EDISON

4SC

FY13 results

Clarity on resminostat strategy

Pharma & biotech

4SC has clarified and simplified its development strategy for resminostat in first-line liver cancer. Having previously considered an adaptive Phase II/III study, requiring a partner and/or significant investment today, the company now plans to conduct a Phase II study with the aim of confirming the drug's efficacy and fully validating the proposed biomarker, ZFP64. This could deliver a more compelling partnering and development case for pivotal studies. We welcome this revision, although funding for the Phase II study will need to be secured and a longer clinical timeline (launch in 2021 vs 2019) reduces our overall valuation to €105m, or €2.07 per share.

Year end	Revenue (€m)	PBT* (€m)	EPS* (€)	DPS (€)	P/E (x)	Yield (%)
12/12	4.35	(11.7)	(0.25)	0.0	N/A	N/A
12/13	4.90	(8.0)	(0.16)	0.0	N/A	N/A
12/14e	5.10	(4.1)	(0.08)	0.0	N/A	N/A
12/15e	5.30	(9.1)	(0.18)	0.0	N/A	N/A

Note: *PBT and EPS are normalised, excluding intangible amortisation, exceptional items and share-based payments.

Encouraging data…

The 57-patient, open-label, Phase IIa SHELTER study produced encouraging progression-free survival (PFS) and overall survival (OS) rates for resminostat in second-line liver cancer. The survival benefit appeared to be more pronounced in patients with high levels of the blood-based biomarker ZFP64. However, the ZFP64-correlated benefit was identified in a post-hoc analysis (ie not pre-defined in the trial design) and the patient numbers were relatively small.

…but further validation required

The previously proposed adaptive Phase II/III pivotal study design, with ZFP64 an integral part of patient stratification/selection, could have been achievable, but the hurdles to gaining regulatory approval and securing the finance and/or a pharma partner for this plan were probably too high. We therefore welcome the more straightforward intention to conduct a Phase II study, to provide further evidence to support resminostat's benefit in combination with sorafenib (Nexavar) and validate ZFP64 (and potentially others) as a biomarker to inform the pivotal study design.

Creating a more valuable asset

Generating this Phase II data should increase resminostat's value/attractiveness to prospective partners, although the size, scope and timelines are to be determined. 4SC will now ascertain support for the plan with regulators and potential investors/partners and expects to submit the study protocol by the end of 2014.

Valuation: Reduced to €105m (€2.07 per share)

Opting for stepwise Phase II then Phase III studies (not Phase II/III) pushes back the expected launch for resminostat from 2019 to 2021. This reduces our valuation to €105m (vs €122m) or €2.07/share (€2.41). However, we view this as a more realistic approach and are hopeful that the required funds (c €15m) can be secured.

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Price	**€1.24**
Market cap	**€63m**

Net cash (€m) at end-FY13	4.9
Shares in issue	50.4m
Free float	30%
Code	VSC
Primary exchange	Frankfurt
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	(18.4)	(24.6)	(27.2)
Rel (local)	(19.8)	(24.7)	(41.4)
52-week high/low		€2.10	€1.24

Business description

4SC is a Munich-based drug discovery and development company focused on small-molecule drugs for cancer and inflammatory diseases. It has three NCEs in active clinical development, a Japanese partnership for resminostat, and a number of early-stage R&D collaborations.

Next events

4SC-202 Phase I data	Q214
4SC-205 Phase I data	Q314
Potential Phase II financing and/or partnership for resminostat	H214
Start resminostat Phase II study in first-line liver cancer	H115

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Valuation

Primarily due to the change in expected launch for resminostat in hepatocellular carcinoma (HCC; liver cancer) from 2019 to 2021, our overall valuation reduces to €105m, or €2.07 per share. We have also pushed back the potential launch for resminostat in Japan for non-small cell lung cancer (NSCLC) from 2020 to 2021. We welcome the timing of the decision to opt for a Phase II-only strategy now, rather than in 12 months' time, should the regulators and/or partners not have been receptive to 4SC's Phase II/III study proposal.

Our valuation model (Exhibit 1) is based on a risk-adjusted NPV analysis of the key products and lead indications, and uses a 12.5% discount rate. We have maintained our previous peak sales estimates (and underlying assumptions) and probabilities of success, which are in keeping with the stage of development and data generated so far.

Exhibit 1: 4SC valuation model and key assumptions

Product	Indication	Status	NPV (€m)	Probability of success	rNPV (€m)	rNPV/ share (€)	Launch	Peak sales (€m)	Net royalty estimate
Resminostat	Front-line HCC (WW)	Phase II	186.2	40%	74.5	1.48	2021	590	Japan 17.5% US/EU 20%
Resminostat	Second-line NSCLC (Japan)	Phase I/II	51.6	25%	12.9	0.26	2021	205	Japan 17.5%
4SC-202/4SC-205	Haematological/solid tumours	Phase I			20.0	0.40			
R&D expenses					(3.7)	(0.07)			
Admin expenses					(4.0)	(0.08)			
Net cash (as at 31 December 2013)					4.9	0.10			
Total					**105**	**2.07**			

Source: Edison Investment Research

Although resminostat will not now be entering a potentially pivotal Phase II/III study, the need for funding and/or a partnership remains. Indeed, opting for a Phase II study alone reduces the complexity and costs involved, such that the estimated €15m trial expense (direct costs) is lower than the previous expectation of €20-25m required to fund the Phase II portion of the Phase II/III study. We also note that the revised plan to conduct a Phase II study to potentially validate ZFP64 as a biomarker for the drug's effectiveness could position resminostat as a personalised medicine and therefore increase the chances of success in the long run.

We await further details of the proposed study design, but would assume it aims to recruit >100 patients with first-line HCC, testing a combination of resminostat with sorafenib (Nexavar), the standard of care for first-line HCC, versus sorafenib alone (1:1 randomisation). We estimate this trial could cost €15m, which includes the cost of purchasing Nexavar. The aim would be to demonstrate a survival benefit (PFS and/or OS) from the combination treatment, while also providing the data to support ZFP64 as a predictive biomarker (other potential biomarkers would also be assessed). In prior clinical studies in HCC and Hodgkin's lymphoma (HL), patients who had high levels of ZFP64 (zinc finger protein 64) at baseline had a longer OS benefit (median near doubling) than those with low expression of ZFP64. 4SC estimates that approximately two-thirds of HCC patients over-express ZFP64, which is also relatively easy to measure by real-time PCR (simple blood-based test). 4SC has also filed patent applications to provide IP protection for its findings on ZFP64.

Aside from resminostat, we include an indicative contribution from the active Phase I programmes (4SC-202, 4SC-205) of €20m. Results from the Phase I TOPAS dose-finding study with the epigenetic compound 4SC-202 in patients with advanced haematological tumours are expected in Q214. For 4SC-205 (Eg5 kinesin inhibitor), the inclusion of additional dosage regimes in the Phase I AEGIS study, in patients with solid tumours, means data are not now expected until Q314. 4SC will consider entering into partnerships for these programmes on completion of the Phase I trials. Underlying R&D expenses attributed to the development of the Phase I oncology candidates are

reduced as these studies near completion. 4SC's active clinical programmes are summarised in Exhibit 2.

Exhibit 2: 4SC's clinical development programmes

Product	Indication	Notes
Resminostat	Front-line HCC (Japan)	Up to 164-pt Phase I part of Phase I/II study initiated in May 2013, conducted by partner Yakult.
	Front-line HCC (US, EU)	57-pt Phase IIa SHELTER study in second-line HCC showed encouraging efficacy and good safety/tolerability of resminostat in combination with sorafenib. Planned move into front-line HCC, with a Phase II trial testing a resminostat/sorafenib combination vs sorafenib alone in advanced front-line HCC. Study will include a comprehensive biomarker panel analysis, focusing on ZFP64 (zinc finger protein 64), given that high levels appeared to confer a survival benefit in prior clinical studies in HCC and HL. Study protocol under preparation and to be discussed with the FDA and EMA in H214.
	Advanced Hodgkin's lymphoma (HL)	37-pt Phase II SAPHIRE study as monotherapy in relapsed or refractory Hodgkin's lymphoma. Overall response rate of 34% and a clinical benefit in 54% of the patients, with good safety and tolerability.
	Second-line CRC (EU)	Resminostat in combination with FOLFIRI in SHORE study in pts with advanced KRAS-mutant CRC; encouraging Phase I data at ASCO 2013.
	Second-line NSCLC (Japan)	Up to 118-pt Phase I/II study of docetaxel ± resminostat, initiated in July 2013 by partner Yakult.
4SC-202	Haematological cancers	Up to 36-pt Phase I TOPAS study has reported encouraging interim results. Data expected Q214.
4SC-205	Solid tumours	Up to 58-pt Phase I AEGIS trial met its safety/tolerability objectives in initial 46 patients. Further patients (approximately six to 12) being currently tested with novel dosing scheme. Data expected Q314.

Source: 4SC, Edison Investment Research

No value is ascribed to vidofludimus, a Phase IIb-ready agent for Crohn's disease, so resumption of development by an external party (4SC will not invest further) would increase the valuation. We also attribute no value to 4SC's multiple discovery programmes (Exhibit 3) in our rNPV. As such, any future success-based milestones and/or progress into the clinic would represent additional upside to our base case valuation.

Exhibit 3: 4SC partnerships

Partner	Product/programme	Territory	Deal terms
4SC development			
Yakult Honsha	Resminostat	Japan	Signed 2011. €6m upfront payment, up to €127m in development/commercial milestones plus double-digit royalties on sales (which includes provision of the API). Yakult pays all Japanese development costs.
4SC Discovery			
BioNTech	Cancer immunotherapy	Global	Signed December 2012. Focused on small molecule toll-like receptor (TLR) agonists as anti-cancer immunotherapy. €2.5m upfront payment, share of potential sublicensing proceeds, specific sales milestones plus royalties.
BioNTech	Cancer	Global	Initiated January 2013. Three-year research collaboration. 4SC to identify new small molecule anti-cancer drugs for defined targets and optimise these for BioNTech. Four cancer therapy projects ongoing. 4SC receives cost-based service fees, success-based payments on achievement of specific sales milestones plus royalties on sales.
LEO Pharma	Psoriasis	Global	Signed February 2013. Aim to identify and develop an oral therapy for inflammatory skin disease. €1m upfront payment, research funding, further potential milestones of up to €95m plus royalties.
Panoptes Pharma	Inflammatory eye disorders (uveitis)	Global	Signed September 2013. Patent and development rights for a pre-clinical compound transferred to Panoptes (4SC Discovery holds a 24.9% stake).
CRELUX	Discovery platform		Signed April 2012. Strategic alliance for joint drug discovery services – integrated drug discovery platform i2c (idea to candidate).
UCB	Neurology	Global	Discovery collaboration for 4SC Discovery and CRELUX to identify novel small molecule compounds for neurological disorders. Uses i2c platform to deliver candidates to UCB. Financial details not disclosed.
AiCuris	Infectious diseases	Global	Signed November 2013. Discovery collaboration for 4SC Discovery, CRELUX and AiCuris to identify novel small molecule compounds for infectious diseases. Uses i2c platform.

Source: 4SC; Edison Investment Research

Sensitivities

4SC is subject to sensitivities typical of biotech drug development, including the unpredictable nature of clinical trials, the success or failure of competitors, changing market dynamics and a reliance on partnerships to commercially exploit its products. The investment case hinges on 4SC's ability to secure financing and/or a deal for resminostat (ex-Japan) to advance the product for HCC. Another key sensitivity is the outcome of the Phase III trial of Eisai's lenvatinib in front-line HCC in 2015; positive data versus sorafenib could shift the standard of care in advanced HCC. 4SC has a limited free float (c 30%) with a large single shareholder, Santo Holding, having a 48% share.

Financials

4SC reported net cash of €4.9m as of 31 December 2013. The company's guidance is for a monthly operating cash burn of €0.4m in 2014, with significantly lower R&D expenses in 2014 than 2013; we estimate €5.5m in R&D costs for 2014 compared to €10.2m reported in 2013. This assumes that the Phase II study for resminostat in HCC does not start in 2014. Administrative expenses are also expected to be lower in 2014 (estimated at €3.4m) than 2013 (€3.8m) as a result of restructuring and staff reductions in 2013. Current cash is therefore sufficient for at least the next 12 months (excluding the cost of the planned Phase II HCC study), which can be supplemented by drawing up to €15m from a convertible note agreement with Yorkville (signed in February 2014). These bonds can be issued in tranches of €0.5m, and the first tranche was issued in March 2014.

For FY13, 4SC recorded a net loss of €10.5m, of which one-time extraordinary charges amounted to approximately €0.9m, which included an impairment charge of €0.72m for programme discontinuations (ie 4SC-203, 4SC-207 and two early-stage programmes), and staff reduction compensation expenses of €0.14m.

Revenues in FY13 reached €4.9m, a 13% increase compared to €4.4m in 2012. Specifically, revenues from 4SC's discovery subsidiary were €3.3m (vs €3m in 2012), while development milestones (primarily from Yakult Honsha, a partner in Japan for resminostat) were €1.6m (vs €1.4m). We model modest increases in revenues for 2014 and 2015 at €5.1m and €5.3m, respectively. 4SC's discovery business generated an operating cash surplus in 2013 and is expected to be at least cash-flow neutral in 2014.

For 2015 and 2016, we have added the estimated costs for conducting the Phase II HCC study for resminostat to our financial model, such that R&D costs increase significantly, to €11m and €15m, respectively. This creates a financing requirement over the next three years, which we have assigned to debt and model as follows: €2m in 2014 (Yorkville), €15m in 2015 and €5m in 2016 (Yorkville). The existing agreement with Yorkville expires in December 2016. The additional €15m could come from debt, equity, partners, or a combination of all three. Our financial model, which has been extended to 2016, is summarised in Exhibit 4.

Exhibit 4: Financial summary

€000s	2011	2012	2013	2014e	2015e	2016e
Year end 31 December	IFRS	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS						
Revenue	**780**	**4,353**	**4,904**	**5,100**	**5,300**	**5,500**
Cost of sales	(123)	(327)	(1,474)	(1,533)	(1,593)	(1,653)
Gross profit	657	4,026	3,430	3,567	3,707	3,847
R&D expenditure	(15,012)	(12,909)	(10,243)	(5,500)	(11,000)	(15,400)
Administrative, distribution and other	(4,438)	(4,483)	(3,779)	(3,400)	(3,100)	(3,100)
Operating profit	**(18,793)**	**(13,366)**	**(10,592)**	**(5,333)**	**(10,393)**	**(14,653)**
Intangible amortisation	(903)	(1,403)	(1,593)	(1,200)	(1,200)	(1,200)
Exceptionals (impairment / restructuring costs)	0	0	(862)	0	0	0
Share-based payments	(313)	(130)	(53)	(55)	(55)	(55)
EBITDA	**(17,088)**	**(11,522)**	**(7,804)**	**(3,828)**	**(8,913)**	**(13,198)**
Operating profit (before GW and except.)	**(17,577)**	**(11,833)**	**(8,084)**	**(4,078)**	**(9,138)**	**(13,398)**
Net interest	278	126	48	20	15	10
Other (profit/loss from associates)	31	33	19	19	19	19
Profit before tax (norm)	**(17,299)**	**(11,707)**	**(8,036)**	**(4,058)**	**(9,123)**	**(13,388)**
Profit before tax (FRS 3)	(18,484)	(13,207)	(10,525)	(5,294)	(10,359)	(14,624)
Tax	(587)	(10)	0	(70)	0	0
Profit after tax (norm)	**(17,855)**	**(11,684)**	**(8,017)**	**(4,109)**	**(9,104)**	**(13,369)**
Profit after tax (FRS 3)	(19,071)	(13,217)	(10,525)	(5,364)	(10,359)	(14,624)
Average number of shares outstanding (m)	41.5	46.2	50.4	50.4	50.4	50.4
EPS - normalised (€)	**(0.43)**	**(0.25)**	**(0.16)**	**(0.08)**	**(0.18)**	**(0.27)**
EPS - FRS 3 (€)	(0.46)	(0.29)	(0.21)	(0.11)	(0.21)	(0.29)
Dividend per share (€)	0.0	0.0	0.0	0.0	0.0	0.0
BALANCE SHEET						
Fixed assets	**15,086**	**13,326**	**11,591**	**10,237**	**8,908**	**7,604**
Intangible assets	13,574	12,223	10,651	9,472	8,293	7,114
Tangible assets	1,065	787	602	427	277	152
Investments and other	447	316	338	338	338	338
Current assets	**16,752**	**15,741**	**6,114**	**4,140**	**10,146**	**1,862**
Stocks	25	22	23	23	23	23
Debtors	117	3,084	346	346	346	346
Cash	15,820	12,064	4,899	2,925	8,931	647
Other current assets	790	571	846	846	846	846
Current liabilities	**(3,523)**	**(3,499)**	**(3,587)**	**(3,865)**	**(4,064)**	**(4,264)**
Creditors	(734)	(584)	(675)	(675)	(675)	(675)
Short-term deferred revenue	(894)	(894)	(1,323)	(1,601)	(1,800)	(2,000)
Short-term borrowings	0	0	0	0	0	0
Other current liabilities	(1,895)	(2,021)	(1,589)	(1,589)	(1,589)	(1,589)
Long-term liabilities	**(4,782)**	**(3,755)**	**(2,836)**	**(5,457)**	**(20,454)**	**(25,454)**
Long-term borrowings	0	0	0	(2,000)	(17,000)	(22,000)
Long-term deferred revenue	(4,469)	(3,575)	(2,682)	(3,303)	(3,300)	(3,300)
Other long-term liabilities	(313)	(180)	(154)	(154)	(154)	(154)
Net assets	**23,533**	**21,813**	**11,282**	**5,055**	**(5,464)**	**(20,252)**
CASH FLOW						
Operating cash flow	**(11,888)**	**(15,327)**	**(7,053)**	**(3,828)**	**(8,913)**	**(13,198)**
Net interest	259	163	66	20	15	10
Tax	(600)	(10)	0	(70)	0	0
Capex	(168)	(50)	(99)	(75)	(75)	(75)
Expenditure on intangibles	(465)	(51)	(21)	(21)	(21)	(21)
Acquisitions/disposals	0	10	10	0	0	0
Financing	11,080	11,367	0	0	0	0
Other	0	0	0	0	0	0
Net cash flow	(1,782)	(3,898)	(7,097)	(3,974)	(8,994)	(13,284)
Opening net debt/(cash)	**(17,607)**	**(15,820)**	**(12,064)**	**(4,899)**	**(925)**	**8,069**
Other	(5)	142	(68)	0	0	(0)
Closing net debt/(cash)	**(15,820)**	**(12,064)**	**(4,899)**	**(925)**	**8,069**	**21,353**

Source: Edison Investment Research, 4SC accounts. Note: A €2m funding requirement in 2014 is assigned to debt, which should be covered by the Yorkville convertible note agreement (worth up to €15m, valid until December 2016).

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