TITLE: KPL-716, anti-oncostatin M receptor beta antibody, reduced pruritus in atopic dermatitis

AUTHORS: Zamaneh Mikhak[1], Robert Bissonnette[2], Dareen Siri[3], Stephen K. Tyring[4], Eben Tessari[1], Rohan Gandhi[1], Fang Fang[1], John F. Paolini[1]

[1]Kiniksa, Lexington, Massachusetts, USA
[2]Innovaderm, Montreal, Quebec, Canada
[3]SWIA Research Center, Normal, Illinois, USA
[4]University of Texas Health Science Center – Center for Clinical Studies, Houston, Texas, USA

ABSTRACT: KPL-716 is a fully-human monoclonal antibody against Oncostatin M receptor beta (OSMRβ), the shared receptor subunit for IL-31 and Oncostatin M (OSM) signaling. This First-In-Human, randomized, double-blind, placebo (PBO)-controlled Phase 1b study assessed safety, tolerability, target engagement and Early Signal of Efficacy of single dose KPL-716 in adult subjects with moderate to severe atopic dermatitis (AD) experiencing pruritus (Worst Itch Numeric Rating Scale [WI-NRS] ≥7 at screening). The study consisted of 2 phases: KPL-716 monotherapy period (Day -7 to 28), when other AD medications were prohibited, and adjunctive therapy period (>Day 28), when subjects used topical corticosteroids as needed. Clinical data included weekly average daily e-diary WI-NRS and periodic pruritus and sleep-loss Visual Analogue Scale (VAS) until Day 60. Observation that a single 7.5 mg/kg KPL-716 intravenous (IV) dose provided serum levels >5 μg/mL (5.8-28.2 μg/mL) in 80% of recipients 44-47 days post-dose prompted us to explore KPL-716 efficacy beyond the monotherapy period. This report focuses on Day 29 to Day 60. Using the as-observed dataset, WI-NRS, pruritus VAS, and sleep-loss VAS were compared in 20 subjects randomized 1:1 to receive IV 7.5 mg/kg KPL-716 or PBO. KPL-716 recipients experienced a greater WI-NRS improvement that continued into the adjunctive therapy period and reached a maximum level at 6 weeks: -51% vs -26.3%. A higher percentage of KPL-716 recipients demonstrated a ≥4-point decrease in WI-NRS vs PBO, reaching a maximum differential in the adjunctive therapy period at 5 weeks: 63% vs 0%. Differences between KPL-716 and PBO recipients in improvement in pruritus or sleep loss VAS also extended into the adjunctive therapy period. These data strengthen initial findings demonstrating the anti-pruritic effect of OSMRβ inhibition, supporting further development of KPL-716 in chronic pruritic indications.