MEDICENNA
THERAPEUTICS CORP.

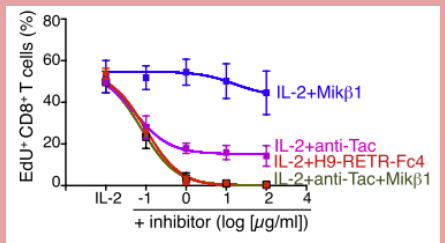
MDNA209: An IL-2 Superkine™ Antagonist For Autoimmune Diseases

PROGRAM OVERVIEW

- Medicenna is developing a pipeline of engineered cytokine products (Superkines and Empowered Cytokines), with pharmacologically-optimized receptor-binding properties
- MDNA209 is an IL-2 mutein with an increased affinity for IL-2Rβ, inhibiting binding of endogenous IL-2, and a decreased γ_c affinity, attenuating IL-2Rβ-γ_c heterodimerization with reduced signaling
- MDNA209 is an IL-2 and IL-15 antagonist with potential therapeutic benefits in autoimmune diseases, such as graft-versus-host disease

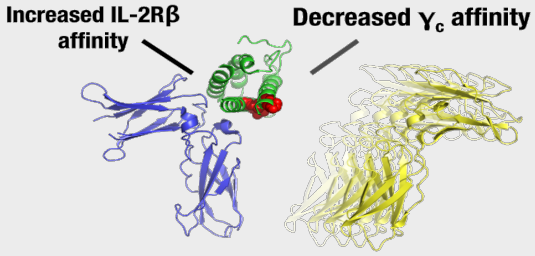
CHARACTERIZATION OF MDNA209

- MDNA209 is characterized as a dominant negative antagonist of IL-2
- In NK cells, MDNA209 has shown to prevent pSTAT5, induce rapid internalization of IL-2Rβ, but not γ_c due to reduced binding to γ_c, and attenuate activation
- MDNA209 has shown to prevent IL-2 and IL-15 signalling via STAT5 in CD8+ T cell STAT5, with reduced CD25 expression, and inhibit Th1, Th9 and Treg cell differentiation, but promoted Th17 cell differentiation
- An Fc-fusion version of MDNA209 (MDNA209-Fc4) is 27,000X more potent than Daclizumab in blocking IL-2 signalling in CD8+ T cells



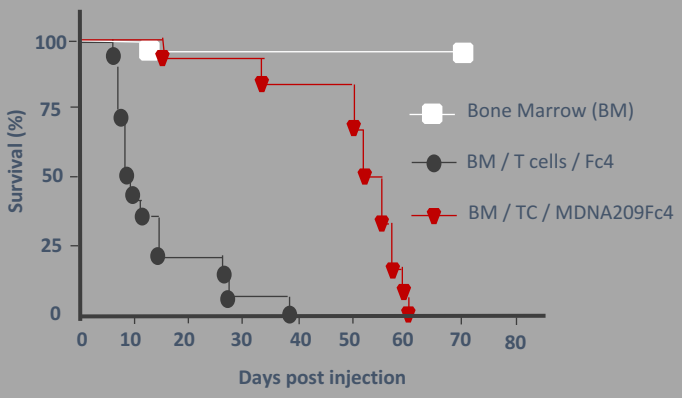
DEVELOPMENT OF MDNA209

- MDNA209 was selected from a library of IL-2 Superkines with a wide range of receptor binding and immunomodulating properties
- MDNA209 has enhanced affinity for IL-2Rβ (200X lower K_D), and greatly decreased affinity towards γ_c, leading to simultaneous blockade of IL-2 and IL-15 signalling



TARGETING AUTOIMMUNE DISORDERS

- MDNA209 is intended to dampen overall T cell responses in T-cell mediated autoimmune disorders
- The IL-2 / IL-15 signaling axis has been implicated in several autoimmune diseases, including acute graft-versus-host disease and Alopecia areata
- Mice treated with MDNA209-Fc4 daily for 10 days showed prolonged survival in a full-MHC mismatch acute graft-versus-host disease model compared to control



- MDNA209 demonstrated superior efficacy compared to individual receptor subunit-targeted antibodies (e.g. Hu-Mikbeta1, an anti-CD122 mAb) in preventing proliferation of viral-specific CD8 cells isolated from HTLV-1 associated myelopathy/tropical spastic paraparesis patients