Targeted Small Molecule Therapeutics for Cancer and Autoimmune Diseases

- Experienced management team with a deep understanding of molecule design, drug development and partner requirements
- Pipeline of clinical and preclinical, partnered and internal programme assets addressing emerging, high-value disease targets
- Validated track record from clinical-stage $300M licence deal

Company

Sareum is a specialist drug development company delivering targeted small molecule therapeutics to improve the treatment of cancer and autoimmune disease. The Company aims to generate value through licensing its candidates to international pharmaceutical and biotechnology companies at the preclinical or early clinical trials stage.

Sareum is advancing internal programmes focused on distinct dual tyrosine kinase 2 (TYK2) / Janus kinase 1 (JAK1) inhibitors through preclinical development as therapies for autoimmune diseases (SDC-1801) and cancers (SDC-1802).

Sareum also has an economic interest in SRA737, a clinical-stage oral, selective Checkpoint kinase 1 (Chk1) inhibitor that targets cancer cell replication and DNA damage repair mechanisms. Preliminary Phase 2 and comprehensive preclinical data suggest SRA737 may have broad application in combination with other oncology and immuno-oncology drugs in genetically defined patients. SRA737 was discovered and initially developed by scientists at The Institute of Cancer Research in collaboration with Sareum, and with funding from Cancer Research UK. SRA737 was licensed by CRT Pioneer Fund (CPF) to Sierra Oncology, in a $300m plus royalties licence deal, with Sareum eligible to receive 27.5% of all payments to CPF under the agreement.

Pipeline

<table>
<thead>
<tr>
<th>Target</th>
<th>Lead optimisation</th>
<th>Candidate selection</th>
<th>Preclinical</th>
<th>Clinical Phase I</th>
<th>Clinical Phase II</th>
<th>Potential indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>TYK2/JAK1</td>
<td>SDC-1801</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Psoriasis, RA, lupus, IBD, MS</td>
</tr>
<tr>
<td>Cancer</td>
<td>SDC-1802</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>T-ALL, ccRCC, immunotherapy</td>
</tr>
<tr>
<td>Covid-19</td>
<td>UKRI grant awarded</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Acute respiratory symptoms of viral infections</td>
</tr>
<tr>
<td>Autoimmune diseases</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monotherapy</td>
<td>SRA737</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Solid tumours</td>
</tr>
<tr>
<td>Low dose gemcitabine (LDG) combination</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Anaplastic</td>
</tr>
<tr>
<td>PARP inhibitor combination</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Prostate</td>
</tr>
<tr>
<td>Immunotherapy combination</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lung, colon</td>
</tr>
</tbody>
</table>

TYK2/JAK1 Inhibitors

SDC-1801 and SDC-1802 are potent inhibitors of TYK2 and JAK1 kinases and are selective over JAK2 and JAK3 kinases, thus having potential to avoid the side effects associated with currently marketed JAK inhibitors.

Both compounds are expected to be dosed orally, once or twice daily. They have good safety profiles in assays to date and the CMC synthesis is straightforward.

TYK2 has been clinically validated in Phase 2 psoriasis and psoriatic arthritis studies by BMS and Pfizer.

SDC-1801 - Autoimmune Diseases

SDC-1801 shows compelling activity in disease models of psoriasis and rheumatoid arthritis, and closely related compounds show good activity in models of IBD and lupus.

Figure 1: Oral dosing of SDC-1801 in CIA RA model

Contact:
Dr Tim Mitchell, CEO  tim.mitchell@sareum.co.uk, +44 1223 497703

Sareum Ltd is the trading subsidiary of Sareum Holdings plc (AIM: SAR)  www.sareum.co.uk
SCD-1801 – Covid19

Sareum has been awarded UKRI grant funding to explore the use of SDC-1801 against severe respiratory inflammation caused by Covid-19 and other viral infections.

Many of the cytokines involved in the “cytokine storm” immune system over-reaction signal via JAK-family kinases.

Sareum believes TYK2/JAK1 inhibition by SDC-1801 has the potential to be less toxic and also give better protection against secondary bacterial pneumonia than the authorised JAK-family inhibitor, baricitinib.

SDC-1802 – Cancer Immunotherapy

SDC-1802 shows compelling activity in disease models of: Blood cancers that are dependent on TYK2/STAT signalling (e.g. T-ALL and B-cell lymphoma); solid tumours dependent on TYK2-dependent interleukin signalling (e.g. kidney and colon cancers) and; solid tumours via local immune system modulation (including kidney, colon, pancreatic and skin cancers).

Chk1 Kinase Inhibitor SRA737

Chk1 is a clinically validated target for cancer therapy, having shown clinical efficacy in multiple cancer types. SRA737 is emerging as the potential class leader, and has completed two Phase 2 studies, preliminary results of which were reported at ASCO 2019.

In combination with low-dose gemcitabine (LDG), SRA737 demonstrated >33% tumour shrinkage in 30% of evaluable anogenital cancer patients, and stable disease in a further 30%. Anogenital cancer is a clear unmet medical need, with no second-line therapies available.

As a monotherapy and in combination with LDG, SRA737 was well-tolerated, with the majority of adverse events being mild or moderate. The safety profile was markedly superior to recently discontinued Chk1 inhibitors from Lilly and Genentech.

Preclinical data supports the combination of SRA737 with PARP inhibitors and immune checkpoint blockers in future clinical trials.

SDC-1802 gives significant reduction of Panc-02 tumour growth in immune-competent mice (but SDC-1802 has little effect in immuno-deficient mice)

SRA737 in combination with LDG and anti-PD-L1 in a SCLC model

Intellectual Property

Patents related to these programmes can be found at www.sareum.com/news/patents-and-publications.

Management

Sareum’s executive team comprises Dr Tim Mitchell, CEO and Dr John Reader, CSO. Between them, they have over 50 years’ drug discovery experience in big pharma, biotech and chemistry service companies. Non-executive directors are Dr Stephen Parker, Dr Mike Owen and Mr Clive Birch, who bring a wealth of corporate finance, research management and corporate governance expertise to the Company.

Commercialisation

Sareum is seeking investment to advance its TYK2/JAK1 programmes into proof-of-concept clinical trials, or licence/collaboration partners to progress one or both of these programmes on an exclusive or co-development basis.