, given their sedating effects and the development of tolerance, they are not generally considered appropriate for long-term treatment. Anti-depressants such as SSRIs can be prescribed for patients with depression, which is common in dementia patients, and frequently have agitation as a comorbidity. Anti-psychotics can be helpful in alleviating underlying psychosis, which may be a causative factor in agitation, and these agents have gained the most widespread use of pharmacologic treatments. However, all antipsychotics carry a black-box warning for the treatment of dementia patients because their use is associated with increased mortality.

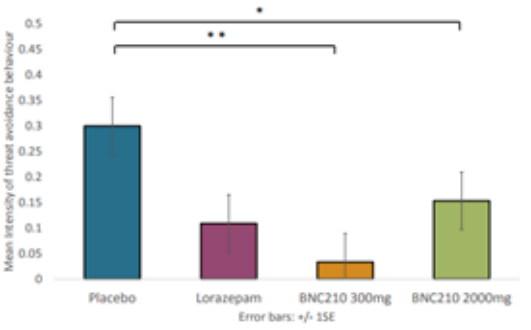
BNC210's novel mechanism of action positions it as a potential solution to the limitations associated with other pharmaceutical treatments. It has anxiolytic activity, which may provide acute relief from symptoms, similar to benzodiazepines but without the sedating side effects that limit routine use. Moreover, the company previously demonstrated in its Phase IIa study that BNC210 reduces the activation of the amygdalae (Exhibit 1), a region of the brain associated with fear and emotion. One manifestation in this study (among others) was decreased threat avoidance behaviour in the Joystick Operated Runway Task (JORT) (Exhibit 2). It is therefore plausible that the drug may reduce emotional arousal in dementia patients.

Exhibit 1: Reduction in amygdala activation from low-dose BNC210



Source: Bionomics. Note: *p<0.05.

Exhibit 2: Threat avoidance behaviour in the JORT



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

The Phase IIa study will be randomized, double-blind and placebo controlled. Approximately 40 patients from geriatric hospital wards in Australia will be enrolled and monitored over a five-day

[1] Steinberg M, et al. (2008) Point and 5-year period prevalence of neuropsychiatric symptoms in dementia: the Cache County Study. *Int J Geriatr Psychiatry* 23, 170-177.

[2] Morris S, et al. (2015) Monetary costs of agitation in older adults with Alzheimer's disease in the UK: prospective cohort study. *Brit J Med Open* 5, e007382.

treatment and a two-day follow-up period. Based on these parameters, the study should be quick, and the company expects to report results in Q1 of calendar year 2019. The primary endpoint of the study will be improvement in agitation symptoms as measured on the Pittsburgh Agitation Scale (PAS). The PAS is a 16-point assessment over four behaviour groups: vocalization (complaints, yelling), motor agitation (pacing, banging), aggressiveness (threats, violent gestures) and resisting care. Secondary endpoints for the study include safety and tolerability and improvement in clinical global impression scale (CGI-I).

PTSD trial fully enrolled

In April 2018, the company reported that it had fully enrolled its Phase II PTSD study. The study was designed for enrolment of up to 192 patients. 193 patients were enrolled and are being monitored over the course of 12 weeks. The primary endpoint of the study is improvement in CAPS-5, with secondary endpoints of impact of the drug on individual symptom clusters of the CAPS-5 (arousal and reactivity, avoidance, negative alterations in cognition and mood, intrusion symptoms), anxiety using the Hamilton Anxiety Rating Scale and on depression using the Montgomery-Asberg Depression Rating Scale. Given the range of effects being investigated, we expect the data from this study to be rich and to inform future clinical directions outside of PTSD. The company announced that top-line results are expected in H2 of calendar year 2018.

Valuation

We have increased our valuation of Bionomics to A$492m or A$1.02 per basic share from A$418.7m or A$0.87 per basic share. This increase is largely driven by the inclusion of the agitation indication in our models. We assign a 20% probability of success for the programme given the limited data on BNC210 and the difficulty in developing a drug for this particular indication. We assume that the company will be able to bring the drug to market in FY23 following a 320-person Phase III. We model peak penetration of 10% into the market of institutionalized dementia patients with aggression in Europe and the US.

Our valuation is additionally increased by advancing our NPVs to the most recent period. We expect to update our valuation with the release of data from the ongoing PTSD study in calendar H218. We may add indications at this time if the results are suggestive of broader applications. The company has completed the Phase I clinical study of BNC101 in colorectal cancer (CRC). The company previously stated at an interim update that no safety issues were observed, and it provided an update in a poster presentation at the AACR 2018 meeting that no biomarkers of gut toxicity were observed. However, it has not released detailed results from the trial. We expect to update our valuation following the release of these data.

Exhibit 3: 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%	349.7
BNC210	Agitation	20%	2023	259.0	52%	47.6
BNC101	CRC	10%	2025	1103.3	55%	80.2
Merck collaboration milestones	Alzheimer's associated cognitive dysfunction	10%	2025	1821.0	5%	17.1
CRO business				6.6	4%	1.3
Unallocated costs						(16.7)
Total						$479.2
Net cash and equivalents (FQ318) (A$m)						$12.9
Total firm value (A$m)						$492.1
Total shares (m)						482.8
Value per share (A$)						$1.02
Dilutive warrants and options (m)						52.34
Total diluted shares						535.1
Value per diluted share (A$)						0.97

Source: Edison Investment research, Bionomics reports

Financials

The company recently provided an update on cash flows for fiscal Q318. Operational cashflow was roughly breakeven for the period following the receipt of A$8.1m in government incentive payments, leaving the company's cash balance largely unchanged at A$32.2m. Debt also remained steady at A$19.4m. Our forecasts remain largely unchanged at this time. We record the company's future financing shortfall as A$35m in illustrated debt in FY20, although these needs can potentially be met through licensing activity.

Exhibit 4: Financial summary

$'000	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)	(677)	(813)
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)	(7,138)	(28,409)
Profit Before Tax (reported)	(17,277)	(17,324)	(6,227)	(8,928)	(30,199)
Reported tax	328	732	(523)	1,920	1,275
Profit After Tax (norm)	(15,786)	(16,031)	(4,810)	(5,603)	(27,209)
Profit After Tax (reported)	(16,949)	(16,592)	(6,750)	(7,008)	(28,923)
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)	(5,603)	(27,209)
Net income (reported)	(13,637)	(15,624)	(6,864)	(7,008)	(28,923)
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)	(1.08)	(5.02)
EPS - basic reported (c)	(4.06)	(3.63)	(1.40)	(1.39)	(5.45)
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	50,085	22,602
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	38,615	11,066
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)	(37,089)	(35,060)
Long term borrowings	(9,317)	(18,437)	(10,014)	(19,365)	(19,365)
Other long term liabilities	(14,143)	(15,824)	(19,719)	(17,724)	(15,695)
Net Assets	31,966	44,163	40,454	34,208	5,788
Minority interests	0	0	0	0	0
Shareholders' equity	31,966	44,163	40,454	34,208	5,788
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	(1,657)	(3,343)
Tax	0	0	0	0	0
Net operating cash flow	4,936	(15,360)	(1,440)	(6,254)	(28,337)
Capex	(846)	(197)	(248)	(323)	(323)
Acquisitions/disposals	(391)	69	0	0	0
Net interest	941	1,232	1,201	1,204	1,111
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)	(5,090)	(27,549)
Opening net debt/(cash)	(6,856)	(11,781)	(24,281)	(24,364)	(19,250)
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)	(19,250)	8,299

Source: Edison Investment research, Bionomics reports

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