# 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 final data for our single-ascending-dose Phase 1 study in healthy volunteers for KPL-404, supporting further development in patients. KPL-404 was well tolerated and showed dose-dependent increases in concentration across cohorts. Subjects dosed with KPL-404 10 mg/kg intravenous (IV) showed full receptor occupancy through Day 71 and complete suppression of T-cell Dependent Antibody Response (TDAR) to keyhole limpet hemocyanin (KLH) challenge and re-challenge through at least Day 57. Subjects dosed with KPL-404 5 mg/kg SC showed full receptor occupancy through Day 43 and suppression of TDAR after KLH challenge through at least Day 29. The 3 mg/kg IV dose level had previously demonstrated complete suppression of memory TDAR response to a second KLH challenge on Day 29. Kiniksa plans to initiate a Phase 2 proof-of-concept trial of KPL-404 in the second half of 2021.

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