CD200R1 was identified as a promising immune-oncology target by the 23andMe Advanced Solid Malignancies genetic database.3 This finding was based on the observation that CD200R1 expression is reduced in tumor tissues compared to normal tissues.4,5 Patients with tumors that express lower levels of CD200R1 may be more susceptible to immune-mediated disease control.

CD200 and CD200R1 are Highly Expressed in a Subset of Human Tumors

Table 2. IHC Expression of CD200 and CD200R1 in Select Tumor Types

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>CD200</th>
<th>CD200R1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ovarian Cancer</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Small Cell Lung</td>
<td>+++</td>
<td>+</td>
</tr>
</tbody>
</table>

Study Objectives

- Determine safety, tolerability, MTD and/or RP2D of 23ME-00610 in patients with locally advanced or metastatic solid cancers.
- Evaluate clinical activity of 23ME-00610 in evaluable patients with locally advanced or metastatic solid cancers.
- Assess the relationship between germline genetics and clinical outcomes using lead SNPs in 23ME-00610.

Study Assessments

- PK, PD, ADA, and Biopsy
- Safety, tolerability, MTD, RP2D
- Clinical activity
- Germline genetics

Disease Criteria for Expansion Cohorts

- Eligible patients must have advanced or metastatic solid cancers who have progressed following standard therapy, including:
  - Neuroendocrine cancer
  - Merkel cell carcinoma
  - Carcinomas with mismatch repair deficiency
  - Metastatic solid tumors with actionable mutations

Key Eligibility Criteria

- Patients must have a solid tumor histology consistent with an actionable mutation.
- Patients must have progressed following standard therapy.
- Patients must have an Eastern Cooperative Oncology Group (ECOG) performance status of 0-1.
- Patients must have adequate organ function.
- Patients must be willing to undergo a fresh biopsy during screening.
- Patients must be able to provide a blood sample for genotyping.
- Patients must have written informed consent.

Clinical trial data will be summarized using descriptive statistics. Safety, tolerability, MTD, and RP2D will be evaluated using the 3+3 dose-escalation method. Efficacy will be evaluated using the tumor response rate.

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Figure 1: CD200-CD200R1 signaling cascade.

Distinct Cell Types Express CD200 and CD200R1 in Cancer Lesions

23ME-0616

- CD200 is expressed by macrophages, T cells, and B cells.
- CD200R1 is expressed by tumor cells, stromal cells, and immune cells.
- CD200 and CD200R1 are co-expressed in tumor tissues.

Part A: Dose Escalation

- Patients with advanced solid malignancies will be enrolled in a dose-escalation phase to determine the maximum tolerated dose (MTD) and recommended phase 2 dose (RP2D).
- Patients will be followed for 21 days after the last dose to assess any delayed adverse events.

Part B: Dose Expansion

- Patients with advanced solid malignancies who have progressed following standard therapy will be enrolled in a dose-expansion phase to further evaluate clinical activity.
- Patients will be followed for an additional 21 days after the last dose to assess delayed adverse events.

Genotyping Rationale and Methods

- Polygenic risk scores for autoimmune AEs were shown to predict adverse event and disease activity.
- Patients with HIV, hepatitis B, and hepatitis C will be excluded from the study.
- Patients with active autoimmune disease will be excluded from the study.

Current Status and Future Perspectives

- The study sponsor is committed to the inclusion of diverse populations, with a focus on enrolling patients from underrepresented communities.
- The study is ongoing and will be updated as new data become available.

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Figure 1: Key milestones for 23ME-00610.

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