In vitro Treg activation (CD25)
Vehicle (C57BL/6)
CD4 Treg, CD25 MFI
Day 5
Ki67+ Treg

INTRODUCTION

• Impaired IL-2 production and regulatory T cell (Treg) dysfunction have been implicated as immunological mechanisms in multiple autoimmune disorders
• Low-dose IL-2 is used to stimulate Tregs for clinical benefit
• Poor pharmacokinetics (PK) and daily delivery of low-dose IL-2
• Treg increases are modest and short-lived

Nektar Therapeutics has developed NKTR-358, a novel product with the goal of selectively restoring Treg homeostasis
• Utilizes the interleukin (IL)-2 receptor pathway
• Chemically conjugated with stable polyethylene glycol (PEG) moieties
• Intended for low dose, subcutaneous administration
• Minimal impact on conventional T cell (Tcon) function

METHODS

A single administration of NKTR-358 promotes greater Treg mobilization than multiple administrations

NKTR-358: a selective, first-in-class IL-2 pathway agonist, which increases number and suppressive function of regulatory T cells for the treatment of immune inflammatory disorders

RESULTS

NKTR-358 demonstrates attenuated affinity for the IL-2R relative to IL-2Rα and favors activation of Treg over Tcon

NKTR-358 mobilizes Treg in cynomolgus monkey

NKTR-358 increases Treg suppressive function

NKTR-358 suppresses antigen-driven inflammation in the mouse DTH model

NKTR-358 is efficacious in a mouse model of systemic lupus erythematosus

CONCLUSIONS

• NKTR-358 delivers sustained, preferential activation of Tregs; in cynomolgus monkey this effect is sustained for >14 days
• NKTR-358 is currently being investigated in a Phase 1 study in healthy subjects to evaluate Treg mobilization, functional activity, PK, and safety, with the goal of establishing a range of dose levels to advance into a multiple-ascending dose trial in patients with SLE
• Nektar Therapeutics and Eli Lilly and Company have entered into a strategic collaboration to develop and commercialize NKTR-358