

24 July 2008

Neuropharm

Year End	Revenue (£m)	PBT* (£m)	EPS* (p)	DPS (p)	PE (x)	Yield (%)
06/06	0.0	(0.3)	(6.6)	0.0	N/A	N/A
06/07	0.0	(2.7)	(13.8)	0.0	N/A	N/A
06/08e	0.0	(6.1)	(18.3)	0.0	N/A	N/A
06/09e	0.0	(6.5)	(19.5)	0.0	N/A	N/A

Note: *PBT and EPS are normalised, excluding goodwill amortisation and exceptional items.

Investment summary: Fragile X trial data

Results of two early-stage open-label Phase II studies of Neuropharm's programmes for Fragile X syndrome were released earlier this week, ahead of its presentation at the International Fragile X Conference starting today. Results of both studies were positive and highlight Neuropharm's broader R&D base, although the investment case still relies on NPL-2008 for autism. Neuropharm has confirmed recruitment for the SOFIA trial is on track and should complete the clinical phase by the year end. Completion of filing of the rolling NDA is due in Q209.

NPL-2005: Significant reduction in hyperactivity score

The 10-patient Phase IIa study of NPL-2005 (valproate) showed a statistically significant reduction in hyperactivity and a trend on cognitive impairment, with a majority of the completers classified as responders.

NPL-2009: Safety and early evidence of response

A 12-patient study showed a favourable safety profile (no CNS adverse effects) and indications of potential efficacy after a single dose, with four of six males and two of six females classified as responders.

SOFIA update

Out of 128 target recruitment, 120 patients have now completed the screening phase. Given the study's 14-week treatment period, read-out of the study should be possible in Q109. The open-label phase, codenamed EMMA, should begin shortly, enrolling patients as they complete the study.

Valuation: rNPV of £250m

We are maintaining our risk-adjusted NPV valuation of £250m, which represents a multiple of Neuropharm's EV. Neuropharm's share price has held up well in the turbulent market conditions of recent months, which we would suggest is a reflection of its clear strategy, near-term catalysts and steady progress on projects.

Price 172.5p
Market Cap £54m

Share price graph



Share details

Code NPH
Listing AIM
Sector Pharmaceuticals & Biotechnology
Shares in issue 31.5m

Price

52 week High 191p Low 166p

Balance Sheet as at 30 June 2008*

Debt/Equity (%) N/A
NAV per share (p) 28.0
Net cash (£m) 10.8

* Estimated

Business

Neuropharm is an emerging speciality pharmaceutical group focused on the development of medicines for the treatment of neuro-developmental disorders.

Valuation

	2007	2008e	2009e
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
	100%	0%	0%	0%

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Background

Neuropharm is a UK-based emerging speciality pharmaceutical company focused on CNS conditions, in particular, neuro-developmental disorders affecting children (autism, Fragile X syndrome and paediatric obsessive-compulsive disorder). Its principal product is a novel formulation of fluoxetine (a widely-used, off-patent SSRI antidepressant) for the treatment of the core symptoms of autism. The company has orphan drug designation for this and two other programmes and intends to establish its own salesforce in the US, allowing it to capture a significantly greater proportion of the value of its products than is normally the case for biotech companies.

The current status of Neuropharm's R&D pipeline is summarised in Exhibit 1 below.

Exhibit 1: Neuropharm R&D Summary

Project	Indication	Development stage/notes
NPL-2008 (Zydis Fast-melt formulation of fluoxetine)	Autism	The trial is moving towards completion of enrolment, with 120 patients having completed screening out of the target recruitment of 128. The Phase III SOFIA study has a 14-week treatment period, with flexible dosing up to the minimum effective dose (eg 2mg, 4mg, 6mg, 9mg and 18mg). Completion of the clinical phase is expected by the year end. The planned rolling NDA is expected to start in early Q4 (with the CMC package) and complete with clinical data. FDA fast-track status and likely priority review mean US launch is possible in Q409. The open-label phase will continue into 2010, examining IQ. Potential out-licensing opportunity in Europe, where the regulatory route is to be the Paediatric Use Marketing Authorisation (PUMA). US orphan drug designation held. Commercial agreements. Original clinical trial data and orphan drug designation acquired from Mount Sinai School of Medicine in return for a 5% royalty on US net sales. Agreement with Catalent Pharma Solutions covering the Zydis technology provides for transfer prices and a profit share equivalent to 10% of gross margin for the first three years, reducing to 3% in year seven and thereafter.
NPL-2005 (valproate)	Fragile X syndrome (behavioural symptoms)	Pilot open-label Phase IIa study in 10 young males (aged 7-16 years) with Fragile X Syndrome and co-morbid attention deficit hyperactivity disorder (ADHD) showed significant reduction in Connors' Parent Rating Scale hyperactivity scores ($p < 0.05$) and non-significant trend in cognition. Six of eight children completing the study were classified as responders, achieving a clinically meaningful reduction in symptom severity. Strategy is to develop a novel formulation in this indication (valproate is a marketed, off-patent anticonvulsant used for epilepsy and bipolar disorder). US orphan drug designation held.
NPL-2009 (fenobam)	Fragile X syndrome	12-patient, open-label dose-escalation Phase II study of escalating single doses 50mg-150mg in male and female adults showed the drug was well tolerated with no CNS effects (primary endpoint was safety). PK showed NPL-2009 levels were dose-dependent but variable. Four of six males and two of six females in the study were defined as responders. US orphan drug designation held. Commercial agreements. Preclinical data acquired from FRAXA in return for a 3% royalty on net sales; right of reference to the original IND from J&J in return for a 3% royalty interest for 10 years. (Prior clinical exposure extends to c 300 patients from Phase II studies for anxiety conducted in 1970s.)
NPL-2003 (undisclosed)	Paediatric OCD	Phase II study was closed, part-recruited, with data expected to be reported in Q4. Neuropharm has already agreed to facilitate further studies through an independent investigator in the adult population. Active agent is a marketed antibiotic.

Source: Edison Investment Research

Investment summary: New data broadens R&D pipeline

Earlier this week, Neuropharm announced the first clinical trial results for two of its clinical development programmes, NPL-2005 and NPL-2009 for Fragile X syndrome, ahead of presentations of the data at the National Fragile X Foundation's 11th International Fragile X Conference, starting today. Results of both studies were positive and highlight the company's broader R&D base, although the investment case for Neuropharm still relies on NPL-2008 for autism. As noted in Edison's recent note, the SOFIA study of NPL-2008 is also progressing well – recruitment is almost complete – and the clinical phase should complete around the year end.

Neuropharm expects to be in a position to present its plans how it will proceed with further studies of NPL-2005 and NPL-2009 at the time of its preliminary results in October.

NPL-2005

The open-label exploratory study of NPL-2005 (valproate) was conducted in 10 young males (aged between 7 and 16 years) with Fragile X syndrome and co-morbid ADHD symptoms. This was believed to be the first clinical study of valproate in Fragile X, although it is already in use off-label. The study had dose titration up to the maximum level indicated by the current label as an anti-epileptic (side-effects at higher doses are known to include sedation and some cognitive impairment). The duration of treatment in the study was six months, during which safety and efficacy, as measured by the Connors' Parent Rating Scale, were assessed.

The data will be presented by joint lead investigators Professors Giovanni Neri and Maria-Giulia Torrioli at the Università Cattolica del Sacro Cuore, Rome, who conducted the study.

NPL-2005 was well tolerated in the study population and no treatment-emergent adverse events were reported. A significant reduction in Connors' hyperactivity score was observed ($p=0.03$) and a non-significant trend in Connors' cognitive score ($p=0.14$). Six of the eight completers were classified as responders, achieving a clinically meaningful reduction in symptom severity.

NPL-2009

The study of NPL-2009 was an open-label single-dose Phase IIa study in 12 adults, which was primarily designed to investigate safety, although there were surrogate efficacy-related outcome measures. The study had a single dose escalation design (of 50mg to 150mg) on a per patient basis (ie the first two patients received the lowest dose, the next two an intermediate dose, and the final eight the highest dose).

The trial data will be presented by Professor Randi Hagerman of the UC Davis MIND Institute and Professor Elizabeth Berry-Kravis of the RUSH University Medical Center. NPL-2009, or fenobam, is an off-patent NCE that has been studied but not approved in another indication.

The study showed NPL-2009 to be well-tolerated with no significant adverse reactions and pharmacokinetic analysis showed that NPL-2009 levels were dose-dependent, although variable. In terms of efficacy, four of six males and two of six females were defined as responders, based on the pre-pulse inhibition and continuous performance task tests. There was anecdotal evidence of clinical improvement in nine patients (five males, four females).

Neuropharm intends to determine the next steps for both NPL-2005 and NPL-2009 over the next few months, and aims to be in a position to confirm its strategy at its preliminary results in October.

Fragile X syndrome

Fragile X syndrome is an X-linked mutation that prevents production of FMRP, a protein needed for normal brain functioning. In people with Fragile X, the *FMR1* gene has a large number of repeats of the CGG codon, which causes methylation of the DNA and silences expression of the FMRP protein. This methylation of the *FMR1* locus is also believed to result in constriction of the X chromosome, which consequently appears 'fragile' when viewed under the microscope, the observation that gave the syndrome its name.

Although rare, Fragile X is the largest cause of inherited mental retardation (although in a third of patients, the genetic abnormality occurs spontaneously) affecting around one in every 3,600 males and one in 4,000-6,000 females. There are around 80,000 patients with Fragile X in the US and 130,000 in the EU27.

Features of the condition include mental impairment, ranging from learning disabilities to mental retardation, attention deficit and hyperactivity, anxiety, unstable mood and autistic behaviour. Boys are more severely affected than girls (who would have one normal X chromosome). Most Fragile X boys have mental retardation (eg the IQ of an adult male would be likely to be 40-50). Girls with Fragile X exhibit a high incidence of anxiety disorders, while a smaller proportion (30%-50%) has intellectual impairment (and some can have normal intelligence). Emotional and behavioural problems are, however, common to both sexes.

About one third of patients with Fragile X syndrome meet the DSM IV criteria for autism and a further third for autism spectrum disorder. It is possible that NPL-2008 may be suitable for treating the autistic behaviour of patients with Fragile X syndrome and Neuropharm could pursue this potential indication in the future. A diagnosis of autism would normally exclude Fragile X (and other rare chromosomal disorders with similar symptoms), which may cause the symptoms.

There is currently no approved specific treatment for Fragile X syndrome, although there are a number of therapies available for treating the symptoms (eg epilepsy, hyperactivity, emotional problems).

Financials

Our model indicates Neuropharm will record an operating loss of around £7m for the year to 30 June 2008, reflecting the spending on its programmes, and will end the year with cash of £10.6m. Full-year results are due to be reported in October.

The company raised £20m gross (£18.2m net) in its 2007 AIM listing. Neuropharm operates with a low fixed cost base and would not need to incur most of the costs in establishing its US sales force until it can be reasonably confident of approval of its NPL-2008 programme in autism in H209.

Exhibit 3: Financials

Note: 2006 was the year of incorporation. US launch of NPL-2008 is possible in FY2010, although forecasts do not anticipate this, pending the outcome of the SOFIA study.

Year end 30 June	£'000	2006 IFRS	2007 IFRS	2008e IFRS	2009e IFRS	2010e IFRS
PROFIT & LOSS						
Revenue		0	0	0	0	0
Cost of Sales		0	0	0	0	0
Gross Profit		0	0	0	0	0
EBITDA		(277)	(3,006)	(7,011)	(6,904)	(3,353)
Operating Profit (before GW and except.)		(277)	(3,009)	(7,016)	(6,911)	(3,361)
Intangible Amortisation		0	(3)	(3)	(3)	(2)
Exceptionals		0	0	0	0	0
Other		(86)	(544)	(150)	(550)	(550)
Operating Profit		(363)	(3,556)	(7,169)	(7,464)	(3,913)
Net Interest		0	320	900	400	200
Profit Before Tax (norm)		(277)	(2,689)	(6,116)	(6,511)	(3,161)
Profit Before Tax (FRS 3)		(363)	(3,236)	(6,269)	(7,064)	(3,713)
Tax		0	0	350	350	350
Profit After Tax (norm)		(277)	(2,689)	(5,766)	(6,161)	(2,811)
Profit After Tax (FRS 3)		(363)	(3,236)	(5,919)	(6,714)	(3,363)
Average Number of Shares Outstanding (m)		4.2	19.5	31.5	31.5	31.5
EPS - normalised (p)		(6.6)	(13.8)	(18.3)	(19.5)	(8.9)
EPS - FRS 3 (p)		(8.7)	(16.6)	(18.8)	(21.3)	(10.7)
Dividend per share (p)		0.0	0.0	0.0	0.0	0.0
BALANCE SHEET						
Fixed Assets		0	59	66	71	75
Intangible Assets		0	47	44	41	39
Tangible Assets		0	12	22	30	36
Investments		0	0	0	0	0
Current Assets		570	18,109	11,429	5,508	2,339
Stocks		0	0	0	0	0
Debtors		101	458	800	800	800
Cash		469	17,651	10,629	4,708	1,539
Current Liabilities		(146)	(1,365)	(2,600)	(2,000)	(2,000)
Creditors		(146)	(1,365)	(2,600)	(2,000)	(2,000)
Short term borrowings		0	0	0	0	0
Long Term Liabilities		0	(101)	(101)	(101)	(100)
Long term borrowings		0	0	0	0	0
Other long term liabilities		0	(101)	(101)	(101)	(100)
Net Assets		424	16,702	8,794	3,478	314
CASH FLOW						
Operating Cash Flow		(232)	(2,144)	(7,907)	(6,307)	(3,355)
Net Interest		0	320	900	400	200
Tax		0	0	0	0	0
Capex		0	(15)	(15)	(15)	(14)
Expenditure on intangibles		0	0	0	0	0
Acquisitions/disposals		0	0	0	0	0
Financing		701	19,021	0	0	0
Dividends		0	0	0	0	0
Net Cash Flow		469	17,182	(7,022)	(5,922)	(3,169)
Opening net debt/(cash)		0	(469)	(17,651)	(10,629)	(4,708)
HP finance leases initiated		0	0	0	0	0
Other		0	0	0	0	0
Closing net debt/(cash)		(469)	(17,651)	(10,629)	(4,708)	(1,539)

Source: Edison Investment Research

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