Sareum Holdings

Pharma & biotech

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SDC-1801's clinical plan modified

Sareum's lead asset SDC-1801 is inching closer to completing its preclinical toxicology studies, although the decision to pursue a capsule alternative to the original suspension formulation, at the cost of a further delay in the clinical trial application (CTA) filing (now expected mid-2022), comes as a surprise. Management asserts that the new formulation adds value to the programme (removing the need to develop capsules at a later stage) and is supported by £4.6m of funds raised in calendar Q221/Q321. While we see merits in the strategy, continued delays may concern the market. Encouragingly, out-licensed asset, SRA737, seems to be gaining traction after Sierra Oncology's decision to reassess it in combination with other targeted therapies. We expect that the next few months will be crucial for Sareum.

SDC-1801 to be developed in capsule formulation

SDC-1801, Sareum's lead TYK2/JAK1 inhibitor, is on-track to complete the final preclinical toxicology studies by the end of 2021 and the company has appointed external consultants to help develop the clinical plan and choose the optimal first indication for the clinical studies. A key development in SDC-1801's clinical plans has been Sareum's decision to develop its drug in a capsule form versus the original dry powder suspension. We believe these efforts towards optimising the formulation/administration could be a sensible step, although the repetitive delays in taking the asset to the clinic may concern investors.

Encouraging signals for SRA737

The recent in-licensing by Sierra of BET inhibitor AZD5153 from AstraZeneca and subsequent disclosure by Sierra that it may test the compound in combination with SRA737 in two Phase I trials (haematological malignancies and solid tumours) is a positive sign for Sareum, which owns a 27.5% economic interest in SRA737. Sierra will also be undertaking a third Phase I study assessing SRA737 along with immunotherapy/low-dose gemcitabine. First patient dosing in any one study will trigger a $2m milestone payment (thus $0.55m to Sareum).

Financing in place after equity raise

Equity raisings in calendar Q221/Q321 (totalling £4.6m) should allow Sareum to advance SDC-1801 to the clinic and complete preclinical studies on SDC-1802, as per the management. However, additional funds would be required (possibly through out-licensing deals or equity raises) to progress the programmes further.

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

Price	3.95p
Market cap	£133m

Share price graph

Share details

Code	SAR
Listing	AIM
Shares in issue	3.37bn
Net cash at 30 September 2021	£4.4m

Business description

Sareum is a UK-based drug development company, specialising in small molecule kinase inhibitors. Its lead programmes are its preclinical 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.
- Possible COVID-19 opportunity with UK funding.

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.

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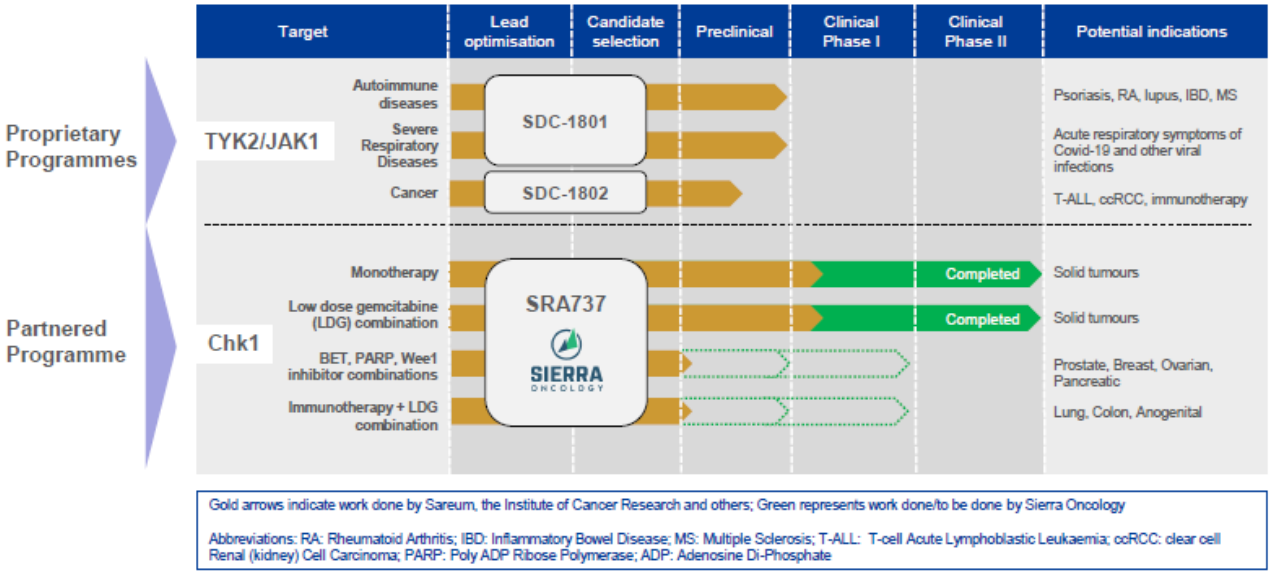
Sareum's pipeline

As part of its FY21 (June 2021) results, Sareum apprised the market on the developmental progression of its pipeline assets (Exhibit 1).

Exhibit 1: Sareum's asset pipeline



Source: Company presentation, November 2021

SDC-1801's modified path to the clinic

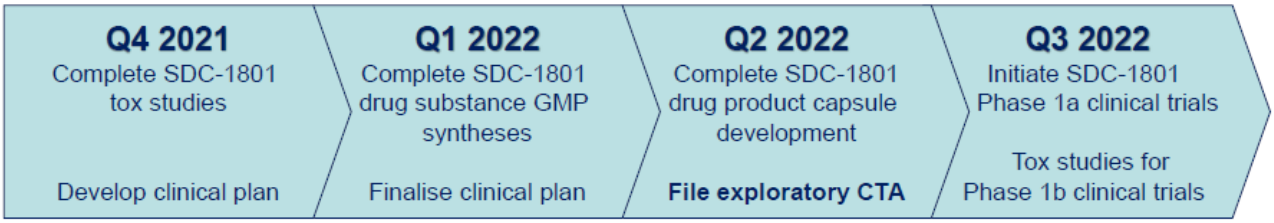
The company's core asset, the TYK2/JAK1 inhibitor SDC-1801, is on track to conclude preclinical studies, with the completion of the final toxicology and safety studies expected by management by the end of calendar year 2021. As indicated by the company, consultants have been recruited to guide the study design as well as the optimal first indication in the target autoimmune space for the first in-human study planned in calendar H222. A manufacturing route to produce the SDC-1801 active ingredient under Good Manufacturing Practice (GMP) conditions has been developed and a specialist Contract Manufacturing Organisation has been appointed to provide GMP drug product for clinical trials.

Given more advanced TYK2 assets under development (see our initiation report for more details) have all targeted psoriasis (PS) as the first indication, it would seem to be a likely first choice for SDC-1801 although Sareum may evaluate other, less explored, autoimmune conditions such as lupus where the company has reported encouraging preclinical data. The recent failure of category leader Bristol Myers Squibb's highly selective TYK2 asset deucravacitinib to meet primary and secondary efficacy endpoints in a Phase II trial for ulcerative colitis is concerning but may also create an opportunity for Sareum courtesy its dual TYK2/JAK1 action, which may potentially offer greater therapeutic gains in the inflammatory bowel disease space, given the role of IL-6 cytokine in its pathogenesis, which can be targeted by both TYK2 and JAK1 inhibitors.

Another key development highlighted in Sareum's FY21 results was SDC-1801's modified path to the clinic, where Sareum has decided to develop a capsule formulation for its drug rather than the originally planned orally dosed solution/suspension. Sareum claims the capsule formulation would be more advanced than the typically used solution/suspension in Phase I clinical trials and removes the need to develop capsules at a later stage, in turn increasing the attractiveness of the asset to potential buyers. The additional time required is likely to push out the exploratory CTA and commencement of the Phase Ia clinical trial (assessing SDC-1801's safety in healthy volunteers) to

calendar mid-2022 and Q322, respectively. Sareum is actively seeking partnerships/out-licensing opportunities and the possibility of SDC-1801 being monetised before the Phase I trial cannot be ruled out. SDC-1801's path to the clinic, as depicted by Sareum, is presented in Exhibit 2 below.

Exhibit 2: SDC-1801's timeline to clinical progression



Source: Company presentation, November 2021

Read across from Pfizer exiting its mid-stage TYK2 assets

On 2 November 2021, Pfizer announced it is offloading its two Phase II TYK2 clinical assets to a new company formed by Pfizer in partnership with an undisclosed autoimmune player, in return for a 25% stake in the venture (plus retention of certain ex-US rights). The out-licensed assets include Pfizer's TYK2/JAK1 asset brepocitinib (PF-06700841) and the pure TYK2 compound PF-06826647. The company has indicated this would 'enable the allocation of resources to advance development of brepocitinib and TYK2 while allowing Pfizer to focus on diversifying its pipeline'. It is possible the recent FDA safety concern disclosure on multiple JAK inhibitors (on toxicity/safety concerns) has played a role in Pfizer's decision to reduce pipeline exposure to this asset class as a whole, although the company continues to hold other clinically advanced JAK inhibitors in its portfolio, including JAK1 inhibitor abrocitinib (PF-04965842) and JAK3/TEC Inhibitor ritlecitinib (PF-06651600). As a reminder, the toxicity issues related to the class have been widely attributed to broader activity across the JAK2 and JAK3 sub-types. While selective action (against TYK2 and JAK1) of the newest class of drugs (such as SDC-1801) is designed to overcome this issue, clinical validation would be crucial to assuage these concerns.

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

The six-month UK Research & Innovation (UKRI) funded preclinical research study assessing the therapeutic potential of SDC-1801 in severe COVID-19 was completed in June 2021 with Sareum reporting encouraging results. The project concluded that SDC-1801 reduced the levels of cytokines associated with acute respiratory distress syndrome (ARDS) in human lung cells infected with SARS-CoV-2 and demonstrated a superior profile to the anti-inflammatory steroid Dexamethasone and similar to the JAK1/JAK2 inhibitor, baricitinib. Sareum plans to secure further funding from the UK government's AGILE development platform (launched in February 2021 to support novel COVID-19 treatments) to progress the treatment to clinical trials, although the timing and design of the clinical trials has not yet been crystallised.

Sareum's other TYK2/JAK1 candidate, SDC-1802 (targeting multiple oncology indications, in both haematological (blood related) malignancies and solid tumours), is undergoing translational studies to identify an optimal cancer indication and patient population before undertaking further toxicology studies. A second US patent grant in October 2021 strengthens the company's intellectual property (IP position), although we maintain that the clinical progression would be contingent on the headway made with SDC-1801.

SRA737: Early signs of revival

Sareum's out-licensed CHK1 inhibitor SRA737 (licensed to Sierra Oncology) had been deprioritised by Sierra since June 2019, but has seen a revival in interest following Sierra'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. Since then, Sierra has expanded the potential therapeutic applications for SRA737 as combination therapy in both haematological malignancies and solid tumours, presenting the pipeline plan in its latest November 2021 corporate presentation. The plan lays out a potential three separate trials in combination with SRA737, two with SRA515 in haematological malignancies and solid tumours in combination with standard of care, respectively, and another one in combination with immunotherapy/low-dose gemcitabine.

Sareum holds a 27.5% economic interest in the deal (up to $79.75m in milestone payments plus royalties) and stands to benefit from this development. Sierra, in its latest Q321 results announced that they may initiate new clinical trials for SRA737 in 2022. First patient dosing in any of these studies will trigger a milestone payment of $2m (translating to $0.55m to Sareum).

FY21 results

Sareum's FY21 operating loss stood at £1.72m (including the receipt of a £0.17m UKRI grant), up from £1.12m in FY20, driven by higher R&D expenses related to preclinical activities. The majority of these expenses were incurred in H221 (operating loss stood at £0.6m in H121) indicating the heightened pace of activities in the second half of the year. Net loss came in at £1.5m in FY21 versus £1.0m in FY20 (£0.55m in H121). We believe it is likely for the operating expenses to continue to increase as the pipeline approaches the clinic.

The cash balance at the end of FY21 was £2.7m (£1.3m at the end of half-year ending December 2020), supported by two equity issues to high-net-worth individuals in June 2021 (£0.9m and £1.47m, respectively). The cash position has been bolstered by two rounds of fund raising in July and August 2021, raising a combined £2.18m. The company reports the net cash position at the end of September 2021 at £4.4m. If the FY21 cash burn rate (£1.6m) is maintained, the cash balance would be projected to provide funding into FY24 although we believe future spending (FY22 and beyond) is likely to be higher as the assets approach the clinic. Management has indicated the cash balance is sufficient to advance SDC-1801 into clinical trials and complete the preclinical work on SDC-1802. Additional funds (secured either through partnerships and/or equity issues) would be required to advance the programmes further.

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