

QEL-005: CD19 Directed CAR Regulatory T Cell Therapy for the Treatment of Complex Autoimmune Diseases including Rheumatoid Arthritis and Systemic Sclerosis



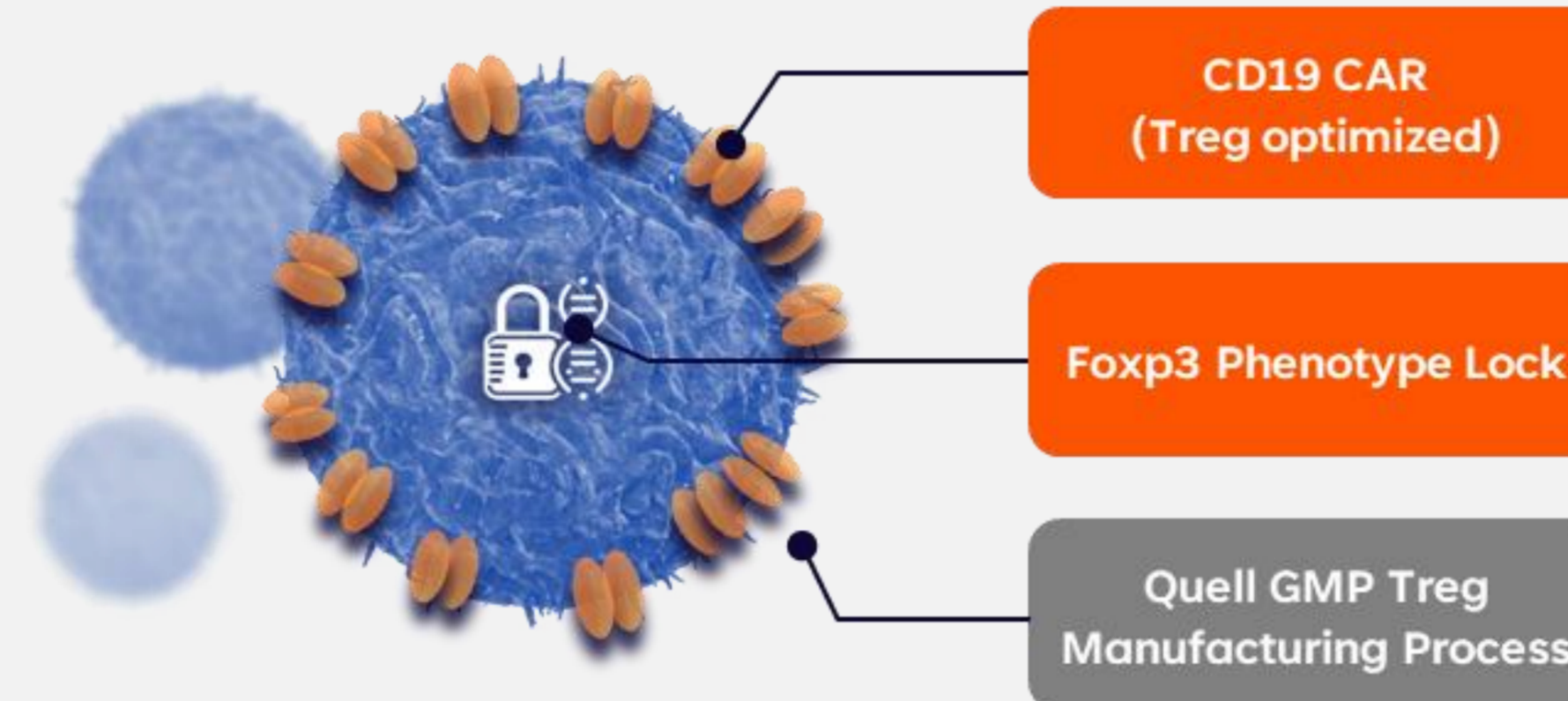
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Introduction: Clinical Opportunity for Treg cell therapy

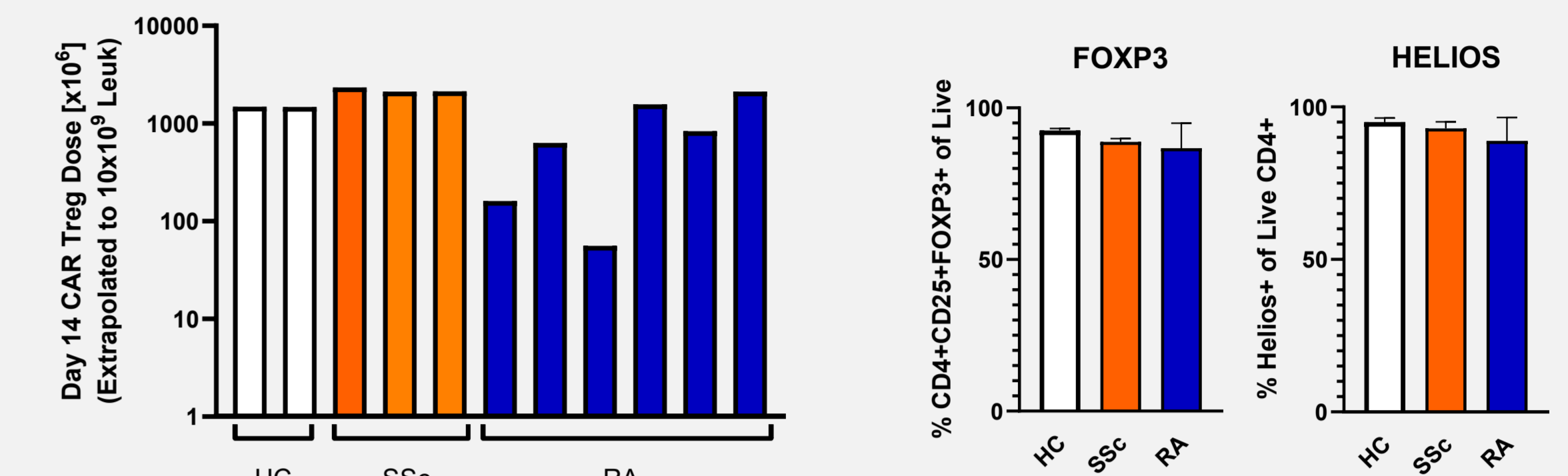
- Rheumatoid Arthritis (RA) and Systemic Sclerosis (SSc) are complex autoimmune diseases involving a chronic loop of inflammation and ongoing tissue damage
- Regulatory T cells (Tregs) have an essential role in restraining autoimmunity and are key mediators of immune and tissue homeostasis through the modulation of an array of immunological pathways
- B cell depletion approaches highlight the contribution of B cells in rheumatological diseases but are limited to targeting a single immune cell type and carry safety and tolerability risks in some patient populations
- We propose that a CD19-directed CAR-Treg cell will be activated by B cells in disease tissue, as well as secondary and tertiary lymphoid organs to control chronic inflammatory responses driven by B cells, T cells and Macrophages to restore tissue homeostasis

QEL-005 Treg Cell Therapy

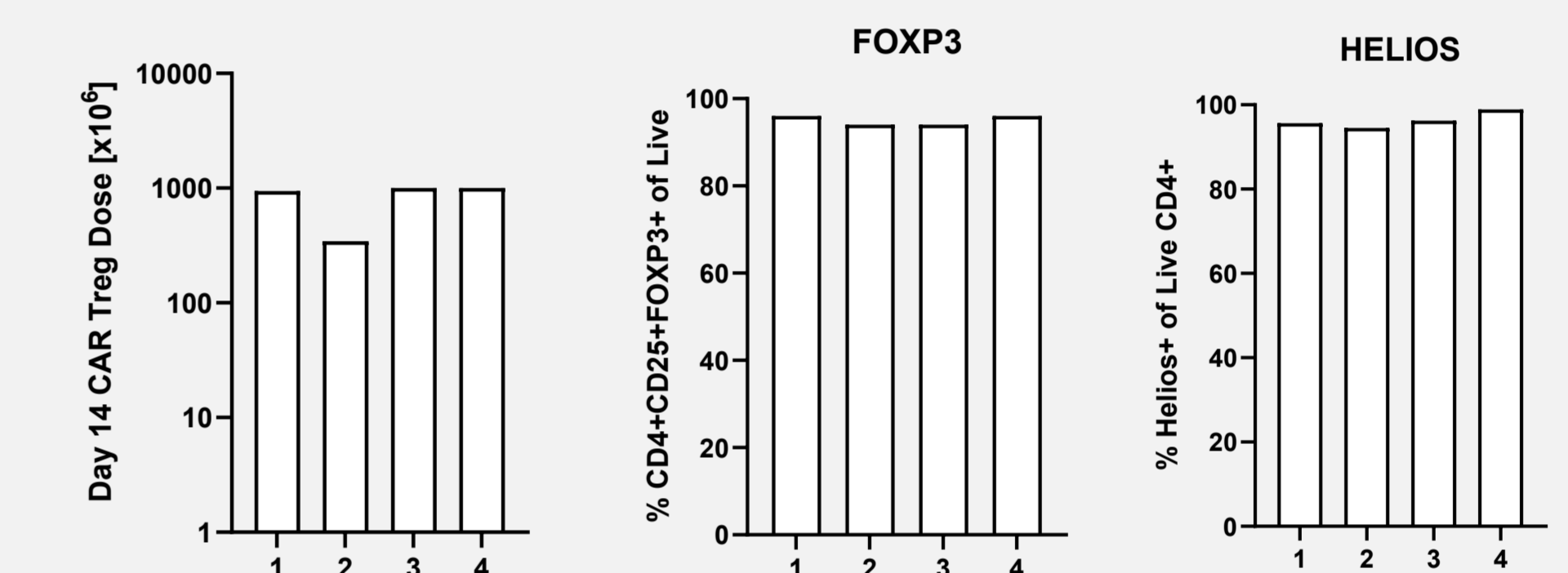


GMP readiness

Patient Material at Manufacturing Scale



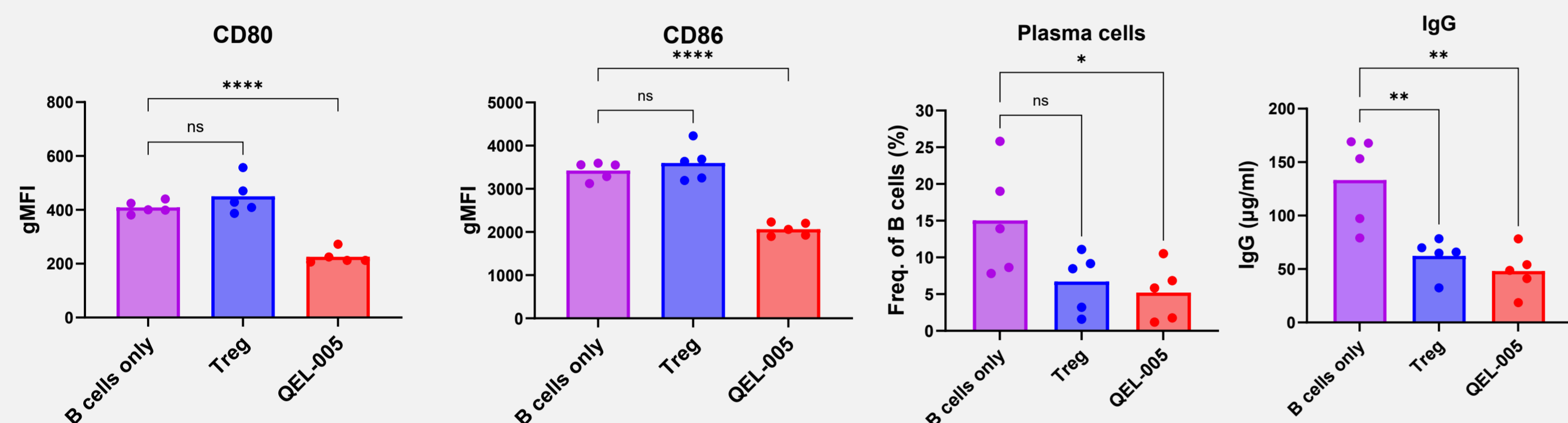
GMP Manufacturing Runs



QEL-005 Tregs: Broad Mechanism of Action Across Pathogenic Immune Cell Types

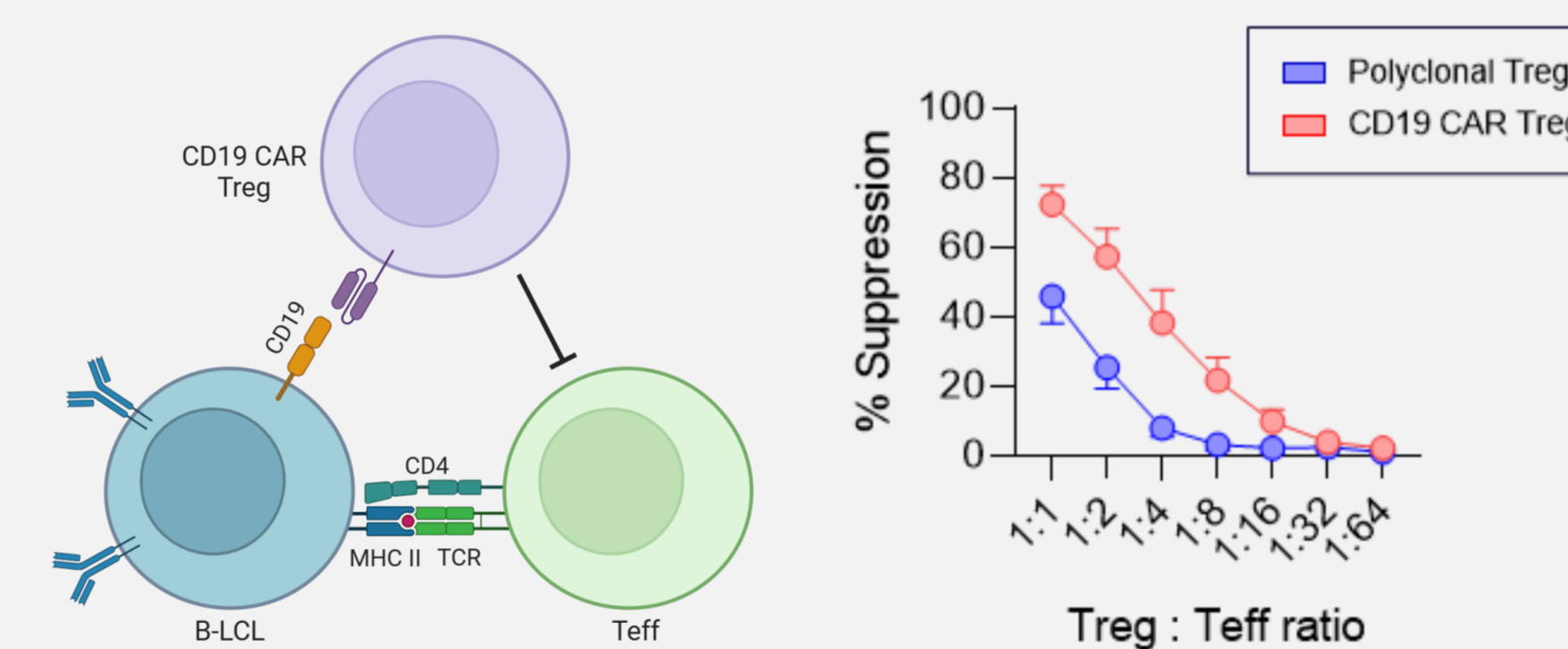
B cells

QEL-005 reduces antigen-presentation potential of B cells, reduces plasma cell differentiation and reduces IgG production



T cells

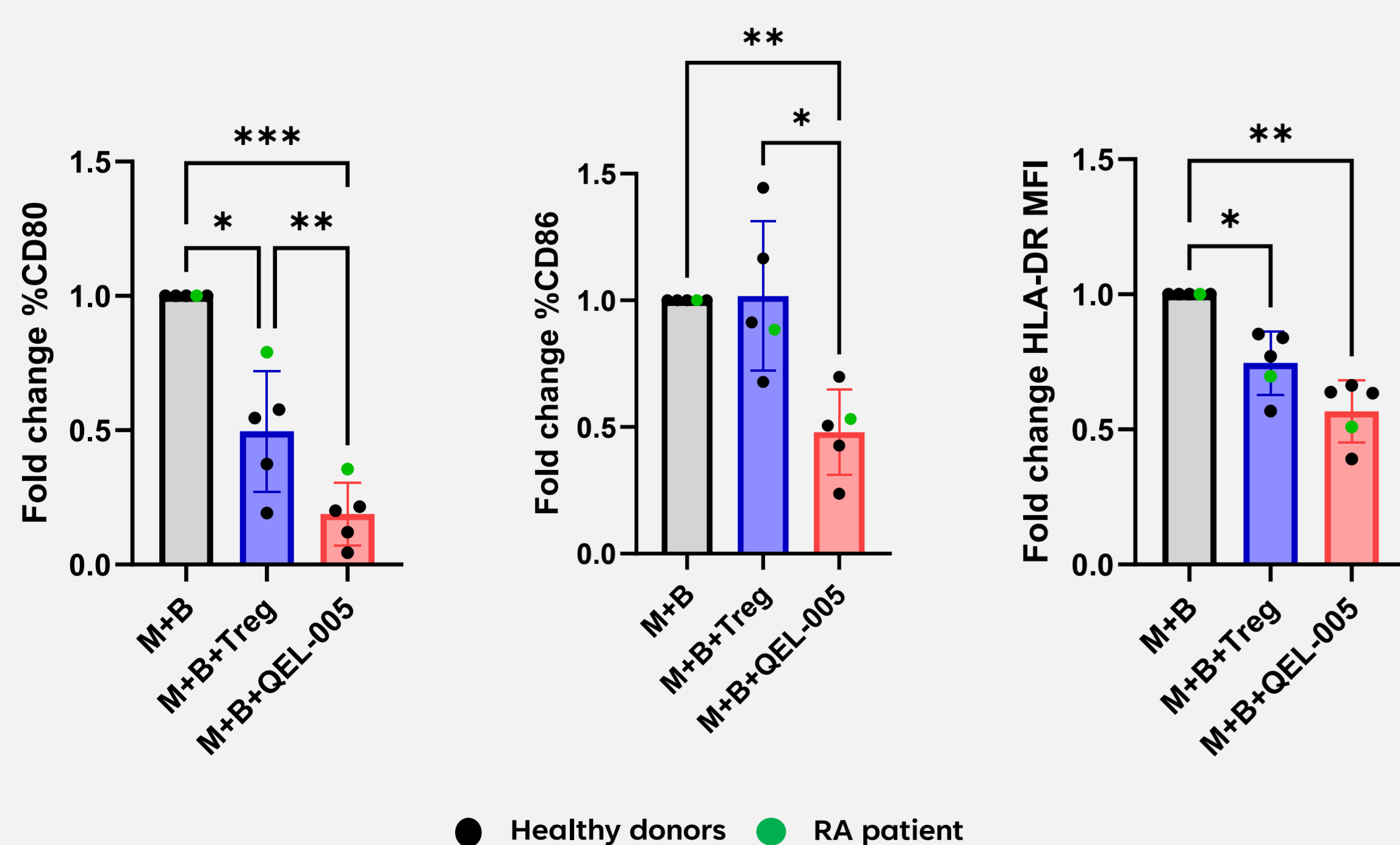
QEL-005 activation by CD19+ B cells controls T cell proliferation through bystander suppression



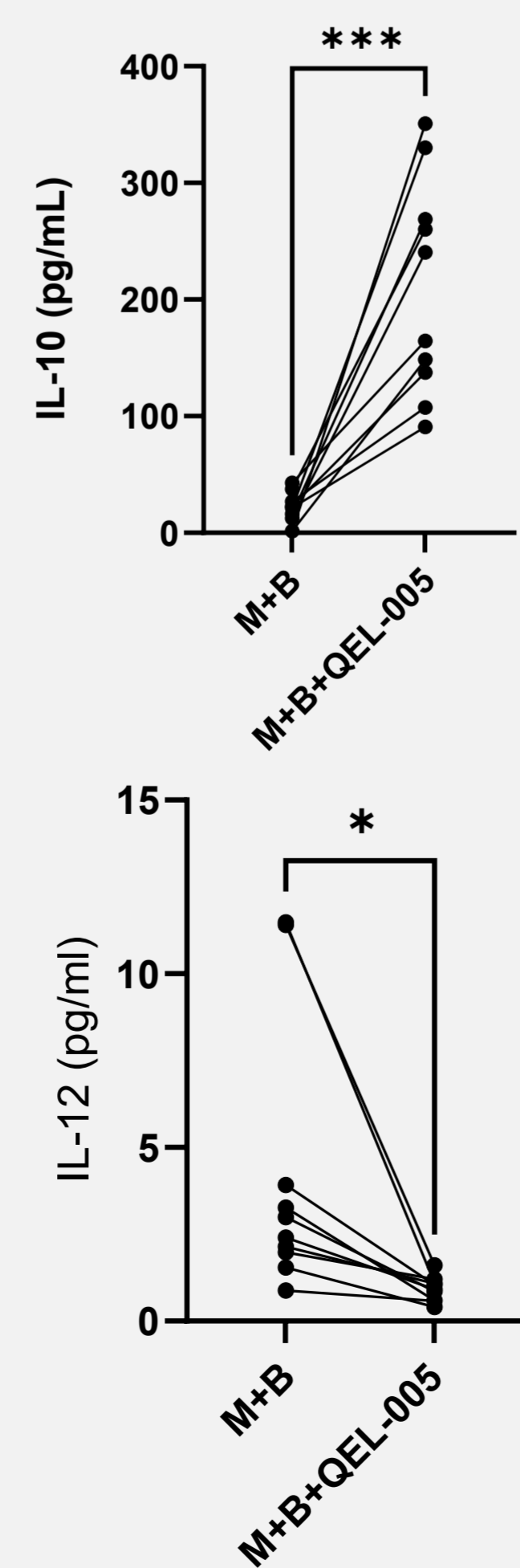
Macrophages

CD19 CAR-Tregs modulate the phenotype of fully differentiated macrophages from healthy controls and RA patients towards a pro-resolving phenotype

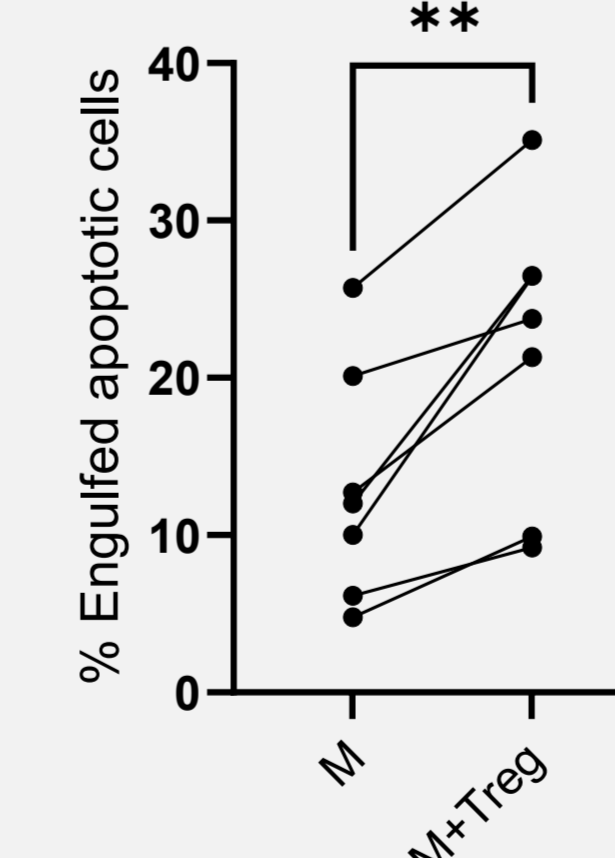
Antigen-specific regulation of macrophage phenotype



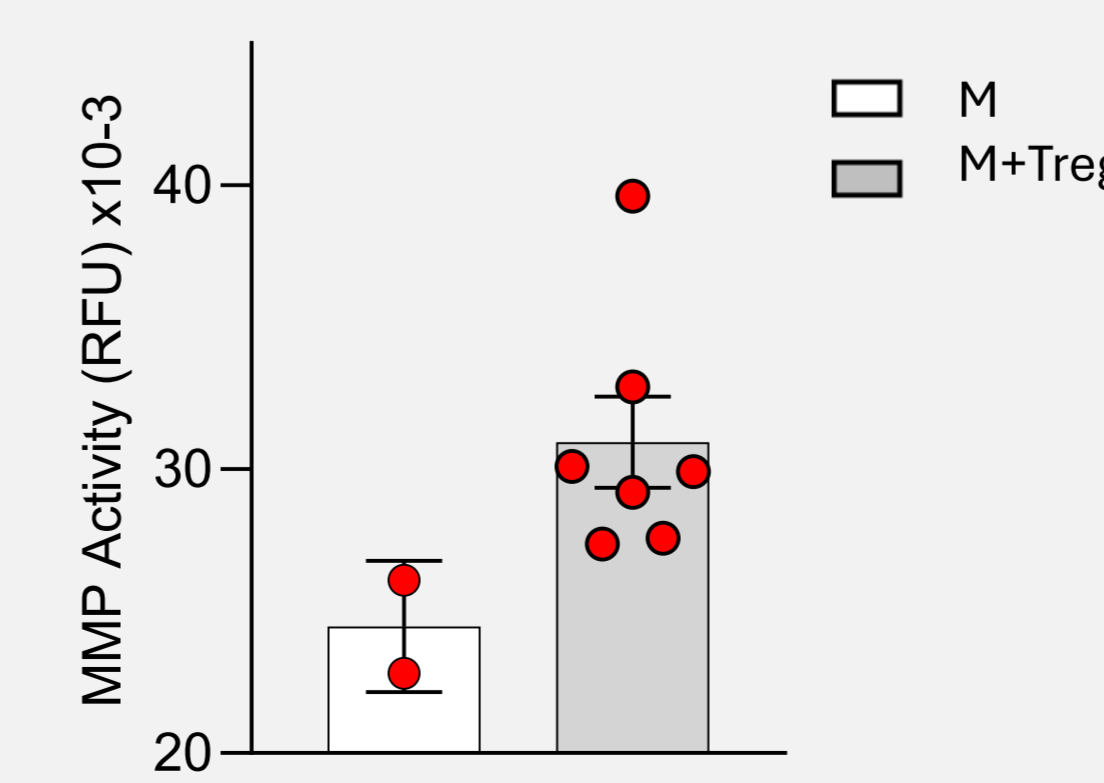
M = macrophage alone M+B = Macrophage+Bcells Treg = Polyclonal Tregs



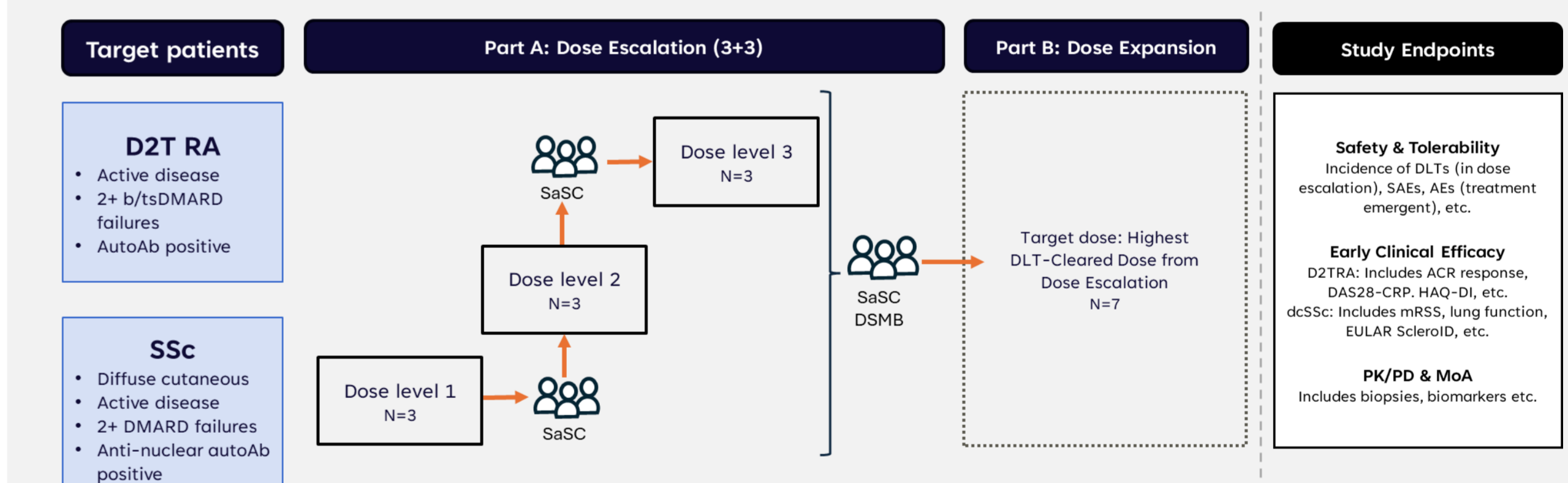
Efferocytosis



MMP activity



CHILL Trial Design



ACR = American College of Rheumatology; AEs = Adverse events; AutoAb = Autoantibody; D2TRA = Difficult-to-treat rheumatoid arthritis; DAS28-CRP = Disease Activity Score 28 C-Reactive Protein; dcSSc = Diffuse systemic sclerosis; DLT = Dose-limiting toxicity; b/tsDMARD = biologic/targeted synthetic Disease-Modifying Anti-Rheumatic Drugs; DSMB = Data Safety Monitoring Board; EULAR-ScleroID = European Alliance of Associations for Rheumatology Systemic Sclerosis Impact of Disease; HAQ-DI = Health Assessment Questionnaire Disability Index; mRSS = Modified Rodnan Score; MoA = Mechanism of Action; N = Number of Participants; PD = Pharmacokinetics; PK = Pharmacokinetics; SAEs = Serious adverse events; SaSC = Study Safety and Steering Committee.

QEL-005 Tregs have the potential to reduce chronic inflammation and restore tissue homeostasis in SSc, RA and other complex autoimmune diseases