Safety, efficacy, and PKPD of 23ME-00610, a first-in-class anti-CD200R1 antibody, in patients with advanced neuroendocrine cancers: Results from a multi-center multi-country Phase 1/2a expansion cohort.

**METHODS**

- **CD200R1** was identified as a promising immuno-oncology target in the Pan02 study.
- **Free soluble CD200R1** Concentration-time profiles, PK parameters by NCA.
- **23ME-00610** is currently in the Phase 2a portion of a Phase 1/2a clinical trial in patients with advanced solid malignancies (NCT05199272). 1
- **Participants** with advanced solid malignancies (NCT05199272) (Figure 2).
- **Preclinical studies** for 3 critical components of the CD200R1 pathway, including CD200R1, its sole ligand CD200, and the downstream signaling protein PDGFRB.
- **23ME-00610** is expressed on immune cells and antibodies to CD200. Its only known ligand is CD200.
- Binding of 23ME-00610 to CD200 can downregulate immune cells to suppress immune response and immunosuppressive microenvironment in human cancers, where CD200 is highly expressed.2 (Figure 1).
- **23ME-00610** is a first-in-class IgG1 antibody that binds CD200 with high affinity, Fc - C1r/C1s, and enables immunosuppressive signaling leading to restoration of T-cell activity and killing of CD200 expressing tumor cells in preclinical studies.3 (Figure 1).
- **23ME-00610** is currently in the Phase 2a portion of Phase 1/2a clinical trial in patients with advanced solid malignancies (NCT05199272). Figure 2.
- From the 28-patient Phase 1 portion, 23ME-00610 has demonstrated acceptable safety, antitumor activity, objective responses, and partial target engagement with peripheral saturation of doses (10 mg) and pharmacodynamic evidence of activity, including target-immune related AEs - >50% stable disease rate, and tumor shrinkage.1-2

**RESULTS**

- **Patient Demographics** and Disease Characteristics (Table 1).
- **PD-1** blockade (n=2).
- **CD200 IHC**: Prior genotyping identified 3 critical components of the CD200R1 pathway, including CD200R1, its sole ligand CD200, and the downstream signaling protein PDGFRB.
- **Patient with No Clinical Benefit**. Ovarian cancer2 cases have different clinical outcomes in this patient with No Clinical Benefit. Ovarian cancer2 cases have different clinical outcomes in this phase of the trial.
- **Patient from vignette with partial response**.

**CONCLUSIONS**

- **23ME-00610** shows acceptable safety, tolerability, and minimal PD-1/cost of treatment.
- Patients with advanced solid malignancies treated with 23ME-00610 have prolonged survival and significant reductions in tumor burden compared to historical controls.
- **Presumptive RP2D of 1400 mg achieves prespecified PK target and saturates solCD200R1**, the PK profile generally supports Q3W dosing, and there was negligible ADA with no adverse impact on clinical activity.
- **9/14** patients had partial response and ongoing treatment duration > 72 weeks for a well-differentiated pNET with H-score of Target Lesions and CD200 Tumor Expression.
- Tumor CD200 and CD200R1 Expression Shows >50% Neuroendocrine Patients with Moderate or High Tumor CD200.
- **High CD200 expression** in tumors that progressed (PD). Enlarged dots represent the H-scores of the tumors in the IHC panel.23ME-00610 treatment as demonstrated by these two grade 3 pancreatic NETs that have different clinical outcomes in this phase of the trial.
- **Tumors of patients deriving benefit may have more immune suppressive phenotype at baseline.**

**Figure 1. 23ME-00610, a Fully Humanized, Efectorsless IgG1, Inhibits Immunosuppressive CD200R1 Signaling via High Affinity Binding to CD200R1**

**Figure 2. Phase 1/2a Study Design in Patients with Locally Advanced or Metastatic Solid Malignancies (NCT01992172)**

**Figure 3. Schedule of Assessments**

**Figure 4. Overall 23ME-00610 AE Profile, including TEAEs, TRAEs, and AEs**

**Figure 5. 23ME-00610 Optimized PKPD Profile at 1400 mg Q3W**

**Figure 6. 23ME-00610 Treatment Duration and Tumor Response per RECIST v1.3**

**Figure 7. Tumor CD200 and CD200R1 Expression Shows >50% Neuroendocrine Patients with Moderate or High Tumor CD200**

**Figure 8. Tumors of patients deriving benefit may have more immune suppressive phenotype at baseline.**

**Figure 9. Best % Change of Summary of Diameters (SoD) of Target Lesions and CD200 Tumor Expression**

**Figure 10. 23ME-00610 showed acceptable safety, tolerability, and minimal PD-1/cost of treatment.**

**Figure 11. 23ME-00610 showed acceptable safety, tolerability, and minimal PD-1/cost of treatment.**

**Figure 12. 23ME-00610 showed acceptable safety, tolerability, and minimal PD-1/cost of treatment.**