Sareum Holdings PLC

SRA737 update

01 March 2018

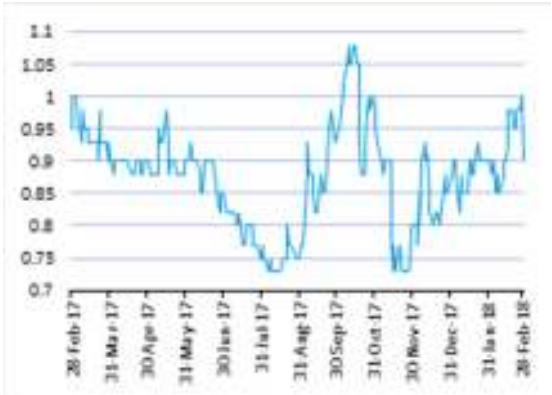
HYBRIDAN
DEDICATED TO BROKING

Key Statistics:

Code	SAR.L
Listing	AIM
Sector	Pharma & Biotech
Market Cap	£26.1m
Share in issue	2.745bn
Current Price*	0.95p
12 mnth High/Low	1.08p/0.72p

*Priced at close on 28 February 2018

Stock Performance



Source: Yahoo Finance

Financials y/e Jun

£'m	FY 15A	FY 16A	FY17A	FY18E
Net Profit	(1.3)	(1.0)	0.4	(1.6)
Cash	1.5	1.3	2.3	1.4

Source: Published results and Hybridan LLP Forecasts

Company Description

An AIM quoted drug discovery Company, Sareum Holdings Plc, focuses its research primarily on cancer and autoimmune diseases. The Company and its partners (Sareum 27.5%) have secured its first licensing agreement, on its Chk1 clinical programme for a headline value of $328.5m. The Company leverages its proprietary technology platform, SKIL, to develop most of its research programmes, which are focused on novel small molecule drugs. Sareum has shown good preclinical results on all its remaining programmes and has international partners collaborating on Aurora+FLT3 and TYK2 for autoimmune and inflammatory disorders.

HYBRIDAN LLP
20 Ironmonger Lane, London, EC2V 8EP
Website: www.hybridan.com
@HybridanLLP

Derren Nathan
Tel: 020 3764 2344
Email: derren.nathan@hybridan.com

Chk1 program powering ahead

Sareum's licensing partner on its Chk1 inhibitor, Sierra Oncology (NASDAQ:SRRA) this week released an update on its clinical program, the focus of which was on SRA737, the potential driver of further milestone payments and royalties to Sareum. The news release and subsequent conference call updated on both the monotherapy study and low dose gemcitabine (a common chemotherapy agent) combination therapy study. The key take-aways are that safety and tolerability data has been very encouraging in both arms, and continues to demonstrate a potentially superior profile to competing validated Chk1 inhibitors.

The next arm of the Phase 1/2 trials is being expanded from 120 to 200 patients across 10 cancer indications where replication stress, and hence sensitivity to Chk 1 inhibition, which ultimately leads to cancer cell death due to disruption of the DNA Damage Response Network. **The next key reporting date from Sierra will be initial data on efficacy from the phase 2 efficacy-oriented portion of the trials, expected to be delivered in Q4 this year.** As at the end of December 2017 Sierra Oncology had cash balances of $100.3m, which it believes will be sufficient to fund current operating plans through approximately mid-2019.

Monotherapy - Dose Escalation has proceeded through multiple dose levels and SRA737 **has been well-tolerated from 20 mg QD (once daily) to 1000 mg QD as monotherapy. There has been no evidence of cumulative toxicity seen in up to 8 months of daily treatment. This is well in excess of the therapeutic window suggested by preclinical data** and two possible dosing regimes or either 1,000mg QD or 500mg twice a day are being investigated. Dose limiting toxicities have been seen at 1300mg although the nature of these is consistent with Chk1 inhibition and therefore suggests that the drug might be working as hoped.

The monotherapy arm is enrolling genetically-defined patients into indication specific cohorts, including advanced or metastatic: castration-resistant prostate cancer; high grade serous ovarian cancer; non-small cell lung cancer; head and neck squamous cell carcinoma or squamous cell carcinoma of the anus; and colorectal cancer. **Sierra is also adding a sixth indication in CCNE1-driven ovarian cancer cohort. Given the key role of CCNE1 in driving replication stress, SRA737 may be effective in these tumour types and pre-clinical data has been encouraging. We understand that the expected total addressable US patient populations with CCNE1 mutations in ovarian and other cancers to be over 300,000 per annum.**

Low dose gemcitabine combo study- This is an interesting study and contrary to perhaps how one might have originally imagined SRA737 to work in combination with chemotherapy. Rather than looking for SRA737 to augment chemotherapy, a sub therapeutic dose (as a single agent) of gemcitabine is administered. This is hoped to stimulate replication stress in the tumour cells and thereby sensitise them further to Chk1 inhibition with SRA737 being the agent that delivers the knock out blow. **The combination is very well tolerated so far, with no dose limiting tox being reported. Dose escalation continues, with the cohort expansion Phase 2 stage expected to commence in Q2 2018,** in genetically defined patients with uroepithelial (bladder) cancer, small cell lung cancer, soft tissue carcinoma and cervical/anogenital cancers.

As well as a chemotherapy combination study there are two other combination programs with SRA737 in the pipeline. The first which is backed by pre-clinical data referenced in a SRRA press release last week, is a **combination with TESARO's ZEJULA® (niraparib), an orally administered PARP inhibitor which also has a role in regulating the DNA Damage Repair Network.** There are in fact multiple DNA damage repair pathways which is why such a combination makes sense, in effect cutting off all the cell's options to repair itself. **The initiation of the trial is expected in Q4 2018**.

Secondly Sierra presented its **rationale /evidence that DNA Damage Response Inhibition can potentiate immunotherapy responses. A related clinical trial application could potentially be submitted in Q4.**

SRA737 is becoming interesting in so many indications and combinations, that this starts to increase the number of 'shots on goal' that Sierra (and indirectly Sareum) has, and of course the size of the potential end market for Chk1 inhibitors.

Although SRA737 is not the only game in town, this week's conference call reconfirmed that **Chk 1 has been clinically validated as a target already by the likes of Lilly's Prexasertib. However, SRA737 has arguably a better safety and tolerability profile and a more selective mechanism of action**. Lilly's compound has a much higher effect on 'Chk2' than SRA737 and it is thought that this potentially exacerbates toxicity in healthy cells.

Should the current trials be successful Sierra will need to move to full scale Phase 2 trials. If these are then compelling Sierra plans to discuss an accelerated pathway with the regulatory authorities, which may negate the need for a Phase 3 trial before marketing approval can be applied for. **This could potentially bring forward approval by two to three years.** Clearly there are many hoops to get through before this can be achieved. **We have previously set out indicative risked and un-risked valuations for the Chk1 1 programs of 1.05p and 4.83p respectively. Clearly any**

increase in the eventual market size for SRA737, and/or a reduction in timelines to potential approval would have a material uplift on these values, which have been derived through a DCF of our hypothesised milestone and royalty schedules should SRA737 get all the way to market. Meanwhile we look forward to news on Sareum's earlier stage programs as they progress towards the clinic where our combined indicative value stands at circa 1p per share.

Profit & Loss Account

Year-end June (£m)	2015A	2016A	2017A	2018E
Revenue	0.00	0.00	0.00	0.00
Expenditures	(0.81)	(1.00)	(1.45)	(1.80)
Total expenditures	(0.81)	(1.00)	(1.45)	(1.80)
Share of loss of associates	(0.50)	(0.33)	1.78	0.00
Other Income	0.00	0.12	0.02	0.00
Operating Profit/ Loss	(1.31)	(1.20)	0.35	(1.80)
Finance income	0.03	0.00	0.00	0.00
Finance Costs	(0.14)	0.00	0.00	0.00
Pre-tax Profit	(1.41)	(1.20)	0.35	(1.80)
Taxation	0.15	0.19	0.05	0.20
Profit after tax	(1.26)	(1.01)	0.40	(1.60)
Attributable Profit/ (Loss)	(1.26)	(1.01)	0.40	(1.60)
PER SHARE DATA				
EPS - (p)	**(0.06)**	**(0.04)**	**0.015**	**(0.06)**

Source: Published accounts and Hybridan LLP Forecasts

Cash Flow Statement

Cash Flow Statement

Year-end June (£m)	2015A	2016A	2017A	2018E
Profit before Tax	(1.41)	(1.20)	0.35	(1.80)
Dep and Amort	0.02	0.00	0.00	0.00
Dec (Inc) trade/ other receivables	0.05	(0.03)	0.01	0.00
Inc (Dec) in trade/ other payables	0.00	0.03	0.06	0.00
Deferred income payment	0.00	0.00	0.00	0.00
Loss from associate	0.50	0.33	0.19	0.00
Share Based Charges	0.04	0.01	0.08	0.00
Taxation	0.00	0.19	0.15	0.20
Finance Costs	0.14	0.00	0.00	0.00
Finance Income	(0.03)	(0.00)	0.00	0.00
Other	0.00	0.00	0.00	0.00
Cashflow from operating activities	**(0.70)**	**(0.68)**	**0.85**	**(1.60)**
Purchase of tangible fixed assets	0.00	(0.60)	(0.02)	(0.02)
Purchase of intangible fixed assets	0.00	0.00	0.00	0.00
Purchase of fixed asset investments	0.00	0.00	0.00	0.00
Repayment of investment funds			0.23	0.00
Equity Swap Arrangement	0.06	0.00	0.00	0.00
Interest received	0.00	0.00	0.00	0.00
Cashflow from investing activities	**0.07**	**(0.59)**	**0.22**	**(0.02)**
Financing Activities				
Loan to director				
Issue of Ordinary Share Capital	1.36	0.04	0.00	0.67
Share premium on issue of shares	0.00	1.00	0.00	0.00
Repayment of borrowings	0.00	0.00	0.00	0.00
Borrowings	0.00	0.00	0.00	0.00
Cashflow from Financing Activities	**1.36**	**1.04**	**0.00**	**0.67**
Net increase (dec) in cash/ cash eq	**0.72**	**(0.23)**	**1.07**	**(0.95)**
Cash and Cash equivalents	1.48	1.25	2.32	1.37

Source: Published accounts and Hybridan LLP Forecasts

Balance Sheet

Balance Sheet

Year-end 30 June (£m)	2015A	2016A	2017A	2018E
Non-current assets				
Intangible Assets	0.00	0.00	0.00	0.00
Investments	0.20	0.48	0.01	0.01
Property, plant and equipment	0.00	0.00	0.05	0.07
	0.20	0.48	0.07	0.08
Current assets				
Trade and other receivables	0.05	0.08	0.08	0.08
Cash and equivalents	1.48	1.25	2.32	1.37
Investments	0.00	0.00	0.00	0.00
Tax receivable	0.19	0.15	0.02	0.02
Assets for disposal classed held for sale	0.00	0.00	0.00	0.00
	1.72	1.49	2.42	1.47
Total Assets	1.92	1.96	2.49	1.55
Non-current Liabilities				
Borrowings	0.00	0.00	0.00	0.00
Deferred Income	0.00	0.00	0.00	0.00
Financial liabilities	0.00	0.00	0.00	0.00
Provisions	0.00	0.00	0.00	0.00
Deferred tax	0.00	0.00	0.00	0.00
Liabilities for disposal	0.00	0.00	0.00	0.00
	0.00	0.00	0.00	0.00
Current				
Trade and other payables	0.07	0.10	0.16	0.16
Deferred income	0.00	0.00	0.00	0.00
Provisions	0.00	0.00	0.00	0.00
Borrowings	0.00	0.00	0.00	0.00
Financial liabilities	0.00	0.00	0.00	0.00
Other liabilities	0.00	0.00	0.00	0.00
	0.07	0.10	0.16	0.16
Total Liabilities	0.07	0.10	0.16	0.16
Net Assets	**1.85**	**1.86**	**2.33**	**1.39**
Shareholders' Equity				
Called up share capital	0.62	0.66	0.66	0.66
Share premium	10.76	11.77	11.77	12.43
Other reserves	0.00	0.00	0.00	0.00
Retained profit/ loss	(9.65)	(10.67)	(10.27)	(11.87)
Translation reserve	0.00	0.00	0.00	0.00
Convertible loan note reserve		0.00	0.00	0.00
Share based payment reserve	0.11	0.11	0.19	0.19
Total Equity	1.84	1.86	2.35	1.41

Source: Published accounts and Hybridan LLP Forecasts

HYBRIDAN
DEDICATED TO BROKING

Research Disclaimer – Sareum Holdings plc

This document should not be relied upon as being an impartial or objective assessment of the subject matter and does not constitute **investment research** for the purposes of the Conduct of Business Sourcebook (**"COBS"**) issued by the Financial Conduct Authority (**"FCA"**) to reflect the requirements of Regulation 600/2014/EU (the **MIFID II Regulation**) and Directive 2014/65/EU (the **MIFID II Directive**) and all rules made in connection therewith (together, known as **MIFID II**). The individuals who prepared this document may be interested in shares in the company concerned and/or other companies within its sector. As a consequence the research (a) has not been prepared in accordance with legal requirements designed to promote the independence of investment research under MIFID II; and (b) is not subject to any prohibition on dealing ahead of the dissemination of investment research (although Hybridan does impose restrictions on personal account dealing in the run up to publishing research as set out in our Conflicts of Interest Policy).

Hybridan LLP is involved in providing other financial services to Sareum Holdings **plc** (the **"Company"**) and, as a result, Hybridan LLP may have responsibilities to the Company which conflict with the interests of the persons who receive this document.

This document has been issued by Hybridan LLP for **information purposes only** and should not be construed in any circumstances as an offer to sell or solicitation of any offer to buy any security or other financial instrument, nor shall it, or the fact of its distribution, form the basis of, or be relied upon in connection with, any contract relating to such action. This document has no regard for the specific investment objectives, financial situation or needs of any specific entity. Hybridan LLP and/or connected persons may, from time to time, effect transactions in any investment or related investment mentioned herein and may provide financial services to the issuers of such investments. The information contained herein is based on materials and sources that we believe to be reliable, however, Hybridan LLP makes no representation or warranty, either express or implied, in relation to the accuracy, completeness or reliability of the information contained herein. Opinions expressed are our current opinions as of the date appearing on this material only. Any opinions expressed are subject to change without notice and Hybridan LLP is under no obligation to update the information contained herein. None of Hybridan LLP, its affiliates or employees shall have any liability whatsoever for any indirect or consequential loss or damage arising from any use of this document.

In the United Kingdom, this report is directed at and is for distribution only to persons who (i) fall within article 19(1) (persons who have professional experience in matters relating to investments) or article 49(2) (a) to (d) (high net worth companies, unincorporated associations, etc) of the Financial Services and Markets Act 2000 (Financial Promotions) Order 2005 (SI 2005/1529) (as amended) or (ii) persons who are each a **professional client** or **eligible counterparty** (as those terms are defined in COBS (issued by the FCA) of Hybridan LLP (all such persons together being referred to as **"relevant persons"**). This report must not be acted on or relied upon by persons in the United Kingdom who are not relevant persons.

Neither this report, nor any copy or part thereof may be distributed in any other jurisdictions where its distribution may be restricted by law and persons into whose possession this report comes should inform him or her self about, and observe any such restrictions. Distribution of this report in any such other jurisdictions may constitute a violation of securities laws in the United Kingdom, the United States (or any part thereof) or any other jurisdiction in any other part of the world.

Investments in general involve some degree of risk, including the risk of capital loss. The services, securities and investments discussed in this document may not be available to or suitable for all investors. Investors should make their own investment decisions based upon their own financial objectives and financial resources and, if in any doubt, should seek advice from an investment advisor. Past performance is not necessarily a guide to future performance and an investor may not get back the amount originally invested. Where investment is made in currencies other than the investor's base currency, movements in exchange rates will have an effect on the value, either favourable or unfavourable. Levels and bases for taxation may change. When Hybridan LLP comments on AIM or NEX Exchange shares investors should be aware that because the rules for those markets are less demanding than the Official List of the London Stock Exchange the risks are higher. Furthermore, the marketability of these shares is often restricted.

Hybridan LLP and/or its associated companies may from time-to-time provide investment advice or other services to, or solicit such business from, any of the companies referred to in this document. Accordingly, information may be available to Hybridan LLP that is not reflected in this material and Hybridan LLP may have acted upon or used the information prior to or immediately following its publication. In addition, Hybridan LLP, the partners, directors and employees thereof and/or any connected persons may have an interest in the securities, warrants, futures, options, derivatives or other financial instrument of any of the companies referred to in this document and may from time-to-time add or dispose of such interests. Neither the whole nor any part of this material may be duplicated in any form or by any means. Neither should any of this material be redistributed or disclosed to anyone without the prior consent of Hybridan LLP.

Hybridan LLP is authorised and regulated by the FCA and is a member of the London Stock Exchange.

Dissemination of Research: Reports are made available to all relevant recipients at the same time. Issuers may, in certain circumstances, be permitted to review investment analysts' investment research prior to publication for review of factual accuracy only. Investment research prepared and disseminated by Hybridan LLP is monitored to ensure that it is only provided to relevant persons. Research prepared by Hybridan LLP is not intended to be received and/or used by any person who is categorised as a **retail client** under COBS.

Hybridan LLP

20 Ironmonger Lane, London, EC2V 8EP

T +44 (0) 20 3764 2341

F +44 (0) 20 7600 1586

www.hybridan.com

Hybridan LLP

Research Disclosures

Investment analyst certification:

All research is issued under the regulatory oversight of Hybridan LLP. Each investment analyst of Hybridan LLP whose name appears as the author of **this Investment Research** hereby certifies that the opinions expressed in such Investment Research accurately reflect the investment analyst's personal and objective views about any and all of the companies or the Company discussed herein that are within such investment analyst's coverage universe.

The investment analyst who is responsible for the preparation of this Investment Research is Derren Nathan, who is an employee of Hybridan.

Investment Research Disclosures:

1. In the past 12 months, Hybridan LLP has [had corporate finance mandates as broker or managed or co-managed a public offering of the Company's securities or received compensation for corporate finance services from the Company.

2. Hybridan LLP may receive compensation for corporate finance services from this Company in the next twelve months.

3. Hybridan LLP acts as broker to the Company.

4. Hybridan may provide investment banking services to the Company and in that capacity may have received confidential information relevant to the securities mentioned in this research report which is not known to the researcher who has compiled this research report.

Hybridan, its partners, officers or employees or any connected persons may at the time of publication have an interest in the equity of the Company through the holding of warrants, securities, futures, options, derivatives and any other financial instrument of any of the companies referred to in this document. Hybridan at the time of publication currently has [no] interest of this nature in the Company discussed herein. If exercised this interest would not be required to be notified as it would comprise less than 3% of the Company's issued share capital. Hybridan reserves the right to increase or dispose of this interest and/or the underlying shares resulting from exercise, without further notice. Any disposal or acquisition of warrants or shares will be undertaken under the FCA Disclosure Guidance and Transparency Rules Sourcebook.

No Research recommendations:

In line with our conflicts of interest policy Hybridan LLP does not produce recommendations or publish target prices on companies who are corporate clients of Hybridan LLP.

MIFID II status of Hybridan LLP research:

The cost of production of our corporate research is met by retainers from our corporate broking clients. In addition, from time to time we issue further communications as market commentary (such as our daily newsletter, Small Cap Breakfast), which we consider to constitute a minor non-monetary benefit which is capable of enhancing the quality of service provided by Hybridan LLP and which is of a scale and nature which could not be judged to impair the duty of Hybridan LLP to act in the best interest of its client falling within article 24(7)(b) of the **MIFID II Regulation**.