# Sareum Holdings

## A decisive period ahead for SDC-1801

**Sareum Holdings' H124 results highlighted the company's swift progress for lead asset SDC-1801, since gaining regulatory approval in Australia to start human studies in mid-CY23. SDC-1801, a TYK2/JAK1 inhibitor targeting the autoimmune space, has reported a good safety profile to date and top-line data for the ongoing Phase Ia study are expected in Q2 CY24, a key catalyst for the company. The TYK2 class's safety and efficacy has been validated by the likes of Sotyktu and TAK-279, and SDC-1801's dual inhibition may provide differentiation, in our opinion. Funding, however, remains an overhang (period-end cash of £0.4m; operating loss of c £2.5m in H124) and will likely dictate the timing/pace of the Phase IIa study in psoriasis patients, currently planned for end-CY24. We expect the recent £2.3m capital raise and upcoming tax credits (£0.7m) to offer some headroom but anticipate the need for further funds in CY24.**

### Pressing on with SDC-1801 in the clinic

Since initiating the three-part Phase Ia study in heathy volunteers (n=96) in May 2023, Sareum has completed part 1 (single ascending dose) and part 3 (food effects) of the study, with initial data indicative of a good safety profile and supporting once-daily oral dosing. The multiple ascending dose arm (part 2) is expected to conclude in Q2 CY24, by which time the company plans to announce full safety data from the Phase Ia study. Should data continue to be favourable and contingent on Sareum securing further funding (we expect the company is likely to seek non-dilutive funding in the form of a partnership), the company expects to start a Phase IIa study in psoriasis patients (n=24) before end-CY24.

### Tightening the belt on costs

Given downward stock price pressure, Sareum has been unable to make drawdowns from the remaining c £2.5m of its RiverFort facility and it enacted stringent cost cutting measures to preserve cash. Sareum announced a £2.3m (gross) conditional equity raise, issuing 23m shares at 10p each (c 30% discount to 27 March closing). While dilutive, we see the raise as being necessitated by the company's focus on timely completion of the Phase Ia study. At the H124 cash burn rate of c £1.9m (excluding the £760k finance charge related to the RiverFort facility), the pro-forma funds (£0.4m gross cash at end-H124, £0.4m in R&D tax credit received in Q1 CY24 and the £2.3m equity raise) would be projected to support runway extension into H2 CY24, past the Phase Ia study completion. Should data be positive, we expect the company to seek additional funds and/or partnering opportunities to undertake further clinical development for SDC-1801.

**Historical financials**

| Year end | Revenue (£m) | PBT (£m) | EPS* (p) | DPS (p) | P/E (x) | Yield (%) |
|---|---|---|---|---|---|---|
| 06/20 | 0.04 | (1.1) | (1.6) | 0.0 | N/A | N/A |
| 06/21 | 0.00 | (1.7) | (2.3) | 0.0 | N/A | N/A |
| 06/22 | 0.00 | (2.6) | (3.2) | 0.0 | N/A | N/A |
| 06/23 | 0.00 | (4.0) | (4.7) | 0.0 | N/A | N/A |

Source: Company data. Note: *EPS figures have been adjusted retrospectively for the 50:1 share consolidation in March 2022.

**Pharma and biotech**

**3 April 2024**

| | |
|---|---|
| Price | 10.30p |
| Market cap | £7m |

**Share price graph**


**Share details**

| | |
|---|---|
| Code | SAR |
| Listing | AIM |
| Shares in issue (excluding the 23m shares to be issued under the March 2024 offering) | 71.76m |
| Gross cash at 31 December 2023 (excluding £2.3 from Mar 2024 equity raise) | £0.4m |

**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. Sareum initiated clinical trials for SDC-1801 in Australia in May 2023 (Phase Ia), with safety data expected in H1 CY24. Other programmes include the CHK1 inhibitor SRA737, which was out-licensed to an unnamed private US-based pharma company by co-development partner CRT Pioneer Fund LP in January 2024.

**Bull**

- SDC-1801's novel TYK2/JAK1 selectivity may be attractive to partners, pending clinical validation.
- First-in-class opportunity for SDC-1802 in multiple cancer indications.
- Approval of Sotyktu provides regulatory feasibility for TYK2 inhibitors.

**Bear**

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

**Analysts**

Soo Romanoff +44 (0)20 3077 5700

Jyoti Prakash, CFA +44 (0)20 3077 5700

healthcare@edisongroup.com

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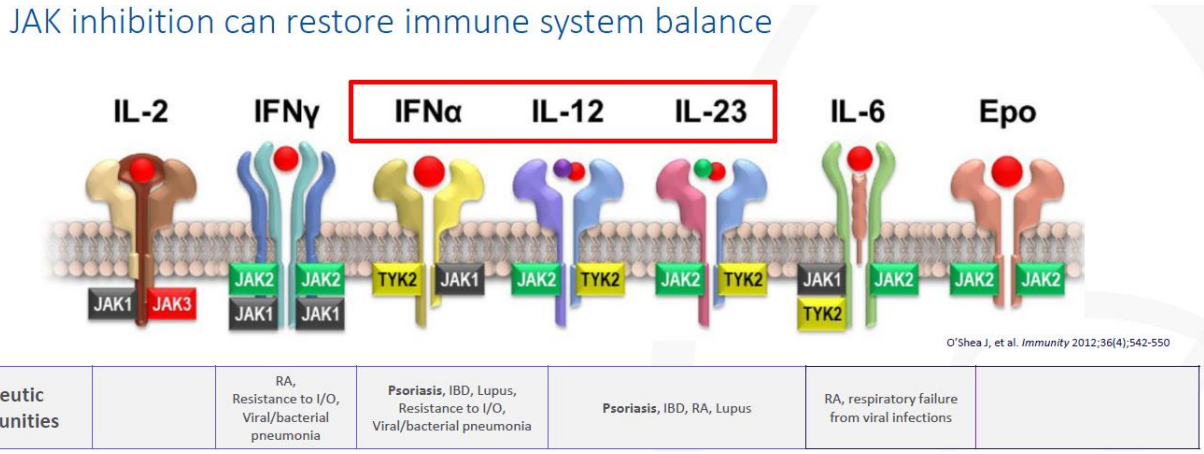
# Approaching a key inflection point

## TYK2/JAK1, a promising target in inflammatory conditions

SDC-1801, Sareum's lead asset, is an inhibitor of both tyrosine kinase 2 (TYK2) and Janus kinase 1 (JAK1) enzymes, both part of the JAK family of proteins (four isoforms – JAK1, JAK2, JAK3 and TYK2) recognised for their role in immune regulation. These isoforms are known for their role in facilitating downstream signalling of a number of extracellular, pro-inflammatory cytokines, which lack their own enzymatic activity (Exhibit 1).

**Exhibit 1: Jak isoforms implicated in downstream signalling of selected cytokines**




Source: Sareum Holdings corporate presentation, October 2023

An oral administration targeting multiple cytokine pathways could offer theoretical advantages over single target agents such as biologics. TYK2, for example is instrumental in mediating the downstream signalling of IL-6, IL-10, IL-12, IL-23 and type I interferons (IFNs), recognised for their role in driving autoimmunity and associated inflammation. We also believe that a dual kinase approach, such as that of SDC-1801, accords applicability in a broad range of potential indications, particularly in the autoimmune space.

While effective, a non-selective and broad inhibition of certain JAK enzymes (particularly JAK2 and JAK3) has been associated with off-target toxicities, highlighted by the black box warnings (increased risk of malignancy, thrombosis and cardiac events) associated with the approved JAK1 inhibitors, Xeljanz, Olumiant and Rinvoq. SDC-1801 has been engineered to selectively target the TYK2/JAK1 enzymes with the aim of circumventing the safety/toxicity issues related to the JAK2 and JAK3 isoforms. Although SDC-1801 is designed to target a range of autoimmune diseases, the initial focus is on psoriasis, a serious dermatological condition affecting more than 125 million people globally (7.5–8.0 million in the US alone). The global psoriasis treatment market was valued by Fortune Business Insights at US$26.4bn in 2022 and is expected to grow to US$51.5bn by 2030.

The psoriasis treatment market has hitherto been dominated by biologics – anti-TNF and interleukin antibodies – although the approval of Bristol Myers Squibb's first-in-class, selective TYK2 asset, Sotyktu (deucravacitinib) in September 2022 could potentially start to change that. Sotyktu was approved without a black box warning and without restricted usage (such as limitations to patients refractory to biologics and other available treatments), demonstrating the potential of this class of drugs (Sotyktu recorded global sales of US$170m in 2023, its first full year on the market). Sareum claims that the dual TYK2 and JAK 1 inhibition offered by SDC-1801 could result in better efficacy (without safety trade-offs) in psoriasis compared to agents that target only one of the two kinases, although this would have to be proved in large clinical trials.

### SDC-1801 moving steadily through the clinic

Sareum initiated clinical studies for SDC-1801 in Australia in June 2023 (Phase Ia), following approval of its clinical trial application by the Australian authorities in May 2023. The Phase Ia study is a randomised, placebo-controlled trial (targeted n=96) evaluating safety, tolerability and pharmacokinetics/pharmacodynamics of SDC-1801 in healthy adults. The study includes 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). In February 2024, the company announced that part 1 and part 3 of the study have been completed, indicating a favourable safety profile and supporting once-daily oral dosing to achieve therapeutic drug levels in the bloodstream. The SAD part randomised participants in a 3:1 ratio to a single ascending dose xof SDC-1801 or placebo in six dose cohorts with eight subjects each. Part 2 (MAD) is ongoing (four sequential and ascending doses tested on four dose cohorts with eight participants each) and is expected to complete by Q2 CY24. Full safety data from the Phase Ia study is planned to be reported in Q2 CY24 and we believe this could be a key inflection point for the company. Sareum had previously planned to initiate the follow-up Phase IIa study (with 24 psoriasis patients) in H2 CY24 (with a planned completion by end-CY24) but given the funding constraint, the timeline for trial initiation has now been pushed out by a few months to end-CY24, subject to the Phase Ia data review and access to financing. If the Phase Ia data are positive, we believe Sareum will likely seek potential out-licensing opportunities, whereby a prospective partner would be responsible for undertaking the next phase of clinical development as well as subsequent commercialisation.

In March 2024, Sareum received a notice of allowance from the European Patent Office, related to SDC-1801's (application (EP3864009) in the treatment of autoimmune diseases, and certain methods of synthesis. This follows the approval in China in June 2023 (CN113056456), which was the first patent granted to SDC-1801 and Japan. Patent applications in several other regions are under review, including the US (US2021387981).

## A broader pipeline, beyond SDC-1801

While Sareum has other assets in its pipeline (including another TYK2/JAK1 inhibitor, SDC-1802, targeting cancer immunotherapy), we understand that development work on these assets has been put on hold to focus resources on the clinical development of SDC-1801. We believe that development work may be reinitiated following a partnering deal for the lead asset.

**SDC-1802:** management has indicated that work on translational studies is ongoing to identify an optimal cancer indication and patient population before undertaking further toxicology and manufacturing studies. We remind readers that in June 2023, Sareum was granted a patent for SDC-1802 in the US for autoimmune disorders, extending its scope beyond the initial focus immuno-oncology. The first patent for the compound was granted in April 2022, covering the molecular and pharmaceutical preparations of SDC-1802 in the treatment of T-cell acute lymphoblastic leukaemia and other cancers.

**SRA737:** SRA737 is an oral checkpoint kinase 1 (CHK1) inhibitor, in which Sareum owns a 27.5% economic interest (the remaining stake is held by CRT Pioneer Fund). Rights to the drug (previously out-licensed to Sierra Oncology, which was subsequently acquired by GSK) were returned to the original owners (Sareum and CRT Pioneer Fund) in November 2022. In December 2023, CRT Pioneer Fund out-licensed SRA737 to a privately-held US biopharma for an upfront payment of US$0.5m, additional fees of up to $1m in cash and 500,000 shares of the partner and potential milestone payments of up to $289m. The deal also allows for tiered high single-digit royalties on net sales. As part of the deal, Sareum received $137.5k as an upfront payment and is also entitled to receive 27.5% of any future payments.

# Financials

## Widened operating loss on increased clinical activity

Sareum reported an H124 (six months ending December 2023) operating loss of £2.53m, up from £1.75m in H123, driven by increased investments in preparatory activities related to the Phase Ia clinical trial of SDC-1801. The H124 net loss was £2.51m, with the R&D tax credit of £0.77m received during the period offset by the £0.76m finance charge resulting from the £5m RiverFort prepayment facility entered into on 3 August 2023 (£2.3m drawn down to date in two tranches). This finance charge reflects the difference between the amount due to RiverFort as at 31 December 2023 in respect of shares issued to it, and the market value of the shares it still held at that date. Reflecting the higher operating expenses during the period, the net cash outflow from operating activities increased to £2.69m in H124 from £1.34m in H123.

The economics of the deal with RiverFort included Sareum issuing shares to cover the drawdown amount, which RiverFort would subsequently sell in the market. With the recent downward pressure on Sareum's share price (59.5p at 31 December 2023 vs 100p at the time of deal signing), shares sold (worth £0.7m) and held (worth £0.5m) by RiverFort fall short of covering the loaned amount, resulting in the non-case finance charge of £0.76m in Sareum's books. Note that this charge is subject to change with the movement in Sareum's share price and the sale of further shares by RiverFort. Exhibit 2 presents a snapshot of the drawdowns/conversions to date and the outstanding balance.

**Exhibit 2: Deal details for the RiverFort facility**

| | Value of shares issued/converted (£m) | Held as cash (£m) | Total (£m) |
|---|---|---|---|
| **Drawdown and conversion** | | | |
| Balance drawn down by Sareum | 2.0 | 0.3 | 2.3 |
| Realised value by RiverFort on sale of shares | (0.7) | 0.0 | (0.7) |
| **Balance due to Riverfort as at 31 December 2023** | **1.3** | **0.3** | **(1.6)** |
| | | | |
| **Accounting** | | | |
| Market value of shares still held by RiverFort | 0.5 | 0.0 | 0.5 |
| Cash advanced by Riverfort | 0.0 | 0.3 | 0.3 |
| Finance charge | 0.8 | 0.0 | 0.8 |
| **Total** | **1.3** | **0.3** | **1.6** |
| **Balance due by Sareum** | **0.8** | **0.3** | **1.1** |

Source: Sareum H124 filing.

As of 26 March 2024, £1.1m remains outstanding for repayment under the facility, which Sareum expects to fulfil through share issuances (or cash payment) on or before August 2025. With the SDC-1801 clinical trial in full force, operating expenditure rates may remain at comparable levels (vs H124) in H224, although we note that the company may generate some savings following its decision to minimise cash utilisation (as highlighted by its decision to settle pending salaries of directors/advisors in shares and deferring a portion of their salaries to a future date).

## New funds extend runway

The gross cash balance at end H124 stood at £0.4m versus £1.0m at end FY23 and £2.9m at end H123. This was further supported by the £0.4m tax credit received in January 2024 and the £2.3m conditional equity fund raise (before expenses) announced by the company on 28 March 2024 and subsequently updated on 2 April 2024. This fund raise would result in an issuance of 23.2 million new ordinary shares at the placing price of 10p/share (a ~30% discount to the closing price of 14.5p on 27 March). This includes 9.55m shares in an open placement ('placing'), 2.255m shares under a direct issue to certain high net worth individuals ('subscription'), 195k shares to company directors

and 11.2m shares in a retail offering (WRAP retail offer) to existing shareholders. The WRAP retail offer closed on 2 April 2024, and new shares are expected to be admitted for trading on AIM on 5 April 2024.

The completion of the placing is conditional, among other things, on the company receiving a commitment of a minimum of £0.205m under the subscription prior to 4 April 2024 and on admission of the new ordinary shares for trading on the AIM exchange. We believe that the need to raise external equity capital was triggered by the company's inability to make further drawdowns from the £5m prepayment facility with RiverFort.

Management estimates that, along with cash at hand, the tax credits of £0.4m received in January 2024 and the net proceeds from the fundraise will be sufficient to complete the Phase Ia clinical trial of SDC-1801, and it expects to report top-line safety data from the trial in Q2 CY24. Furthermore, the company anticipates receiving tax credits of £0.7m in September 2024, which would support the company in meeting working capital needs. At the company's current run-rate (cash burn of £1.9m in H124, excluding the £0.76m finance charge), it may need to secure additional funds in H2 CY24 to advance SDC-1801 to the Phase IIa trial.

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London | New York | Frankfurt
20 Red Lion Street
London, WC1R 4PS
United Kingdom