EDISON

4SC

Company update

Resminostat refocused cancer strategy begins

Pharma & biotech

4SC's recent €29m capital increase has provided vital funds to advance the epigenetic lead candidate resminostat. Focus is now on an EU Phase II trial in CTCL, rather than liver cancer (HCC). HCC would have been more costly and time-consuming compared with CTCL. Clinical data in 2016 in HCC and NSCLC from the Yakult collaboration will allow 4SC to revisit, with less risk, the prospects for resminostat in other cancers ex-Asia. Combination of resminostat with new immunotherapies is also being explored. Our valuation increases from €115m to €141m to reflect the cash increase and fresh development plans for resminostat in CTCL (EU).

Year end	Revenue (€m)	PBT* (€m)	EPS* (€)	DPS (€)	P/E (x)	Yield (%)
12/13	4.9	(8.0)	(0.80)	0.0	N/A	N/A
12/14	7.1	(8.8)	(0.88)	0.0	N/A	N/A
12/15e	5.0	(10.7)	(0.73)	0.0	N/A	N/A
12/16e	6.8	(10.2)	(0.54)	0.0	N/A	N/A

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

Resminostat EU CTCL trial to start in H116

This year 4SC decided to redirect efforts into CTCL rather than HCC. The funding roadshow for this new focus raised gross proceeds of €29m (€27.5m net) from the issue of 7.25m shares at €4.00 per share. The resminostat EU CTCL study is expected to start in Q216 and EMA scientific advice is anticipated before year end. The trial is potentially pivotal and 4SC hopes to file for conditional approval on the back of Phase II data. Assuming positive results (due in H218), we view this as a plausible outcome given the FDA has approved HDAC inhibitors in the US on Phase II data alone. EU filing/approval could therefore be secured in H219.

Positioning in CTCL will be key

Resminostat will be assessed as a maintenance therapy for advanced CTCL (>IIB stage) patients, after failure on standard systemic treatment, like bexarotene but in responders to chemotherapy. We note nine drugs in Phase II/III development, but closer inspection reveals a limited competitive threat.

What about liver cancer and other opportunities?

Yakult is conducting two Phase II studies in Japan in HCC and lung cancer (NSCLC). Positive data (especially validation of the ZFP64 biomarker) in 2016 would therefore bring development of resminostat for solid tumours into play once more, subject to partnerships and/or fresh finance.

Valuation: Increased to €141m from €115m

We now include the EU CTCL opportunity for resminostat in our valuation model, with peak sales of €123m by 2028. Adjusting for FY15e net cash of €20m and increased R&D expenses, our overall valuation rises to €141m (vs €115m), but on a per share basis drops to €7.43 (vs €11.32), with 8.75m new shares in issue (7.25m capital increase + 1.5m loan repayment to Santo).

6 October 2015

Price	**€2.7**
Market cap	**€51m**

Pro forma net cash (€m) at end July 2015 (post €27.5m net capital raise)	26.5
Shares in issue	18.97m
Free float	38%
Code	VSC
Primary exchange	Xetra
Secondary exchange	Frankfurt

Share price performance

%	1m	3m	12m
Abs	68.4	36.8	3.4
Rel (local)	70.9	20.3	(16.4)
52-week high/low		€7.3	€2.7

Business description

4SC is a Munich-based drug discovery and development company focused on small molecule compounds for cancer. Resminostat (HDAC inhibitor) is in Phase II in the EU for CTCL, partnered with Yakult (Japan, Phase II HCC/NSCLC) and Menarini (Asia). Two agents (4SC-202, 4SC-205) have completed Phase I.

Next events

Q315 results	11 November 2015
Phase II EU CTCL begins	Q216
EMA advice of EU CTCL study	Q415
Phase II data HCC/NSCLC (Yakult)	2016

Analysts

Tim Franklin +44 (0)20 3077 5734

Christian Glennie +44 (0)20 3077 5727

healthcare@edisongroup.com

Edison profile page

What is cutaneous T-cell lymphoma (CTCL)?

Our revision to the company's fair value includes a valuation assessment of resminostat in CTCL.

CTCL is a type of non-Hodgkin lymphoma (NHL) and is caused by a chronic malignancy of mature T-cells. T-cell lymphomas account for more than 70% of all cutaneous lymphomas, the remainder being B-cell. Mycosis fungoides (MF) and Sézary syndrome (SS) are the most common subtypes of CTCL, with MF making up around 50% of all CTCL s and SS 5%. CTCL usually affects people aged between 40 and 60 and is more common in men than in women.

Malignant T-cells initially migrate to the skin, causing red patches and plaques (Stage I). In many individuals the disease does not progress beyond Stage I/IIA, but in others CTCL eventually leads to skin tumours (Stages IIB), erythroderma (Stage III) and, in approximately 10-20% of cases, spreads to other organs of the body such as the liver, blood and lymph nodes (Stage IV).

MF is an 'indolent' form of CTCL, with slow/no progression and symptoms largely confined to the skin. Sézary syndrome is a more aggressive form and characterised by a generalised erythroderma (red rash), lymph node involvement and blood leukaemia. More generally, CTCL symptoms include intolerable itching, disfigurement, difficulty walking and using hands, and frequent *Staphylococcus* or *Pseudomonas* infections, which in extreme cases can cause death in CTCL patients.

Patients with early disease (Stages I and IIA) have a median survival of more than 12 years. Those with more advanced disease (Stages IIB, III and IVA) have a median survival of five years.

CTCL is a niche orphan indication. The exact number of CTCL cases is difficult to determine due to the lack of definitive diagnosis at its early stages when the disease symptoms can mimic benign skin conditions such as eczema, psoriasis and dermatitis. It can take an average of six years from the onset of disease until diagnosis of CTCL is confirmed.

Incidence in many countries appears to be increasing, which may reflect improving diagnosis. Analysis of EU data indicates an age-adjusted incidence of 6.4 cases per million (of which around 50% are MF), but reports are highly variable with rates in the region of 2,000 to 4,600 cases per year. Since most are lower-grade cases, the average survival rate is around 12-15 years. There is a wide range on prevalence, from 18,000 to 60,000 cases. Diagnosis data would appear to be correlated with incidence data, but the actual presentation of disease is a mixture of true new cases plus prevalent cases. So there is a challenge and an opportunity for 4SC to influence diagnosis rates in the future to increase the number of diagnosed patients.

Exhibit 1: Incidence and prevalence estimates of CTCL in EU28 in 2015

	Incidence rate	Incidence	Prevalence
EU28	6.4 per million	2,000-4,600	18,000-60,000

Source: Edison Investment Research, BMJ Best Practice, EMA 2008, NHS UK, Agar et al, JCO, 28, 4730-4739, 2010

Current treatments for CTCL

The treatment of CTCL (in particular MF and SS) depends on disease stage. At the early stages (I-IIA) therapy is skin-directed and includes PUVA (psoralen plus UVA), narrow band UVB and topical corticosteroids. At more advanced stages (Stage IIB-IV) systemic agents are employed and the notable difference is that two HDAC inhibitors have been approved for the treatment of CTCL in the US and some other countries but not, to date, in Europe. The two US-approved HDACs failed approval by EMEA in the EU, mostly as a result of the poor study designs, questionable or low efficacy, lack of comparators and safety issues. The Vorinostat application for the indication advanced CTCL was rejected by the European Medicines Agency (EMA) in February 2009 for the following reasons:

1. The applicant presented efficacy data on a single uncontrolled pivotal study in 76 patients.

2. The EMA questioned whether the response rate of 30% was clinically meaningful in this target indication.
3. It was not possible to identify a suitable target population in this study where efficacy was meaningful.
4. The safety data suggested a potential safety concern relating to thromboembolic disease. Given the absence of comparator data, putting this concern into context was difficult.

In July 2012 romidepsin was another HDAC that was refused marketing authorisation by the EMA in a non-cutaneous T-cell lymphoma subtype, Peripheral T-cell Lymphoma (PTCL) for the following reasons:

1. The study design did not include a comparison with any other treatment.
2. It was not possible to assess the effect on overall survival or progression-free survival in comparison with treatments currently used for PTCL in patients that no longer respond to or who return after previous therapy.
3. The company failed to provide an adequate certificate of good manufacturing practice (GMP) for the site where the medicine is manufactured, which is legally required. Therefore, at that point in time, the Committee for Medicinal Products for Human Use (CHMP) was of the opinion that there was insufficient evidence on the benefits of romidepsin and that the balance of its benefits and risks could not be established. Hence, the EMA's CHMP recommended that the marketing authorisation be refused.

Exhibit 2: CTCL treatment options

	Europe	US
Early-stage (I-IIA) – skin-directed agents		
Topical corticosteroids	Yes	Yes
Phototherapy (PUVA/UVB)	Yes	Yes
Topical chemotherapy (carmustine, nitrogen mustard)	Yes	Yes
First-line advanced stage (IIB-IV) - systemic treatments		
PUVA +/- IFN-alpha	Yes	Yes
Second-line advanced stage (IIB-IV) – systemic treatments		
ECP (extracorporeal photopheresis)	Yes	Yes
Oral bexarotene	Yes	Yes
Radiation: total body electron beam	Yes	Yes
Chemotherapy (methotrexate, chlorambucil, gemcitabine/cladribine, liposomal doxorubicin, CHOP chemotherapy)	Yes	Yes
Targeted immunotherapy: alemtuzumab (anti-CD52)	Yes	Yes
Allogeneic stem cell transplant	Yes	Yes
HDAC inhibitors (vorinostat, romidepsin)	**No**	**Yes**

Source: Edison Investment Research

Histone deacetylase (HDAC) inhibitors in CTCL

Histone deacetylases (HDACs) are epigenetic enzymes that regulate gene expression by modifying the chromatin structure as a result of binding to and removing acetyl groups from histones. These HDACs are often dysregulated in human tumours and thus HDAC inhibitors are being investigated as an emerging class of novel anti-tumour agents. Eleven cellular HDACs have been identified so far. The effect of their inhibition is still being characterised, but can include various effects on tumour cells including cell death (apoptosis), senescence, cell cycle arrest, differentiation, autophagy and tumour immunogenicity. 4SC has a particular focus within oncology on epigenetic targets, as two out of three pipeline products have an epigenetic mode of action (resminostat, an HDAC inhibitor and 4SC-202, a selective inhibitor of LSD1 and HDACs 1, 2, and 3).

The two HDAC inhibitors that were refused authorisation in the EU – vorinostat and romidepsin – have so far been approved by the FDA for use in relapsed/refractory CTCL: Merck's vorinostat (Zolinza) for third-line therapy of CTCL in 2006 and Celgene's romidepsin (Istodax) for second-line therapy of CTCL in 2009 (see Exhibit 3).

Neither appears likely to pursue approval in Europe following previous negative opinions for both drugs by the CHMP.

Exhibit 3: Approved histone deacetylase (HDAC) inhibitors

Compound	MoA	Company	Approved indication	Approval geography
Vorinostat (Zolinza)	Pan-HDAC (oral)	Merck & Co	CTCL in patients who have progressive, persistent, or recurrent disease after two systemic therapies.	US (2006), Canada, Taiwan, Japan, Australia EU filing withdrawn in 2009 (EMA concerns about risk/benefit and thromboembolic events).
Romidepsin (Istodax)	Class-1 selective (iv)	Celgene	CTCL in patients who have received at least one prior systemic therapy. Relapsing/refractory PTCL.	US (2009 CTCL, 2011 PTCL), Canada, Australia (PTCL) Europe: July 2012 CHMP negative opinion for PTCL filing (no conclusive clinical benefit).
Belinostat (Beleodaq)	Pan-HDAC (iv)	Spectrum (Onxeo)	Relapsing/refractory PTCL, second-line after failure of standard chemotherapy. Phase III in first-line PTCL planned for H116.	US (2014). Europe – Phase III planned 2016.
Panobinostat (Farydak)	Pan-HDAC (oral)	Novartis	Relapsing/refractory multiple myeloma, third-line after two prior treatments (in combination with bortezomib + dexamethasone).	US, Chile (2015). Europe: September 2015.

Source: Edison Investment Research, company reports

Of the other approved HDACs, belinostat is used in the very niche indication of PTCL and there are no plans for panobinostat in CTCL. Novartis's panobinostat (Farydak) recently received EMA approval as a third-line treatment of relapsed and/or refractory multiple myeloma and is therefore the first HDAC inhibitor to reach the EU market. Belinostat (Beleodaq) is approved in the US for second-line treatment of PTCL and Onxeo is currently preparing Phase III European trials for its use in first-line PTCL.

There was another HDAC inhibitor in development for CTCL, quisinostat (JNJ-26481585). Quisinostat showed very low response rates in Phase II in 2012 and does not appear on the company's pipeline list. Resminostat is similar to vorinostat in the number and type of HDAC isoforms it targets, but has shown a more benign side-effect profile in the clinic to date.

4SC's resminostat could be the first HDAC inhibitor approved for CTCL in Europe

4SC is currently preparing a Phase II trial of resminostat in CTCL. It is scheduled to start in Q216 pending scientific advice from the regulatory authority EMA at the end of this year. Success in this trial and subsequent regulatory approval would make resminostat the first HDAC for CTCL in Europe.

According to current plans before scientific advice from the EMA, the randomised placebo-controlled Phase II trial will test resminostat in CTCL patients who have progressed beyond Stage IIA, have failed previous standard systemic therapy like oral bexarotene treatment and have stable disease (or a partial or complete response) after debulking therapy, eg chemotherapy. Patients meeting these criteria will be randomised to receive resminostat plus best supportive care vs placebo and best supportive care until progression or intolerability. The study is likely to run until H218. Assuming data are positive, 4SC could file for EU conditional approval on the back of Phase II data.

The level of adverse events will clearly be key to an EU approval given the failure of Merck's vorinostat (Zolinza), which was withdrawn after the CHMP expressed doubts over the clinical benefit and the level of side effects including thromboembolic events (4.7% of patients had pulmonary embolisms). To date, no significant adverse effect of resminostat on the cardiovascular system has been observed. The most frequent (>5%) grade 3/4 adverse events reported for resminostat in clinical trials with non-Asian patients were thrombocytopenia (6.4%), anaemia (5.4%) and diarrhoea (5.4%). The majority of adverse events were mild to moderate, manageable and reversible.

In a historical comparison between resminostat and vorinostat in Hodgkin's lymphoma (HL) Phase II trials, vorinostat grade 3/4 adverse events included anaemia in 32%, thrombocytopenia in 16%

and lymphopenia in 12% of patients, while resminostat demonstrated a safer adverse event (AE) profile in HL, with anaemia in 8% and thrombocytopenia in 14% of patients.

The clinical positioning that 4SC is targeting for resminostat appears similar to other HDAC inhibitors that have been approved in the US – second/third-line treatment after at least one prior systemic treatment, but with the aim of maintaining progression-free survival and prolonging time to progression after debulking systemic therapy. Compared with the monoclonal antibody products, we would expect resminostat to have a pricing advantage given the significantly higher cost of goods of biological products.

Drug pipeline competition in CTCL is not strong

The pipeline of therapies according to ClinicalTrials.gov shows there are 12 products in clinical development for CTCL. Four of these are in late-stage pivotal trials, with clinical data due from Q1-Q416. Phase II data are expected before the end of 2015 for two products. However, after closer examination, direct competition for resminostat in advanced CTCL appears very low. Resminostat is currently the only compound for development as a maintenance therapy after debulking systemic therapy.

The most advanced drugs in Phase III are the monoclonal antibodies brentuximab vedotin and mogamulizumab. Both are monoclonal antibodies that target a subpopulation of patients who in most cases still progress with their disease. Patients would therefore ultimately still be available for therapy with resminostat. Furthermore, the likely high pricing of these products would make them less competitive than resminostat. The arrival of these products will also help to stimulate market awareness of CTCL and improve diagnosis rates.

Brentuximab vedotin

One of the most advanced CTCL drugs in development is brentuximab vedotin, which is an antibody-drug conjugate (ADC) comprised of an anti-CD30 monoclonal antibody attached by an enzyme-cleavable linker to the antimicrotubule agent, monomethyl auristatin E (MMAE), targeting a CD30+ subpopulation of CTCL. In 48 evaluable patients, the overall response rate was 73%. Usually response rates ranges vary by up to 50%. Peripheral neuropathy was the most common adverse event of concern, occurring in 31 (65%) of 48 patients at least once. Dose reductions resolved peripheral neuropathy in 14 (45%) of the 31 patients; it was unresolved in the remaining 17 (55%) patients. Despite impressive response rates, there was long-lasting peripheral neuropathy in half the patients tested. Clinical data from this study are expected in 2016, with launch possible in 2017/18 if data are supportive.

Exhibit 4: Drugs in development for CTCL

Drug	Company	Type	Phase	Study data	Comment
Mogamulizumab (KW-0761)	Kyowa Hakko Kirin	mAb: Defucosylated anti-CCR4 mAb	Phase III	Mar-16	
Brentuximab vedotin	Takeda/Millennium	mAb: Anti-CD30 mAb-drug conjugate	Phase III	2016	Subgroup of CD30+ patients.
SGX-301	Soligenix	PDT utilizing visible light	Phase III	Dec-16	Topical application for earlier disease stages.
E7777 (Ontak)	Eisai	IL-2 + diphtheria toxin	Phase III	Sep-16	New formulation of already approved product.
A-dmDT390-bisFv	Angimmune	mAb + diphteria toxin	Phase II	Sep-15	Earlier-stage patients. No overlap with resminostat.
Quisinostat (JNJ-26481585)	JNJ	HDACi (1&2)	Phase II	Nov-15	Assume low competitive potential given previous clinical data.
Everolimus (Afinitor)	Novartis	mTOR inhibitor	Phase II	Apr-16	
SHAPE (SHP-141)	TetraLogic	HDACi, topical gel	Phase II	May-16	Topical application for earlier disease stages.
Alemtuzumab (Campath)	Sanofi-Genzyme	mAb: Anti-CD52	Phase II	Aug-16	Trial with already approved product (enrolment completed 2010).
Resminostat	4SC	HDACi	Phase II	2019	Maintenance therapy after debulking chemotherapy for advanced stages.
Carfilzomib + romidepsin	Onyx	proteosome inhibitor + HDACi	Phase I	Oct-15	All stages of CTCL.
Bortezomib (Velcade) + romidepsin	Takeda/Celgene	proteasome inhibitor + HDACi	Phase I	Dec-15	Various leukemia and lymphoma.

Source: ClinicalTrials.gov

Mogamulizumab

Mogamulizumab is a humanised, anti-CC chemokine receptor four monoclonal antibody, which has already been approved in Japan in CTCL in this patient subgroup only. The most frequent treatment-emergent adverse events were nausea (31.0%), chills (23.8%), headache (21.4%) and infusion-related reaction (21.4%); the majority of events were grade 1-2. There were no significant hematologic effects. Among 38 evaluable patients, the overall response rate was 36.8%; the product appeared to be safe and efficacious. There will be some data in Q116, but study completion is in 2017 with potential launch in 2018.

Resminostat has shown efficacy and safety in HCC and HL

Resminostat shows encouraging anti-tumour activity with good tolerability. To date, it has been tested in more than 250 patients in Phase I and II in a range of blood and solid tumours, both as monotherapy and in combination with chemotherapies in the EU and Asia. In 2016 4SC will know if resminostat has a future in HCC and NSCLC following the clinical readout of the Yakult trials. The two randomised Phase II trials currently conducted by Yakult are testing resminostat plus sorafenib vs sorafenib mono in first-line HCC and resminostat plus docetaxel vs docetaxel mono in second-/third-line NSCLC, respectively, in Asian patients.

The move by 4SC to focus on CTCL in the near term was due to the recognised activity on the tumour by HDAC inhibitors plus an assumed fast-to-market opportunity in the EU at reduced cost and risk. On the other hand, as 4SC was within reach of the Yakult Phase II data in HCC, it seemed more rational from a risk and efficiency standpoint for the company to defer the start of its own planned first-line development in Western HCC until Yakult's randomised data on OS and the ZFP64 biomarker are available to use these data for 4SC's own study design. By establishing a collaboration with Yakult, 4SC can concentrate its near-term efforts on a high-need orphan indication such as CTCL in Europe, but also benefit from its partners' studies.

Resminostat is being investigated in Phase II trials in its lead indication of first-line HCC, as well as in second/third-line NSCLC in Japan with partner Yakult. The first readout in HCC in Japan is expected during 2016, and the intention for Yakult is to initiate pivotal Phase III trials in HCC in Japan in 2017. Yakult has started Phase I trials in GI pancreatic and biliary tract cancer in Japan in June 2015, while the deal signed with new partner Menarini in April 2015 allows it to conduct resminostat trials elsewhere in Asia (ex-Japan, indications to be determined).

ZFP64, a potential biomarker for resminostat

In post-Phase IIa of both HCC and HL tumour indications, 4SC has identified zinc finger protein 64 (ZFP64) as a potential new biomarker whose gene expression levels appear indicative of overall survival benefit following treatment with resminostat. Patients with a high level of ZFP64 gene expression at baseline showed a statistically significant increase of median overall survival compared with patients with low ZFP64 expression. Future trials (including the HCC Phase II ongoing in Japan) will therefore include measurements of this biomarker.

Valuation

Our valuation model now includes a value for resminostat in CTCL (EU market). Our rNPV for this opportunity is €9.7m with peak sales of around €123m by 2028 (Exhibit 6). This represents around 3,000 patients treated with resminostat pa before loss of the core patent in 2029.

Our main assumptions for CTCL evaluation include an incidence rate of 6.4 per million, survival of 12 years after diagnosis, growth in diagnosed cases of 3% per year, rate of failure of first/second-line of 80%, price of resminostat per cycle of €6,000 and seven cycles per year. Although there is the chance of regulatory approval in 2019, we have conservatively assumed a full year of sales from 2020 (Exhibit 5).

Exhibit 5: EU CTCL sales forecast for Resminostat

EU28	2019e	2020e	2021e	2022e	2023e	2024e	2025e	2026e	2027e	2028e	2029e	2030e
	File	Launch	Sales	Sales	Sales	Sales	Sales	Sales	Sales	Sales	Expiry	Expiry
EU population	507	507	507	507	507	507	507	507	507	507	507	507
CTCL incidence	3,550	3,550	3,550	3,551	3,551	3,551	3,551	3,551	3,552	3,552	3,552	3,552
CTCL prevalence	42,599	42,602	42,605	42,607	42,610	42,612	42,615	42,617	42,620	42,623	42,625	42,628
Diagnosed cases	4,114	4,361	4,623	4,900	5,194	5,506	5,836	6,186	6,558	6,951	7,368	7,810
Suitable for therapy	3,086	3,271	3,467	3,675	3,896	4,129	4,377	4,640	4,918	5,213	5,526	5,858
Failure on first/second-line	2,469	2,617	2,774	2,940	3,116	3,303	3,502	3,712	3,935	4,171	4,421	4,686
Market share resminostat		262	555	882	1558	1982	2276	2598	2754	2919	2652	1406
Market share resminostat %		10	20	30	50	60	65	70	70	70	60	30
Price (€)		42,000	42,000	42,000	42,000	42,000	42,000	42,000	42,000	42,000	42,000	42,000
Sales (€m)		11.0	23.3	37.0	65.4	83.2	95.6	109.1	115.7	122.6	111.4	59.0

Source: Edison Investment Research

Exhibit 6: NPV sum-of-the-parts fair value

Product	Indication	Region	Status	Partner	NPV (€m)	Prob. of success (%)	rNPV (€m)	rNPV/ share (€)	Launch	Peak sales (€m)	Net royalty estimate
Resminostat	First-line HCC	Japan	Phase II	Yakult Honsha	94.8	40	37.9	2.00	2021	198	17.5%
		China	Phase I	Menarini	83.6	20	16.7	0.88	2022	259	15%
		USA	Phase II	-	52.3	30	15.7	0.83	2021	191	20%
		EU	Phase II	-	56.4	30	16.9	0.89	2021	201	20%
Resminostat	Second-line NSCLC	Japan	Phase II	Yakult Honsha	61.7	40	24.7	1.30	2021	204	17.5%
Resminostat	Second-line CTCL	EU	Phase II	-	48.5	20	9.7	0.51	2020	123	25.0%
4SC-202/4SC-205	Haematological/solid tumours	WW	Phase I	-			25.0	1.32			
R&D expenses							(18.1)	(0.96)	2016-18 expenses (risk-adjusted)		
Admin expenses							(7.5)	(0.40)	2016-18 expenses (risk-adjusted)		
Net cash (FY15e)							20.0	1.05			
Total							**141**	**7.43**			

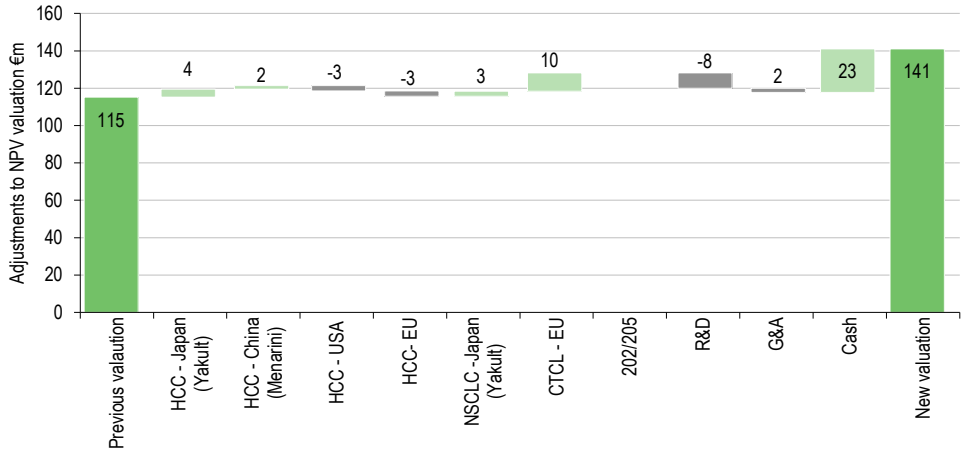
Source: Edison Investment Research

Since our last report the increase to our fair value is driven mostly by the capital increase (€20m cash vs €3m debt), and the addition of a CTCL forecast for the EU (rNPV €9.7m). The CTCL model assumes the company out-licenses for CTCL in Europe and receives a net royalty rate of 25% of sales. If the company decides to go alone with CTCL in Europe, the economics could be expected

to be more favourable after factoring-in manufacturing costs, sales and marketing and general overheads to support the product. If the company decides to go alone, we see potential upside to our fair value.

We have also rebased our model to 2016 vs 2015, and apply our standard discount rate of 12.5%. These are partially offset by downward adjustments in the probability of success of HCC in the US and EU from 40% to 30%, given current uncertainty over further development in these regions in the absence of adequate funding or development partners. The capital increase will be used to fund the resminostat CTCL trial, so this is now reflected in increased R&D costs in 2016-18 (rNPV €18m vs €10m). We retain the US/EU component for resminostat in HCC in our model, as positive data from Yakult in 2016 could spark fresh partnership and/or finance opportunities.

Exhibit 7: Adjustments to valuation



Source: Edison Investment Research

Financials

The 2015 net cash balance sheet forecast is based on reported cash of €908k at H115, plus the net proceeds of the capital increase in July (€27.52m after €1.48m transaction fee), and the revised annual guidance of a monthly cash burn of approximately €1m for FY15. The capital increase was essential to start the EU CTCL trial, so costs will increase. Company Q215 guidance was revised and increased for cash burn, operating expenses and net loss (Exhibit 8).

We note that the major life science fund Wellington Partners invested €5m in the capital increase, alongside new institutional investors from the US and Europe, and is a new cornerstone investor in 4SC (6.6% holding).

At the time of the capital increase, €6m of a €7.5m loan drawn down from major shareholder Santo was removed through the issue of 1.5m shares to Santo at €4.00 per share. As of 30 June 2015 there was €1.89m outstanding on the Santo loan (€1.5m + 8% pa interest), which is repayable by end 2016; we currently assume this remaining balance will be repaid in cash in 2016, but acknowledge that it may be refinanced or met through the issue of new equity.

The total number of new shares issued, including both capital increase and loan repayment, was 8.75m (7.25m capital increase + 1.5m loan repayment).

Exhibit 8: Current guidance and Edison estimates

Item	FY15 4SC guidance	FY14 4SC actual (€m)	Edison FY15e previous (€m)	Edison FY15e new (€m)
Cash burn rate	€1m/month	0.7	0.35	1.0
Op expenses	Higher than 2014	12.4	9.5	13.6
Consolidated net loss	Higher than 2014	9.7	10.5	11.5

Source: 4SC Q2 results, Edison Investment Research

Our revised financial forecast predicts sufficient cash into 2018 and could enable completion of the Phase II CTCL trial in Europe. The timing and value of potential milestones from Yakult and Menarini in 2016/17 could help improve the cash position. The outcomes of the two Yakult Phase II trials in Japan in 2016 could also affect the cash position if a deal and/or further capital injection becomes an option on the back of positive results.

Exhibit 9: Financial summary

€000s	2013	2014	2015e	2016e	2017e
Year-end 31 December	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS					
Revenue	4,904	7,055	5,000	6,800	7,300
Cost of sales	(1,474)	(4,080)	(2,601)	(3,060)	(2,920)
Gross profit	3,430	2,975	2,399	3,740	4,380
R&D expenditure	(10,243)	(8,504)	(10,016)	(11,000)	(10,000)
Administrative, distribution and other	(3,779)	(3,908)	(3,605)	(3,867)	(3,983)
Operating profit	(10,592)	(9,437)	(11,221)	(11,127)	(9,603)
Intangible amortisation	(1,593)	(819)	(819)	(819)	(819)
Exceptionals (impairment / restructuring costs)	(862)	0	0	0	0
Share-based payments	(53)	(3)	(15)	(20)	(20)
EBITDA	(7,804)	(8,339)	(10,137)	(10,063)	(8,539)
Operating profit (before GW and except.)	(8,084)	(8,615)	(10,387)	(10,288)	(8,764)
Net interest	48	(228)	(269)	75	150
Other (profit/loss from associates)	19	39	39	39	39
Profit before tax (norm)	(8,036)	(8,843)	(10,656)	(10,214)	(8,614)
Profit before tax (FRS 3)	(10,525)	(9,626)	(11,451)	(11,014)	(9,414)
Tax	0	(70)	(40)	0	0
Profit after tax (norm)	(8,017)	(8,874)	(10,657)	(10,175)	(8,575)
Profit after tax (FRS 3)	(10,525)	(9,696)	(11,491)	(11,014)	(9,414)
Average number of shares outstanding (m)	10.1	10.1	14.6	19.0	19.0
EPS - normalised (€)	(0.80)	(0.88)	(0.73)	(0.54)	(0.45)
EPS - FRS 3 (€)	(1.04)	(0.96)	(0.79)	(0.58)	(0.50)
Dividend per share (€)	0.0	0.0	0.0	0.0	0.0
BALANCE SHEET					
Fixed assets	11,591	10,639	10,193	9,302	8,436
Intangible assets	10,651	9,836	9,400	8,584	7,768
Tangible assets	602	425	375	300	250
Investments and other	338	378	418	418	418
Current assets	6,114	4,295	22,551	11,376	2,412
Stocks	23	25	25	25	25
Debtors	346	652	225	225	225
Cash	4,899	3,202	21,916	10,741	1,777
Other current assets	846	393	385	385	385
Current liabilities	(3,587)	(4,842)	(4,055)	(3,475)	(3,725)
Creditors	(675)	(993)	(625)	(625)	(625)
Short-term borrowings	0	(317)	0	0	0
Deferred revenue (short term)	(1,589)	(2,638)	(2,330)	(1,750)	(2,000)
Other current liabilities	(1,323)	(894)	(1,100)	(1,100)	(1,100)
Long-term liabilities	(2,836)	(8,042)	(3,991)	(1,750)	(1,750)
Long-term borrowings	0	(6,131)	(1,891)	0	0
Deferred revenue (long term)	(2,682)	(1,788)	(2,000)	(1,650)	(1,650)
Other long-term liabilities	(154)	(123)	(100)	(100)	(100)
Net assets	11,282	2,050	24,698	15,453	5,373
CASH FLOW					
Operating cash flow	(7,052)	(8,302)	(10,100)	(9,133)	(8,789)
Net interest	66	0	(7)	2	4
Tax	0	(70)	(40)	0	0
Capex	(99)	(100)	(100)	(150)	(175)
Expenditure on intangibles	(21)	(3)	(3)	(3)	(3)
Acquisitions/disposals	10	0	0	0	0
Financing	0	477	27,521	0	0
Other	0	0	6,000*	0	0
Net cash flow	(7,096)	(7,998)	23,271	(9,284)	(8,963)
Opening net debt/(cash)	(12,064)	(4,899)	3,246	(20,025)	(10,741)
HP finance leases initiated	0	0	0	0	0
Other	(69)	(147)	0	0	0
Closing net debt/(cash)	(4,899)	3,246	(20,025)	(10,741)	(1,777)

Source: Edison Investment Research, company accounts. Note: *Balancing item in 2015 for €6m Santo loan pay-off through the issue of 1.5m new shares at €4.00 to Santo in July 2015.

Frankfurt +49 (0)69 78 8076 960
Schumannstrasse 34b
60325 Frankfurt
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 1161
Level 25, Aurora Place
88 Phillip St, Sydney
NSW 2000, Australia

Wellington +64 (0)48 948 555
Level 15, 171 Featherston St
Wellington 6011
New Zealand