Eligibility Criteria (Part A)

- Age ≥ 18 years, with a predicted life expectancy of ≥ 3 months
- Eastern Cooperative Oncology Group (ECOG) performance status (PS) ≤ 2

Clinical cutoff date: September 7, 2021

The recommended Part B dose of 1500 mg q3w has been chosen based on the results from oropharynx cancer patients.

In Part A2, 10 patients were dosed with 1500 mg q3w, which would provide flexible dose frequency when combining with different anti-PD-L1 therapy. Safety

Safety endpoints include AE, clinical observations (e.g., vital signs, physical examination), laboratory tests, electrocardiograms, and echocardiograms. DLT evaluation period was 21 days for q3w regimen and 14 days for q2w regimen.

Response is assessed using RECIST v1.1 by PI; the scan is performed during screening, 6 weeks after first dose, every 9 weeks, and every 6 months of treatment, and 12 weeks thereafter; central reads are also being conducted, with a comprehensive review of the central reads to be performed once completed across the cohorts. As biomarker strategy to assess both the immune status and TGFβ pathway activity as well as orthogonal approaches are being developed.

Determination of MTD and Recommended Dose for Part B

As of October 12, 2021, no DLTs were observed up to 3000 mg q3w and 2000 mg q2w in Part A1; and up to 1600 mg q3w in Part A2.

The recommended Part B dose is 1500 mg q3w (1500 mg q2w in Part A2) in the mouse pharmacodynamic efficacy model (Background, the observed Cmax for SRK-181 was ~80 µg/mL at 10 mg/kg).

The recommended dose of 1500 mg q3w has been chosen based on the ability to attain Cmax ~80 µg/mL at the lower end of the 90% CI.

The dose of 1500 mg q3w was chosen since it allows for equivalent Cmax exposure to 1500 mg q2w, which would provide flexible dose frequency when combining with different anti-PD-L1 in Part B.

Part A1

Part A2

<table>
<thead>
<tr>
<th>Dose (mg)</th>
<th>q3w</th>
<th>q2w</th>
</tr>
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<tbody>
<tr>
<td>800</td>
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<td>3000</td>
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</tbody>
</table>

All dose levels were administered q3w except 2000 mg, which was administered q2w in Part A1; and up to 1600 mg q3w in Part A2.

Phase 1 Clinical Trial Overview

- The DRAGON trial (NCT04291079) is a multicenter, open-label, Phase 1/II, dose-escalation, and dose-expansion trial to evaluate the safety, tolerability, PK, pharmacodynamics, and efficacy of SRK-181 alone and in combination with anti-PD-(L)1 therapy in patients with advanced solid tumors.

- SRK-181 may potentially decrease PD-1/L1 inhibitor resistance and toxicity of nonselective TGFβ pathway inhibitors in human cancer patients.

Study Objectives (Part A)

- Evaluate the safety and PK profile of SRK-181
- Evaluate anti-tumor activity
- Evaluate biomarkers

Secondary Objectives

- Evaluate the PK and ADA proﬁle
- Evaluate tumor activity
- Evaluate biomarkers

Primary Objectives

- Evaluate the safety and PK of SRK-181 alone (Part A1) and in combination with anti-PD-(L)1 (Part A2)
- Determine the MTD or MAD, and recommended dose for Part B