

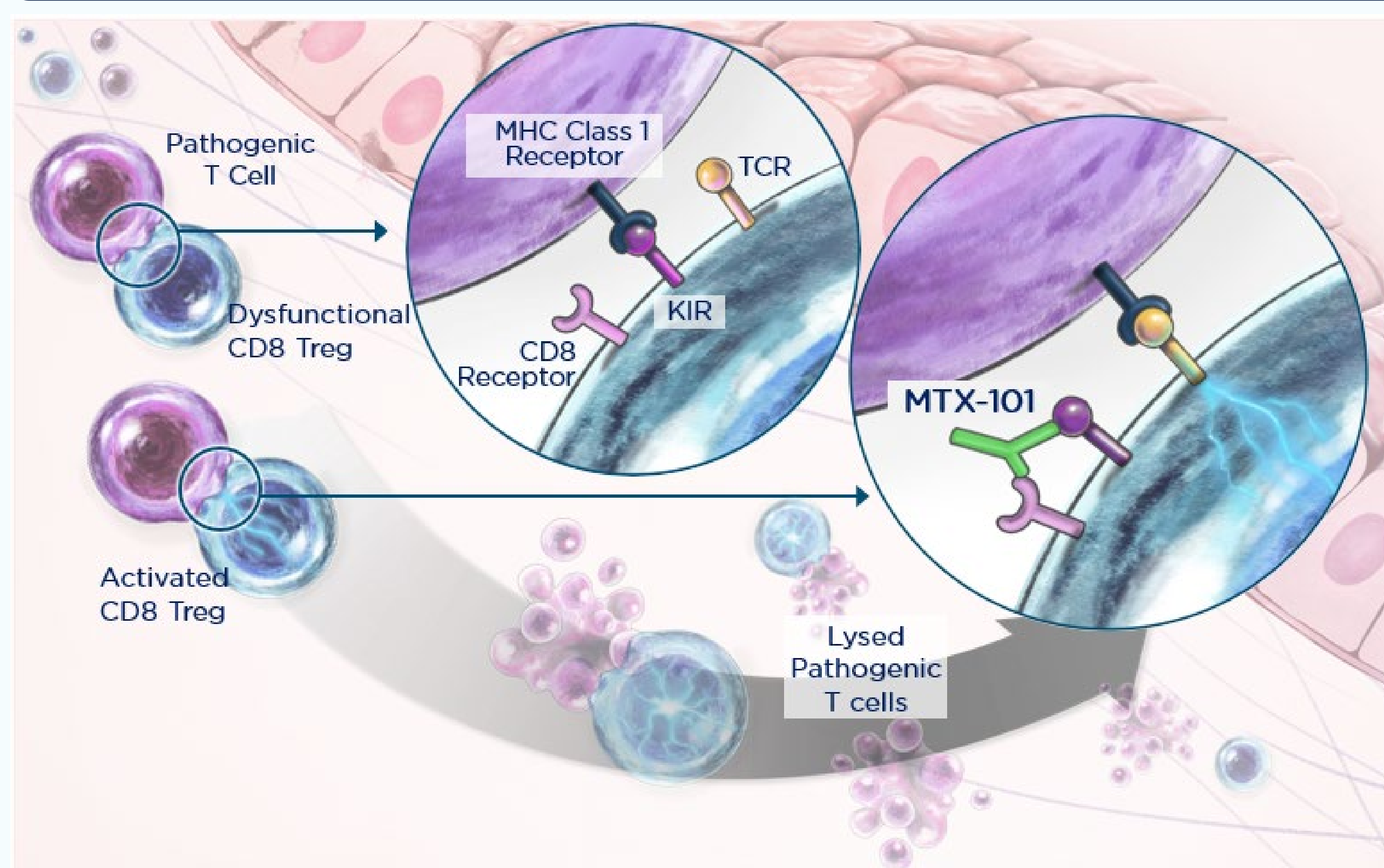
Phase 1 study evaluating the safety, pharmacokinetics, and pharmacodynamics of MTX-101 in healthy adults and patients with type 1 diabetes

Jason W. Chien, Catherine J. McMahan, Jean S. Campbell, Roxana E. Rojas, Heather Wroe, Jasmine C. Labuda, Daniel R. Boster, Daniel T. Patton, Eyayu K. Belay, Allison R. O'Rourke, Meghan E. Maurer, Cong Tan, Sean Summers, Kaelen S. Encarnacion, Nadine M. Morgan, Monica M. Childs, Kristi L. Manjarrez, Kristine M. Swiderek, John M. Wentworth, Courtney A. Crane

Background

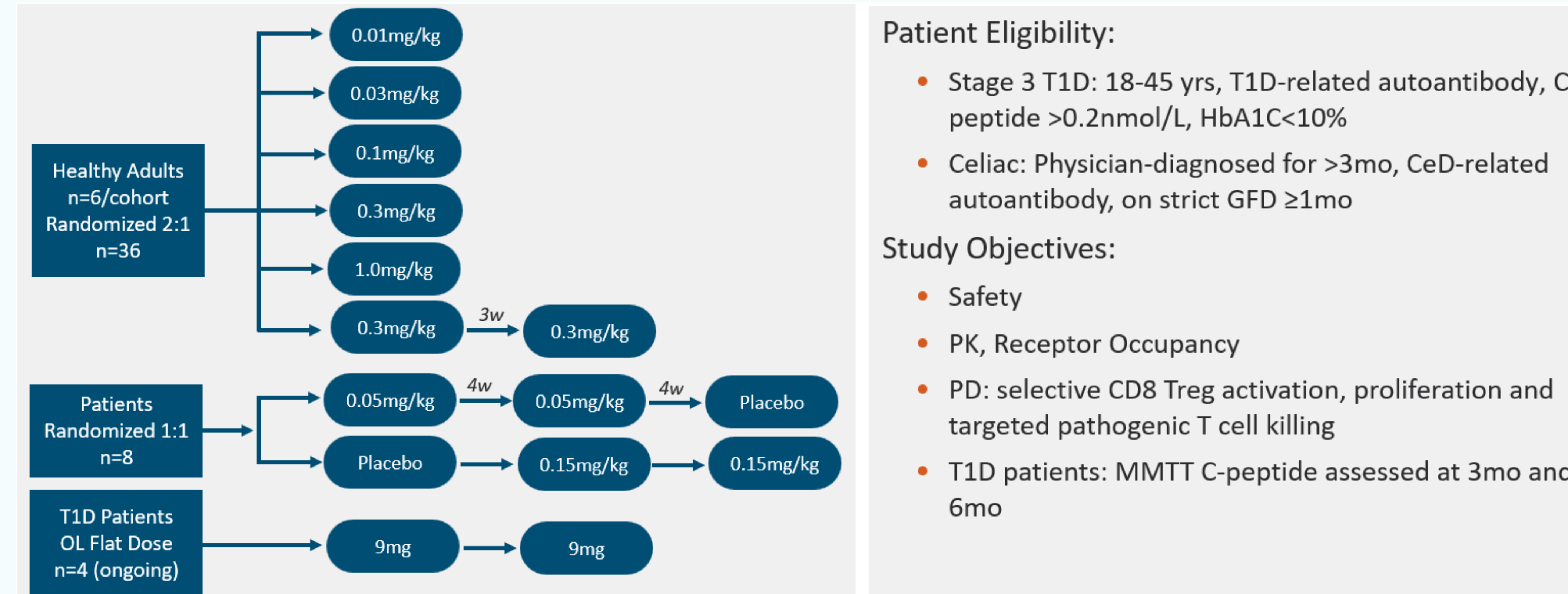
Regulatory CD8 T cells (CD8 Treg) selectively kill pathogenic T cells which can attack host tissues. In autoimmune disease, CD8 Treg are dysfunctional and fail to control the expansion of pathogenic T cells. This dysfunction is related to the expression of inhibitory killer immunoglobulin-like receptors (KIR; KIR2DL isoforms 1-3) on CD8 Treg. MTX-101 is a bispecific antibody that targets inhibitory KIR and CD8 to restore CD8 Treg's ability to kill pathogenic T cells. We conducted a Phase 1a/ 1b study to evaluate the safety, pharmacokinetics, and pharmacodynamics of MTX-101 in healthy adults and adults with Stage 3 Type 1 Diabetes. We found that MTX-101 was well tolerated, reduced pathogenic T cells and preserved C peptide in patients with Stage 3 T1D.

Therapeutic Hypothesis



Model of the postulated mechanism of action for MTX-101. MTX-101, a bispecific antibody targeting inhibitory KIR and CD8, supports TCR restricted CD8 Treg activation and cytolytic capacity, restoring immune tolerance and preventing downstream inflammation and tissue destruction.

Study Schema



Summary of MTX-101 Clinical Safety

Adverse Events n (%)	MTX-101 (mg/kg)			All Placebo n=6 ^a
	Low Dose (3.1–4.5 mg) n=5	High Dose (8.5–13.8 mg) n=7	All MTX-101 n=12	
Any AE	4 (80)	7 (100)	11 (92)	4 (67)
Grade 1	4 (80)	5 (71)	9 (75)	4 (67)
Grade 2	2 (40)	4 (57)	6 (50)	2 (30)
Grade 3	1 ^b (20)	3 ^b (42)	4 ^b (33)	0
Grade 4	0	1 ^c (14)	1 ^c (8)	0

^a Includes n=3 participants who received placebo (Day 1 to Day 28) prior to receiving MTX-101 on Day 29.

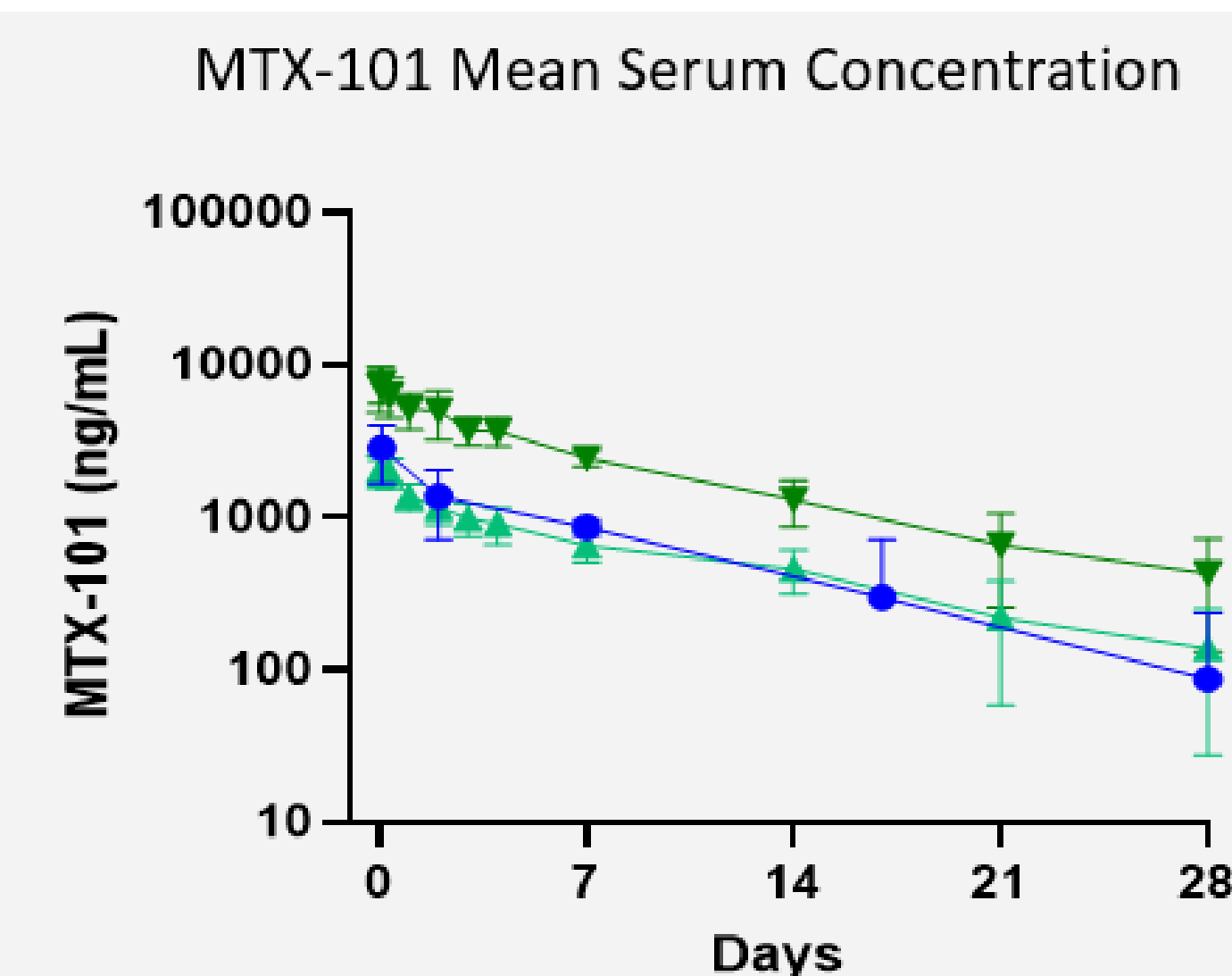
^b n=1 fracture of humerus (low dose; unrelated); n=1 vasovagal reaction (0.15 mg/kg; related to MTX-101); n=1 CRS and sinus bradycardia (0.15 mg/kg; related); n=1 alkaline phosphatase increased (0.15 mg/kg; related to MTX-101)

^c Decreased lymphocyte and neutrophil counts (transient [≤48 hr] and self-limiting), elevated AST, and elevated ALT, occurred in the participant with Grade 3 CRS (related to MTX-101)

Note: All events ≥Grade 3 occurred in the same participant, excepting Grade 3 fracture of the humerus, Grade 3 vasovagal reaction and Grade 3 alkaline phosphatase increase.

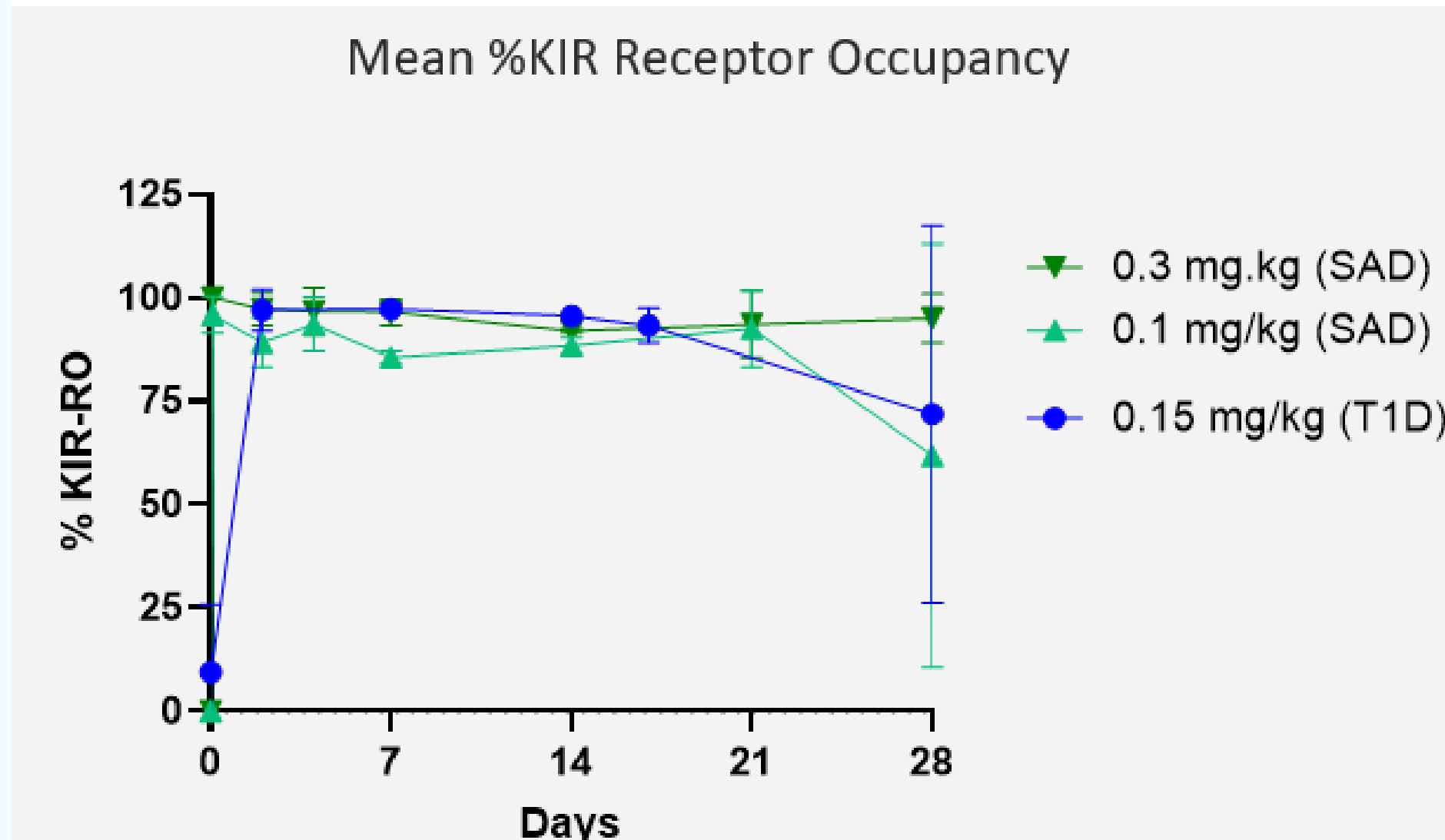
Interim PK & Receptor Occupancy Data Support Convenient Dosing

PK is dose-proportional



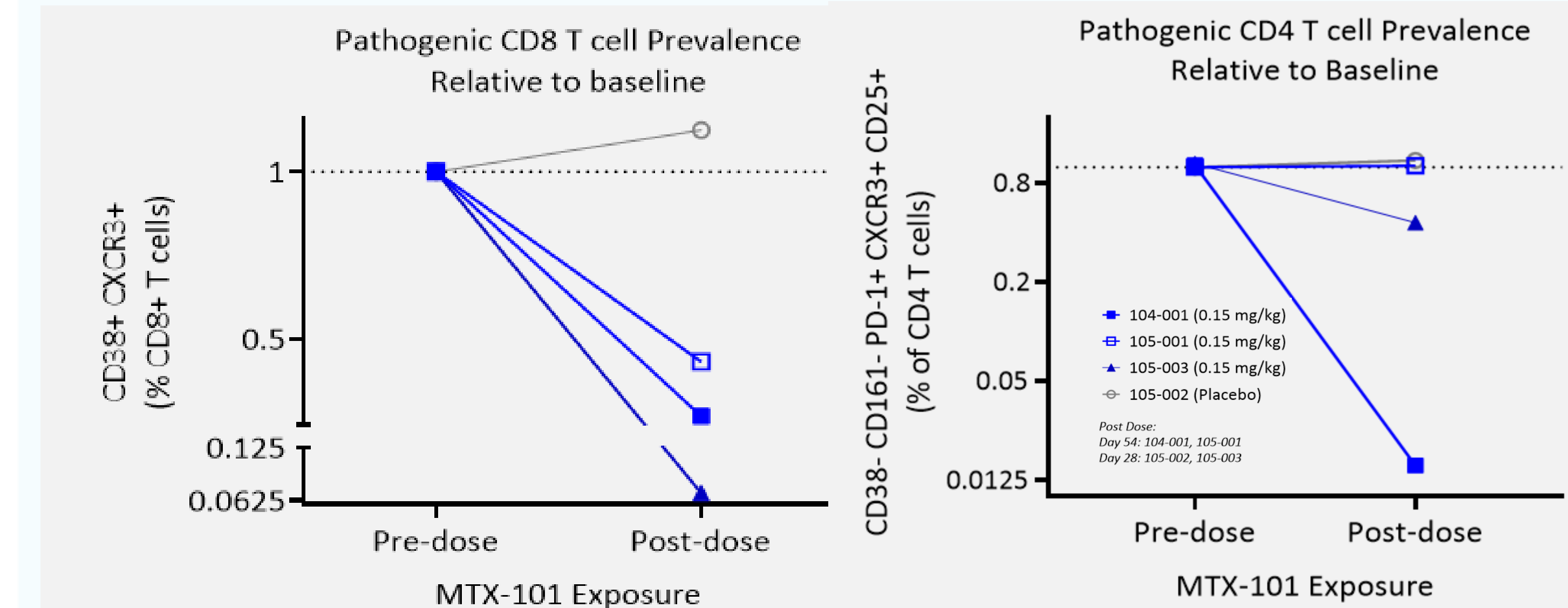
• Mean serum PK concentration by dose level

CD8 Treg RO is sustained at higher dose levels

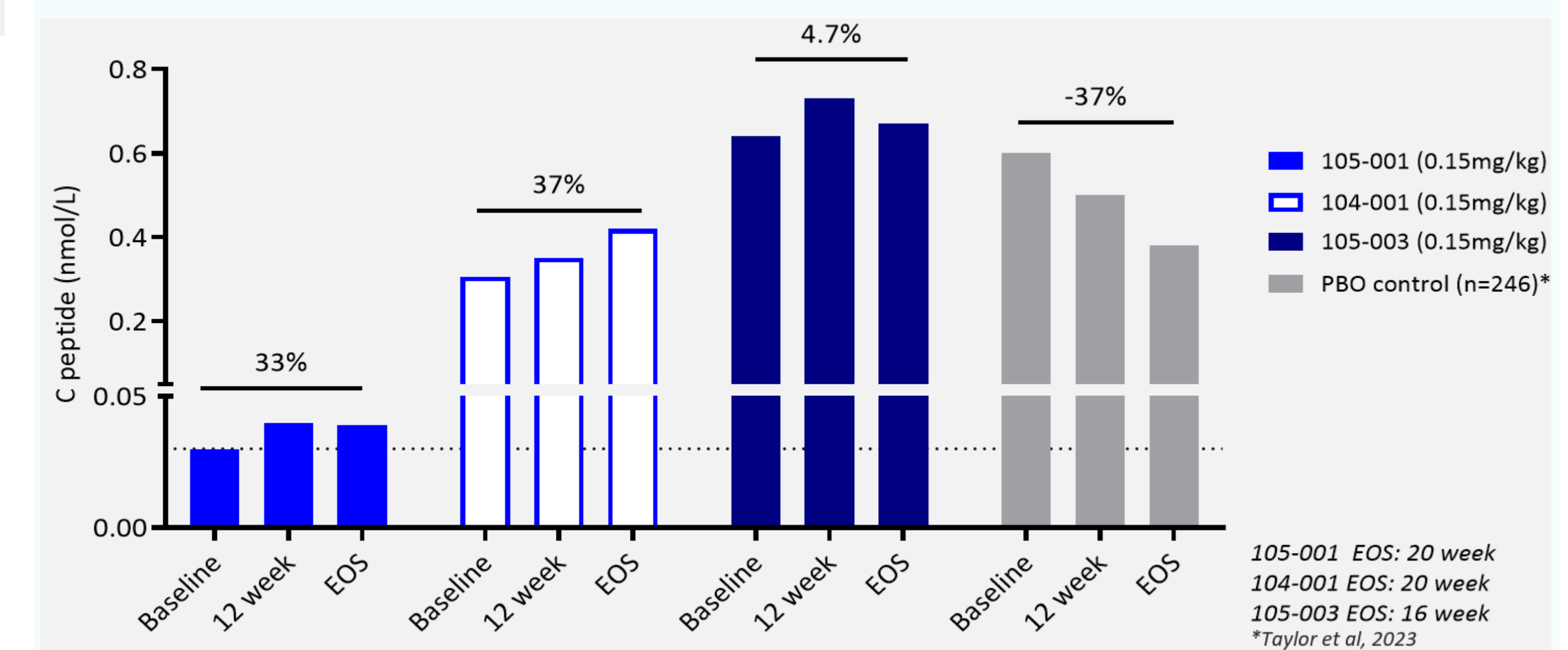


• Mean RO by dose level

Reduction of Pathogenic CD4 and CD8 T Cells



MTX-101 Effect on C-Peptide



Summary

- Stage 3 T1D—MTX-101 can shift the treatment paradigm
- First CD8 Treg modulator for Stage 3 T1D to preserve C-peptide and delay progression of a disease where daily insulin injections are the standard of care for symptom management
- 38 adult participants, including 4 Celiac and 10 T1D patients, treated with MTX-101 in Ph1 study
- Consistent findings that MTX-101 restores the selective reduction of pathogenic T cells without broad immunosuppression
- Strong mechanistic readthrough with notable maintenance of C-peptide at 20 weeks after a single dose
- Formulation and PK will provide opportunity for convenient and infrequent subcutaneous dosing

MTX-101 can safely and selectively modulate the CD8 Treg network to restore durable immune homeostasis and preserve endogenous insulin production