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Preliminary Data from KPL-404 Single-Ascending-Dose Phase 1 Study

November 2020

Forward Looking Statements

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This presentation also contains estimates, projections, and/or other information regarding our industry, our business and the markets for certain of our product candidates, including data regarding the estimated size of those markets, and the incidence and prevalence of certain medical conditions. Unless otherwise expressly stated, we obtained this industry, business, market and other data from reports, research surveys, clinical trials, studies and similar data prepared by market research firms and other third parties, from industry, medical and general publications, and from government data and similar sources. Information that is based on estimates, forecasts, projections, market research, or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information.

KPL-404

Monoclonal antibody inhibitor interaction between CD40 and CD40L

Disease Area: External proof-of-concept previously established in broad range of autoimmune diseases: Sjogren's disease, systemic lupus, rheumatoid arthritis, solid organ transplant and Graves' disease[1]

Scientific Rationale[2,3]: Attractive target for blocking T-cell dependent, B-cell–mediated autoimmunity

Status: RO and TDAR suppression shown through Day 29 at 3mg/kg IV in Phase 1; Data to-date support subsequent study in patients, including potential monthly IV or SC monthly administration; Final data from all cohorts expected in 1H 2021

Economics: Clinical and regulatory milestones and royalty on annual net sales

Rights: Worldwide

1) Poster presentation at the Keystone Symposia: Antibodies as Drugs: New Horizons in the Therapeutic Use of Engineered Antibodies: KPL-404, a CD40 antagonist, blocked antigen-specific antibody responses in an in vivo NHP model and demonstrated strong PK/PD correlation; 2) Elgueta, et al. Immunol Rev 2009, 229 (1), 152-172; 3) Peters, et al. Semin Immunol 2009, 21 (5) 293-300; CD40L = CD40 ligand; RO = receptor occupancy; TDAR = T-cell Dependent Antibody Response

KPL-404: Potential Molecule for Evaluation in a Broad Range of Autoimmune Diseases

Mechanism	**Humanized mAb inhibitor of CD40-CD40L interaction[1]**	• Designed to inhibit CD40-CD40L, a T-cell co-stimulatory pathway critical for B-cell maturation and immunoglobulin class switching
Rationale	**External POC for CD40-CD40L inhibition observed in a range of autoimmune diseases[2,3]**	• **Published Positive Class-Related Clinical Data**: Sjogren's syndrome, systemic lupus erythematosus, solid organ transplant, rheumatoid arthritis, Graves' disease • **Ongoing Class-Related Studies**: type 1 diabetes, ulcerative colitis, lupus nephritis, hidradenitis suppurativa, kidney transplant and focal segmental glomerulosclerosis
Preclinical Data	**Robust preclinical package supports development potential**	• Favorable pharmacokinetic and pharmacodynamic findings, including engagement of CD40 target and block of antigen-specific primary and secondary antibody responses in a T-cell dependent antibody response cynomolgus monkey model
Competition	**Potential differentiation**	• KPL-404 at 10mg/kg achieved/maintained ~100% receptor occupancy in 7/7 non-human primates (NHP) through 4 weeks • KPL-404 10mg/kg suppressed T-cell dependent antibody responses (TDAR) in NHP model to tetanus toxoid (TT) and keyhole limpet hemocyanin (KLH) for >4 weeks
Status	**Enrolling first-in-human study**	• Receptor occupancy and TDAR suppression shown through Day 29 at 3 mg/kg intravenous; Data to-date support subsequent study in patients, including potential intravenous or subcutaneous monthly administration; Final data and safety follow-up from all cohorts expected in 1H 2021

1) Poster presentation at the Keystone Symposia: Antibodies as Drugs: New Horizons in the Therapeutic Use of Engineered Antibodies: KPL-404, a CD40 antagonist, blocked antigen-specific antibody responses in an in vivo NHP model and demonstrated strong PK/PD correlation; 2) Elgueta, et al. Immunol Rev 2009, 229 (1), 152-172; 3) Peters, et al. Semin Immunol 2009, 21 (5) 293-300; TDAR, T-cell Dependent Antibody Response

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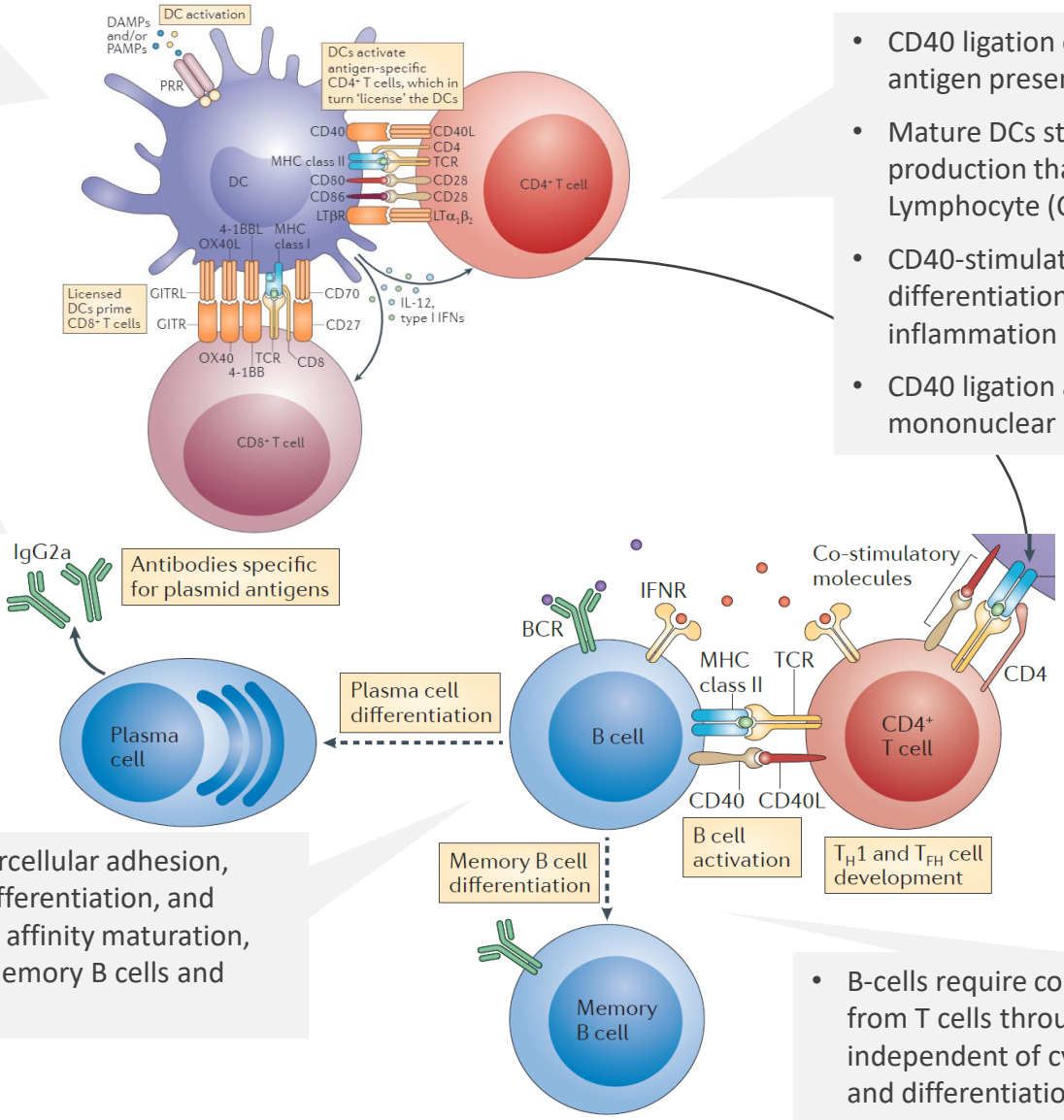
CD40/CD40L is an Essential Immune Pathway for T-Cell Priming and T-Cell Dependent B-Cell Responses

- CD40 is expressed on the surface of dendritic cells, B-cells, antigen-presenting cells and non-immune cell types
- Its ligand, CD40L (CD154), is expressed by activated T-cells, platelets, and other cell types



- CD40 ligation on DCs induces cell maturation by promoting antigen presentation and enhancing their costimulatory activity
- Mature DCs stimulate activated T-cells to increase IL-2 production that facilitates T-helper cells (Th) and cytolytic T-Lymphocyte (CTL) expansion
- CD40-stimulated DCs also secrete cytokines favoring Th1 cell differentiation and promoting Th cell migration to sites of inflammation
- CD40 ligation also provides a pro-inflammatory signal within the mononuclear phagocyte system

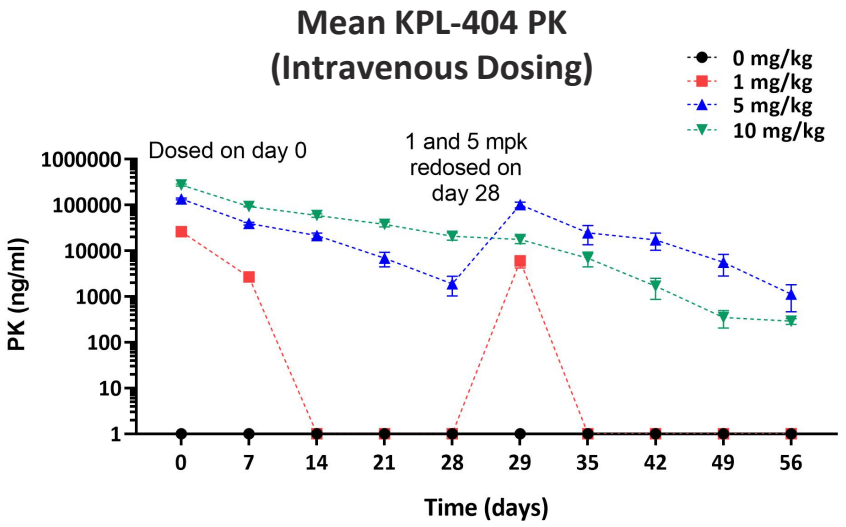
- Humoral immunity is dependent on a thriving B cell population and activation by Th cells; blockade of CD40/CD40L interaction has been shown to completely ablate primary and secondary TDAR response

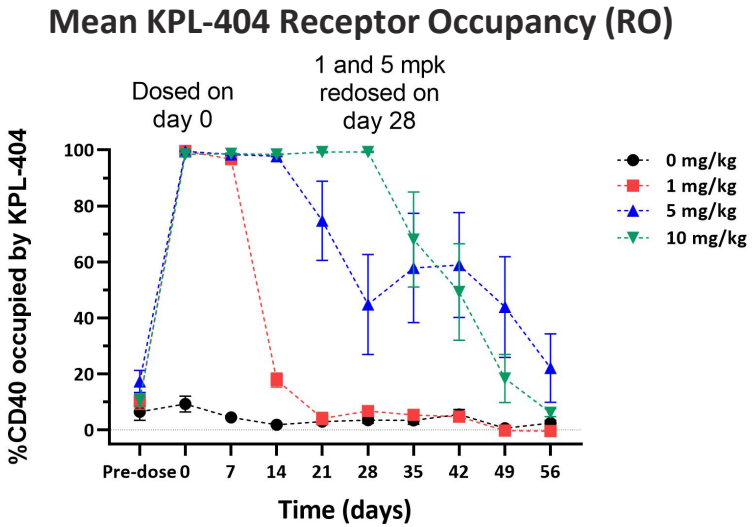
- CD40 engagement triggers B-cell intercellular adhesion, sustained proliferation, expansion, differentiation, and antibody isotype switching leading to affinity maturation, which is essential for generation of memory B cells and long-lived plasma cells

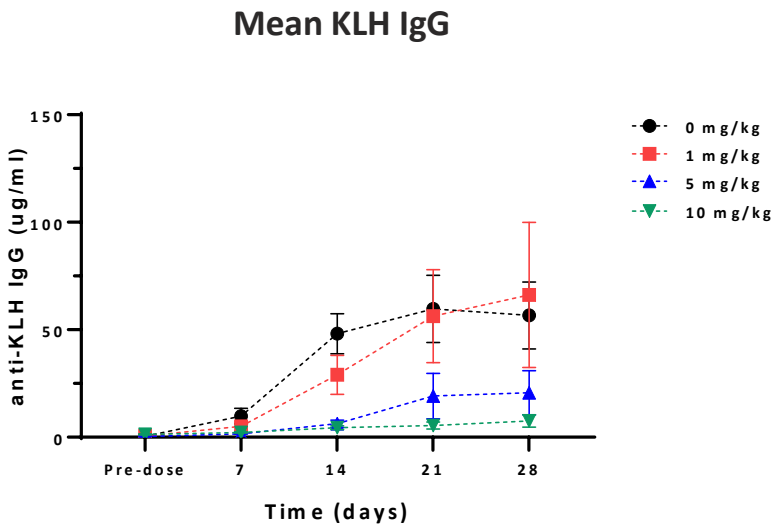
- B-cells require contact-dependent stimulus from T cells through CD40/CD40L interaction independent of cytokines to trigger growth and differentiation

Sources: Elgueta et al., Immunol Rev, 2009; Peters et al., Semin Immunol, 2009; Kambayashi et al., Nature Reviews: Immunology, 14, 2014; Desmet et al., Nature Reviews: Immunology, 12, 2012

KPL-404 Showed Encouraging Results in a Non-Human Primate Model of TDAR







Showed linear pharmacokinetic profile with low variability between non-human primate subjects (n=7)

KPL-404 achieved 100% receptor occupancy for 2 weeks in all animals at 5mg/kg and 4 weeks in all animals at 10mg/kg

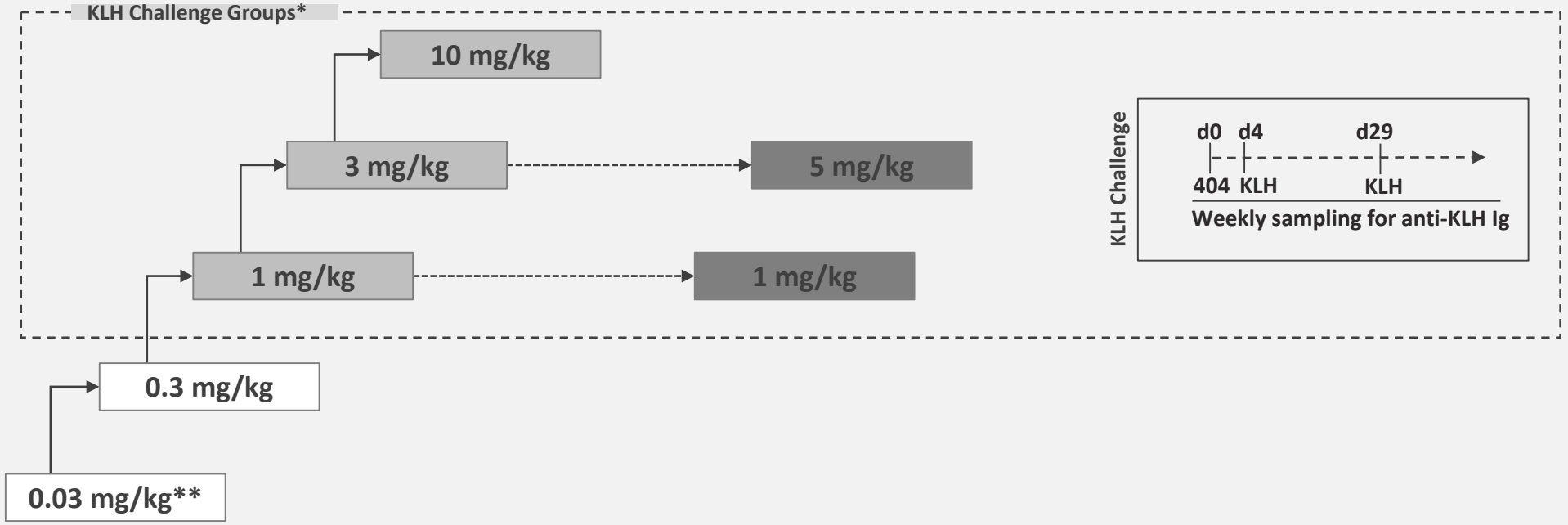
Complete suppression of primary T-cell dependent antigen response correlated with 100% receptor occupancy

Source = 1) Poster presentation at the Keystone Symposia: Antibodies as Drugs: New Horizons in the Therapeutic Use of Engineered Antibodies: KPL-404, a CD40 antagonist, blocked antigen-specific antibody responses in an in vivo NHP model and demonstrated strong PK/PD correlation; TDAR = T-cell dependent antibody response; KLH = keyhole limpet hemocyanin

KPL-404 Single-Ascending-Dose Phase 1 Study

First-in-human study to provide safety data and pharmacokinetics as well as receptor occupancy and TDAR

Part A (Single IV dose) | Part B (Single SC Dose)



- **Primary endpoints:** Safety and Tolerability
- **Secondary endpoints:** PK and ADA / CD40 RO in blood / Serum anti-KLH Ig levels
- **Exploratory endpoints:** Serum CXCL13 levels

Notes: Unless otherwise noted dose groups included 6 active/2 placebo subjects; *1° KLH challenge for all SAD dose groups except 0.03 and 0.3 mg/kg, 2° KLH re-challenge only in 1, 3, and 10 mg/kg IV; ** Cohort included 2 active and 2 placebo subjects

SAD = single-ascending-dose; TDAR = T-cell dependent antibody response; KLH = keyhole limpet hemocyanin; RO = receptor occupancy; ADA = anti-drug antibodies

Preliminary Data from KPL-404 Single-Ascending-Dose Phase 1 Study

The randomized, double-blind, placebo-controlled first-in-human (FIH) study is designed to investigate the safety, tolerability, PK and PD properties of single-ascending intravenous (IV) and subcutaneous (SC) doses of KPL-404 in healthy subjects.

- 2 single-ascending-dose arms (SAD):
  - Single-dose KPL-404 0.03 mg/kg, 0.3 mg/kg, 1 mg/kg, 3 mg/kg or 10 mg/kg IV and
  - Single-dose KPL-404 1 mg/kg or 5 mg/kg SC

Primary Endpoint: Safety and tolerability of single ascending intravenous (IV) and subcutaneous (SC) doses of KPL-404 in healthy subjects.

- KLH challenge in 1 mg/kg, 3 mg/kg, and 10 mg/kg IV and 1 mg/kg and 5 mg/kg SC cohorts

Secondary Endpoints: Pharmacokinetics and anti-drug antibody response following single IV and SC doses of KPL-404 in healthy subjects, receptor occupancy of KPL-404 on CD40 in healthy subjects, serum anti- keyhole limpet hemocyanin (KLH) IgG levels.

- KLH re-challenge only in 1 mg/kg, 3 mg/kg, and 10 mg/kg IV

Topline Observations:

- 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 IV and 5 mg/kg SC, is ongoing.
- The data to-date support subsequent study in patients, including potential IV or SC monthly administration. Kiniksa expects final data and safety follow-up from all cohorts in the first half of 2021.

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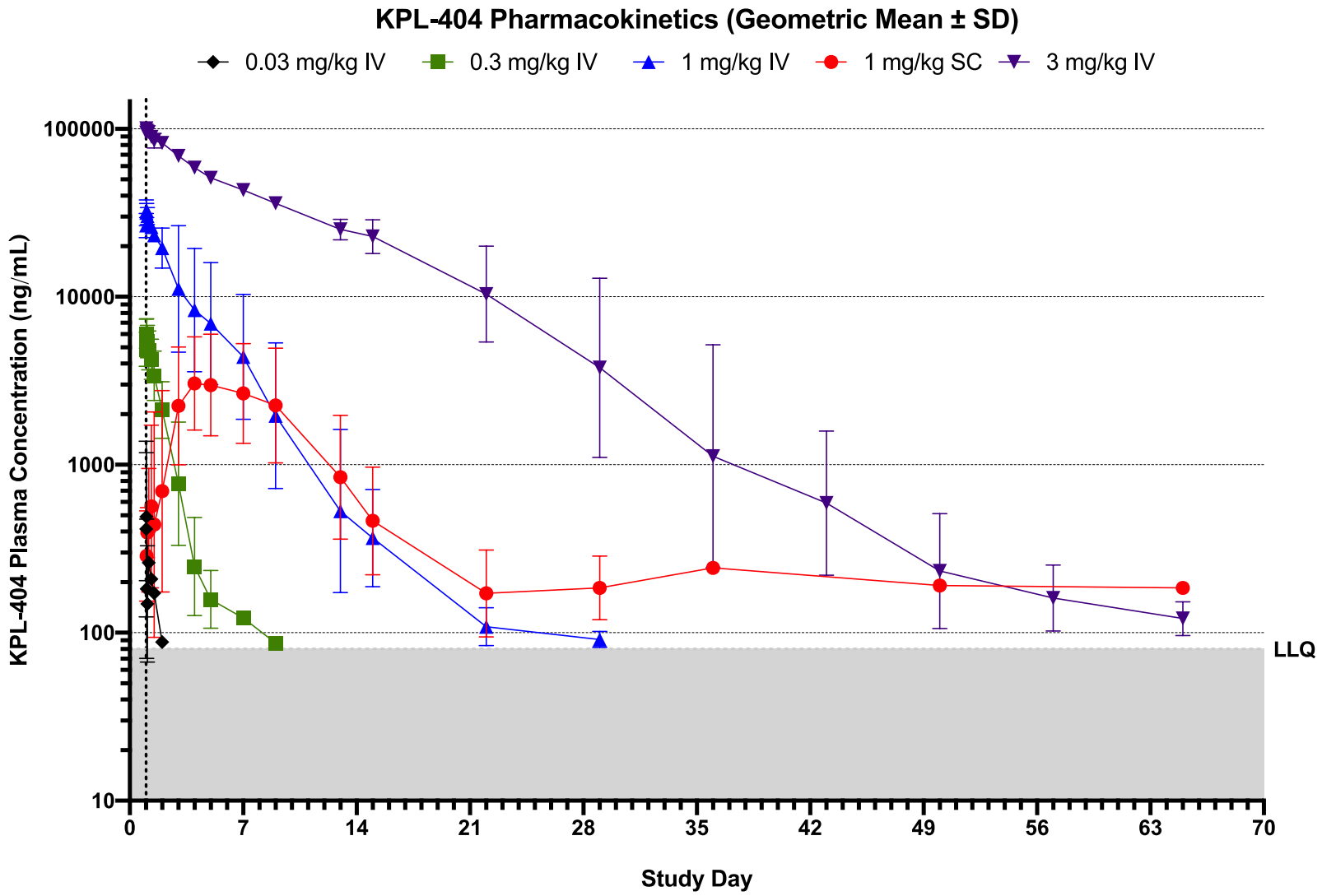
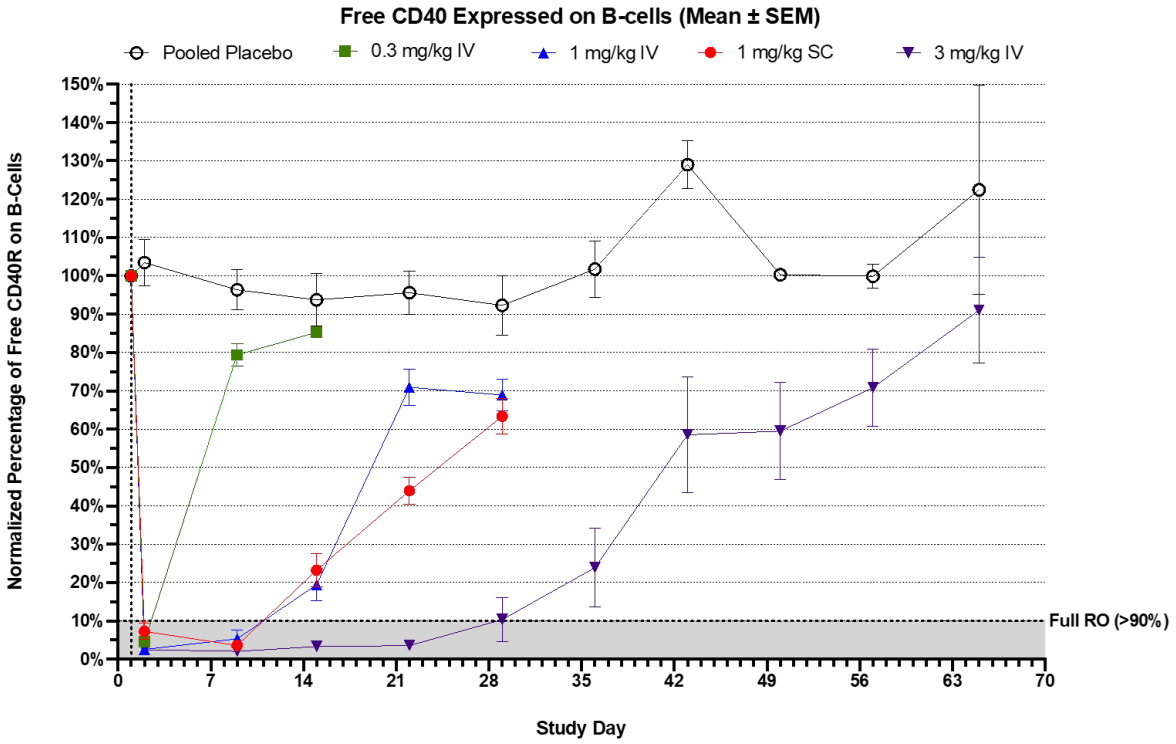
Preliminary Data from KPL-404 Single-Ascending-Dose Phase 1 Study

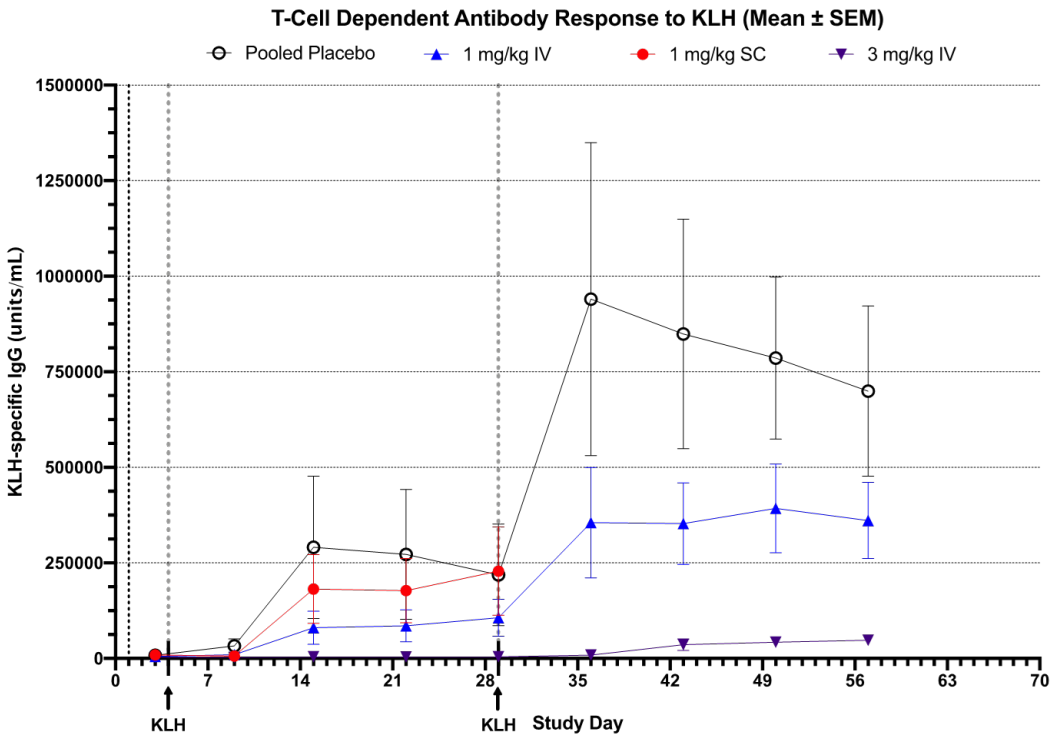
Pharmacokinetic summary



Preliminary Data from KPL-404 Single-Ascending-Dose Phase 1 Study

Receptor occupancy and KLH antigen challenge TDAR summary

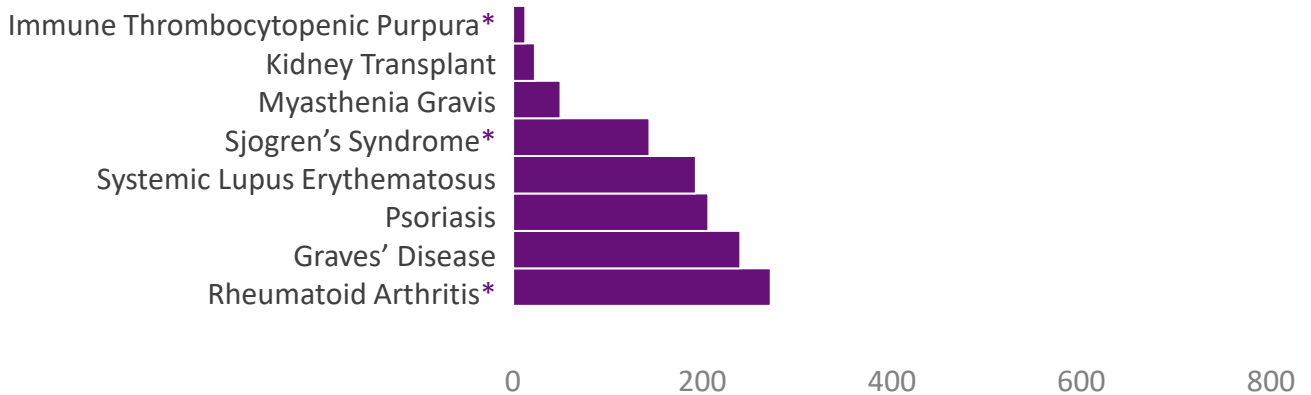




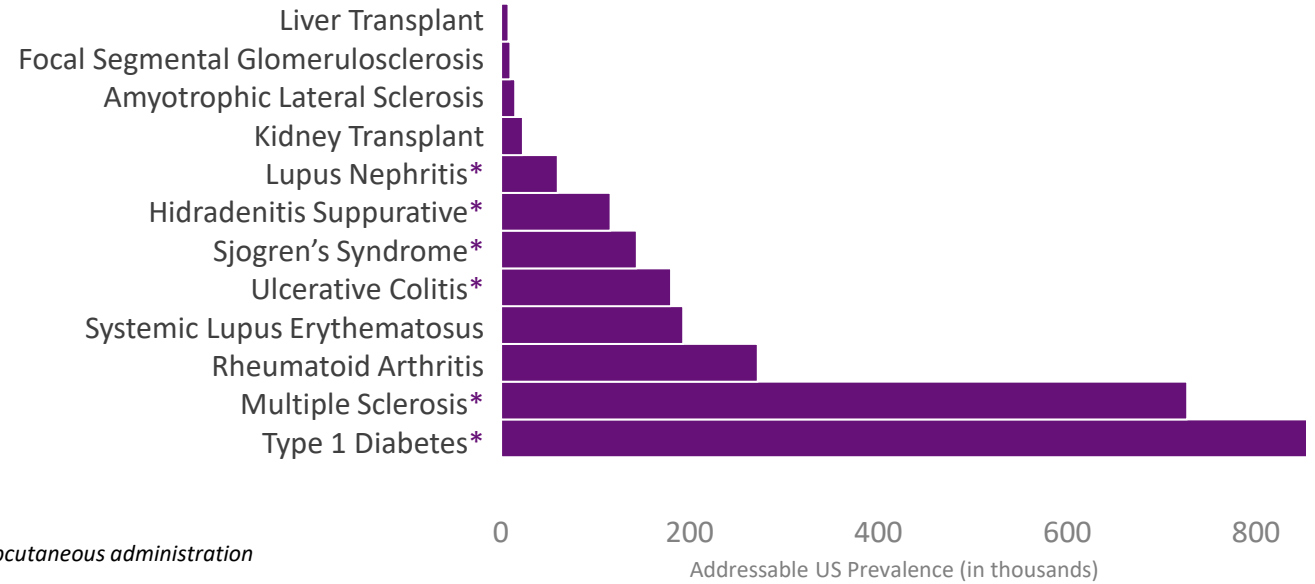
1) Free CD40R = inverse of receptor occupancy; KLH = keyhole limpet hemocyanin; TDAR = T-cell dependent antibody response

Potential for Evaluation of KPL-404 in a Broad Range of Autoimmune Diseases

Indications with Published Data[1]



Indications with Pending Data & Trials Ongoing[1]



Indication Selection Criteria

- **Robust Data or proof-of-concept supporting mechanism**
- **Differentiation vs. Competitors**
- **Commercial Attractiveness**

**Indications evaluated with subcutaneous administration*

1) With the CD40 mechanism

Sources: 2019 numbers: https://unos.org/data/transplant-trends/; Hunter et al. Prevalence of rheumatoid arthritis in the United States adult population in healthcare claims databases, 2004-2014; Rheumatol Int. 2017 Sep;37(9):1551-1557; Overall Prevalence: Maciel et al, Arthritis Care Res (Hoboken) 2017; Qin et al, Ann Rheum Dis 2015; UpToDate; Baldini et al. Prevalence of Severe Extra-Glandular Manifestations in a Large Cohort of Patients with Primary Sjögren's Syndrome; 2012 ACR/ARHP Annual Meeting, ABSTRACT NUMBER: 2185; Wallin et al. The prevalence of MS in the United States A population-based estimate using health claims data, Neurology, March 5, 2019; Somers et al.; Prevalence of Systemic Lupus Erythematosus in the United States: Preliminary Estimates from a Meta-Analysis of the Centers for Disease Control and Prevention Lupus Registries; 2019 ACR/ARP Annual Meeting ABSTRACT NUMBER: 2886; Garg et al. JAMA Dermatol. 2017;153(8):760-764. doi:10.1001/jamadermatol.2017.0201 Sex- and Age-Adjusted Population Analysis of Prevalence Estimates for Hidradenitis Suppurativa in the United States; MayoClinic.org; Yale J Biol Med. 2013 Jun; 86(2): 255–260. N Engl J Med 2016;375:2570-81; https://www.diabetesresearch.org/diabetes-statistics; Nephcure.org; Kitiyakara C, Eggers P, Kopp JB. Twenty-one-year trend in ESRD due to focal segmental glomerulosclerosis in the United States. Am J Kidney Dis. 2004 Nov;44(5):815-25; Rachakonda et al. J Am Acad Dermatol . 2014 Mar;70(3):512-6. doi: 10.1016/j.jaad.2013.11.013. Epub 2014 Jan 2. Psoriasis prevalence among adults in the United States; Yeung et al. Psoriasis severity and the prevalence of major medical co-morbidities: a population-based study; JAMA Dermatol. 2013 Oct 1; 149(10): 1173–1179; Hoover etal. Kidney Int. 2016 Sep; 90(3): 487–492. Insights into the Epidemiology and Management of Lupus Nephritis from the U.S. Rheumatologist's Perspective.

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