

Sareum Holdings

Approaching the clinic

Sareum's H122 results (to end-December 2021) provided an update on the company's progress with its therapeutic pipeline. With final toxicology and safety studies for lead asset SDC-1801 completed in Q4 of CY21 (final report expected by end-Q122), the company is on track to file an exploratory clinical trial application (CTA) in mid-2022 and start clinical studies in H222. The cash balance of £5.6m at the end of H1 should be sufficient to take SDC-1801 through Phase Ia clinical trials and accelerate SDC-1802's preclinical progress, with the company continuing to assess options to further clinical development. Sareum completed the 50:1 share consolidation it announced at the December 2021 AGM, with the new shares starting trading on 1 March.

SDC-1801 remains on track to enter the clinic in 2022

SDC-1801, Sareum's lead TYK2/JAK1 inhibitor, is on track for a mid-2022 CTA filing and a subsequent clinical entry in H2 CY22 after completion of final pre-clinical toxicology studies in Q421. While the full study will be available towards the end of March, early findings are encouraging and Sareum says they support its clinical plans. Development of the capsule formulation is progressing on schedule, with the synthesis of the drug's active pharmaceutical ingredient (API) under Good Manufacturing Practice (GMP) conditions nearing completion.

SDC-1801 trial design

As per available information, the Phase Ia study would be a safety and dose-finding (ascending doses) study in healthy volunteers, with the initial target indication to be decided thereafter. The trial will also investigate early efficacy signals by looking at SDC-1801's effect on certain biomarkers of autoimmune disease. The company indicated it is working with specialist clinical trial consultants to design the trial and we expect more details in the coming months. According to management, cash at end-December 2021 (£5.6m) remains sufficient to complete the Phase Ia study, after which the company will assess further fundraising or outlicensing/partnerships to progress SDC-1801's clinical development.

Share consolidation complete

After the company's communication of a planned share consolidation in 2022, Sareum effected a 50:1 share consolidation from 1 March. The key objective was to help improve Sareum's attractiveness to institutional investors.

Historical financials

Year end	Revenue (£m)	PBT (£m)	EPS (p)	DPS (p)	P/E (x)	Yield (%)
06/18	0.0	(1.5)	(0.06)	0.0	N/A	N/A
06/19	0.0	(1.5)	(0.05)	0.0	N/A	N/A
06/20	0.04	(1.0)	(0.03)	0.0	N/A	N/A
06/21	0.0	(1.5)	(0.05)	0.0	N/A	N/A

Source: Company data

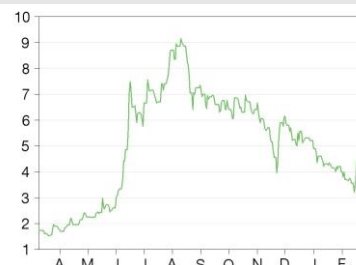
Pharma & biotech

9 March 2022

Price £1.5

Market cap £102m

Share price graph



Share details

Code	SAR
Listing	AIM
Shares in issue	68.07m
Net cash at 31 December 2021	£5.6m

Business description

Sareum is a UK-based drug development company, specialising in small molecule kinase inhibitors. Its lead programmes are its pre-clinical TYK2/JAK1 inhibitors, SDC-1801 for autoimmune diseases and SDC-1802 for cancer. SDC-1801 is undergoing advanced toxicology studies with a target to file a CTA in mid-2022. Other programmes include the CHK1 inhibitor SRA737, out licensed to Sierra Oncology (Sareum holds a 27.5% stake of the economics of the licence agreement) and the de-prioritised FLT3+Aurora kinase.

Bull

- SDC-1801's novel TYK2 selectivity may be attractive to partners, pending clinical validation.
- First-in-class opportunity for SDC-1802 in multiple cancer indications.
- Potential income generation opportunity from SRA737 offers additional upside

Bear

- Safety profile of combined TYK2/JAK1 inhibitor not certain or proved yet.
- Potential funding challenges delaying clinical progress of SDC-1801 and SDC-1802.
- Markets sought by SDC-1801 and SDC-1802 are highly competitive.

Analyst

Jyoti Prakash, CFA +91 981 880 0393

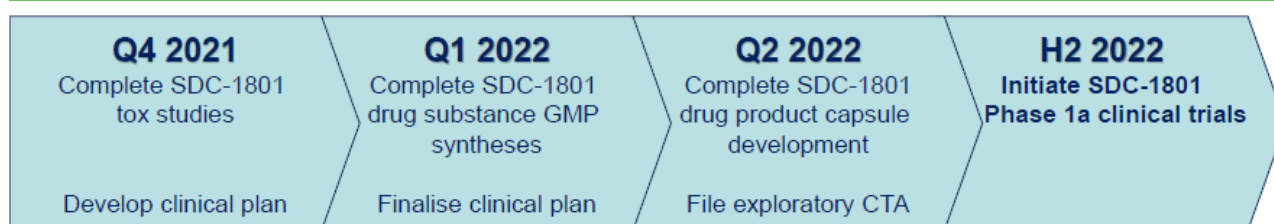
healthcare@edisongroup.com
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SDC-1801's clinical transition progressing to plan

Completion of final pre-clinical toxicology and safety studies for SDC-1801 in Q421 marks a key milestone for the company. While we are encouraged by this, final results from the study (data analysis underway, with results expected by the end of March 2022) would be instrumental in shaping Sareum's plans for a CTA filing, particularly in light of ongoing toxicity concerns around the janus kinase (JAK) class of assets. Management has indicated that preliminary data from the studies appear promising (meeting the objective of identifying organs/tissues susceptible to high-dose toxicity and determine the appropriate first-in-human dose range) and support SDC-1801's progression to the clinic. Sareum expects to initiate Phase Ia clinical trials in H222 pending successful CTA filing (with the Medicines and Healthcare products Regulatory Agency) and approval in mid-2022. While the study design is still being finalised (with guidance from external consultants), Sareum has disclosed the trial will investigate the safety of ascending doses of SDC-1801 in healthy volunteers, before the selection of an initial indication for further clinical studies in patients. In addition to safety, the first trial would aim to assess initial efficacy signals by analysing SDC-1801's effect on certain predictive biomarkers of autoimmune disease. Progress on the manufacturing front remain on track with the SDC-1801 API and oral capsule formulation under GMP conditions expected to be available by the time the trial starts in H222. Sareum's depiction of SDC-1801's path to the clinic is presented in Exhibit 1.

Exhibit 1: SDC-1801's timeline to clinical progression



Source: Company presentation, February 2022

Recent approvals for JAK inhibitors encouraging

While market sentiment around the JAK inhibitor class has been affected by the FDA diktat on class-level boxed warnings (increased risk of malignancy, thrombosis and cardiac events), JAK inhibitors remain an important treatment optionality in autoimmune/inflammatory conditions given their strong efficacy potential. After months of stalemate, we see the recent FDA approvals of second-generation JAK1 inhibitors for moderate to severe atopic dermatitis, Pfizer's [Cibinqo](#) (abrocitinib) and AbbVie's [Rinvoq](#) (upadacitinib), as a positive development and a potentially encouraging signal for the newer-generation JAK inhibitors. Despite the ongoing effects of class-wide label restrictions, the large market size and scope of the autoimmune/anti-inflammatory space means both drugs continue to hold blockbuster potential; [Evaluate Pharma](#) estimates 2026 sales for Cibinqo and Rinvoq to be \$1bn and \$2.2bn, respectively, for the indication.

The TYK2 selectivity of Bristol Myers Squibb's deucravacitinib and Sareum's SDC-1801 is more likely to side-step the toxicity issues, although it looks increasingly probable these assets may be subjected to the same black-box warning. Further clarity will be available after the FDA's decision on deucravacitinib for plaque psoriasis (expected in September 2022) and we feel this will be a major upcoming catalyst for Sareum. However, we also note the mechanism of action for deucravacitinib is different to that of SDC-1801 (allosteric approach, which allows it to bind to TYK2's non-active regulatory domain versus the traditional adenosine triphosphate approach Sareum uses) and any read-across may not be completely accurate.

Progress with SDC-1801 (COVID-19) and SDC-1802

Sareum expects the Phase Ia results for SDC-1801 to potentially support future clinical trials assessing it in COVID-19 indications and the company is in talks with experts to evaluate the timing and design of these trials. As noted in our earlier update, Sareum plans to secure further funding from the UK government's AGILE development platform (launched in February 2021 to support fast-track development and fund Phase I studies for novel COVID-19 treatments) or equivalent programmes to fund development for this indication.

Sareum's other TYK2/JAK1 candidate, SDC-1802 (targeting multiple oncology indications, in both haematological, or blood-related, malignancies and solid tumours), continues to undergo translational studies to identify an optimal cancer indication and patient population before undertaking further toxicology studies. The company expected the recent fundraising to accelerate pre-clinical development for this asset. We highlight that SDC-1802's TYK2 selectivity accords it a first-in-class potential for therapeutic treatment in cancer, although it remains a risky undertaking given past failures in this space (see our [initiation note](#) for more details). We maintain that the clinical progression for SDC-1802 would be contingent on the headway made with SDC-1801.

SRA737 update

As highlighted in our [previous note](#), Sareum's out-licensed CHK1 inhibitor SRA737 has seen a revival in interest after partner Sierra Oncology's in-licensing of the BET inhibitor AZD5153 (now known as SRA515) from AstraZeneca (August 2021) and subsequent potential combinations with SRA737 as a possible pipeline expansion opportunity. [As reiterated by Sierra in a January 2022 presentation](#), the plan lays out the potential for three separate trials in combination with SRA737, two with SRA515 in haematological malignancies and solid tumours in combination with the standard of care and another in combination with immunotherapy/low-dose gemcitabine. While Sierra has given no update on the design and timing of these trials, the company's lead asset momelotinib's potential market entry after [positive results](#) from its Phase III studies in myelofibrosis could free up some of Sierra's cash and other resources, possibly accelerating Sierra's plans for SRA737. We also note Sierra recently raised \$135m through a [public offering](#), which ameliorates any funding-related constraints in pipeline development and progression. First-patient dosing in any of these SRA737-involving studies will trigger a milestone payment of \$2m (translating to \$0.55m to Sareum).

Share consolidation complete

After Sareum's announcement of its plans for a share consolidation (announced in December 2021), the company concluded a 50:1 share consolidation on 1 March 2022 (every 50 ordinary shares consolidated into one). As a result, the number of outstanding shares dropped from 3.4bn to 68.07m, trading at £1.28 on 8 March 2021. The main reason for this was to generate increased interest from institutional investors (who may otherwise have been dissuaded by the previously large volume of shares outstanding and the low absolute trading price). As a reminder, Sareum's ownership allocation remains heavily skewed towards retail investors.

Financials

Sareum's H122 operating loss was £1.02m, up from £0.61m in H121, driven by higher R&D expenses related to pre-clinical activities, in particular for SDC-1801 as the asset nears the clinic. Net loss came in at £0.86m during the period, including R&D tax credit of £0.16m. Given the higher R&D expenses related to clinical trials, operating expenses will likely continue to increase as the pipeline approaches the clinic.

The cash balance at the end of H122 was £5.6m, supported by three equity issues to high-net-worth individuals in July, August and December 2021, raising total gross proceeds of £3.9m. This was in addition to two previous rounds raised in June 2021 (total proceeds of £2.4m). If the current run-rate (cash burn of £0.8m in H122) is maintained, the cash balance would provide funding into FY25, although we believe spending (H222 and beyond) is likely to be materially higher as the assets approach the clinic. Management has indicated cash is sufficient to complete SDC-1801's Phase Ia clinical trials and accelerate the preclinical work on SDC-1802. Additional funds (secured either through partnerships and/or equity issues) would be required to advance the programmes further. We anticipate that Sareum may evaluate outlicensing opportunities following completion of the Phase Ia clinical trials for SDC-1801, using the data from the study to potentially secure a partnership deal at attractive terms.

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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
1185 Avenue of the Americas
3rd Floor, New York, NY 10036
United States of America

Sydney +61 (0)2 8249 8342
Level 4, Office 1205
95 Pitt Street, Sydney
NSW 2000, Australia