MARTEN & CO

Update | Healthcare

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Sareum Holdings

Key ‘737 data coming up

Sareum’s investment case stands on two pillars: the development by licensee Sierra Oncology of the Chk1 inhibitor, SRA737; and the development and potential licensing of internally-generated TYK2 candidates for autoimmune disease and cancer.

This year should see the first clinical data on SRA737, as well as further data from preclinical studies, that may support a valuation uplift. Preclinical data on SRA737 in combination with low-dose gemcitabine and an anti-PD1 antibody in small cell lung cancer are due at AACR (29 March-3 April) and have the potential to surprise to the upside. Early clinical data on SRA737, and potentially on the competitor, prexasertib, are expected at ASCO, about two months later (abstracts revealed 15 May).

Several other developments have affected the investment case, most notably the proposed acquisition of Celgene by Bristol-Myers Squibb. BMS has featured its lead TYK2i prominently in presentations supporting the deal, which has increased attention on the drug class. Moreover, the acquisition, if completed, will also almost certainly mean that Celgene will not be able to exercise its option over Nimbus Therapeutics’ competing TYK2i.

Marten & Co values Sareum’s 27.5% economic interest in SRA737 at £20.3m and places an indicative value on its TYK2 assets of £8-16m, representing a modest upgrade from its previous position. This suggests an overall value for Sareum of £25-35m (0.87-1.14p/share), which offers up to 63% upside to the current share price.

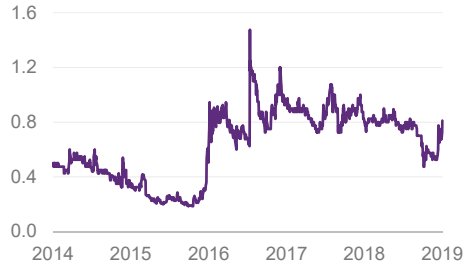
Year ended	Rev (£m)	PBT (£m)	EPS (p)	DPS (p)
30/06/16	0.0	(1.2)	(0.05)	0.0
30/06/17	0.0	0.4	0.02	0.0
30/06/18	0.0	(1.7)	(0.06)	0.0
30/06/19	0.0	(1.7)	(0.06)	0.0

Source: Marten & Co

Sector	Healthcare
Ticker	SAR LN
Base currency	GBP
Price	0.81p
Daily volume (1-year average)	5.3m shares
1-year high	0.90p
1-year low	0.475p
1-year performance	15.7%
5-year performance	(33.3%)
Yield	nil

Share price over five years

Time period 19/03/2014 to 19/03/2019



Source: Bloomberg

Domicile	England & Wales
Market cap	£23.3m
Shares outstanding	2.88bn
Net cash	£1.4m

Click here for our initiation note

Data summary

Figure 1: Sareum's R&D pipeline

Compound	Mechanism	Indication(s)	Stage	Notes
SRA737	CHK1 inhibitor	High-grade serous ovarian cancer (HGSOC) and other solid tumours, especially with mutations likely to cause increased replication stress and therefore sensitivity to Chk1 inhibition.	Phase I/II	Licensed to **Sierra Oncology** in a deal with a headline value of $328.5m, in which Sareum holds a 27.5% interest. Majority interest held by CRT Pioneer Fund. Future studies could include two/three drug combinations with low-dose gemcitabine, PARP inhibitors and immune checkpoint inhibitors.
SDC-1801	TYK2/JAK1 inhibitor	Potential indications include psoriasis, RA, lupus, IBD and MS. Candidate SAR-20347 showed activity in models of psoriasis, RA and colitis.	Preclinical	Efficacy demonstrated in psoriasis, RA and colitis models. Entering non-GLP tox studies. US DoD funding for lupus model.
SDC-1802	TYK2/JAK1 inhibitor	T-cell acute lymphoblastic leukaemia (T-ALL); anaplastic large cell lymphoma (ALCL), solid tumours.	Preclinical	Efficacy demonstrated in model of T-ALL. Innovate UK funding award for T-ALL model.
-	Aurora/FLT3	Acute myeloid leukaemia (AML)/ acute lymphoblastic leukaemia (ALL).	Preclinical	**HMUBEC** is entitled to a low-mid single digit royalty.

Source: Sareum, Marten & Co. RA = rheumatoid arthritis; MS =multiple sclerosis; IBD = inflammatory bowel disease.

Figure 2: SRA737 trial schedule

Indication	N	Design	Study ID	Data
Ovarian/ Other cancers	112	Monotherapy. Five indication-based cohorts: HGSOC with 65 pts with/without CCNE1 mutation and four smaller cohorts of up to 20 pts each in prostate, NSCLC, head & neck/anal and colorectal cancer. SRA737 is administered each day as monotherapy. See here.	NCT02797964 / SRA737-01	Sep-19
Ovarian/ other cancers	140	Combination with low-dose gemcitabine. Expansion cohort consists of four cohorts of 20 pts each in HGSOC (prioritised), small cell lung cancer, soft tissue sarcoma and cervical/anogenital cancer. All pts must have one or more mutations likely to confer sensitivity of Chk1 inhibition. Pts receive low-dose gem on days 1 and SRA737 on days 2,3 weeks for three weeks every 28 days. See here.	NCT02797977 / SRA737-02	Dec-19
Prostate cancer	N/A	Planned combination study of SRA737 + niraparib.	SRA737-03	N/A

Source: Marten & Co. Note: HGSOC = High-grade serous ovarian cancer; NSCLC = non-small cell lung cancer.

Figure 3: Potential stock catalysts relating to SRA737

Time	Catalyst	Comment/notes
29 Mar-1 April	American Association for Cancer Research (AACR)	Preclinical study on SRA737, low-dose gemcitabine and anti-PDL1 in small cell lung cancer (1 April). Results of Phase I study of prexasertib combined with olaparib in HGSOC (2 April).
15 May	American Society of Clinical Oncology (ASCO) abstracts revealed.	Expected update on SRA737, possible updates on prexasertib.
31 May-4 Jun	ASCO	Data presentations
2019	Initiation of IST combination trial of SRA737 and niraparib in prostate cancer	Note: niraparib provided by J&J, partner of GSK (which acquired Tesaro).
27 Sep-1 Oct	European Society of Medical Oncology	Potential venue for SRA737 and prexasertib data updates.
H2 19	Final data on mono and combo studies of **SRA737**	Will inform selection of indications for further development.

Source: Marten & Co

Investment summary.

More information is available on the company's website www.sareum.com

- Sareum's investment case rests on two pillars: the development of SRA737 by partner Sierra Oncology (Nasdaq: SRRA) and the early development and potential out-licensing of its two TYK2/JAK1 candidates for autoimmune disease and cancer.
- Sareum holds a 27.5% economic interest in the licensing deal covering SRA737, with the remainder held by CRT Pioneer Fund. SRA737 is one of three compounds with the Chk1 mechanism in active development (the two others are Lilly's prexasertib and Esperas Pharma's LY2880070). SRA737 is in two clinical trials and may enter a third this year, and prexasertib, the principal competitor is in six studies.
- Marten & Co values Sareum's interest in SRA737 at £20.3m and expects this figure to rise by £2-3m/year over the next two years, before doubling to £52m in 2021. Sareum's enterprise value (market cap less cash) of £19m suggests investors either undervalue SRA737 or ascribe little, if any, value to its TYK2/JAK1 assets.
- Marten & Co places an indicative value on Sareum's TYK2 assets of £8-16m ($10-20m), a modest upgrade relative to that in the initiation note.
- Sareum is exposed to risks normally associated with drug development, including the uncertain outcome of clinical trials and the success or failure of competing molecules. The most important of these risks at present relate to Sierra's priorities for SRA737 and its continued ability to fund a development in the context of a broader R&D pipeline.
- With reasonable assumptions for R&D spending, overheads and tax, Marten & Co suggests an indicative valuation for Sareum of £25-35m (0.87-1.14p/share), which suggests up to 63% upside to the current share price.

SRA737 development

Highly selective inhibitor of Checkpoint kinase 1, a key regulator of cell-cycle progression and DNA damage response

SRA737 is a highly selective inhibitor of Checkpoint kinase 1 (Chk1), a key regulator of cell-cycle progression and DNA damage repair/replication stress response. Cancer cells are normally in a state of intrinsic replication stress caused by oncogenes (eg *CCNE1* or *MYC*), mutations in DNA repair machinery (eg *BRCA1* or *FANCA*), a dysregulated cell cycle (eg *p53* or *RAD50*) or other genomic alterations. This replication stress leads to a dependency on Chk1 for survival. Thus, targeted inhibition of Chk1 should cause the selective death of cancer cells in replication stress, a process known as "synthetic lethality".

One of just three Chk1 inhibitors in development

SRA737 is one of two main Chk1 inhibitors in development. SRA737 has several potential advantages over prexasertib: its oral route of administration (Lilly's compound is only available IV) and a higher specificity for the Chk1 target. Both agents are in single-arm Phase I/II clinical trials in solid tumour types, but with a focus on high-grade serous ovarian carcinoma (HGSOC, especially OC patients who are unresponsive to PARP inhibitors (another DNA damage repair/synthetic lethality mechanism). HGSOC accounts for the majority of ovarian cancers.

Phase I/II studies are underway as monotherapy and in combination with low-dose gemcitabine

SRA737 is being evaluated in two separate Phase I/II trials, both of which have an initial dose-escalation Phase I stage (to define the optimal dose) followed by a Phase II dose expansion stage, designed to provide some evidence of efficacy. The first study examines SRA737 as a monotherapy, administered daily, and includes a 65-patient cohort in HGSOC in patients with and without the CCNE1 mutation. The second study tests the combination, given intermittently with a sub-therapeutic (potentially as low as 5% of standard) dose of gemcitabine. Gemcitabine is a commonly-used chemotherapeutic agent, but at a low dose it is hypothesised to potentiate the

anticancer effect of Chk1 inhibition. In this study, SRA737 is administered on two of seven days in each week.

Monotherapy study has completed recruitment with 112 patients

The monotherapy study has recently completed recruitment with 112 patients, presumably having reached 65 HGSOC with the remainder across the other four cohorts and in the Phase I dose-escalation phase.

The combination study currently remains open with an enrolment target of 140 patients across four cohorts but is prioritised for ovarian cancer. The study's earlier dose-escalation stage also included a triple combination with cisplatin, although this was not included in the dose expansion stage.

Dose expansion stages enrol patients with one or more mutations that are expected to confer sensitivity to Chk1 inhibition.

In both studies, subjects in the dose expansion stages enrol patients who must have tumours with one or more mutations that are expected to confer sensitivity to Chk1 inhibition. These fall into four categories: oncogenic drivers (CCNE1 or MYC); genes involved in the DNA repair process or mismatch repair (MMR) genetic alterations and/or high microsatellite instability; and, key tumour suppressor genes regulating G1 cell cycle progression/arrest or genetic indicators of replicative stress. Patients with head and neck or anal cancers must also be positive for HPV, a main causative agent for these malignancies.

Upcoming conference publications

Initial clinical data are targeted for ASCO

Sierra aims to present preliminary clinical data on SRA737 at ASCO, the scientific conference that is widely considered to be the industry's most prestigious venue. Abstract headlines for ASCO are disclosed in mid-April, with the texts revealed on May 15. Assuming an abstract(s) is accepted, they would contain that data from a cut-off that would have occurred in January at the latest (as the submission deadline is 12 February). However, companies typically update the material presented at the conference. Data that could be submitted are likely to include safety, pharmacokinetics, and dosing with possibly some preliminary evidence of activity.

Sierra also recently upgraded the monotherapy study's protocol to add objective response rate (ORR) to the primary endpoints (the others relate to safety and PK). ORR is typically measured by RECIST, a standardised approach, that allocates patients to one of four groups based on their response. There are three responding outcomes: complete response (CR, complete reduction of the tumour); partial response (PR, a >30% reduction in the tumour's size); and, stable disease (SD, a change in the tumour size of <30%, either increase or decrease). The fourth category is progressive disease (PD, an increase in the tumour size of >30%).

A key benchmark will be the comparison with Lilly's prexasertib, which achieved an ORR of 59% (eight PRs and five SDs from 24 evaluable) in heavily pre-treated HGSOC or high-grade endometrioid ovarian carcinoma.

Late breaking oral presentation due at AACR

Meanwhile, Sierra has been given a late-breaking oral presentation (which are reserved for higher impact results) at the American Association for Cancer Research (29 March-3 April), another prestigious conference typically used for preclinical data. The presentation will describe preclinical results of SRA737, low-dose gemcitabine and an anti-PDL1 antibody in xenograft model of small cell lung cancer (SCLC). The abstract title notes the triple combination produced "profound synergy with inducing durable tumour regression and modulation of the immune microenvironment". Abstract details have not yet been disclosed (which may occur on 29 March).

Previous (preclinical) data disclosures on SRA737 are shown in Figure 4.

Figure 4: Previous preclinical publications on SRA737

Conference	Finding	Conclusion/notes
AACR Conference on Tumor Immunology and Immunotherapy, November 2018	Efficacy in anti-PD-L1 refractory SCLC model.	SRA737 inhibits tumour growth and synergises with an anti-PD-L1 antibody to induce tumour regression in an anti-PD-L1 refractory small cell lung cancer model.
EORTC-NCI-AACR Symposium - November 2018.	Efficacy in CCNE1 and MYCN-overexpressing HGSOC.	SRA737 shows promising efficacy in CCNE1-amplified and MYCN over-expressing preclinical models of HGSOC.
AACR, April 2018	Activity in PARP inhibitor resistant and CCNE1 amplified HGSOC.	SRA737 demonstrates single agent activity in acquired PARP-resistant cells, as well as in combination with a PARP inhibitor. Synergistic tumour growth inhibitory activity shown for SRA737 in combination with PARP inhibitor in a HGSOC model.
AACR, April 2018	Synergy with niraparib, a PARP inhibitor in ovarian and breast cancer *in vitro* models.	The combination of SRA737 and niraparib (a PARP inhibitor) in HRR proficient ovarian and breast tumour cell lines elicited enhanced tumour cell death compared to either agent alone.
EORTC-NCI-AACR Symposium, November 2017.	SRA737 demonstrates synthetic lethality with replication stress-inducing agents in preclinical models	SRA737 synergises with a range of chemotherapeutic agents that induce replication stress, resulting in tumour cell death in *in vitro* and *in vivo* models via synthetic lethality. Profound synergy between SRA737 and gemcitabine was observed in bladder cancer cell lines. Significant anti-tumour activity shown in an aggressive gemcitabine-resistant bladder carcinoma model. Anti-tumour activity observed for SRA737 combined with a sub-therapeutic dose of gemcitabine in colorectal cancer and osteosarcoma models.

Source: Marten & Co, Sierra Oncology.

Prexasertib – key Chk1 competitor

Lilly's prexasertib, the key competitor molecule, is in four Phase II trials, all single arm, as well as several pilot Phase I studies examining combinations with other agents (shown in Figure 5). Data from these studies are due from the middle of 2019 and would presumably, if positive, support a move into registration trials.

Figure 5: Phase I/II studies underway with Lilly's prexasertib (competitor Chk1 inhibitor)

Indication	N	Design	Study ID	Data
ED-SCLC	131	3 arm study (Pt-resistant, Pt-sensitive and exploratory)	NCT02735980	Jul-17
SCCHN	70	Combination with cisplatin or cetuximab with radiation.	NCT02555644	Jan-19
Pt-resistant/refractory recurrent ovarian cancer	180	Four cohorts: BRACA negative, ≥3 lines of prior Tx; BRACA-negative <3 lines of prior Tx; BRACA positive, prior PARP inhibitor; and Pt refractory.	NCT03414047	Apr-19
BRCA1/2 mut. breast or ovarian, TNBC, HGSOC and mCRPC	153	NCI-sponsored pilot study of monotherapy.	NCT02203513	Jun-19
Adv solid tumours*	205	Five arms test prexasertib in combination with cisplatin, cetuximab, G-CSF, pemetrexed, fluorouracil and LY3023414 (a PI3K/mTORi).	NCT02124148	Feb-20
Adv solid tumour	50	Three cohorts: HR deficiency, replicative stress, and CCNE-1 amplification.	NCT02873975	Apr-20

Source: Marten & Co. Note: * Phase I, Extensive Stage Disease Small Cell Lung Cancer; TNBC = triple negative breast cancer.; SCCHN =squamous cell carcinoma of the head and neck.

Lilly also has three publications on prexasertib due at AACR, including data from a Phase I study of prexasertib and olaparib (AstraZeneca/Merck & Co's PARP inhibitor, Lynparza) in HGSOC and other advanced solid tumours (abstract not yet disclosed), and preclinical data that show synergistic activity in combination with LY3023414 (a PI3K/mTORi) in HGSOC and triple negative breast cancer.

Lilly has previously published data from four early clinical studies (shown in Figure 6), which describe the activity of its agent.

Figure 6: Clinical trial publications on prexasertib

Time	Title (abbreviated)t	Efficacy findings/notes
Lancet Oncology, Feb 2019	28 heavily pre-treated women with HGSOC, most (22 [79%]) with Pt-resistant or refractory disease.	24/28 were evaluable for response by RECIST. 8/24 (33%) had PR, of which 6/19 pts (32%) had Pt resistant or refractory disease, and 5 pts (26%) had SD>6 mos, with a median treatment duration of 9.5 mos. All pts were BRCA wild-type.
Cancer Science. October Oct 2018	Dose-finding study in Japanese pts with advanced solid tumours.	Open-label phase I study testing two doses: 80mg/m^2 and 105mg/m^2, admin IV once every 14 days (n=6 for each dose). Eight patients had SD.
Clin Cancer Ressearch. 2018 Jul.	Phase Ib study in 101 heavily pre-treated pts with squamous carcinoma, including 26 with SCC of anus, 57 with SCCHN and 16 with squamous NSCLC.	Median PFS was 2.8 mos for SCC of anus, 1.6 mos for SCCHN, and 3.0 mos for sqNSCLC. CBR at 3 mos was 29% (23% SCC of the anus, 28% SCCHN, 44% sqNSCLC). Four pts with SCC of anus had PR or CR (ORR=15%) and three pts with SCCHN had PR (ORR=5%).
J Clinical Oncology, May 2016.	Phase I study in 45 pts with advanced cancer.	2/45 pts (4.4%) had a PR; one had SCC of anus and one had SCCHN. 15 pts (33.3%) had SD (range: 1.2 to 6.7 mos), six of whom had SCC.

Source: Marten & Co. PR=Partial response. SCCHN =squamous cell carcinoma of head and neck; NSCLC =non-small cell lung cancer.

Investment sensitivities specific to SRA737

Additional risk arises from Sierra's relative early-stage and its dependence on capital markets for funding

For Sareum investors, there are two important risks/sensitivities related to SRA737 over and above those normally associated with any drug development undertaking. These arise from the fact that Sierra itself is an early-stage, pre-revenue company (market capitalisation $138m, cash of $106m as of 30 December) and thus is dependent on raising capital to support development of SRA737 as well as its other programmes. Furthermore, Sierra's principal R&D focus is on the development of a Phase III-stage asset, momelotinib. Nevertheless, Marten & Co presumes that Sierra will at some point seek to sub-license SRA737 either globally or ex-US and it is possible that the company may become attractive as a M&A opportunity. This could be driven either by momelotinib or SRA737 or both. If this were to occur, responsibility for development of SRA737 would transfer to the acquiring company, which could accelerate its development.

TYK2 – autoimmune disease

One of five companies that have identified TYK2 inhibitors

Sareum's other assets are its TYK2/JAK1 inhibitors, which are being readied for studies in autoimmune disease and cancer. Sareum is one of five companies developing TYK2 inhibitors, two of which are in mid/late clinical stage - Bristol-Myers Squibb (BMS-986165) and Pfizer (PF-06700841). BMS has two registration trials underway for psoriasis and both companies have multiple mid-stage studies underway in other indications including systemic lupus erythematosus, Crohn's and ulcerative colitis (UC), psoriasis or psoriatic arthritis and vitiligo (see Figure 7). Pfizer also has a topical version of its molecule entering mid-stage studies for psoriasis.

Competitor data validate TYK2 in psoriasis and alopecia

Phase II data from the Pfizer and BMS compounds in psoriasis and alopecia areata, an AI condition that causes patchy or complete hair loss, have validated the TYK2 mechanism in these indications. It is not yet possible to compare efficacy across trials in the same indication and thereby gauge whether there is an advantage of dual TYK2/JAK1 inhibition over pure TYK2 approach (BMS's molecule is a pure TYK2 inhibitor while Pfizer's agent is a dual TYK2/JAK1 inhibitor (as is that of Sareum)). Pfizer's Phase II study in alopecia areata, also examined a JAK3 inhibitor and in this

case, the efficacy for its TYK2/JAK1 was marginally better. Possibly for commercial reasons, Pfizer advanced the JAK3 inhibitor into Phase III trials in this indication.

JAK1 mechanism is validated in multiple indications

JAK1 inhibition can be considered validated by approved products in RA (Xeljanx and Olumiant) as well as multiple positive studies in other indications (psoriasis, atopic dermatitis, Crohn's and UC). Xeljanz, a JAK1/3 inhibitor, gained approval in 2012 for rheumatoid arthritis (RA) and subsequently for psoriatic arthritis and ulcerative colitis. Xeljanz has sales of $1.8bn in 2018 despite carrying a "black box" warning for infections and lymphoma.

Lilly's Olumiant, the second JAK inhibitor to be approved, has peak sales forecast of $2bn/year and it also carries a black-box warning for serious infections, lymphoma and thrombosis. Olumiant is in late-stage development for other indications including atopic dermatitis, in which it has positive Phase III studies, and lupus. Two other companies have selective JAK1 inhibitors in late development, both initially targeting RA. These are AbbVie (updacitinib, filed) and Gilead (filgotinib, target filing H2 19). Pfizer has a pure JAK1 inhibitor, abrocitinib (PF-04965842), which is in Phase III for atopic dermatitis.

Figure 7: TYK2 competitive landscape in autoimmune disease

Company	Compound	Specificity	Indications/stage	Notes
Bristol-Myers Squibb	BMS-986165	TYK2	Phase III (psoriasis). Phase II (lupus, Crohn's, ulcerative colitis, psoriatic arthritis).	Positive Phase II in psoriasis.
Pfizer	PF-06700841	TYK2/ JAK1	Phase II (Crohn's disease, psoriasis, ulcerative colitis, lupus, vitiligo).	Positive Phase II studies in alopecia areata and psoriasis.
BMS	N/A*	TYK2	Phase I	
Nimbus	N/A	TYK2	Preclinical. Targeting IND filing year end 2019.	Subject to an option deal with Celgene, but unlikely to be exercised due to that company's proposed acquisition by BMS.
Sareum	SD-1801	TYK2/ JAK1	Preclinical. IND preparation studies underway, target filing by 2020.	Target first indication to be confirmed.

Source: Marten& Co. * Note: possibly BMS-986235.

Figure 8: Ongoing later-stage clinical studies with the Pfizer and BMS' TYK2 inhibitors

Drug	Stage	N	Design	Endpoint(s)	NCT ID
BMS-986165					
Plaque psoriasis	III	600	Double blind, 3 arm (one dose vs pbo vs aprelimast).	Co-primary: sPGA score of 0 or 1 at wk16 and PASI 75 at 16 wks.	NCT03624127 /POETYK-PSO-1
Plaque psoriasis	III	1,000	Double blind, 3 arm (one dose level vs pbo vs apremilast) with rand. withdrawal and retreat.	Co-Primary: sPGA score of 0 or 1 and PASI 75, both at wk 16.	NCT03611751/POETYK-PSO-2
SLE	II	360	3 does levels vs pbo.	SLE Responder Index at 24 wks.	NCT03252587
Crohn's disease	II	240	3 dose levels vs pbo.	Co-primary: CDAI at 12 wks and endoscopic response.	NCT03599622
PF-06700841					
SLE	II	448	3 dose levels vs pbo	SRI-4 at wk 52	NCT03845517
Plaque psoriasis	II	212	7 diff. doses (some with higher induction) vs pbo.	PASI score at wk 12	NCT02969018
Psoriasis (topical)	II	240	6 doses (QD and BID) vs pbo	PASI score at wk 12	NCT03850483
Crohn's disease*	II	250	4 arms: both actives vs pbo for 12 wks, plus 52 wk OLE.	Endoscopic improvement (>3pts) at wk 12.	NCT03395184
Ulcerative colitis *	II	360	12 arm: (3 doses vs pbo for each drug) for 8 and 24 wks.	Total Mayo Score (wk 8).	NCT02958865
Vitiligo*	II	330	12 arm (induction and maintenance) for 20 wks.	VASI index at wk 24.	NCT03715829

Source: Marten & Co. Note: SLE = systemic lupus erythematosus. *Also testing PF-06651600 (JAK3i) in parallel.

SDC-1802: cancer opportunity

Sareum's other TYK2 asset, SDC-1802, has shown activity in cellular and disease models of T-cell acute lymphoblastic leukaemia (T-ALL) and B-cell lymphoma. T-cell ALL is a rare cancer that largely affects children and accounts for 10-15% of newly diagnosed cases of ALL. Sareum estimates there may be 2,000 cases/year in Europe and the US. The condition is currently treated with chemotherapy and stem-cell transplant, but no targeted therapies (or chimeric antigen T-cell therapies) have yet been developed.

Sareum has also generated evidence in disease models of kidney, colon, skin and pancreatic cancer that suggests that TYK2 inhibition can modulate the host's immune system to block tumour-cell proliferation. Further work may elucidate a strategy in solid-tumour indications, possibly with immune checkpoint inhibitors.

Investment thesis - valuation

Marten & Co considers SRA737 and the two TYK2/JAK1 compounds to form the investment case.

Valuation of Sareum's interest in SRA737 reflects assumptions on size and timing of milestones and royalties

To establish a value for the interest in SRA737, Marten & Co has made assumptions about the size and timing of future milestones (which, as is usual, have not been disclosed). Our main assumptions are that the remaining $319.5m is comprised of $195m in development and regulatory milestones and $125 of sales milestones, a roughly 60:40 split. We assume SRA737 is launched in 2022 (in the US only, with accelerated approval) with a broader worldwide launch in 2023. For the purposes of modelling royalties, we have assumed the product has a commercial life until 2034, when IP may expire (unless extended).

We have modelled milestone and royalty income from SRA737, broadly on the basis that Sierra continues development with a focus on HGSOC and on a site-agnostic approach for tumours driven by CCNE1 (or similar) mutations. CCNE1 mutations are thought to be present in 21% of ovarian cancers

Figure 9: SRA737 modelling assumptions - summary

Assumption	Detail	Notes
R&D milestones	$45m on entry into pivotal trials	$20m (2019), $25m (2022)
Regulatory milestones	$150m on approval and launch	$50m (2022), $100m (2023).
Sales milestones	$125m on key thresholds	$50m when sales >$250m/year (2025), $75m when global sales >$500m/year (2027)
Royalties	"High single rising to low double digit".	Assumed 9% on sales up to $500m/year, 12% on sales >$500m/year
Peak sales	$922m in 2034	Not modelled based on incidence and pricing but by reference to other tyrosine kinase inhibitors using a similar tumour agnostic approach.
Key indication	HGSOC and CCNE1 mutant solid tumours	Monotherapy in CCNE1 mutant/wild type/combination with low-dose gemcitabine. CCNE1 (or similar) mutations are present in other solid tumour types such as bladder (25%), endometrial (21%), colorectal (14%) and NSCLC (9%)

Source: Marten & Co.

We have assumed peak sales of SRA737 of $920m/year in the late 2020s. Given the product's potential indications, pricing, duration of use and competition are all unknown at this point; this is clearly a rough estimate. However, this figure would be in line with projections for sales of Zejula in ovarian cancer (one of three PARP inhibitors approved in ovarian cancer) and, is also in line with sell-side estimates for other developmental cancer drugs that target specific driver mutations across several tumour types.

This approach values Sareum's interest in SRA737 at £20.2m based on a risk-adjusted NPV, assuming a 25% probability of success, a 12.5% discount rate with a USD/GBP FX rate of 1.3.

Our valuation approach for the TYK2 assets is less sophisticated, as the potential indications here are still unknown. We have instead used common benchmarks to provide a base case valuation of £8-15m ($10-20m). With reasonable assumptions for R&D spending, overheads and tax, Marten & Co suggests an indicative valuation for Sareum of £28-35m (0.87-1.14p/share), which suggests up to 63% upside to the current share price.

Investment sensitivities

Sareum is exposed to the risks typical of biotech drug development, including the uncertain outcome of clinical trials and reliance on third parties (notably Sierra) to advance the development of SRA737 and its own TYK2 assets. Specific sensitivities related to Sierra's funding and priorities have been noted earlier. Sareum will also have to raise further funds to advance its TYK2 assets, particularly SDC-1801.

We note that for commercial reasons a potential partner(s) for the TYK2 compounds may insist on rights to both autoimmune and cancer indications and thus it may not be possible to license the two compounds separately and our indicative valuation does not assume this. The value of the TYK2 assets may be affected by the success or failure of competitors, both within the TYK2/JAK class and - to a lesser extent - for other oral molecules addressing autoimmune/inflammatory indications. In order to be commercially successful, new oral agents will likely have to show levels of efficacy that approach or match those of biological agents while offering side-effect advantages, such a lower tendency for immunosuppression.

Financials

Sareum reported cash of £1.3m at half year end (30 December), which if current spending levels are maintained should provide a runway into 2020. The financial model has not changed since the initiation and is not a major factor in the investment thesis, except in relation to Sareum's ability to fund its planned future development activities.

Figure 10: Income statement

Year ending Jun £'000	2016	2017	2018	2019e	2020e
Revenue	123	20	0	0	0
Cost of sales	(1,326)	334	(1,717)	(1,717)	(1,717)
EBITDA	(1,203)	354	(1,717)	(1,717)	(1,717)
Depreciation	(2)	(4)	(5)	(5)	(5)
Operating profit	(1,205)	350	(1,722)	(1,722)	(1,722)
Net financials	4	3	4	3	0
Profit before tax	(1,201)	353	(1,718)	(1,719)	(1,722)
Tax	0	153	47	47	47
Net income	(1,201)	505	(1,671)	(1,672)	(1,675)

Source: Marten & Co

Figure 11: Balance sheet

Year ending Jun £'000	2016	2017	2018	2019e	2020e
Cash	1,253	2,306	1,375	156	35
Receivables	79	80	138	138	138
Other	155	48	254	254	254
Total current assets	1,487	2,434	1,767	548	427
Tangible assets	1	13	8	5	4
Other	475	54	41	29	29
Total fixed assets	476	67	49	34	33
Total assets	1,963	2,501	1,816	582	460
Accounts payable	(100)	(156)	(183)	(183)	(183)
Short-term debt				(500)	(1,600)
Total current liabilities	(100)	(156)	(183)	(683)	(1,783)
Shareholder equity	1,864	2,346	1,633	(102)	(1,324)

Source: Marten & Co

Figure 12: Cash-flow statement

Year ending Jun £'000	2016	2017	2018	2019e	2020e
Operating profit	(1,205)	350	(1,722)	(1,722)	(1,722)
Depreciation	2	4	5	3	1
Change in debtors	(79)	(1)	(57)	0	0
Change in creditors	100	56	28	0	0
Other	321	281	110	0	0
Net operating cash inflow/(outflow)	(862)	690	(1,636)	(1,719)	(1,721)
Capex	0	(16)	0	0	0
Tax	184	154	43	43	43
Financial income (charge)	4	3	4	0	0
Free cash flow	(674)	831	(1,589)	(1,675)	(1,678)
Acquisition spend	(597)	0	0	0	0
Net cash flow before financing	(1,271)	831	(1,589)	(1,675)	(1,678)
Equity issues	0	0	656	791	0
Other	0	229	0	0	0
Net cash inflow/(outflow)	(1,271)	1,060	(933)	(885)	(1,678)
Other	0	(7)	3	(43)	0
Change in net debt	(1,271)	1,053	(930)	(928)	(1,678)

Source: Marten & Co

Previous publications

Readers interested in further information about Sareum may wish to read our initiation note, Tyking the boxes, which was published on 7 November 2018. You can read the note by clicking on the link or by visiting our website.

MARTEN & CO

Authorised and regulated by the Financial Conduct Authority
123a Kings Road, London SW3 4PL
0203 691 9430

www.martenandco.com

Registered in England & Wales number 07981621,
2nd Floor Heathmans House
19 Heathmans Road, London SW6 4TJ

Sales:

Edward Marten
(em@martenandco.com)

Nick Potts
(np@martenandco.com)

David McFadyen
(dm@martenandco.com)

Research:

Healthcare analyst – Robin Davison
(rd@martenandco.com)

Matthew Read
(mr@martenandco.com)

James Carthew
(jc@martenandco.com)

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