Sareum Holdings

Broader pipeline, bigger milestones

Sareum Holdings' H125 results (to 31 December 2024) summarised a period of operational progress and an improved capital position, with successful fund-raising. Since the completion of the Phase I trial for lead asset SDC-1801 in June 2024, the focus has been on formulation optimisation and drug product manufacturing for the toxicology study, which we believe will now commence in May 2025, with completion likely in Q4 CY25 (Q2 CY25 previously). We expect this to extend the timeline for a Phase II trial start into 2026 although, with period-end cash of £4.1m, inflows from the subsequent private placement (£1.07m) and R&D credits (£0.2m), Sareum appears sufficiently funded to reach this milestone. We see the recent licence acquisition for SRA737 as a positive development as it adds another clinical-stage asset to the portfolio, which should help manage downside risks related to a more concentrated clinical pipeline.

Near-term focus on SDC-1801 Phase II readiness

The requirement for a 16-week toxicology study for SDC-1801 was driven by Sareum's decision to prepare for a Phase II study for its lead asset (rather than Phase Ib as previously planned), given the encouraging Phase I data. While we had expected the toxicology study to start by Q4 CY24/Q1 CY25, we understand that Sareum has been focusing on optimising the formulation and drug product re-synthesis to align with Phase II requirements, which has pushed the timeline to May 2025, with completion by Q4 CY25. We expect partnering discussions to gather speed in H2 CY25, as the drug progresses towards Phase II readiness.

SRA737 licence acquisition de-risks pipeline

We view the licence acquisition for SRA737 (giving Sareum a 63.5% economic interest vs 27.5% previously) as a positive step for Sareum, giving it greater control over the development plans and commercial pathway for SRA737. SRA737 is a checkpoint kinase 1 (CHK1) inhibitor, which has shown a favourable safety profile and efficacy signals in earlier Phase I/II clinical trials. We believe Sareum will seek to out-license the asset to a strategic buyer, leveraging existing clinical data.

Latest funding provides headroom into 2026

Sareum started 2025 with a cash balance of £4.1m, which was bolstered post period by the £1.07m private placement in March 2025 (against the issue of 8.56m shares) and another £0.2m in R&D tax credits. Based solely on historical burn rates, we project the funds will provide a runway into 2026, which may be sufficient time for the company to secure a partner for SDC-1801, and potentially SRA737.

Historical financials

Year end	Revenue (£m)	PBT (£m)	EPS (p)	P/E (x)
6/21	0.0	(1.7)	(2.30)	N/A
6/22	0.0	(2.6)	(3.20)	N/A
6/23	0.0	(4.0)	(4.70)	N/A
6/24	0.0	(4.6)	(4.20)	N/A

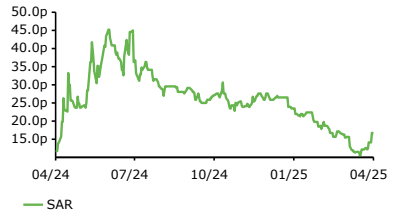
Source: Company data

Healthcare

10 April 2025

Price	**17.50p**
Market cap	**£23m**

Share price performance



Share details

Code	SAR
Listing	AIM
Shares in issue	133.5m
Net cash/(debt) at 31 December 2024	£4.1m

Business description

Sareum Holdings is a UK-based drug development company, specialising in small molecule kinase inhibitors. Its lead programmes are TYK2/JAK1 inhibitors, SDC-1801 for autoimmune diseases and SDC-1802 for cancer. Lead asset SDC-1801 reported positive Phase I data in June 2024, with Phase II readiness expected by Q4 CY25. Other programmes include the CHK1 inhibitor SRA737, for which Sareum acquired the licence in March 2025, corresponding to a 63.5% economic interest versus 27.5% held previously.

Bull points

- SDC-1801's dual TYK2/JAK1 selectivity may provide a competitive edge to peers, pending clinical validation of efficacy.
- First-in-class opportunity for SDC-1802 and SRA737 in multiple cancer indications.
- Approval of Sotyktu provides regulatory feasibility for TYK2 inhibitors.

Bear points

- Potential funding challenges due to possible partnering delays affecting clinical progress of SDC-1801 and SDC-1802.
- Safety/efficacy profile of TYK2/JAK1 inhibitors needs to be proved in larger randomised trials.
- Markets sought by SDC-1801 and SDC-1802 are highly competitive.

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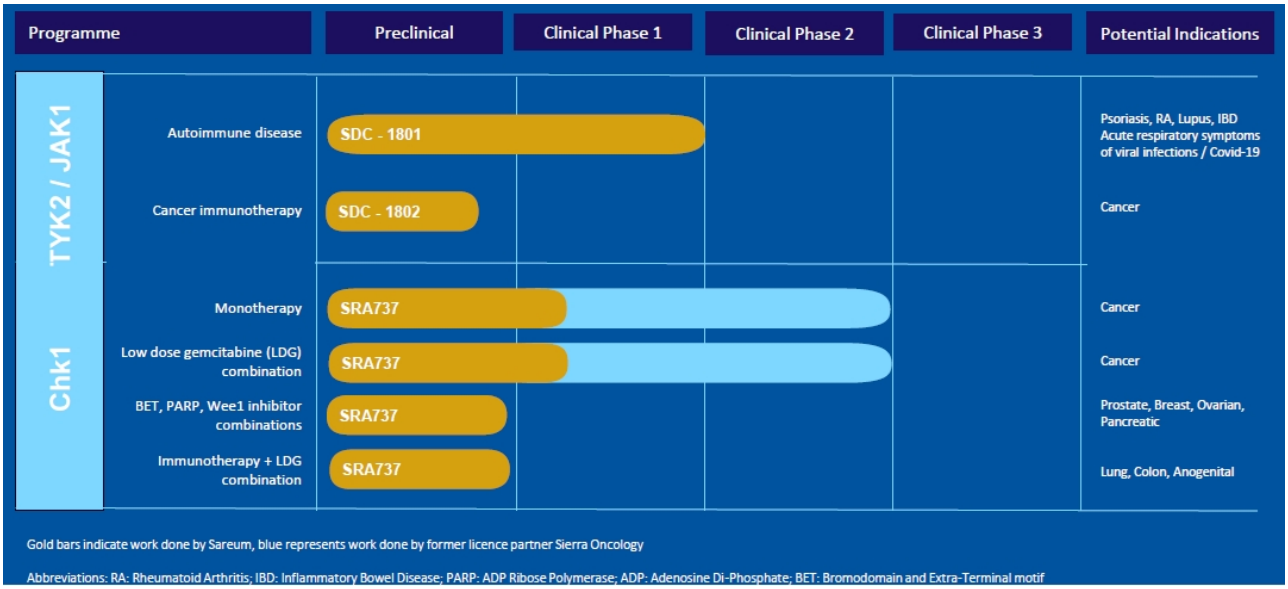
A broader pipeline with recent licence acquisition

Sareum is a clinical-stage company focused on developing novel small molecule kinase inhibitors, targeting autoimmune and cancer indications. Its core portfolio includes two tyrosine kinase 2/Janus kinase 1 (TYK2/JAK1) inhibitors, SDC-1801 and SDC-1802, with current focus on progressing the more advanced asset, SDC-1801, towards Phase II trials and, potentially, an out-licensing/partnering deal. Following encouraging data from the Phase I study in June 2024 (discussed in more detail below), the immediate goal is to initiate the 16-week toxicology study (now expected to start in May 2025, with completion in Q425) required ahead of the Phase II trial initiation, with psoriasis as the likely initial target indication. We expect the toxicology data, if positive, to support the company's discussion with prospective licensing partners to undertake the Phase II trial, potentially in 2026. Note that Sareum has recently strengthened its IP position for the drug, given new patent allowances in the US (application number US2021387981) and China (application number 2021800259993), which could provide further leverage in partnering discussions. The other TYK2/JAK1 asset, SDC-1802, is being developed for oncology indications and management has communicated that translational and preclinical studies to establish the appropriate target indication have been accelerated, with support from recent fund-raises (in October 2024 and March 2025, respectively).

While the primary focus remains on SDC-1801, the company expanded its clinical pipeline in March 2025 with the acquisition of the licence for SRA737, a CHK1 inhibitor, in which it had previously held a 27.5% economic interest. Sareum initially developed SRA737 in collaboration with the Institute of Cancer Research (ICR), Cancer Research Technology (CRT) and the CRT Pioneer Fund (CPF), before it was out-licensed to Sierra Oncology and subsequently to an undisclosed private US biopharma. The rights to the drug were returned to CPF in December 2024. Following the recent licence acquisition (which we believe was negotiated at no cost to Sareum in return for partners CPF, CRT and ICR continuing to hold a 36.5% economic interest in the asset), Sareum will hold complete decision-making rights on SRA737, along with a 63.5% economic interest. Exhibit 1 shows the company's expanded development pipeline.

Exhibit 1: Sareum's development pipeline



Source: Sareum corporate presentation, March 2025

Focus on advancing SDC-1801 to Phase II readiness

Positive Phase I data

H125 (six months ending 31 December 2024) was marked by Sareum undertaking a deeper analysis of the completed Phase I trial data for SDC-1801 and preparatory activities for the 16-week toxicology study before initiation of the Phase II trial. Undertaken in Australia, the Phase I study was a randomised, placebo-controlled trial (targeted n=96) evaluating the safety, tolerability and pharmacokinetics/pharmacodynamics (PK/PD) of SDC-1801 in healthy adults. The study

included three parts: a single ascending dose (SAD) study (part 1), a multiple ascending dose (MAD) study (part 2) and a food effects study (part 3). Parts 1 and 3 of the study were completed in February 2024 and indicated a favourable safety profile, with data from the MAD portion (reported in June 2024) and full unblinded data, released in October 2024, confirming the initial findings. The full data confirmed SDC-1801's favourable safety profile, with no serious adverse events or deaths (all adverse events were reported to be either mild or moderate) and the frequency of adverse events similar to placebo. Note that despite promising efficacy, safety has remained a key issue for JAK inhibitors, with previous-generation JAKs (such as Xeljanz, Olumiant and Rinvoq) coming under scrutiny for strong off-target toxicities and cardiovascular issues associated with non-selective targeting of the JAK isoforms (in particular JAK2 and JAK3). Newer-generation JAK inhibitors like SDC-1801 claim to circumvent this issue with more selective targeting of JAK1 and TYK2. This was evidenced by approval of the selective TYK2 inhibitor Sotyktu (deucravacitinib) in September 2022, without any black box warnings on safety issues.

In addition to a favourable safety profile, the Phase I study demonstrated that SDC-1801 was able to achieve materially higher plasma exposure than predicted therapeutic levels, with a relatively long half-life (17–20 hours), which supports convenient once-daily dosing. Unblinded data from participants in the MAD cohort, who received SDC-1801 for 10 days, also demonstrated dose-dependent reductions in three biomarkers of JAK1 and TYK2 activity (Interferon gamma-induced protein 10, high-sensitivity C-reactive protein and interferon alpha-induced STAT phosphorylation), which are key mediators of major inflammatory pathways.

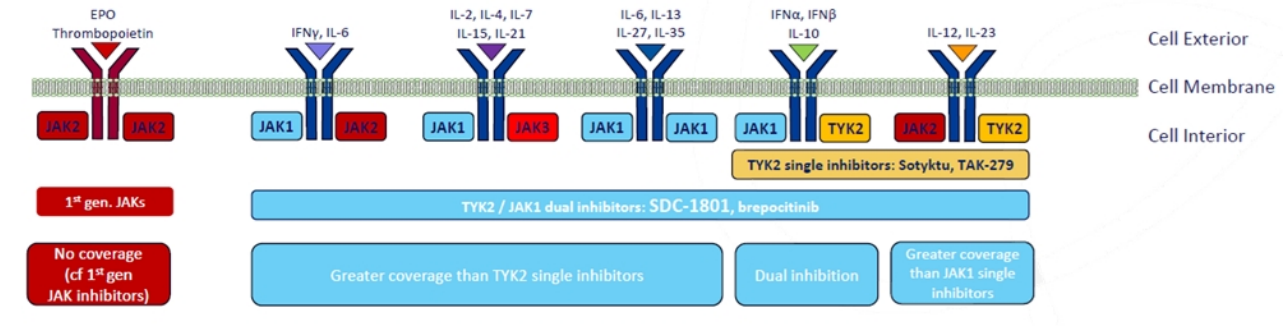
Sets the stage for the next phase of development

The encouraging Phase I data resulted in Sareum amending its development plans to prepare for a Phase II study versus Phase Ib as originally planned for SDC-1801. As a regulatory requirement, the company will need to conduct a 16-week toxicology study, matching the dosing period for the planned Phase II trial. In its H125 results, management said that preparatory work is ongoing for the toxicology study, which the company expects to start in May 2025 and complete in Q4 CY25. While we had previously expected the study to have started sooner (Q4 CY24 or Q1 CY25), we understand that Sareum is in the process of completing synthesis of additional drug substance required for the toxicology studies. In parallel, we believe that Sareum is optimising the drug formulation to improve absorption and develop capsule sizes consistent with the planned Phase II doses. Management has also communicated that it is already in talks with potential licensing partners and we expect discussions to intensify as the drug progresses towards Phase II readiness. Management has indicated that while a licensing agreement for SDC-1801 remains a top priority, Sareum is open to undertaking the Phase II trial independently if sufficient funding is available. Note that the typical cost of a 150-patient Phase II study (the likely size of the SDC-1801 study) can range from $7m to $15m and therefore would likely require a sizeable capital outlay.

A worthy, oral challenger to the supremacy of biologics

In spite of the success seen by biologics in autoimmune conditions, the treatment landscape has broadened over the last few years, with increased emphasis on more convenient, targeted oral treatments such as JAK inhibitors. JAK isoforms (JAK1, JAK2, JAK3 and TYK2) are widely recognised for their role in facilitating downstream signalling of a number of cytokines which play a pivotal role in inflammatory diseases. The JAK family of inhibitors works by blocking the cytokine messaging pathway (aka the JAK-STAT pathway), in effect calming the immune system and relieving disease symptoms. (Exhibit 2).

Exhibit 2: JAK isoforms implicated in downstream signalling of selected cytokines



Source: Sareum corporate presentation, March 2025

As shown in the chart above, multiple cytokine pathways are mediated by the four JAK isoforms, which could therefore offer theoretical advantages over biologics, which tend to target one particular cytokine (such as TNF-α , IL-12, IL-17

and IL-23). By contrast, TYK2 for example mediates downstream signalling of IL-10, IL-12, IL-23 and type I interferons (IFNs), recognised for their role in driving autoimmunity and associated inflammation. In addition, JAK1 mediates signalling for a number of other cytokines such as IL-6, IL-7, IL-10, IL-27 and IL-35.

In the past few years, several JAK inhibitors have received approval across various dermatological indications, indicating the effectiveness of this class of drugs for such conditions. Key approvals in recent years include Cibinqo (abrocitinib) and Rinvoq (upadacitinib) for atopic dermatitis in 2022, Sotyktu (deucravacitinib) for plaque psoriasis in 2022 and Olumiant (baricitinib), Litfulo (ritlecitinib) and Leqselvi (deuruxolitinib) for alopecia areata in 2022, 2023 and 2024, respectively.

Sareum maintains that SDC-1801's dual kinase approach, along with the benefits of oral administration, could offer even broader applicability and efficacy in autoimmune diseases than JAK inhibitors with single targets. Moreover, by not targeting JAK2 and JAK3, which have been implicated in the toxicity issues related to the first-generation JAK inhibitors, SDC-1801 also promises a more benign safety profile, which was validated by the Phase I data. For further details on the key takeaways from the Phase I top-line and unblinded data, as well as the competitive landscape, we direct readers to our previous update note.

SDC-1802 inching closer to the clinic

The improved liquidity afforded by the recent fund-raises (c £4.5m combined from the October 2024 and March 2025 equity issues) has allowed Sareum to accelerate its development plans for the second TYK2/JAK1 asset, SDC-1802 which is being developed for oncology indications. The company holds a patent covering the molecular and pharmaceutical preparations of SDC-1802 in the treatment of T-cell acute lymphoblastic leukaemia and other cancers (granted in April 2022). Sareum is undertaking translational and preclinical development work on SDC-1802 to identify an optimal cancer indication and patient population before undertaking further toxicology studies. Management aims to commence drug substance manufacturing, followed by preclinical studies in 2025.

Note that unlike autoimmune indications, the applicability of JAK inhibitors has not been as well established across cancer types. Currently, JAK inhibitors have largely been approved for treating myelofibrosis, a rare blood cancer. These include Jakafi (ruxolitinib) in 2011 (also approved for another rare blood cancer, polycythemia vera), Inrebic (fedratinib) in 2019, Vonjo (pacritinib) in 2022 and Ojjaara (momelotinib) in 2023. While this raises clinical risks for SDC-1802 when targeting other cancer indications, it presents increased commercial opportunities given the limited competition. We note that the potential remains significant for drug candidates with improved efficacy/safety profiles versus existing approved drugs. For instance, momelotinib's parent company, Sierra Oncology, was acquired by GlaxoSmithKline (GSK) in April 2022 for $1.9bn, based on the Phase III results for the drug, which demonstrated lower toxicity than previously approved JAK inhibitors.

SRA737's opportunistic acquisition de-risks the pipeline

In March 2025, Sareum announced that it had acquired the licence for SRA737, in which it had previously held a 27.5% economic interest. Following this acquisition, Sareum will be eligible for 63.5% of all future returns from the programme. SRA737 a highly selective CHK1 inhibitor targeting the DNA damage response network for the treatment of solid tumours. Checkpoint kinases (CHK1 and CHK2) are key regulators of DNA damage (eg damage caused by chemotherapy), allowing for DNA repair by temporarily pausing cell replication and division. Blocking this process, therefore, inhibits cancer cell survival.

The compound was developed by Sareum in collaboration with the Institute of Cancer Research and CPF before being out-licensed to Sierra Oncology in 2016 for up to $328.5m (including development, regulatory and commercial milestones and royalties on sales), which was revised down to $290m (total potential proceeds) in November 2020. Sierra Oncology tested SRA737 in two Phase I/II trials (both monotherapy and in combination with low-dose gemcitabine) with positive results. Following GSK's acquisition of Sierra in April 2022, the SRA737 licence was returned to CPF and was subsequently acquired by a privately held US biopharma in December 2023 for an upfront payment of $0.5m, additional fees of up to $1m in cash and 500,000 shares in the licensee company (depending on the US partner achieving a financing objective), as well as potential milestone payments of up to $289m (comparable to the $290m allocated under its revised deal with Sierra Oncology). The rights were subsequent returned to CPF in December 2024, before being acquired by Sareum in March 2025. We understand that Sareum's licence acquisition was negotiated on a no-cash basis, in return for partners CPF, CRT and ICR continuing to own a 36.5% economic stake in the asset.

Management has also communicated that an Investigational New Drug application for SRA737, filed by the then US biopharma partner, has been approved by the US FDA, setting the stage for renewed clinical development.

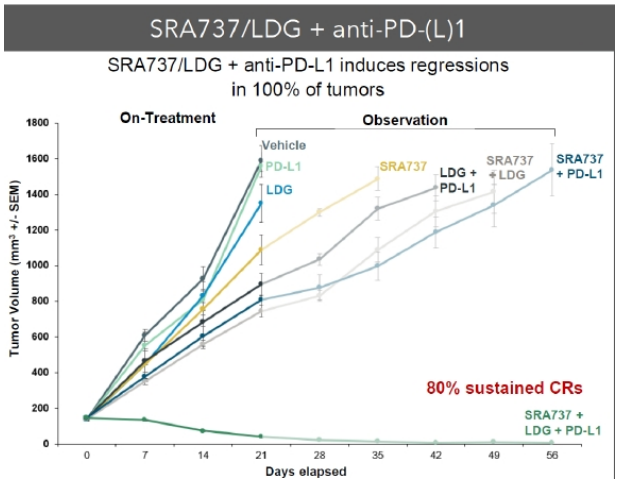
We believe that Sareum will seek to out-license SRA737 to a strategic buyer, leveraging existing clinical data. Note that CHK1 inhibitors, being key regulators of DNA damage, may find broad applicability across solid tumours, although no drugs are currently approved for cancer and clinical progress with first-generation inhibitors has been challenged by off-target toxicities (related to non-selective inhibition of CHK1 and CHK2) and insufficient efficacy as a monotherapy.

Management has endorsed SRA737's favourable safety profile and early efficacy signals, backed by clinical data from two early-stage studies (conducted by Sierra Oncology) as monotherapy and as an adjunct to low-dose chemotherapy:

- A monotherapy study evaluating SRA737 in patients in ovarian, prostate, non-small cell lung, head and neck, and anus and colorectal cancers with specific genetic aberrations (NCT02797964).
- A drug combination study evaluating SRA737 alongside chemotherapy drug low-dose gemcitabine in four cancer indications including ovarian, small cell lung, sarcoma and cervical/anogenital cancers (NCT02797977).

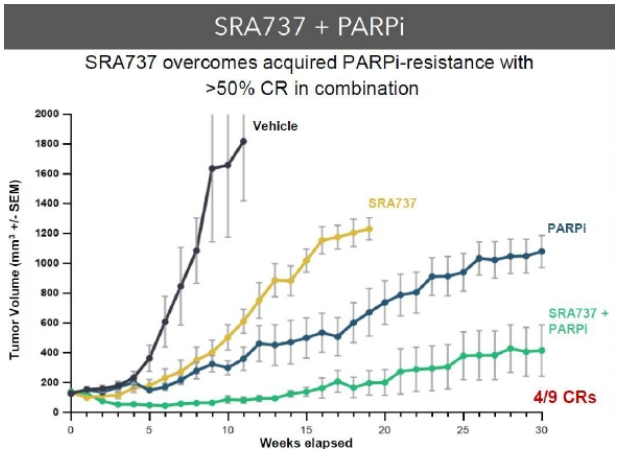
During the earnings presentation, management also highlighted preclinical models showing efficacy benefits from combining SRA737/low-dose gemcitabine with PD-L1 checkpoint inhibitors and SRA737 with PARP inhibitors in small cell lung cancer and ovarian cancer, respectively.

Exhibit 3: SRA737 combination treatment potential in SCLC preclinical model



Source: Sareum corporate presentation, March 2025. Note: SCLC = small cell lung cancer.

Exhibit 4: SRA737 combination treatment potential in ovarian cancer preclinical model



Source: Sareum corporate presentation, March 2025

Given these observations, we see increased potential in pursuing SRA737 as a combination treatment with chemotherapy and/or targeted treatments. We note that SRA737 has properties which position it attractively among peers, including a convenient oral route of administration (once-daily dosing) and high selectivity for CHK1 (a thousand times or more selective for CHK1 compared to CHK2). Management has noted that, based on existing clinical data for the previous Phase I/II studies, anogenital cancer could be an initial target indication.

Financials

Sareum reported an operating loss of £1.3m in H125, materially lower (c 46.8%) than the H124 figure of £2.5m. We attribute this to reduced R&D expenses following the completion of the Phase I study for SDC-1801 in June 2024. This also resulted in lower R&D tax credits (£0.2m in H125 versus £0.8m in H124), which meant Sareum recorded a net loss of £1.2m for the period, down from a loss of £1.7m in H124. Net cash outflow from operating activities was £0.8m, compared to £2.4m in H124.

Sareum ended H125 with net cash of £4.1m, supported by £3.4m in equity proceeds raised in October 2024 along with A$1.9m (c £1.0m) in R&D tax credits received from the Australian authorities. As it relates to the equity financing proceeds, while the initial £2.4m was raised against the issue of 11.8m new shares at a subscription price of 20p/share, the remaining £1.0m was raised against the issue of 4.4m shares at a subscription price of 22.5p/share. Note that the issue also included one five-year warrant per share, exercisable at either the subscription price or at a rebased price, in the case of a fresh issue at a lower price. Post period (in March 2025), the company raised another £1.07m in a

private placement, issuing 8.56m shares at a subscription price of 12.5p/share (a c 24% discount to the last trading price of 16.5p). While this issue did not have attached warrants, we note that it will affect the exercise price of the October 2024 warrants (which will now be adjusted to 12.5p/warrant vs 20p previously). While these financing rounds have been dilutive to existing shareholders, we acknowledge that they serve the broader purpose of securing capital as the company approaches significant milestones for its pipeline. Assuming upcoming cash burn rates will be similar to historical burn rates, we estimate that current cash on hand is sufficient to fund operations into 2026, past the expected completion of the toxicology study for SDC-1801.

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