

25 March 2010

GW Pharmaceuticals

Year end	Revenue (£m)	PBT* (£m)	EPS* (p)	DPS (p)	P/E (x)	Yield (%)
09/08	11.8	(9.5)	(6.2)	0.0	N/A	N/A
09/09	24.1	1.8	1.7	0.0	69.4	N/A
09/10e	29.3	5.7	4.4	0.0	26.8	N/A
09/11e	23.8	(0.5)	(0.4)	0.0	N/A	N/A

Note: *PBT and EPS exclude intangible amortisation and share-based payments.

Investment summary: Positive cancer pain data

GW Pharmaceuticals has reported a positive outcome to its US Phase IIb trial of Sativex in cancer pain, achieving statistically significant improvements in pain scores over placebo in most of the outcome measures. The results support the planned move into Phase III studies with partner Otsuka later this year. This follows last week's news that GW had reached Day 150 of the assessment process of its European submission for Sativex for multiple sclerosis spasticity, a milestone that should lead to the first EU approvals, in the UK and Spain, coming through in Q2.

US cancer pain study positive

The 360-patient Phase IIb study in opioid-refractory cancer pain evaluated three doses of Sativex over a five-week treatment period. The study showed significant ($p < 0.05$) differences versus placebo with two of three response criteria for both the low and mid dose ranges. GW will request an end-of-Phase II meeting with the FDA to confirm the Phase III trial plan; two such trials are expected to be required for US registration. These are expected to begin in H210 and complete in 2012.

UK/Spanish approvals expected in Q2

UK and Spanish approvals should materialise in Q2. The UK launch will be take place immediately; launch in Spain would require a pricing decision. Further approvals in the EU will be sought under the MR procedure in H2.

Sativex approval decision in Canada in H2

A decision on the submission for MS spasticity in Canada, where Sativex has conditional approval (NOC/c) for cancer/neuropathic pain, is expected in H210.

Valuation: £132m EV compares with DCF value of £163m

We indicate a DCF valuation (excluding cash) of £163m, which compares with GW's EV of £130m (£153m market cap less FY10 cash). This applies a 60% development risk to potential cancer pain revenues in the US. Further upside is possible based on the pursuit of new indications for Sativex and progression of GW's other early-stage R&D projects.

Price 118p
Market cap £153m

Share price graph



Share details

Code GWP
Listing AIM
Sector Pharmaceuticals & Biotechnology
Shares in issue 129.3m

Price

52-week High 125.5p Low 70.0p

Balance sheet as at 30 September 2009

Debt/equity (%) N/A
NAV per share (p) 5.2
Net cash (£m) 20.6

Business

GW Pharmaceuticals is a UK company focused on developing cannabinoids as pharmaceuticals. Its lead product, Sativex, is in development for the treatment of neuropathic pain and spasticity associated with MS, cancer pain and peripheral neuropathic pain.

Valuation

	2009	2010e	2011e
P/E relative	476%	231%	N/A
P/CF	N/A	56.1	N/A
EV/sales	5.3	4.4	5.6
ROE	32%	37%	N/A

Revenues by geography

	UK	Europe	US	Other
	6.9%	7.7%	65.9%	19.5%

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Update: Sativex passes key approval hurdle in EU

GW Pharmaceuticals has reported a positive outcome to its US Phase IIb trial of Sativex in cancer pain, achieving statistically significant improvements in pain scores over placebo in two of three predefined outcome measures for two of the three dose ranges tested. The results support the planned move into Phase III studies with partner Otsuka later this year. GW will request an end-of-Phase II meeting with the FDA shortly to confirm the Phase III trial designs. It expects two studies would be required to file a submission in this indication. These studies are expected to begin in late H210 and complete in 2012.

Design

The Phase IIb study evaluated three doses of Sativex over a five-week treatment period in 360 patients (an unusually large number for a Phase II study), all of whom had advanced cancer and were obtaining inadequate analgesia despite optimised chronic opioid therapy. All trial subjects received study drug as an add-on treatment to opioid therapy and were maintained on stable doses during the study.

Patients were randomised to one of three dose arms: low (1-4 sprays per day), mid (6-10 sprays per day), and high (11-16 sprays per day). The randomisation within each arm was 3:1 in favour of Sativex, therefore each dose cohort would have approximately 90 patients on Sativex and 30 on placebo.

The measurement of pain was scored by the patient on a Numerical Rating Scale (NRS), where a score of 0 is "no pain" and 10 is "worst pain imaginable". This is a well-validated scale and is universally accepted for clinical studies in pain.

Results were analysed according to three methodologies: mean absolute change in NRS from baseline, the percentage of patients achieving a 30% change from baseline (30% responder analysis), and continuous response analysis. The latter (where all responders are characterised by percentage improvement) has been the key efficacy parameter in the product labelling of several recently approved medicines for pain in the US.

Results

Preliminary results of the study show significant ($p < 0.05$) differences for Sativex versus placebo for the low and mid dose ranges in the continuous response analysis and mean change from baseline. The 30% responder analysis was numerically in favour of Sativex but did not reach statistical difference for these two dose groups. Outcome data (on an intention to treat (ITT) basis), is shown in Exhibit 1.

Exhibit 1: Sativex cancer pain Phase IIb: outcome data

Note: N/S = not significant ($p > 0.05$); N/A = not available.

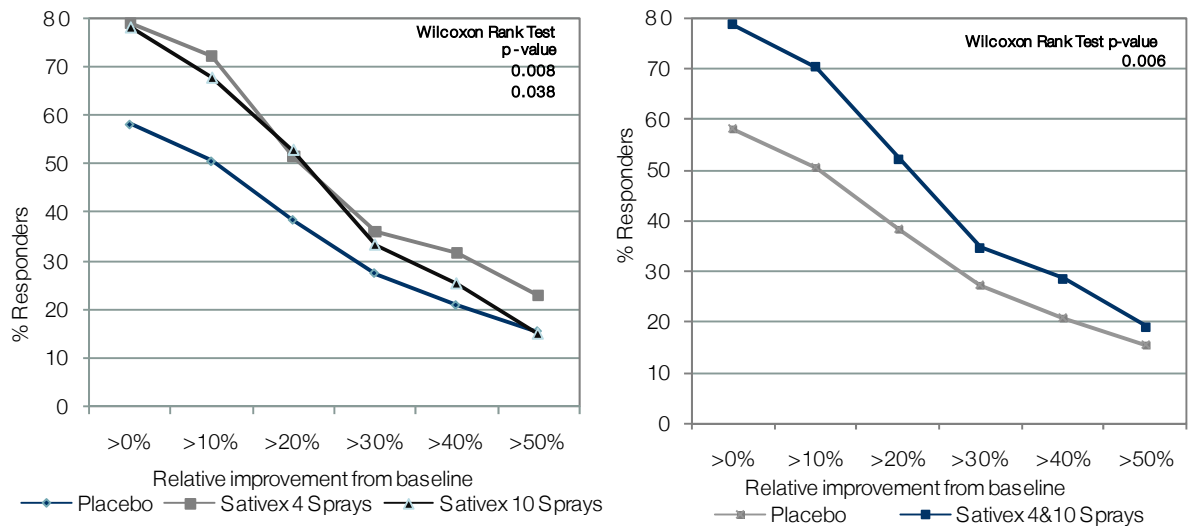
Dose range	Mean change in NRS	30% responder analysis	Continuous response analysis	Sleep disruption	Discontinue rate
Low (1-4 sprays) Sativex n=89, placebo n=91	-1.6, $p=0.006$	Numerically superior, N/S	12.5 (95% CI: -21.3, -3.3), $p=0.008$	$p=0.003$	5%
Mid (6-10 sprays) Sativex n=87, placebo n=91	N/A	Numerically superior, N/S	-8.8 (95% CI: -17.1, 0.0), $p=0.038$	N/A	7%
Low/mid combined (1-10 sprays) Sativex n=176, placebo n=91	-1.4, $p=0.019$	N/A	-10.5 (95% CI: -17.9, -3.1), $p=0.006$	$p=0.016$	N/A
High (11-16 sprays)	N/S	N/S	N/S	N/S	22%

Source: GW Pharmaceuticals, Edison Investment Research

The 30% responder analysis was the pre-determined primary efficacy measure, but since the study was not pivotal, this does not present an issue. According to GW, the study met its key objectives of generating sufficient efficacy and safety information to justify a move into Phase III development, determining the effective dose range of Sativex in this patient population and determining the optimal study parameters to be used in Phase III studies. The data would confirm that the optimal benefit to risk ratio for Sativex is achieved at doses ≤ 12 sprays/day.

Data for the continuous response analysis for the low and mid dose ranges (separately and combined) are illustrated in Exhibit 2.

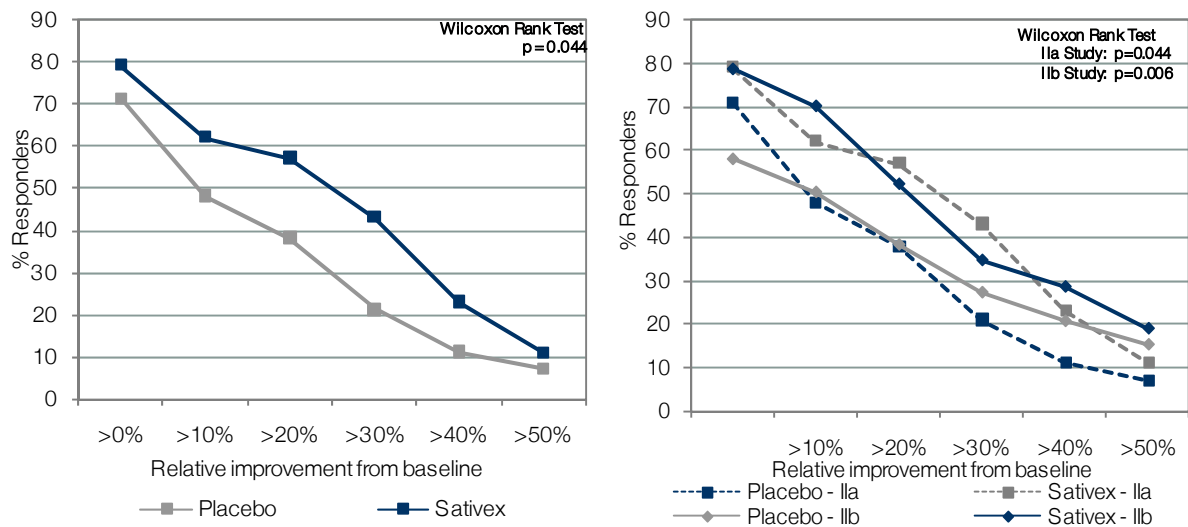
Exhibit 2: Phase IIIb Continuous Response Analysis: low and mid doses (LHS) and combined (RHS)



Source: GW Pharmaceuticals

GW notes that the results are consistent with those from a previous Phase IIa, three-week clinical trial in 177 patients, which were published.¹ For comparison, the Phase IIa data are shown in Exhibit 3 (LHS) and the outcome from the Phase IIIb superimposed, shown in the RHS.

Exhibit 3: Continuous Response Analysis from Phase IIa (LHS) and combined (RHS)



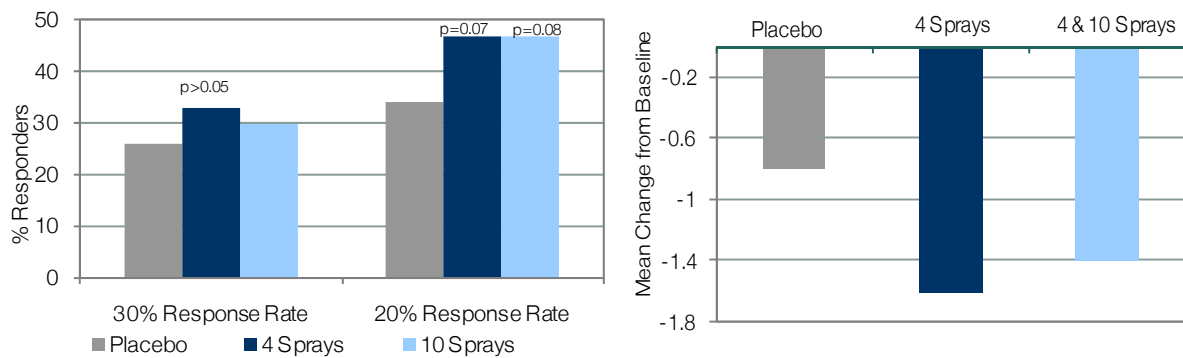
Source: GW Pharmaceuticals

¹ Johnson J *et al*, Journal of Pain and Symptom Management, Vol 39, Issue 2, pp 167-179.

The high dose group was less well tolerated than the low and mid dose groups and as a result saw a higher rate of discontinuations (22%) due to adverse events than low or mid dose or placebo (10%) and showed no improvement in efficacy over placebo. The most common adverse events (>10% for the combined Sativex population) were nausea (22% vs 13% for placebo), dizziness (19% vs 13%), neoplasm progression (18% vs 14%), vomiting (16% vs 8%) and somnolence (15% vs 4%). The adverse event profile for low dose Sativex compared favourably to placebo.

The proportion of patients who achieved a 30% response was numerically superior, but not significant at $p < 0.05$ for the low and mid groups, see Exhibit 4 LHS. Interestingly the results approached statistical significance for the 20% responder group ($p = 0.07 - 0.08$). Mean improvement from baseline is shown in Exhibit 4, RHS.

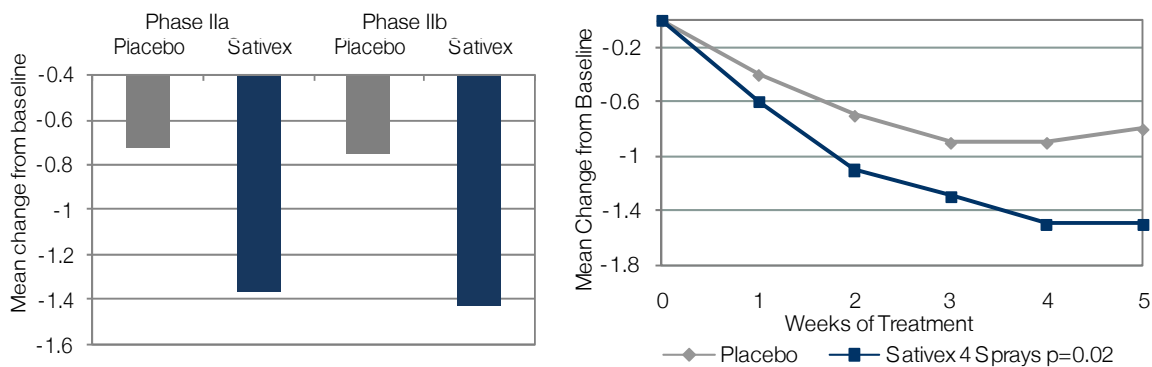
Exhibit 4: Phase IIb 30% & 20% Improvement as Response (LHS) and Mean Improvement from Baseline (RHS)



Source: GW Pharmaceuticals

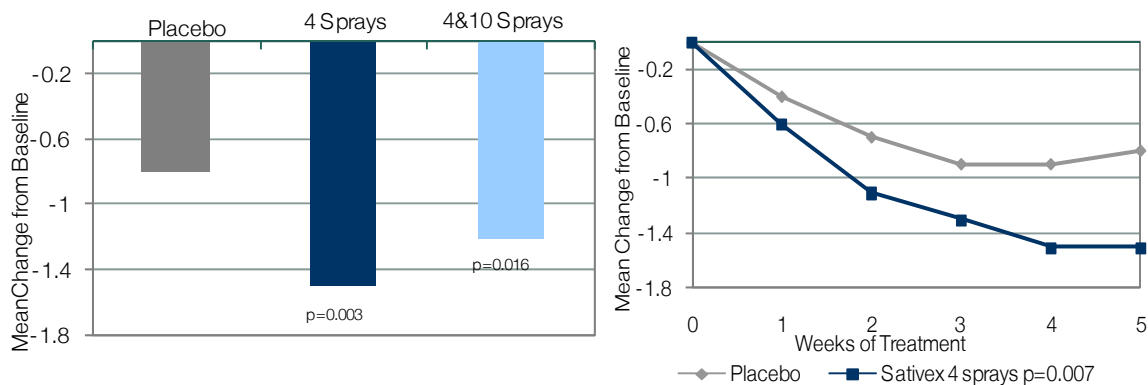
Data showing the mean improvement from baseline for both the earlier Phase IIa and Phase IIb studies and the time course change is shown in Exhibit 5.

Exhibit 5: Mean improvement from baseline (LHS) and Phase IIb time course (RHS)



Source: GW Pharmaceuticals

The study also showed a statistically significant improvement in sleep disruption, a secondary endpoint, both from baseline and over time (Exhibit 6, LHS and RHS panels).

Exhibit 6: NRS Sleep Disruption Score: mean reduction (LHS) and time course (RHS)

Source: GW Pharmaceuticals

Sativex is composed primarily of two cannabinoids, delta 9 tetrahydrocannabinol (THC) and cannabidiol (CBD) and is administered as a metered-dose oromucosal spray; each 100µl spray contains 2.7mg of THC and 2.5mg of CBD. These components bind to cannabinoid receptors distributed throughout the central nervous system and in immune cells.

The current status of Sativex's development in various indications and the other programmes in GW's R&D portfolio are summarised in Exhibit 7 and its licensing arrangements are summarised in Exhibit 8.

Exhibit 7: R&D/clinical trial summary

Product/indication	Trial design/notes
Sativex – spasticity in multiple sclerosis	EU filing in UK (reference member state) and Spain (concerned member state) reaches Day 150 without major issues. Formal approval should be finalised in Q2 allowing approvals to be sought under mutual recognition in other EU countries in H210. Filed in Canada (Nov 2009), approval decision expected H210. Indication is likely to be for symptomatic improvement in patients suffering from spasticity as a result of MS who have not adequate relief with existing medications.
Sativex – cancer pain	360-pt Phase IIb trial in opioid-refractory cancer pain shows significant improvement in various measures of pain. End-of Phase II meeting to be scheduled with FDA to confirm design of studies required for approval. Two Phase III studies are envisaged, which should start recruitment in H2 of 2010. US submission possible in 2012. EU submissions, using the same data, at the same time.
Sativex – neuropathic pain in MS.	66-pt Phase III study demonstrated effectiveness in reducing pain (p=0.005) and sleep disturbance (p=0.003). A 339-pt Phase III study did not show statistical significance in primary endpoint (30% or greater improvement in VAS), although significant results were seen at equal dosing and a randomised withdrawal extension study showed statistical significance.
Sativex – peripheral neuropathic pain	Two of three Phase III trials completed with statistically significant results. Two Phase III studies planned after first EU approval for MS spasticity.
THCV: CBD – metabolic syndrome, type 2 diabetes	Multiple-dose, three month Phase IIa study (testing THCV and CBD combined at different ratios) is planned for H110 in c 48 Type 2 diabetics with residual pancreatic function. The primary endpoint will likely concern measures of blood and liver lipid levels. Single-dose Phase I study completed in 12 healthy volunteers, with no tolerability at relevant doses. Preclinical models suggest that THCV: CBD reduces fasting insulin, leptin and body fat, increases energy expenditure, reduces total cholesterol and increases HDL.
CBD, CBDV, CBC, CBG, THCA, THCV, CBN and others, incl. combinations	Drug candidates under evaluation in collaboration with Otsuka for CNS (anti-psychotic, anti-depressant, anti-epileptic and anxiolytic) and anticancer (antiproliferative, antiangiogenic, proapoptotic, antimigratory) properties. Three-year deal (signed July 2007). First candidate (possibly in a psychiatry indication or epilepsy) could enter clinical trials in 2010. Sativex has shown a synergistic benefit with temozolomide in an <i>in vivo</i> model of glioma and further preclinical studies in other <i>in vivo</i> cancer models (prostate, breast, lung) are currently underway.

Source: Edison Investment Research

Exhibit 8: GW Pharmaceutical licensing arrangements

Partner	Product	Financial terms
Bayer HealthCare	Sativex in UK and Canada	£32.75 total milestones payable, of which £8m have been received to date. £10m payable on first UK approval (Q210). Transfer price less manufacturing cost results in a c 30% effective royalty on sales.
Almirall	Sativex in Europe (excluding UK)	£12m signature fee plus milestones payments of £30m. £8m paid on EU filing, with £2.5m payable on first EU approval (Spain, on completion of pricing negotiations, assumed Q310). Transfer price less manufacturing cost results in a c 25% effective royalty.
Otsuka	Sativex in US	\$18m signature fee, plus \$255m in milestone payments. Transfer price less manufacturing cost results in a c 20% effective royalty. Otsuka funds all development for cancer pain, additional indications and in any future formulations. Joint oversight of all US clinical development and regulatory activities. GW responsible for clinical development in cancer pain indication, with costs reimbursed. Otsuka has responsibility for all subsequent indications.
Otsuka	Global cannabinoid R&D collaboration	Otsuka funds evaluation of cannabinoids as drug candidates in cancer and CNS for an initial three-year term. The research agreement reaches the end of its initial three-year term in July 2010, although it is likely to be extended. Initial \$9m of funding to cover GW operating costs and external collaborations. Additional >\$6m committed to specific research activities.

Source: Edison Investment Research

Other programmes

GW has a number of earlier stage development programmes, which exploit its understanding of plant genetics and know-how in manipulating cannabis plants to produce high concentrations of specific cannabinoid molecules. GW has produced a range of chemovars (plant varieties whose chemical composition varies because of specific breeding and/or different environmental growing conditions), each of which is responsible for expressing a different cannabinoid, eg, delta 9 THC, delta 8 THC, tetrahydrocannabivarin (THCV), cannabidiol (CBD), cannabidivanol, cannabidivarinic acid, cannabigerol, cannabichromene and others.

The chemovars can be propagated vegetatively and grown relatively easily. The cannabinoids produced by each chemovar contribute to what is effectively a proprietary compound library, and this library is being used for early-stage research both in-house and through a partnership with Otsuka. The partnership with Otsuka focuses on the exploitation of this library of cannabinoids for CNS and oncology indications. Early work has focused on laboratory models of psychosis and epilepsy, and CBD and THCV have both shown effects *in vivo* against aggressive generalised seizures. Meanwhile, antipsychotic effects have been seen in certain models using pure CBD and pure THCV alone. There are signs of synergy between an antipsychotic agent and both CBD (synthesised) and THCV (synthesised). Research into possible cancer indications appears to be at an earlier stage.

The selection of a candidate for full development by Otsuka would trigger a separate licensing deal. Its specific terms would be agreed at the time of selection, although this would presumably include funding further development and commercialisation and paying GW licence fees, milestones and royalties, as well as committing to a long-term commercial supply price. The first clinical trial under this collaboration could start in 2010.

GW is conducting proprietary research focusing on diabetes, obesity and metabolic syndrome. This has looked primarily at THCV (a neutral CB1 antagonist thought to decrease food intake and increase energy expenditure), CBD (a non-psychoactive compound believed to alter circulating lipid levels and control fat distribution) and combinations thereof.

GW aims to start a Phase IIa study of THCV/CBD combined at different ratios in H110. The planned three-month study will aim to recruit 48 type 2 diabetes patients with residual pancreatic function and the primary endpoint will likely concern measures of blood and liver lipid levels.

Sensitivities

The approval of Sativex in the UK and Spain significantly reduces the risk associated with GW's investment case. Various assumptions have been made in our valuation model which could vary on both the up and the down side, including the pricing of Sativex (and potentially other products); its use (both approved and off-label) for additional indications; and future value from the early stage R&D portfolio, which is currently excluded.

Valuation

We indicate a valuation of £163m (excluding cash) based on a DCF model to 2017 using a 12.5% cost of capital, which we compare with GW's EV of £130m (based on forecast FY10 cash). This assumes a 60% development risk to potential cancer pain revenues in the US. Pricing is a key sensitivity and we assume Sativex is priced at similar levels to the current named patient basis (Canada C\$125, UK £44 and Spain €75 per 5ml vial), except in the US, where a higher price is assumed. There is upside if GW's partners achieve higher pricing post approval (as is likely), if other indications are pursued and/or other R&D projects progress.

Financials

We expect GW to end the 2010 financial year with cash of c £23m, following receipt of £12.5m of milestones from Bayer and Almirall. A \$5m milestone from Otsuka is payable on start of Phase III studies in cancer pain which is likely in late 2010 (FY11). GW has unutilised tax losses (£43.7m of available as of 30 September 2009), so we do not expect tax to be paid until around 2014. Edison's financial model is shown in Exhibit 9.

Exhibit 9: GW financials

Note: 2009 and 2010 revenue includes milestones received and expected under the Bayer and Almirall deals.

	£'000s	2007	2008	2009	2010e	2011e
Year end 30 September		IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS						
Revenue		5,677	11,774	24,121	29,278	23,808
Cost of sales		(254)	(249)	(433)	(602)	(1,216)
Gross profit		5,423	11,525	23,688	28,677	22,592
EBITDA		(12,059)	(9,862)	2,114	5,983	(398)
Intangible amortisation		0	0	0	0	0
Exceptionals		0	0	0	0	0
Share-based payment		(1,130)	(726)	(634)	(600)	(600)
Operating profit		(13,559)	(11,003)	1,024	4,983	(1,398)
Net Interest		958	809	128	150	250
Profit before tax (excl Intangible amortisation and SBP)		(11,471)	(9,468)	1,786	5,733	(548)
Profit before tax (FRS 3)		(12,601)	(10,194)	1,152	5,133	(1,148)
Tax		2,015	1,974	353	0	0
Profit after tax (FRS 3)		(10,586)	(8,220)	1,505	5,133	(1,148)
Average number of shares outstanding (m)		120.1	120.5	125.0	129.3	129.3
EPS - excl intangible amortisation and SBP (p)		(7.9)	(6.2)	1.7	4.4	(0.4)
EPS - FRS 3 (p)		(8.8)	(6.8)	1.2	4.0	(0.9)
Dividend per share (p)		0.0	0.0	0.0	0.0	0.0
BALANCE SHEET						
Fixed assets		6,292	6,317	7,068	7,668	8,268
Intangible assets		5,210	5,210	5,210	5,210	5,210
Tangible assets		1,082	1,107	1,858	2,458	3,058
Investments		0	0	0	0	0
Current assets		24,316	17,129	22,323	26,877	24,379
Stocks		535	503	551	765	1,587
Debtors		2,815	2,572	1,171	3,288	3,781
Cash		20,966	14,054	20,601	22,824	19,011
Current liabilities		(7,646)	(9,774)	(9,125)	(7,400)	(7,950)
Creditors		(4,186)	(5,363)	(4,531)	(5,500)	(6,050)
Short-term borrowings		0	0	0	0	0
Deferred revenue & advance payments		(3,460)	(4,411)	(4,594)	(1,900)	(1,900)
Long-term liabilities		(17,299)	(15,399)	(13,544)	(11,644)	(9,744)
Long-term borrowings		0	0	0	0	0
Deferred revenue		(17,299)	(15,399)	(13,499)	(11,599)	(9,699)
Other long-term liabilities		0	0	(45)	(45)	(45)
Net assets		5,663	(1,727)	6,722	15,502	14,953
CASH FLOW						
Operating cash flow		(1,453)	(9,588)	(571)	2,720	(3,063)
Net interest		960	821	127	150	250
Tax		2,022	2,191	1,791	353	0
Capex		(500)	(440)	(1,061)	(1,000)	(1,000)
Expenditure on intangibles		0	0	0	0	0
Acquisitions/disposals		0	0	0	0	0
Financing		62	104	6,261	0	0
Dividends		0	0	0	0	0
Net cash flow		1,091	(6,912)	6,547	2,223	(3,813)
Opening net debt/(cash)		(19,875)	(20,966)	(14,054)	(20,601)	(22,824)
HP finance leases initiated		0	0	0	0	0
Other		0	0	0	0	(0)
Closing net debt/(cash)		(20,966)	(14,054)	(20,601)	(22,824)	(19,011)

Source: Edison Investment Research

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