Top-Line Results of a Phase 2, Double-blind, Randomized, Placebo-Controlled Study of a Reversible B Cell Inhibitor, XmAb® 5871, in Systemic Lupus Erythematosus (SLE)

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Introduction:
XmAb5871 is a fully-human anti-CD20 antibody designed to engage FcγR-bearing cells and mediate cell elimination. XmAb5871, an anti-CD19 antibody, has been engineered to enhance binding to FcγR. The engagement of the ir and receptor assembles membrane protein CD20 and FcγR, resulting in a killing of many autoreactive pathways in both healthy and disease cells. It is an important therapeutic in autoimmune diseases without debilitating toxicity.

Study Design:
A double-blind, placebo-controlled study of approximately 168 patients with active SLE patients were randomized. Patients had to have moderate or severe disease activity as defined by either a SLEDAI of ≥ 16 points of which most come from symptoms/frequent disease activity. XmAb5871 results in a reduction of many autoreactive pathways in both healthy and disease cells and might suppress those in the treatment without depleting healthy cells.

Safety:
TEAEs: 168. TEAEs were reported in 61 patients. Of those, 61 events in 41 patients were considered related to XmAb5871 (79.9%) or placebo (43.5%). The most common adverse event in all patients were shown below.

Objectives:
Primary Objective: To determine the efficacy of XmAb5871 to maintain low disease activity improvement achieved by a brief course of disease-suppressing therapy in SLE patients.

Secondary Objectives: To evaluate time to loss of improvement in SLE disease activity improvement and safety in a brief course of disease-suppressing therapy in SLE patients. To indicate the safety and tolerability of XmAb5871 in the treatment of patients with active SLE disease activity in patients.

To evaluate the pharmacodynamics of XmAb5871 and its immunogenicity of every patient with administration of XmAb5871 to patients with active SLE disease activity.

Exploratory Objectives: To determine effects on absolute B cell count, autoreactivity, complement and cytokine levels over time.

Patient Population: Male and female patients aged 18 to ≥ 75 inclusive with active SLE (BILAG≥ M). Patients had to stop all of the immunosuppressive agents by randomization, but were allowed to remain on methotrexate and prednisone equivalent of ≤ 10 mg or less per day. Patients could not have sign-thrombocythemia.

Conclusions:
• Positive trend in primary endpoint, proportion of efficacy-evaluable patients who did not experience loss of improvement (SLEDAI) by Day 225, but did not meet statistical significance at p = 0.05.
• Median time to secondary endpoint (CSAS) was extended by 76% for patients treated with XmAb5871 (median 230 days vs. 133 days for patients on placebo, hazard ratio = 0.24 (0.12, 0.45).
• XmAb5871-treated patients remained without increase in disease activity and on study longer than the placebo patients.
• A total of increased SLE disease activity was reduced by 47% for patients treated with XmAb5871 vs. placebo at 230 days vs. 33 days for patients on placebo, hazard ratio = 0.53 (0.25, 0.95).
• XmAb5871 well-tolerated and safety profile consistent with previous studies, except for discontinuations from infusion reactions. In order to avoid the infusion reactions, a subsequent formulation will be used in future studies. Bioanalytical studies with the CSAS drug showed no infusion reactions or CSAS-related infusion reactions in a healthy population of 40 subjects.