EDISON

4SC

Q218 update

Domatinostat R&D ramp-up in H218

Pharma & biotech

During the Q218 results call, 4SC management announced that with current funds, it plans to initiate some of its additional domatinostat trials including the pivotal Merkel-cell carcinoma (MCC) study and a Phase II skin cancer checkpoint combination study. 4SC will provide further detail in H218. The SENSITIZE study (Phase Ib/II, melanoma) is on track in Europe (data H119), while a new IND will allow expansion of the study into the US in 2019. The EMERGE study (Phase II, GI cancers) is now expected to initiate in Q318 (previously H118). The multiple domatinostat studies in H218/H119 will provide several R&D catalysts while investors wait for pivotal RESMAIN study data. Enrolment for the RESMAIN study (CTCL) continues in Europe and Japan (100/150 patients by end-2018), and top-line data are now expected in H219 (previously H119). Due to this modest delay, we now forecast resminostat launch in 2021 (previously 2020), and therefore slightly lower our valuation to €327m or €10.7/share (vs €11.4/share).

Year end	Revenue (€m)	PBT* (€m)	EPS* (€)	DPS (€)	P/E (x)	Yield (%)
12/16	2.1	(10.9)	(0.54)	0.0	N/A	N/A
12/17	4.2	(10.0)	(0.41)	0.0	N/A	N/A
12/18e	4.7	(17.6)	(0.57)	0.0	N/A	N/A
12/19e	3.1	(19.2)	(0.63)	0.0	N/A	N/A

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

Domatinostat combo strategy revealed late 2018

With current funds, management plans to initiate at least two additional checkpoint combination studies, which will include the pivotal MCC study and the Phase II skin cancer checkpoint combination study (lead-in for the MCC study). Further detail will be provided to investors later in 2018. We expect 4SC's domatinostat programme to become more significant in H218 with multiple catalysts in the period: publication of a data set from the SENSITIZE study (first dose cohort) including safety, efficacy and biological data; initiation of the EMERGE study; fresh preclinical checkpoint combination data; and initiation of an additional combination study.

Financials

In H118 the average cash burn was €1.2m/month, while management's FY18 guidance stays at €1.8-2.0m/month, indicating increased cash burn in H218. For Q218, R&D costs were €4.3m vs €2.2m in Q217. We expect R&D costs to ramp up in H218 reflecting domatinostat trials. Net cash as of 30 June 2018 was €34.1m. 4SC continues to guide cash reach into 2020, providing a number of R&D catalysts.

Valuation: Reduced slightly to €10.7/share

We lower our rNPV-based valuation to €327m, or €10.7/share, from €348m (€11.4/share), due to the updated valuation for resminostat CTCL. We now expect resminostat to launch in 2021 vs 2020 following the announced modest delay in top-line data from the RESMAIN study, which are now due in H219 vs H119. A key near-term catalyst is first interim data from the SENSITIZE study (H218).

17 August 2018

Price	**€4.02**
Market cap	**€123m**
Net cash (€m) at 30 June 2018	34.1
Shares in issue	30.6m
Free float	35%
Code	VSC
Primary exchange	Frankfurt (Xetra)
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	(5.3)	(31.3)	(7.1)
Rel (local)	(2.8)	(27.0)	(6.9)
52-week high/low		€8.5	€3.8

Business description

4SC is a Munich-based cancer biopharmaceutical company. Resminostat (HDAC inhibitor) is the lead candidate for cutaneous T-cell lymphoma (CTCL, pivotal study started in Q416). It has a second compound, domatinostat (Phase Ib/II started in Q317) and a preclinical asset, 4SC-208. 4SC also has several partners including Yakult Honsha for resminostat in Japan in various indications.

Next events

Initiation of EMERGE study	H218
R&D update on domatinostat combination studies	H218
Top-line data from SENSITIZE study (cohort 1)	H218
Top-line data from RESMAIN study	H219

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Domatinostat combination strategy to be revealed soon

As described in our previous note, 4SC intends to carry out a broad clinical programme for domatinostat, beyond SENSITIZE and EMERGE, involving combination studies with checkpoint inhibitors to tackle the high non-responder issue. As of the last update by 4SC, these additional combination studies included a pivotal study in MCC in combination with avelumab, and several other Phase II combination and triple combination studies that were not defined. In the Q218 update, management explained that while these plans are still subject to discussion, it could confirm the company has sufficient capital to initiate 'some' of these additional studies (bearing in mind it has available capital into early 2020), and this will 'certainly' include the MCC pivotal study and a Phase II skin cancer checkpoint combination study. The skin cancer study would be a 'run in' to the pivotal study for MCC. Management aims to release further detail on these studies to investors at the end of 2018. During the Q&A session, 4SC also expressed interested in exploring further new double and triple combinations with domatinostat together with partners.

According to the Q218 update, the SENSITIZE study (domatinostat Phase Ib/II melanoma study in combination with pembrolizumab) is on track with enrolment in Europe, where the second cohort has started treatment following a positive safety review from the first cohort. The company will publish a data set including safety, efficacy and biological data from the first dose cohort in H218, and top-line data from the whole study are expected in H119. Now the FDA has approved 4SC's IND application for domatinostat in melanoma (announced 15 August 2018), it is likely the SENSITIZE study trial will include US trial centres from 2019. Meanwhile, the EMERGE study (domatinostat Phase II MSS GI cancer) is expected to enrol the first patient in Q318. Safety data are expected in Q119 and early efficacy data in H219.

Overall, we see a strong interest and commitment from management to develop the domatinostat pipeline in both Europe and the US, with emphasis on the domatinostat checkpoint combinations.

Mogamulizumab: FDA approval positive for resminostat?

On 8 August 2018, the FDA approved a new drug for CTCL Poteligeo (mogamulizumab, Kyowa Kirin, Inc), which had previously been granted FDA priority review, breakthrough status and Orphan Drug designation. Mogamulizumab is a CC chemokine receptor type 4 (CCR4)-directed monoclonal antibody indicated for the treatment of adult patients with relapsed or refractory mycosis fungoides or Sézary syndrome after at least one prior systemic therapy. It is already approved in Japan and is expected to be approved in Europe in December 2018 (EvaluatePharma).

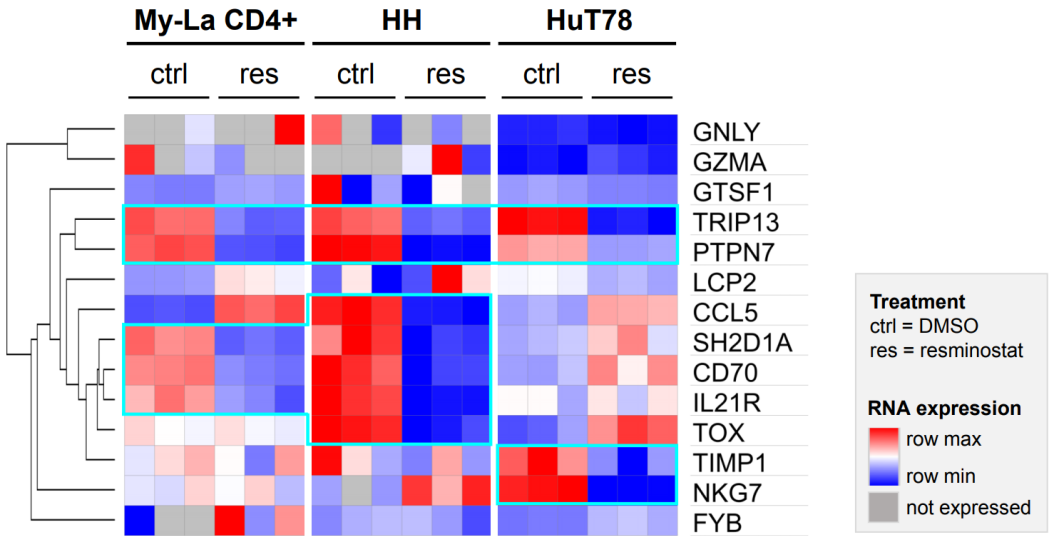
Management believes this news is positive for resminostat, since it demonstrates that the FDA is accepting PFS as an endpoint in CTCL, which is also used as the primary endpoint in the RESMAIN study. Secondly, it demonstrates that HDAC inhibitors are unsuitable for use as a monotherapy for reducing tumour burden in progressive patients. This is because the mogamulizumab trial was compared with HDACi vorinostat, which was only able to achieve 3.1 months PFS compared with 7.6 months with mogamulizumab.

The two drugs are not expected to compete directly since mogamulizumab is targeting relapsed or refractory patients and resminostat is targeting patients who have at least achieved disease control after a previous treatment, although they are both targeting the same subtypes of CTCL (mycosis fungoides and Sézary syndrome). Patients are being enrolled into the RESMAIN study if they have achieved either complete response, partial response or stable disease with previous systemic therapy. According to management, previous systemic therapy would also include mogamulizumab

and so these patients would also be eligible for maintenance treatment with resminostat. Following this logic, if mogamulizumab shows good efficacy in the clinic, it could increase the number of patients achieving at least disease control, thus increasing the number of patients eligible to move onto maintenance with resminostat, and possibly also increase the number of months of treatment with resminostat. It is too early to see how this will shape in clinical practice, however, the rationale appears to be sound.

4SC has been gathering further pre-clinical data to support the unique positioning of resminostat in the maintenance setting. A recent and interesting finding is that resminostat modulates progression-associated genes in CTCL cell lines (Exhibit 1). Management believe these new data support the idea that resminostat can prolong time to progression for CTCL patients.

Exhibit 1: RNA-seq gene expression analysis shows down-regulation of progression-associated genes in resminostat-treated CTCL cell lines compared with control (DMSO)



Source: 4SC Poster Presentation. Note: CTCL cell lines = My-La CD4+, HH and HuT78, ctrl = control (DMSO), res = resminostat.

4SC aims to enrol at least 100 patients in 2018 (previously 150) to the RESMAIN study. Since joining the study in H118, Yakult has five active clinical centres, and has recruited four patients from two of these centres. The company does not have a target for enrolment in Japan. Top-line data from the study are now expected in late 2019 (previously H119). Currently this appears a modest delay and could be related to Yakult jumping on board geographically expanding the trial to Japan, but no specific reasons were mentioned by the company. These delays could affect the filing date, which we previously included in our model as 2019. Depending on how late in 2019 data will be available, 4SC might have to file in 2020, which means market launch in 2021 (previously 2020 in our model).

Upcoming newsflow

Exhibit 2: Upcoming newsflow relating to clinical trials and other activities

	H218	H119	H219	2020
Resminostat clinical studies				
RESMAIN (Pivotal study, CTCL)	• Enrolment of at least 100 patients (n=150)		• **Top-line data expected**	• **Marketing authorisation filing in Europe**
Yakult study (Phase II, biliary tract cancer)				• **Final study results expected by partner Yakult**
Domatinostat clinical studies				
SENSITIZE (Phase Ib/II, melanoma)	• Cohort 2 enrolment expected to complete • Cohort 1 data set published	• Cohort 2 data set published • Cohort 3 enrolment expected to complete • **Cohort 3 data set published**		
EMERGE (Phase II, GI cancers)	• First patient expected to be enrolled	• Safety data published	• **Early efficacy data published**	
Domatinostat in Merkel-cell carcinoma	• MCC preclinical data to be published		• Initiation of MCC Phase II study TBC	
Additional domatinostat combination studies	• Update on R&D strategy • New preclinical triple combination data to be published • Initiation of additional checkpoint combination studies			
Other activities				
Out-licensing	• Further out-licensing of non-core assets			
Fund-raising				• Potential new fund-raise (current cash reach into early 2020)

Source: 4SC, Edison Investment Research. Note: **Bold** indicates key catalysts (efficacy data, marketing authorisation).

Valuation

We revised our valuation of resminostat in CTCL, due to the updated timeline for the RESMAIN pivotal study, as discussed above. Consequently, we have updated our model to reflect market launch in 2021 compared to 2020 before. The rNPV of resminostat CTCL is now €243m (vs €274.2m). All other valuation assumptions remain unchanged. As a result, we have slightly decreased our valuation of 4SC from €348m (€11.4/share) to €327m (€10.7/share). The valuation was also marginally affected by a lower net cash position, offset by rolling the model forward.

Exhibit 3: Financial summary

€'000s	2016	2017	2018e	2019e
Year end 31 December	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS				
Revenue	2,060	4,197	4,724	3,133
Cost of sales	(76)	(574)	(574)	(574)
Gross profit	1,984	3,623	4,150	2,559
R&D expenditure	(10,601)	(11,475)	(19,555)	(19,461)
Administrative, distribution and other	(3,175)	(3,084)	(3,195)	(3,289)
Operating profit	(11,792)	(10,936)	(18,600)	(20,191)
Intangible amortisation	(892)	(892)	(892)	(892)
Exceptionals (impairment / restructuring costs)	0	0	0	0
Share-based payments	0	0	(20)	(20)
EBITDA	(10,900)	(9,819)	(17,463)	(19,054)
Operating Profit (before amort and except.)	(10,900)	(10,044)	(17,688)	(19,279)
Net interest	(14)	9	100	100
Other (profit/loss from associates)	711	0	0	0
Profit before tax (norm)	(10,914)	(10,035)	(17,588)	(19,179)
Profit before tax (FRS 3)	(11,095)	(10,927)	(18,500)	(20,091)
Tax	(71)	(33)	0	0
Profit after tax (norm)	(10,274)	(10,068)	(17,588)	(19,179)
Profit after tax (FRS 3)	(11,166)	(10,960)	(18,500)	(20,091)
Average Number of Shares Outstanding (m)	19.0	24.8	30.6	30.6
EPS - normalised (c)	(54.17)	(40.58)	(57.39)	(62.58)
EPS - FRS 3 (€)	(0.59)	(0.44)	(0.60)	(0.66)
Dividend per share (c)	0.0	0.0	0.0	0.0
BALANCE SHEET				
Fixed assets	7,096	6,365	5,452	4,539
Intangible assets	6,499	5,694	4,806	3,918
Tangible assets	497	570	545	520
Investments and other	100	101	101	101
Current assets	11,959	41,548	22,957	4,522
Stocks	0	0	0	0
Debtors	95	30	30	30
Cash	10,048	41,327	22,736	4,301
Other current assets	1,816	191	191	191
Current liabilities	(3,257)	(2,759)	(3,636)	(2,840)
Creditors	(834)	(1,175)	(1,175)	(1,175)
Short-term borrowings	0	0	0	0
Deferred revenue (short term)	(1,431)	(1,485)	(2,362)	(1,566)
Other current liabilities	(992)	(99)	(99)	(99)
Long-term liabilities	(525)	(461)	(511)	(486)
Long-term borrowings	0	0	0	0
Deferred revenue (long term)	(493)	(394)	(444)	(419)
Other long-term liabilities	(32)	(67)	(67)	(67)
Net assets	15,273	44,693	24,263	5,735
CASH FLOW				
Operating cash flow	(12,320)	(8,508)	(18,390)	(18,234)
Net interest	(531)	0	3	3
Tax	(71)	(33)	0	0
Capex	(404)	(168)	(200)	(200)
Expenditure on intangibles	(60)	(4)	(4)	(4)
Acquisitions/disposals	2,808	39	0	0
Financing	0	39,953	0	0
Other	650	0	0	0
Net cash flow	(9,928)	31,279	(18,591)	(18,435)
Opening net debt/(cash)	(19,514)	(10,048)	(41,327)	(22,736)
HP finance leases initiated	0	0	0	0
Other	462	0	0	0
Closing net debt/(cash)	(10,048)	(41,327)	(22,736)	(4,301)

Source: 4SC, Edison Investment Research

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