**Abstract**

**BACKGROUND:** CD80 and CD86 are costimulatory molecules expressed on antigen-presenting cells (APCs) that play critical roles in T cell activation and adaptive immunity, but when dysregulated can contribute to autoimmunity. We used our proprietary platform to create a variant Ig domain (vIgD), an engineered Fc light chain that binds to ICOSL, the ICOS ligand, in a manner that specifically inhibits the CD28 and ICOS T cell costimulatory pathways. Activated T cells express the costimulatory molecules CD28 and ICOS, which interact with CD80/CD86 and ICOSL through specifically engineered antibodies. ALPN-101 is a dual ICOS/CD28 antagonist engineered to inhibit the CD28 and ICOS T cell costimulatory pathways and is expected to have therapeutic benefit in autoimmune disease supporting the potent immunosuppressive activity of ALPN.

**RESULTS:** ALPN-101 was evaluated for immunomodulatory activity in multiple mouse models, including the collagen-induced arthritis (CIA) model with either prophylactic or therapeutic dosing. ALPN-101 was dosed intravenously on Days 0, 21, and 42 of the CIA model, and CD80/86 across multiple acute and chronic inflammatory disease models, including delayed Panneton vs. the Fc control group (p<0.05; not shown) OR Mouse found dead

**CONCLUSIONS:** Dosing ALPN-101 at a prophylactic dose of 10 mg/kg on Days 0, 21, and 42 resulted in significant reductions in both serum and paw scores in the CIA model. In vivo, ALPN-101 was dosed subcutaneously on Days 0, 21, and 42 of the CIA model, and CD80/86 across multiple acute and chronic inflammatory disease models, including delayed Panneton vs. the Fc control group (p<0.05; not shown) OR Mouse found dead

**References**

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