EDISON

Sucampo Pharmaceuticals

Amitiza approved for OIC

A run on Amitiza

Pharma & biotech

FDA approval for Amitiza to treat opioid-induced constipation (OIC) in adults with chronic, non-cancer pain has sparked a 40% share price rally. OIC affects ~2.5m patients in the US, and with Amitiza the only available therapy and safety concerns over potential competitors, OIC is a significant new market opportunity. We model $215m peak US sales in OIC and have increased our total US peak sales estimate to $665m (vs $590m), on the back of strong Q412 sales in other constipation disorders. We therefore raise our overall valuation of Sucampo to $420m, or $10.00 per share (vs $335m, $8/share). Sucampo is now trading close to its fair value, although upside exists in Amitiza's commercial potential in Europe.

Year end	Revenue ($m)	PBT* ($m)	EPS* ($)	DPS ($)	P/E (x)	Yield (%)
12/2011	54.8	(19.9)	(0.41)	0.0	N/A	N/A
12/2012	81.5	6.2	0.12	0.0	79.3	N/A
12/2013e	93.4	0.4	(0.02)	0.0	N/A	N/A
12/2014e	128.3	21.8	0.42	0.0	22.6	N/A

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

Energising opportunity

Expansion of Amitiza's label to OIC provides US partner Takeda with a great opportunity to energise its promotion of the drug, which had been criticised by Sucampo and was the subject of legal disputes between the companies. With the FDA's safety concerns over mu opioid antagonists potentially stalling a number of competitors (Relistor, naloxegol, bevenopran and TD-1211), Amitiza may have a free run at OIC, an easier market to target (than chronic/irritable bowel-related constipation). OIC patients are actively managed by physicians more aware of treatment options for constipation and more likely to prescribe a drug like Amitiza (vs OTC laxatives), especially if it is approved for multiple constipation types. FDA approval for OIC triggers a $10m milestone payment from Takeda.

Amitiza absorbing Linzess challenge

Our analysis of prescription trend data suggests that, so far, Amitiza has largely been unaffected by the US launch of Linzess (Ironwood/Forest) in December 2012, Amitiza's first direct competitive threat since Zelnorm was withdrawn in 2007. Indeed, with Ironwood reporting that 60% of Linzess prescriptions are for new patients switching from OTC laxatives, the entrance of Linzess would appear to be expanding the market for the use of Rx drugs in constipation (currently <10%).

Valuation: OIC and Amitiza Rx boost to $10.00/share

Removing Amitiza's risk-adjustment for OIC, increasing peak US sales, applying an estimated tiered-royalty rate on increased sales, and a better-than-expected margin on Amitiza transfer revenues to AbbVie for sale in Japan, boosts our overall valuation of Sucampo to $420m ($335m), or $10.00 ($8.00) per share. Sucampo's >40% share price gain to $9.51 on the back of Amitiza's OIC approval brings the stock close to our fair valuation. However, we acknowledge upside potential as our valuation does not currently include Amitiza's commercial opportunity in Europe (peak sales $100-150m), and further line extensions for Amitiza and Rescula.

1 May 2013

Price	**US$9.51**
Market cap	**US$395m**
Net cash ($m)	$18m
Shares in issue	41.5m
Free float	30%
Code	SCMP
Primary exchange	NASDAQ

Share price performance

%	1m	3m	12m
Abs	45.4	83.2	14.3
Rel (local)	42.8	71.8	0.0
52-week high/low	US$9.9	US$3.9	

Business description

Sucampo Pharmaceuticals is a US-based pharmaceutical company focused on developing and commercialising medicines based on prostones. Amitiza (GI disorders) is approved and partnered with Takeda in the US and AbbVie in Japan. Rescula (glaucoma) has gained FDA approval and Sucampo is commercialising in the US.

Next events

Rescula US launch updates	2013
Amitiza regulatory progress in Europe	2013
Start Phase III Amitiza paediatric study	Q313
Start US Phase Ib/IIa cobiprostone study	Q313

Analysts

Christian Glennie +44 (0)20 3077 5727

Robin Davison +44 (0)20 3077 5737

healthcare@edisongroup.com

Edison profile page

Update: Significant opportunity for Amitiza in OIC

Amitiza (lubiprostone; 24mcg twice-daily) is the first and only oral medication approved for the treatment of opioid-induced constipation (OIC) in adult patients with chronic, non-cancer pain. With ~2.5m patients[1] in the US suffering from moderate-to-severe OIC, this is a significant market opportunity for US partner Takeda to ramp up Amitiza sales and help to fight off the competition from Linzess. We expect formal sales force detailing of Amitiza for OIC in mid-May and therefore would look for prescription and sales increases in Q313 and onwards. Ironwood Pharmaceuticals and Forest Labs are investing heavily in Linzess marketing, presenting a direct challenge to Amitiza, although Takeda may use the expected greater awareness (physician and patient) of Rx options for constipation disorders and initiate its own direct-to-consumer (DTC) advertising campaign, a key promotional tool in this market.

Available in the US since 2006, over 7m prescriptions have been written for Amitiza in chronic idiopathic constipation (CIC) and irritable bowel syndrome with constipation (IBS-C). In-market US sales by Takeda in 2012 gained 20% to $271.9m, resulting in royalties to Sucampo of $50.7m (+22% vs $41.5m in 2011). It is estimated that approximately 8-9% of existing Amitiza prescriptions are currently used off-label for OIC.

Opioid-based medicines are widely used in the management of chronic pain, with OIC being a common adverse effect of chronic opioid use. Some patients discontinue opioid therapy and endure pain rather than suffer from the constipation that the opioids cause.

Binding of opioids to peripheral opioid receptors in the gastrointestinal tract can result in electrolyte absorption (eg chloride) and decreased small intestinal fluid, as well as abnormal gastrointestinal motility. Amitiza, a prostone-based medicine, specifically activates ClC-2 chloride channels in the intestinal epithelium, bypassing the anti-secretory action of opiates, to increase fluid content in the small intestine to help soften stools and facilitate stool motility through the intestine. OIC is defined as having <3 spontaneous bowel movements (SBMs) per week, with at least 25% of SBMs associated with one or more of the following: (1) hard stools; (2) moderate-to-severe straining; (3) sensation of incomplete evacuation.

FDA approval, granted through the priority review process (although review took nine months after a three-month extension by the FDA), was based on results from three Phase III efficacy studies (12-week treatment duration) and one long-term safety study (48 weeks). Two of the three efficacy studies (placebo-controlled) met the primary endpoint with Amitiza significantly improving the number of SBMs versus baseline: +3.3 for Amitiza vs +2.4 for placebo-treated patients (week 8; treatment difference = +0.9; p-value = 0.004). The failed study was the subject of a malpractice lawsuit filed by Sucampo against Covance, resulting in a $10m compensation payment to Sucampo. The studies showed effectiveness for OIC in patients taking morphine, oxycodone and fentanyl, although Amitiza's effectiveness against OIC in patients taking diphenylheptane opioids (eg methadone) has not been established (listed as a 'limitation of use' on the drug's label).

Importantly, Amitiza's side-effect profile in OIC patients was broadly similar to that observed in IBS-C and better than in CIC, with nausea (11% vs placebo 5%) and diarrhoea (8% vs placebo 2%) the most common adverse events in the OIC pivotal studies. However, these effects are largely transient, with >85% of cases being mild-to-moderate in nature, while physicians and patients appear to be increasingly comfortable with using the drug.

1 Camilleri M. Opioid-induced constipation: challenges and therapeutic opportunities. Clinical and Systematic Reviews. 2011; 106: 835-842.

Competition stalling?

In November 2012, Salix and Progenics revealed that the FDA has safety concerns over the chronic use of mu-opioid antagonists for OIC in chronic, non-cancer pain, linked to cardiovascular risks as a potential result of opioid withdrawal. The FDA had issued a complete response letter (CRL) in July 2012 to Salix's application for Relistor (subcutaneous injection; an oral form has also completed Phase III trials) for use in OIC patients with chronic, non-cancer pain. Relistor has been available since 2008 for OIC patients with advanced medical illness (FY12e sales ~$32m).

Salix indicated that large cardiovascular outcomes trials may be required for mu-opioid antagonists, such as Relistor, to gain FDA approval, although Salix is seeking clarification on this in 2013. Should the FDA reiterate its safety concerns on this class of drug, a further six pipeline mu-opioid antagonist candidates could be affected, including: naloxegol (AstraZeneca/Nektar), bevenopran (Cubist), TD-1211 (Theravance), naldemedine (Shionogi), Nalcol (S.L.A. Pharma) and CB-01-16 (Cosmo Pharma).

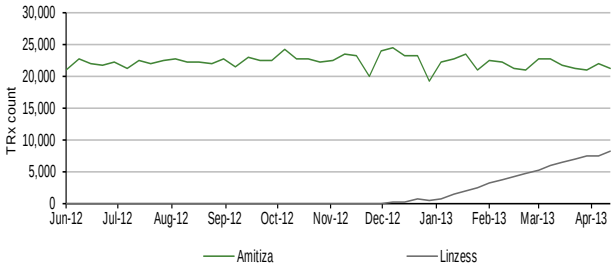
With safety concerns over the chronic use of mu-opioid antagonists, Amitiza's prostone-based mechanism would appear to help distinguish the drug in this field, and boosted by recent label updates (deletion of a pregnancy warning, clarification on Amitiza's mechanism of action), the drug is in a decent position to take advantage of this new opportunity in OIC.

Linzess helping to grow the market

While the recent launch of Linzess certainly presents a challenge to Amitiza, we have long maintained that low brand awareness was one of the reasons behind Amitiza's relatively modest sales so far (when compared to the overall market opportunity), so Linzess's entrance should help to boost awareness of prescription drug options for treating these chronic constipation disorders.

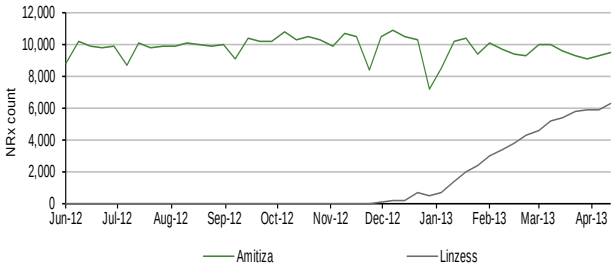
Our review of prescription data since Linzess was launched would tend to support this theory. Exhibits 1 and 2 below show the weekly trend for total (TRx) and new (NRx) prescriptions of Amitiza and Linzess. Although Amitiza prescriptions appear to dip at the time of Linzess's launch, this was short-lived; overall, Amitiza's TRx and NRx have remained fairly stable, on a par with levels prior to Linzess's arrival.

Exhibit 1: Amitiza vs Linzess: TRx count (weekly)



Source: Bloomberg Industries, Symphony Health Solutions

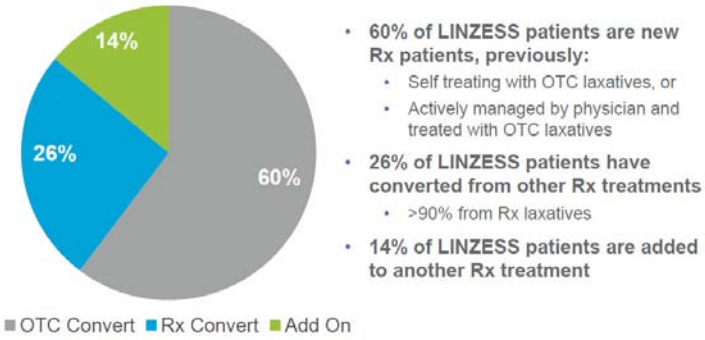
Exhibit 2: Amitiza vs Linzess: NRx count (weekly)



Source: Bloomberg Industries, Symphony Health Solutions

This prescription data would indicate that Linzess is not taking significant direct market share from Amitiza, and indeed is helping to grow the market for the use of prescription drugs for constipation disorders. On Ironwood's Q113 results conference call, the company reported that, of Linzess's prescriptions, 60% are for new Rx patients switching from OTC laxatives, 26% are converting from Rx laxatives, and 14% are added to another Rx treatment (Exhibit 3).

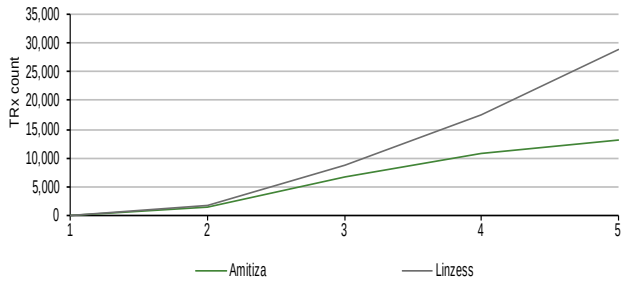
Exhibit 3: Linzess prescription uptake



Source: Ironwood Pharmaceuticals Q113 presentation, 23 April 2013

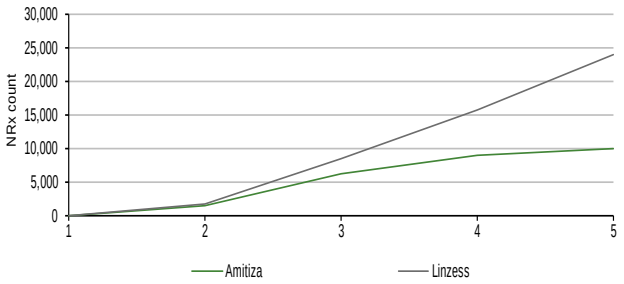
In terms of Linzess's launch trajectory, Exhibits 4 and 5 show TRx and NRx over the first five months of launch for both Amitiza (launched in 2006) and Linzess. Uptake of Linzess appears to be more rapid so far, although the major caveat here is that Amitiza was originally only approved to treat CIC (IBS-C approval came in 2008), whereas Linzess has been launched with both CIC and IBS-C on its label. In addition, Amitiza was initially up against Zelnorm (prior to its withdrawal in 2007), and Linzess is now entering a market where physicians and patients alike appear to be increasingly comfortable with using prescription drugs for constipation disorders.

Exhibit 4: Amitiza vs Linzess: TRx over first five months of launch



Source: Bloomberg Industries, Symphony Health Solutions

Exhibit 5: Amitiza vs Linzess: NRx over first five months of launch



Source: Bloomberg Industries, Symphony Health Solutions

Valuation

We increase our valuation of Sucampo to $420m (vs $335m) or $10.00 per share (vs $8.00), mainly as a result of removing Amitiza's risk-adjustment for OIC (probability raised to 100% vs 85%), increasing peak US sales for existing uses (CIC/IBS-C) to $450m (vs $375m), and a better-than-expected margin on Amitiza transfer revenues to AbbVie for sale in Japan.

Our valuation model is based on a sum-of-the-parts DCF valuation, applying a standard 12.5% discount rate, and a breakdown of our key assumptions is displayed in Exhibit 6. This includes estimated end-Q113 net cash of $18m, with $71m in cash/restricted cash ($53m cash + $18m restricted cash) and $53m in debt.

As a result of increasing our peak sales estimate for Amitiza, we now factor in our own estimates for stepped royalties, given that the terms of the Takeda contract provides for 18-26% in royalties. We assume 19% royalty for annual sales over $150m, 21% royalty on sales over $300m and 23% royalty on sales over $450m. This provides upside to our previous model, which applied a flat 18% royalty.

For Amitiza in Japan, Sucampo sells the product to AbbVie and in Q412 recorded transfer sales of $5m and related COGS of $3m, indicating a 40% gross margin on sales to AbbVie. We have updated our model to now reflect these transfer sales to AbbVie, as opposed to in-market sales, and this is a more profitable arrangement than our previous estimate of a 15% effective royalty rate on in-market sales.

Exhibit 6: Risk-adjusted NPV valuation model and key assumptions

	rNPV ($m)	rNPV / share ($)	Prob. of success	Launch	Peak sales	Royalty estimate	Market exclusivity	Key assumptions
Amitiza for CIC + IBS-C (US)	341	8.11	100%	2006	$450m	18%-23%	2018	10 million patients seeking care beyond OTC/lifestyle options. $750 estimated net annual cost of Rx therapy.
Amitiza for OIC (US)	112	2.66	100%	May-13	$215m	18%-23%	2018	4-7 million patients taking opioids for non-cancer pain, 40-50% experience OIC. $750 net annual cost. $10m milestone on first commercial sale (May 13).
Amitiza for CC (Japan)	125	2.98	100%	Nov-12	$225m	40% gross margin	2020	3-4 million patients seeking care. 40% margin on transfer sales to AbbVie. $15m milestone on first commercial sale (Nov 2012).
Rescula for IOP in glaucoma (US)	113	2.70	100%	Feb-13	$90m	-	2018	3 million patients with open-angle glaucoma in the US; 30 million prescriptions filled per year. $99 WAC per Rescula Rx for 30-day supply.
New pipeline (cobiprostone, SPI-017/SPI-3608)	25	0.60	15%	2017	c $350m	15%	-	
R&D	-90	-2.14						
SG&A	-158	-3.77						
Tax	-64	-1.53						
Net cash	18	0.44						Estimated end-Q113 net cash (includes ~$18m restricted cash)
Valuation	420	10.00						

Source: Edison Investment Research

Our overall valuation of $420m ($10.00 per share) is slightly higher than Sucampo's increased market capitalisation of $399m as a result of the 40% share price gain since the FDA approval of Amitiza in OIC was announced. Hence, we view Sucampo's current share price as close to fair value, although we acknowledge further upside potential to our model given that we do not currently include Amitiza's potential value in Europe (launches for CIC in the UK and Switzerland are expected in 2013, and potential approvals in the same countries in Q114 for OIC), Amitiza's potential in paediatric constipation (a significant opportunity given Linzess's black box warning against use in children (Phase III to start Q313) and Rescula's potential beyond glaucoma (such as retinitis pigmentosa – R-Tech Ueno is conducting a Phase III study in Japan). We await further details on Amitiza's commercial roll-out in Europe to gauge the size and scope of the sales opportunity in this region. A reimbursement decision by the UK's NICE is due by end-2013/ or early 2014.

Sensitivities

The timing and extent of potential generic competition against Amitiza in the US is a key sensitivity for Sucampo. Following Par Pharmaceutical's submission of an ANDA with Paragraph IV certification against Amitiza in the US, we assume that some form of generic competition starts in 2018, with a 50% erosion rate, although an earlier or later entrance of generics would have a significantly negative or positive impact on our valuation. Sucampo, together with its US partner Takeda, filed a patent infringement lawsuit against Anchen Pharmaceuticals, a subsidiary of Par Pharmaceutical, in early-February 2013, triggering a 30-month stay to FDA approval of Par's generic version. Sucampo is claiming infringement against six patents listed in the FDA's Orange Book that expire between 2020 and 2027.

Other sensitivities relate to fresh competition from Linzess in the CIC and IBS-C market, which presents a threat and an opportunity for Amitiza. The challenge for Sucampo and Takeda is to differentiate Amitiza (particularly its proven safety record with long-term use) from Linzess, while

attempting to benefit from the increased patient and physician awareness of the medical need and the availability of prescription treatment options that should result from an extensive promotional effort planned by Ironwood and its US partner Forest Labs.

Financials

Sucampo reported total revenues of $81.5m in FY12 ($54.8m in 2011), boosted by a 22% increase in Amitiza royalties ($50.7m vs $41.5m), a $15m milestone payment from AbbVie for Amitiza launch in Japan and a $5m initial stocking order for Amitiza to AbbVie; Sucampo reported $3m in COGS against this revenue, indicating a 40% gross margin on transfer sales to AbbVie. In-market FY12 US sales of Amitiza by Takeda gained 20% to $271.9m.

For 2013, we now expect revenues of $93m (vs prior estimate $83m), on the back of increased Amitiza royalties ($78m, which includes the $10m milestone from Takeda for OIC launch) and transfer Amitiza sales to AbbVie in Japan of $7.5m. Revenues for 2014 are now estimated at $128m (vs $109m).

Operating expenses in FY12 of $70.1m were in line with our estimate ($70m), and we expect this to rise significantly in 2013 to $86m. We estimate R&D expenses of $31m in 2013 (vs $21m in 2012), to cover the paediatric Phase III study of Amitiza and new trials planned for pipeline drugs (cobiprostone/SPI-017/SPI-3608). G&A costs are expected to be relatively flat ($30.5m vs $30.2m), but we predict S&M expenses to increase to $25m in 2013 (vs $18.7m in 2012), mainly in support of the recent launch of Rescula in the US. Sucampo has indicated that heavy sampling will be required during the first few quarters of commercial launch. Sucampo has guided that the investments being made in Amitiza in Europe, Rescula in the US, and pipeline expansion, will result in a net loss for 2013, but profits should start to flow in 2014 and beyond. Our financial model indicates a $1m net loss in 2013 and a net profit of $17m in 2014.

Sucampo ended 2012 with $77m in total cash/restricted cash ($58.1m cash + $18.9m restricted) and $53m in short-/long-term debt; the bulk of this debt ($41m) is promissory notes payable by 2017, but effectively held by Sucampo's major shareholders, Drs Ryuji Ueno (CEO) and Sachiko Kuno. We do not see a near-term funding requirement for Sucampo, although a potential restructuring of this debt, perhaps linked to a reduction in Ueno and Kuno's combined holding of over 65% to help broaden the shareholder base, cannot be ruled out.

Our financial model is summarised in Exhibit 7.

Exhibit 7: Financial summary

$'000s	2010	2011	2012	2013e	2014e
Year end 31 December	US GAAP	US GAAP	US GAAP	US GAAP	US GAAP
PROFIT & LOSS					
Revenue	61,870	54,761	81,487	93,403	128,308
Cost of Sales	0	0	(3,030)	(4,913)	(12,420)
Gross Profit	61,870	54,761	78,457	88,491	115,888
R&D Expenses	(23,955)	(33,497)	(21,292)	(31,000)	(34,100)
General and Administrative Expenses	(27,867)	(41,270)	(30,157)	(30,459)	(30,763)
Sales and Marketing Expenses	(10,201)	(8,783)	(18,691)	(25,000)	(27,500)
EBITDA	(153)	(17,689)	8,317	2,032	23,525
Operating Profit (before GW and except.)	(153)	(17,689)	8,317	2,032	23,525
Intangible Amortisation	0	0	0	0	0
Exceptionals/Other	0	0	0	0	0
Operating Profit	(153)	(17,689)	8,317	2,032	23,525
Net Interest	533	(2,206)	(2,167)	(1,676)	(1,715)
Other	(3,700)	(2,019)	1,602	0	0
Profit Before Tax (norm)	380	(19,895)	6,150	357	21,810
Profit Before Tax (FRS 3)	(3,320)	(21,914)	7,752	357	21,810
Tax	565	4,608	(2,916)	(1,388)	(4,362)
Deferred tax	0	0	0	0	0
Profit After Tax (norm)	945	(15,287)	3,234	(1,032)	17,448
Profit After Tax (FRS 3)	(2,755)	(17,306)	4,836	(1,032)	17,448
Average Number of Shares Outstanding (m)	41.8	41.8	41.7	41.6	41.5
EPS - normalised ($)	(0.07)	(0.41)	0.12	(0.02)	0.42
EPS - FRS 3 ($)	(0.07)	(0.41)	0.12	(0.02)	0.42
Dividend per share ($)	0.0	0.0	0.0	0.0	0.0
BALANCE SHEET					
Fixed Assets	14,730	42,653	34,882	34,373	34,614
Intangible Assets	3,070	8,364	7,415	6,445	6,202
Tangible Assets	2,025	1,669	1,540	2,001	2,485
Other (incl. restricted cash)	9,635	32,620	25,927	25,927	25,927
Current Assets	134,543	114,916	92,914	96,885	122,597
Stocks	0	0	0	1,997	3,062
Debtors	12,344	17,447	16,267	16,267	16,267
Cash	103,767	75,114	58,057	59,685	84,332
Other (incl. restricted cash)	18,432	22,355	18,590	18,936	18,936
Current Liabilities	(40,002)	(47,081)	(40,071)	(41,662)	(47,086)
Creditors	(20,480)	(26,681)	(20,942)	(22,533)	(27,957)
Short term borrowings	(19,522)	(20,400)	(19,129)	(19,129)	(19,129)
Long Term Liabilities	(55,441)	(71,894)	(44,695)	(48,261)	(51,209)
Long term borrowings	(44,439)	(39,227)	(33,722)	(35,759)	(37,845)
Other long term liabilities	(11,002)	(32,667)	(10,973)	(12,502)	(13,364)
Net Assets	53,830	38,594	43,030	41,336	58,917
CASH FLOW					
Operating Cash Flow	(661)	(20,106)	6,978	5,625	26,867
Net Interest	0	2,288	2,024	(1,676)	(1,715)
Tax	(2,689)	(2,173)	2,998	(1,861)	(850)
Capex	(328)	(3,259)	(3,439)	(461)	(484)
Acquisitions/disposals	(28,118)	0	0	0	0
Financing	14	(581)	(946)	0	0
Dividends	(13,728)	0	0	0	0
Other	(14,900)	(2,187)	(2,081)	0	0
Net Cash Flow	(60,410)	(26,018)	5,534	1,628	23,818
Opening net debt/(cash)	(133,854)	(39,806)	(15,487)	(5,206)	(4,797)
Exchange rate movements	(4,664)	(1,590)	1,605	0	0
Other	(28,974)	3,289	(17,420)	(2,037)	(1,300)
Closing net debt/(cash)	(39,806)	(15,487)	(5,206)	(4,797)	(27,315)

Source: Edison Investment Research, Sucampo accounts

Berlin +49 (0)30 2088 9525
Friedrichstrasse 95
10117 Berlin
Germany

London +44 (0)20 3077 5700
280 High Holborn
London, WC1V 7EE
United Kingdom

New York +1 646 653 7026
245 Park Avenue, 39th Floor
10167, New York
US

Sydney +61 (0)2 9258 1162
Level 33, Australia Square
264 George St, Sydney
NSW 2000, Australia

Wellington +64 (0)4 8948 555
Level 15, 171 Featherston St
Wellington 6011
New Zealand