CGEN-15001: A NOVEL B7-LIKE REGULATOR OF IMMUNE HOMEOSTASIS AND INDUCER OF ANTIGEN-SPECIFIC TOLERANCE

INTRODUCTION

B7 proteins play critical immunomodulatory roles and provide attractive targets for development of novel therapies for cancer and autoimmunity, both of which involve improper immune tolerance. A major medical need in autoimmunity is restoration of immune tolerance to self-antigens and immune homeostasis.

CGEN-15001 is a first-in-class Fc-fusion protein consisting of the extracellular domain of a novel B7-like protein, discovered by Compugen based on shared biochemical characteristics with known B7 members.

CGEN-15001 Induces Antigen Specific Tolerance in Autoimmune Diseases

Unique MOA: Combining tolerance induction and restoration of immunological homeostasis
- Regulates immune homeostasis: inhibiting Th1/Th17 responses while enhancing Th2 and anti-inflammatory cytokines
- Induces durable therapeutic effect following short-term treatment in models of autoimmune diseases
- The therapeutic effect is transferable, and mediated by induction of Ag-specific immune tolerance
- Previous knowledge of the antigen is not required
- Promotes donor-specific tolerance leading to engraftment in bone marrow transplantation models with H-Y mismatch

CGEN-15001 provides potential paradigm shift from "standard of care" addressing a widely anticipated 'next step' therapeutic in autoimmunity through induction of Tregs

TRANSENT TREGS NEUTRALIZATION WITH AN-CD25

CGEN-15001 INHIBITS MOUSE AND HUMAN T CELL ACTIVATION

LONG TERM THERAPEUTIC EFFECT FOLLOWING SHORT TREATMENT WITH CGEN-15001 IN MODELS OF AUTOIMMUNE DISEASES

Long term efficacy in NOD model of type 1 diabetes

- CGEN-15001 administration to pre-diabetic mice prevents disease development
- Long duration of response following short term administration (3x/wk for 2wks), lasting at least 18 weeks after cessation of treatment
- Suggests tolerance induction and opportunity for drug-free remission

CGEN-15001 MOA COMBINES RESTORATION OF IMMUNE HOMEOSTASIS AND RE-ESTABLISHMENT OF TOLERANCE

CGEN-15001 restores homeostasis in vivo: Th1/Th17 to Th2 shift

Adoptive transfer R-EAE model
- Cytokine secretion following in vitro reactivation of splenocytes with PLP139-151 day 45
- Reduction of pro-inflammatory Th1 and Th17 responses
- Enhancement of anti-inflammatory cytokines and Th2 responses
- Similar Th1/Th17 to Th2 shift obtained with human cells

CGEN-15001 INDUCES TREG IN VITRO

In vitro enhancement of iTreg differentiation under Treg driving conditions

CGEN-15001 INDUCED TOLERANCE IS TRANSFERABLE AND ANTIGEN-SPECIFIC

T cells from CGEN-15001-treated mice protect recipients only when disease is driven by the same epitope

CGEN-15001 INHIBITS MOUSE AND HUMAN T CELL ACTIVATION

- Robust inhibition of T cell proliferation following polyclonal or Ag-specific activation

CGEN-15001 IS A NOVEL T CELL INHIBITORY LIGAND

BINDS TO ACTIVATED T CELLS, ACTIVATES INHIBITORY PATHWAY

Antigen specific T cell Activation
- Transient T cells neutralization with anti-CD25
- Robust inhibition of T cell proliferation following polyclonal or Ag-specific activation

CGEN-15001 IS A POTENT MODULATOR OF T CELLS CYTOKINE PRODUCTION TH1/TH17 TO TH2 SHIFT IN VITRO

In vitro T cell differentiation

- DO11.10 treated with CGEN-15001
- DO11.10 CD4+ T cells

CGEN-15001 INHIBITS MOUSE AND HUMAN T CELL ACTIVATION

- Robust inhibition of T cell proliferation following polyclonal or Ag-specific activation