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**Title:** MEMP1972A, an anti-M1 prime monoclonal antibody, reduces serum IgE in healthy and allergic rhinitis subjects

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**Body:** Background: MEMP1972A, a humanized monoclonal antibody specific for the M1 prime epitope of membrane IgE, depletes M1 prime-expressing IgE-switched B cells, IgE memory B cells and IgE plasmablasts. MEMP1972A is in development for the treatment for allergic asthma. Aim: To evaluate the safety, pharmacokinetics (PK) and pharmacodynamics (PD) of MEMP1972A in healthy and allergic rhinitis (AR) subjects. Methods: Two Phase I, randomized, controlled trials investigated the safety, tolerability, PK and PD of MEMP1972A in (1) healthy adults (n=31 MEMP1972A, n=14 placebo [PB]) and (2) AR subjects (n=24 MEMP1972A, n=12 PB [NCT01160861]). In healthy adults, MEMP1972A was given as single escalating doses of 0.003–5 mg/kg intravenous (IV) or 3 mg/kg subcutaneous (SC). In AR subjects, monthly doses were given for 3 months at 1.5 and 5 mg/kg IV and 3 mg/kg SC. Results: MEMP1972A was well tolerated, and the exposure of serum MEMP1972A was dose proportional. Following IV administration, the mean terminal half-life of MEMP1972A was 20–21 days and mean clearance was 2.2–2.7 mL/day/kg. MEMP1972A administration led to a dose dependent reduction in serum IgE in both studies. In healthy adults, a single dose of MEMP1972A at 3 and 5 mg/kg IV significantly reduced serum IgE by ~25% relative to baseline at Day 85, with no significant reductions observed in the PB, lower IV or 3 mg/kg SC cohorts. Monthly doses of MEMP1972A at 5 mg/kg IV or 3 mg/kg SC in AR subjects reduced serum IgE by ~25% relative to baseline at Day 85. Serum IgE reductions were sustained for 6 months. Conclusion: MEMP1972A was well tolerated and reduced serum IgE in adults with or without allergic disease.