

18 March 2009

Neuropharm

Year End	Revenue (£m)	PBT* (£m)	EPS* (p)	DPS (p)	P/E (x)	Yield (%)
06/07	0.0	(2.7)	(13.8)	0.0	N/A	N/A
06/08	0.0	(4.8)	(12.8)	0.0	N/A	N/A
06/09e	0.0	(5.7)	(17.2)	0.0	N/A	N/A
06/10e	0.0	(2.4)	(7.5)	0.0	N/A	N/A

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

Investment summary: Rethink on NPL-2008

Neuropharm is to review its strategy for NPL-2008 in the wake of the failed pivotal SOFIA study in autism. It is currently analysing the SOFIA data and should be able to define the alternatives for further development of NPL-2008 within the next couple of months, which would probably involve some form of corporate partnership. While Neuropharm trades at a quarter of its £10m cash value, there is no obvious short-term catalyst to boost its share price other than a deal on NPL-2008 or M&A. Nonetheless, it remains well funded with c £10m of cash and has a low burn rate.

SOFIA study misses endpoint

The SOFIA study did not meet its primary endpoint of repetitive behaviour, as measured by CYBOCS-PDD, which improved on both NPL-2008 and placebo over the 14-week treatment period (so that there was no significant difference between the two). The study recruited 158 patients – some 30 more than originally planned – suggesting it is unlikely to have been underpowered.

Strategy for NPL-2008 under review

Neuropharm will be in a position to determine its strategy for NPL-2008 once full data from SOFIA have been analysed. Its options include further development in autism or another indication, although this would probably require a corporate partnership. It is well funded with £10m of cash and can avoid the previously budgeted expenditures associated with the planned filing and launch.

Fragile X programmes: Partners sought

Neuropharm is also looking for partners for its two early clinical development programmes for fragile X syndrome, which both reported positive results last year.

Valuation: £13m-50m, depending on NPL-2008 probability

We indicate a valuation range of £13m-50m based on a risk-adjusted NPV, depending on what probability, if any, is assigned to NPL-2008 (the lower figure is 0%, the higher figure 20%). However, it is unrealistic to expect much appreciation in the share price until there is further clarification on corporate strategy.

Price 6.75p
Market Cap £2m

Share price graph



Share details

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

Price

52 week High 177.0p Low 5.6p

Balance sheet as at 31 December 2008

Debt/Equity (%) N/A
NAV per share (p) 31.7
Net cash (£m) 10.2

Business

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

Valuation

	2008	2009e	2010e
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%	0%

Analyst

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Company description: CNS specialist drug developer

Neuropharm is a UK company focused on the development of products for central nervous system (CNS) conditions, principally affecting children (autism, fragile X syndrome and paediatric obsessive-compulsive disorder). The company plans to review its strategy for its lead product NPL-2008, after the failure of after the pivotal Phase III SOFIA study, which put paid to its plan to file and possibly launch the product in the US later this year.

Further analysis and a review of the data on the primary and secondary endpoints from the SOFIA study are underway, which will provide a basis for decisions on the future development, if any, of NPL-2008. It may be possible to continue development of NPL-2008 in autism or a related indication, although Neuropharm would probably have to establish some form of corporate partnership to do so.

Valuation

We indicate a valuation range of £13m-50m based on a risk-adjusted NPV, depending on what probability, if any, is assigned to NPL-2008 (the lower figure is 0%, the higher figure 20%). In advance of the outcome of the detailed SOFIA analysis, it is difficult to ascribe a probability to NPL-2008 reaching the market, hence we present a range of outcomes. Our calculations now use a higher WACC (15%), and longer timelines and assume less favourable partnership economics for all the programmes in the portfolio. However, it is unrealistic to expect much appreciation in the share price until there is some further clarification on corporate strategy.

Sensitivities

At the current share price, there is little downside risk, but at the same time, there is no obvious short-term catalyst (other than a partnership or M&A) that could help restore confidence. There is a reasonable possibility that the full analysis of the SOFIA data may present a viable development strategy for NPL-2008 (there may have been an element in the design that caused the high placebo response or the design that is intended to find a lowest effective dose may have resulted in it being under-dosed, for example). There is a good possibility that Neuropharm may be able to consummate some transaction that recovers value.

Financials

Neuropharm's interim results show cash of £10.2m. Our revised model shows reduced costs, but should be considered tentative until the strategy is clearer. Neuropharm should have a low cash burn going forward, since it has only 12 full-time employees (including two in the US) and operates as a virtual organisation. Our model suggests a cash position in the absence of further studies with NPL-2008 or any significant investment in other programme would now be £6m at the end of financial 2009 and around £4m in financial 2010.

Investment summary: Rethink on NPL-2008

Neuropharm is to review its strategy for lead product NPL-2008 in the wake of the failed pivotal SOFIA study in autism. The company is currently analysing the results of the primary and secondary endpoints from SOFIA and should be able to determine its options for further development within the next few months. Although Neuropharm trades at around a quarter of its cash value, there is no obvious short-term catalyst that could boost its share price, other than a deal on NPL-2008 or M&A. However, when the outcome of the review is clear, there may be a special situation investment case.

Neuropharm will probably have to establish a corporate partnership if there is a viable strategy for further development of NPL-2008. It has indicated that following third party interest, one option of potential is to partner with a larger pharmaceutical company, which would bring in sufficient funding to finance further development. Neuropharm is well funded with c £10m of cash and should have a low burn rate going forward from corporate overhead.

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	158-patient Phase III (SOFIA) study did not achieve statistical significance on the primary endpoint, change versus placebo from baseline over the 14-week treatment period in CYBOCS-PDD (Children's Yale-Brown Obsessive Compulsive Scale modified for pervasive developmental disorders). The study examined three doses (2mg, 9mg or 18mg/day) with flexible titration designed to achieve a 25% improvement in CYBOCS-PDD. Further analysis and review of the data on the primary and secondary endpoints are underway, which will provide the basis for future development decisions. Although Neuropharm has submitted the CMC package, as part of a rolling NDA in September, the SOFIA study result will not support approval for autism. The EMMA open-label extension study is being discontinued. US orphan drug designation held. 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 (7-16 years of age) with FXS and co-morbid attention deficit hyperactivity disorder showed significant reduction in Connors' Parent Rating Scale hyperactivity scores ($p < 0.05$) and non-significant trend in cognition. Six/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 (as valproate is a marketed, off-patent anticonvulsant used for epilepsy and bipolar disorder). US orphan drug designation held. We have also initiated a business development strategy for NPL-2005 relevant to the fragile X syndrome population.
NPL-2009 (fenobam)	fragile X syndrome	12-patient, open-label, dose-escalation Phase IIa study of escalating single 50mg-150mg doses in male and female adults showed that the drug was well tolerated with no CNS effects (primary endpoint was safety). PK showed NPL-2009 levels were dose dependent but variable. Outcome measures included prepulse inhibition (PPI) and a continuous performance test (CPT) obtained before and after dosing on core phenotypic measures of sensory gating, attention and inhibition. PPI met a response criterion of an improvement of >20% over baseline in 6 of 12 individuals (4/6 males and 2/6 females). Results have now been published (Berry-Kravis <i>et al</i> , Journal of Medical Genetics, Jan 2009). Work is underway to identify an appropriate formulation of NPL-2009 for use in further clinical studies. US orphan drug designation held. Preclinical data acquired from FRAXA in return for a 3% royalty on net sales; right of reference to the original IND from Johnson & Johnson 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 (minocycline)	paediatric OCD	Investigator-sponsored 20-patient pilot Phase II study in adults with OCD (results: Q3 2010). Phase IIa study in paediatric OCD was closed, part-recruited in 2008; data are expected to be reported shortly. Active agent is a marketed antibiotic.

Source: Edison Investment Research

SOFIA: Primary endpoint not met

The SOFIA study did not meet its primary endpoint of improving repetitive behaviour in autistic children/adolescents, as measured using the CYBOCS-PDD (Children's Yale-Brown Obsessive Compulsive Scale modified for pervasive developmental disorders). CYBOCS-PDD scores were reduced (ie patients improved) on both NPL-2008 and placebo over the 14-week treatment period, with no statistical difference between the two.

Patients were titrated to one of three doses (2mg, 9mg or 18mg/day) to try to achieve and maintain at least a 25% reduction in CYBOCS-PDD, which was assessed at two-weekly intervals. The study recruited 158 patients (aged between five and 17) – some 30 more than originally planned – suggesting it is unlikely to have been underpowered.

Previous studies with fluoxetine, including a Phase IIb trial (in children and adolescents) and a Phase III trial (in adults), have produced positive results. The earlier Phase IIb study saw an 8% reduction in CYBOCS with fluoxetine (using a different formulation from NLP-2008), versus a 3% increase on placebo, a statistically significant difference ($p=0.039$).

The magnitude of the improvement in both active and placebo has not been disclosed but the active effect is thought to be in line with that achieved in the previous studies. Neuropharm is examining whether some difference in design of the studies led to the higher than expected placebo effect. The Zydys formulation was found to be very patient-friendly and the study achieved a high compliance rate (>95%). It may also be possible that the aspect of SOFIA which sought to identify the lowest effective dose may have meant that patients were under-dosed.

Although a number of trials (mostly open-label) with SSRIs in autism have demonstrated some improvement in global functioning and symptoms, SOFIA is the second large Phase III trial of an SSRI to have failed in autism (the NIH-sponsored STARRT-2 study of citalopram in 149 children over 12 weeks also failed to show an effect). The SOFIA study is the largest randomised clinical trial to have been completed in autism.

There are currently no products specifically approved for treating autism, although Risperdal (risperidone, J&J) is indicated for treating irritability associated with the condition. Current development programmes for the condition are shown in Exhibit 2.

Exhibit 2: Competitive landscape in autism

Note: NIMH = National Institute of Mental Health; part of the NIH.

Product	Company	Development stage/clinical trials/notes
Risperdal (risperidone)	J&J	Approved for the treatment of irritability and associated behaviour in autistic children. 93-p, Phase IV study to evaluate irritability and related behaviours in children or adolescents with autism for six weeks, with a 26-week extension (results: Sept 2009).
Invega (paliperidone)	J&J	30-pt eight-week, open-label study to examine aggression, self-injury and irritability in adolescents and young adults with autism (results: Aug 2009).
Abilify (aripiprazole)	Bristol-Myers Squibb/Otsuka	300-pt, 52-week (flexible dose 2mg to 15mg) in children/adolescents with autistic disorders (results: June 2009). 30-pt, Phase II study on behaviours and development associated with ASD (results due: Jan 2009).
Daytrana (methylphenidate)	Shire	Investigator-sponsored 20-pt Phase II open-label pilot study for treatment of attention and behavioural symptoms in children with autism spectrum disorders (results: Dec 2008).
Strattera (atomoxetine)	Lilly	100-pt, eight-week Phase IV study for symptoms of ADHD in children/adolescents with autism (completion: May 2010). NIMH-sponsored 86-pt, Phase III study in children with ADHD symptoms with autism, Asperger's syndrome and PDD-NOS (completion: Jul 2012).
intranasal oxytocin	various (Novartis)	Investigator-sponsored Phase II to evaluate improvement of mood and social functioning in adults with autism.
oxcarbazepine	various/generic	Investigator-sponsored 12-week, 20-pt study to assess the effectiveness in childhood/adolescent autism.
D-cycloserine	generic	NIMH-sponsored Phase III study in 80 children aged 3-12 in reducing certain symptoms of autism, including some aspects of social impairment.
Aricept (donepezil)	Pfizer	NIMH-sponsored 11-week Phase II study in 40 children/adolescents with autism spectrum disorder, attempting to treat cognitive deficits.
Zyprexa (olanzepine)	Lilly (Zydis formulation)/generic oral	78-pt Phase II study examining effect on disruptive behaviours associated with autism in children aged three to 12 years. The first six weeks are double-blind; the second six weeks all patients are on drug (results: June 2009). NIMH-sponsored Phase II/III (results: Sep 2009).
citalopram	generic	NIMH-sponsored 12-week Phase II study in 149 children. Completed but unpublished.
naltrexone	various/generic	Investigator-sponsored 50-pt study to examine effect of low-dose naltrexone on children with ASD; examines social functioning and language.
minocycline	generic	Open-label NIMH study in 12 children aged 3-12 with regressive autism.
carbetocin	MDRNA	Phase I study of nasal spray formulation to treat autism-related symptoms initiated in 2007.

Source: Edison Investment Research

Other R&D programmes

Neuropharm has two products in development for fragile X syndrome, NPL-2005 and NPL-2009, which have shown positive results in small studies, and another product, NPL-2003, for paediatric OCD. These programmes currently have been a low priority as resources had been devoted to NPL-2008 and no Neuropharm-sponsored clinical trials are underway or planned. It may be possible that these programmes could be given a higher priority in the future.

Fragile X syndrome

FXS is an X-linked mutation that prevents production of FMRP, a protein needed for normal brain functioning. Although rare, it is the largest cause of inherited mental retardation affecting around one in every 3,600 males and one in 4,000-6,000 females. There are around 80,000 patients with FXS in the US and 130,000 in the EU. The features of the condition include mental impairment, ranging from learning disabilities to mental retardation, attention deficit and hyperactivity, anxiety, an unstable mood and autistic behaviour. Boys are more severely affected than girls (who would have one normal X chromosome). Most FXS boys have mental retardation, while girls with FXS exhibit a high incidence of anxiety disorders with a smaller proportion having intellectual impairment. Emotional and behavioural problems are common to both sexes.

There is currently no approved specific treatment for FXS, although there are a number of therapies available for treating the symptoms (eg epilepsy, hyperactivity, emotional problems). Novartis recently started a pilot study of AFQ056, a compound with the same mGluR5 mechanism of action as NPL-2009. Five other products are in development for FXS, as shown in Exhibit 3.

Exhibit 3: Competitive landscape in fragile X syndrome

Product	Company	Development stage/clinical trials/notes
arbaclofen/ STX 209	Seaside Therapeutics	60-patient Phase II study to examine effect on irritability associated with FXS (results: October 2009).
Aricept (donepezil)	Pfizer	Investigator-sponsored 10-patient open-label trial.
Abilify (aripiprazole)	Bristol-Myers Squibb/Otsuka	Investigator-sponsored 12-patient Phase II study in children and adults with FXS (results: April 2009).
AFQ056	Novartis	30-patient Phase II (results: May 2009).
memantine	Forest Labs	180-patient study Phase II study (results: September 2012).

Source: Edison Investment Research

Valuation

In the light of the SOFIA result, we have reviewed our valuation and are now indicating a range of £13m-50m based on a risk-adjusted NPV. This range reflects the probability assigned to NPL-2008 reaching the market (the lower figure is 0%, the higher figure 20%), having previously been much higher. In advance of the outcome of the detailed SOFIA analysis, it is difficult to ascribe a probability to NPL-2008 reaching the market, hence we present a range of outcomes.

In addition, we are also using a higher discount rate/cost of capital of 15%, to reflect the current macroeconomic conditions, and have introduced longer timelines and assume less favourable licensing partnership economics. This also impacts the value of the FXS programmes, because of the increased uncertainty associated with Neuropharm's ability to fund further clinical studies.

A number of other biotech companies are trading below cash following product development disappointments or other setbacks.

Sensitivities

At the current share price, there is little downside risk, but at the same time, there is no obvious short-term catalyst that could boost the share price anywhere near previous levels. There is a reasonable possibility that the full analysis of the SOFIA data may present a viable development strategy for NPL-2008. However, given Neuropharm's current position, we expect it would have to consummate some partnership transaction to fund any further studies of NPL-2008, because of its limited ability to raise new finance (in the light of the markets and the current share price).

Financials

Neuropharm's interim results show cash of £10.2m. We have revised our model to reflect reduced costs of the planned pre-launch promotion, but the forecasts should be considered tentative until the strategy is clearer. (Our model did not previously anticipate any sales of NPL-2008, but also excluded the costs associated with the previously planned US sales force build-up.)

We have forecast R&D costs of £4m for the year to 30 June 2009: the spend in the first half was £2.3m and we have assumed costs of £1.7m in the second half, largely in relation to the now closed EMMA study. Neuropharm booked a one-off gain of £719k in the first half in relation to the value of foreign exchange transactions and forward currency contracts, presumably as a result of the stronger US dollar.

Neuropharm should have a low cash burn going forward, since it has only 12 full-time employees (including two in the US) and operates as a virtual organisation. We suggest its cash position in the absence of further studies with NPL-2008 or any significant investment in other programmes would now be £6m at the end of financial 2009 and £4m in financial 2010.

Edison's financial model is shown in Exhibit 4.

Exhibit 4: Financials

Note: 2006 was the year of incorporation. 2009/2010 forecasts should be considered tentative until the strategy is determined.

Year end 30 June	£'000s	2006 IFRS	2007 IFRS	2008 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)	(2,986)	(5,729)	(6,807)	(2,412)
Operating profit (before GW and except.)		(277)	(2,989)	(5,734)	(6,814)	(2,420)
Intangible amortisation		0	(3)	(3)	(42)	0
Exceptionals		0	0	0	(147)	0
Share-based payments		(86)	(544)	(143)	(600)	(250)
Operating profit		(363)	(3,536)	(5,880)	(7,603)	(2,670)
Net interest		0	320	881	405	70
Profit before tax (norm)		(277)	(2,689)	(4,799)	(5,690)	(2,350)
Profit before tax (FRS 3)		(363)	(3,236)	(4,945)	(6,479)	(2,600)
Tax		0	0	754	250	0
Profit after tax (norm)		(277)	(2,689)	(4,045)	(5,440)	(2,350)
Profit after tax (FRS 3)		(363)	(3,236)	(4,191)	(6,229)	(2,600)
Average number of shares outstanding (m)		4.2	19.5	31.5	31.5	31.5
EPS - normalised (p)		(6.6)	(13.8)	(12.8)	(17.2)	(7.5)
EPS - FRS 3 (p)		(8.7)	(16.6)	(13.3)	(19.8)	(8.2)
Dividend per share (p)		0.0	0.0	0.0	0.0	0.0
BALANCE SHEET						
Fixed assets		0	59	223	184	186
Intangible assets		0	47	42	0	0
Tangible assets		0	12	181	184	186
Investments		0	0	0	0	0
Current assets		570	18,109	13,864	6,485	4,333
Stocks		0	0	0	0	0
Debtors		101	458	704	400	400
Cash		469	17,651	12,658	6,085	3,933
Other		0	0	502	0	0
Current liabilities		(146)	(1,365)	(1,332)	(1,000)	(800)
Creditors		(146)	(1,365)	(1,332)	(1,000)	(800)
Short-term borrowings		0	0	0	0	0
Long-term liabilities		0	(101)	(97)	(101)	(100)
Long-term borrowings		0	0	0	0	0
Other long-term liabilities		0	(101)	(97)	(101)	(100)
Net assets		424	16,702	12,658	5,568	3,619
CASH FLOW						
Operating cash flow		(232)	(2,124)	(5,743)	(6,968)	(2,212)
Net interest		0	320	881	405	70
Tax		0	0	0	0	0
Capex		0	(15)	(185)	(10)	(10)
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	17,202	(5,047)	(6,573)	(2,152)
Opening net debt/(cash)		0	(469)	(17,651)	(12,658)	(6,085)
HP finance leases initiated		0	0	0	0	0
Other		0	(20)	54	0	0
Closing net debt/(cash)		(469)	(17,651)	(12,658)	(6,085)	(3,933)

Source: Edison Investment Research

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