

KPL-404

Phase 1



Mechanism of Action

Monoclonal antibody inhibitor of CD40 signaling. KPL-404 is designed to inhibit CD40-CD40L interaction, a key T-cell costimulatory pathway critical for B-cell maturation and immunoglobulin class switching.

Rationale

CD40-CD40L interaction is an attractive target for blocking T-cell-mediated B-cell-driven autoimmunity and prevention of solid organ transplant rejection. External proof-of-concept for inhibition of this pathway has been previously established in patients with a broad range of autoimmune diseases, including rheumatoid arthritis, Sjögren's syndrome, Graves' disease, systemic lupus erythematosus and solid organ transplant.

Status

We reported preliminary data for our single-ascending-dose Phase 1 study in healthy volunteers for KPL-404 where all dose escalations occurred as per protocol with no dose limiting safety findings. All 6 subjects dosed with KPL-404 3 mg/kg IV showed full receptor occupancy through Day 29, which corresponded with complete suppression of the T-cell Dependent Antibody Response (TDAR) to KLH through Day 29. Consistent dose relatedness was shown in the lower dose level cohorts, including 0.03 mg/kg, 0.3 mg/kg, 1 mg/kg IV and 1 mg/kg SC. Data collection for the higher dose level cohorts, 10 mg/kg intravenous and 5 mg/kg subcutaneous, is ongoing. The data to-date support subsequent study in patients, including potential intravenous or subcutaneous monthly administration. Kiniksa expects final data and safety follow-up from all cohorts in the first half of 2021.

