

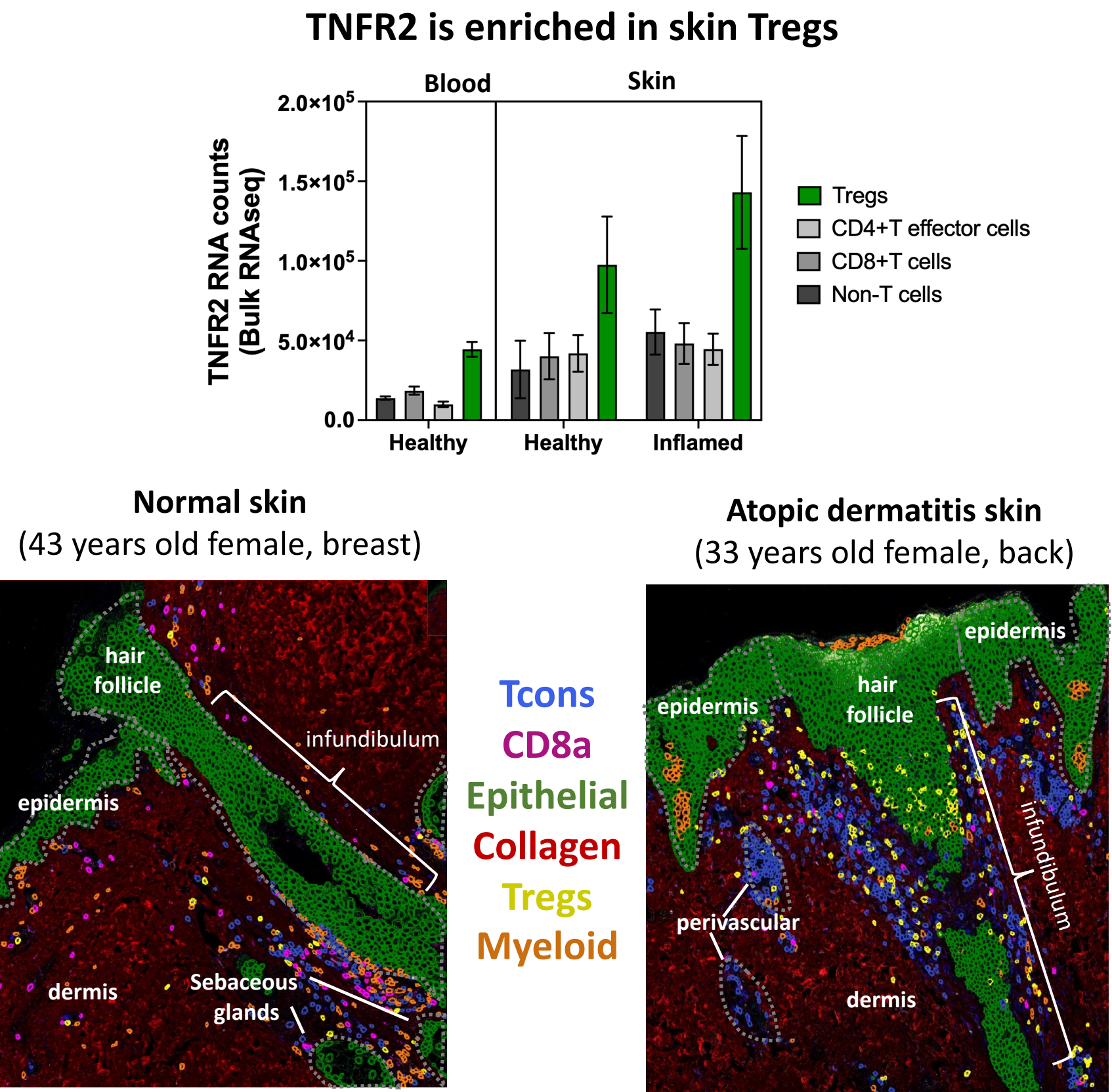


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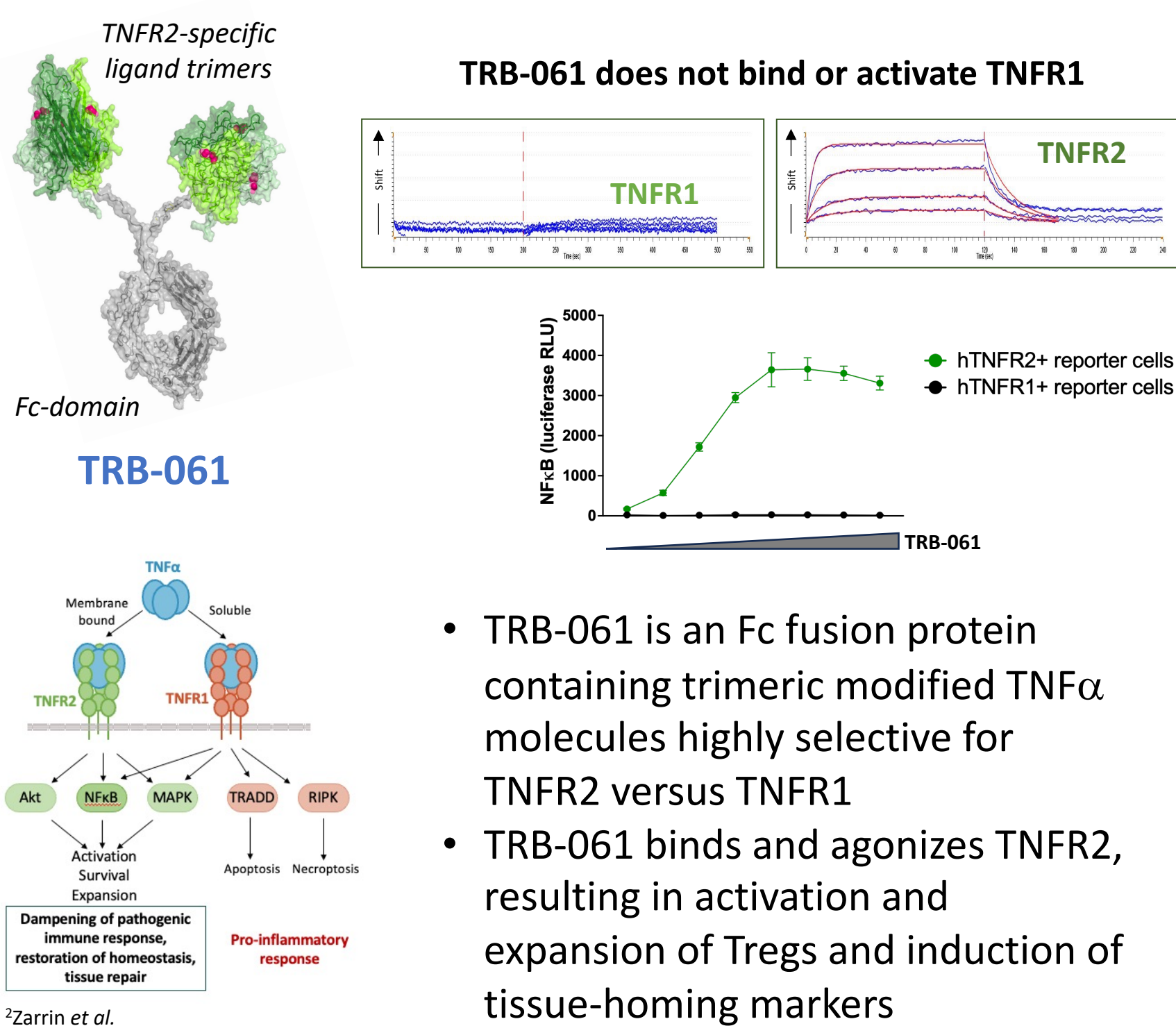
INTRODUCTION

Regulatory T cells (Tregs) play a major role in regulating immune homeostasis and epithelial repair¹. TNFR2 is a cell surface receptor enriched on tissue-localized Tregs, including in the skin. Signaling through TNFR2 activates multiple immunoregulatory pathways to control inflammation. In contrast, defects in TNFR2 impair Treg function and exacerbate inflammatory responses. TRB-061 is a novel, selective, TNFR2-agonist Fc-fusion protein designed to expand and activate TNFR2-expressing Tregs, restoring their functional capacity for the potential treatment of immune-mediated diseases. A first-in-human Ph1b clinical trial of TRB-061 in patients with AD is ongoing. Here we report results of the Ph1a SAD portion of the trial in healthy participants.

TNFR2 is enriched in skin Tregs but Treg niches and immune balance are disrupted in atopic dermatitis



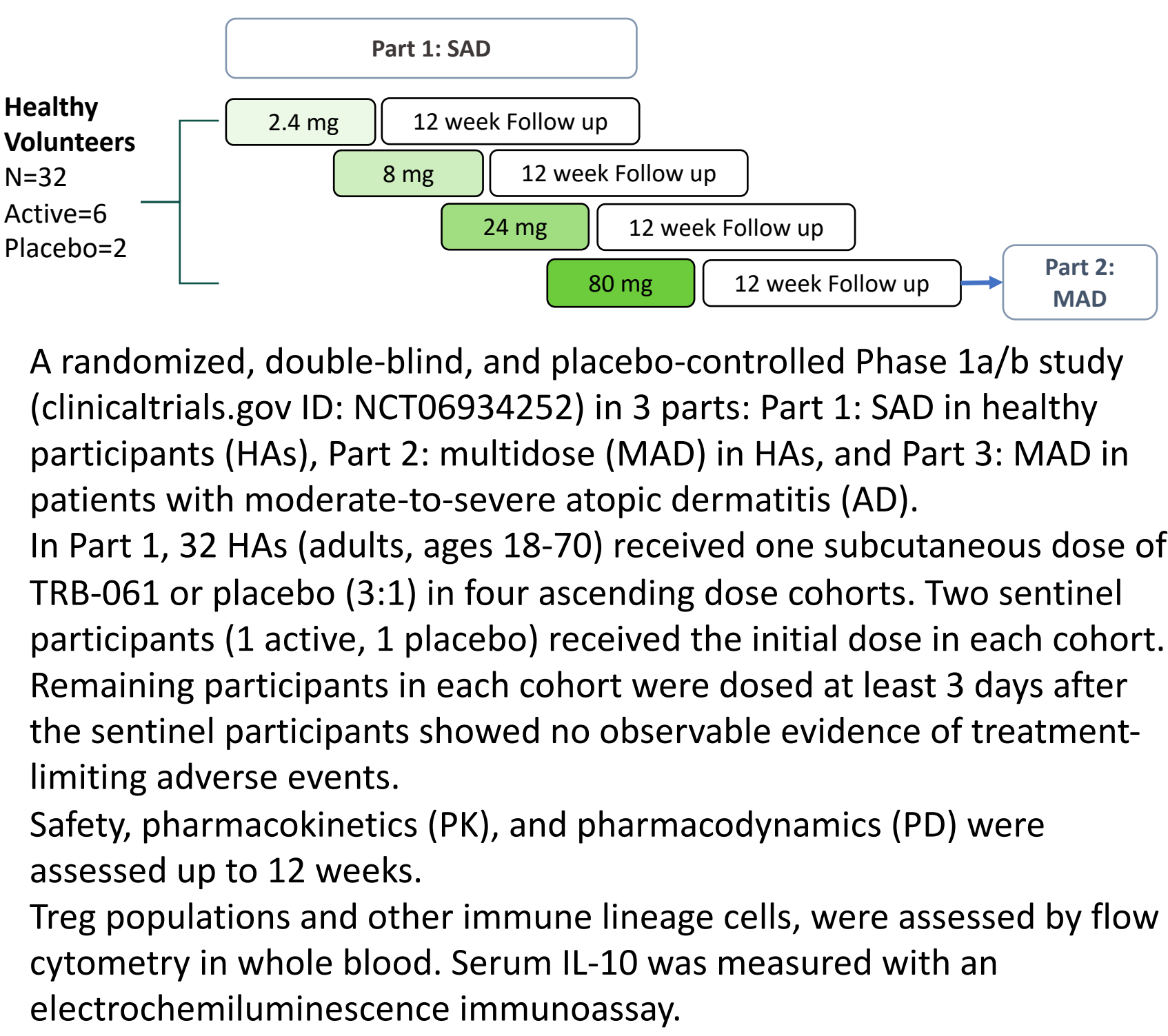
TRB-061 is designed to mimic the structure of membrane-bound TNFα to selectively bind and activate TNFR2



OBJECTIVE

Assess safety, pharmacokinetics, and pharmacodynamics of subcutaneous administration of single-ascending doses of TRB-061 in healthy adult participants

METHODS



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Selective expansion of functional Tregs and induction of clinically relevant regulatory biomarkers in Healthy Volunteers by TRB-061, a novel TNFR2 agonist in development for immune mediated diseases

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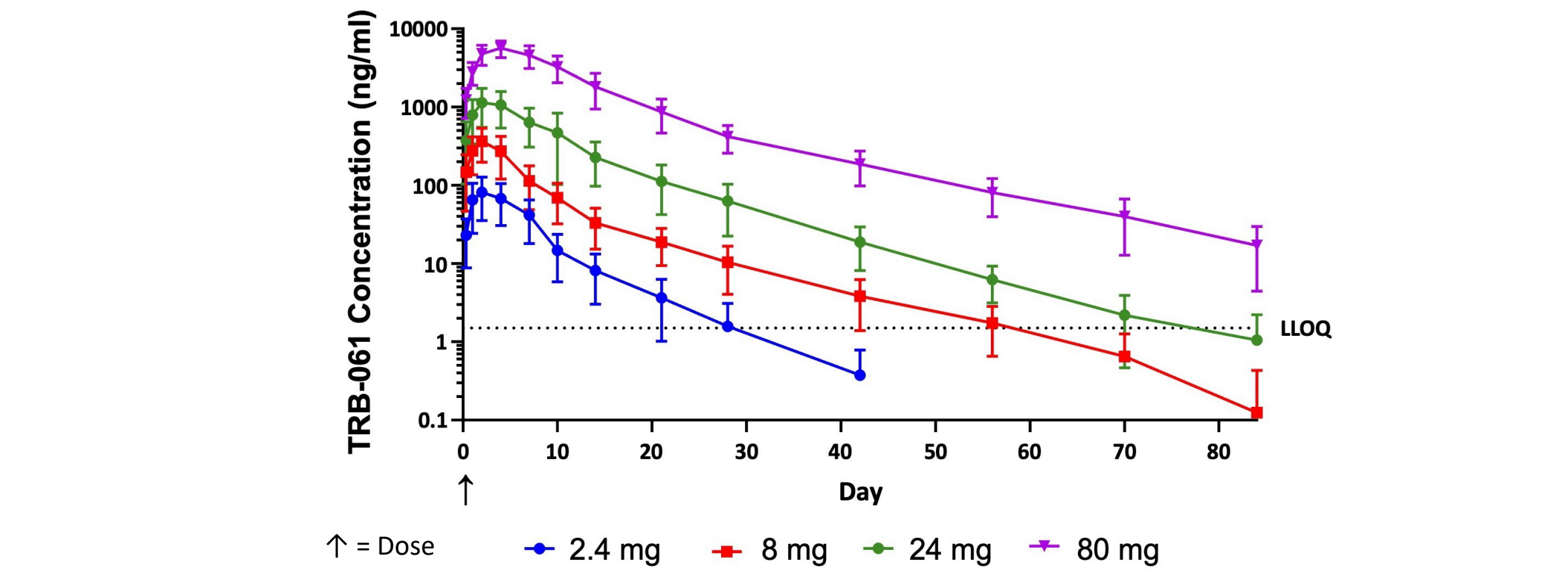
RESULTS

TRB-061 was generally well tolerated across dose levels

Treatment-Emergent Adverse Events (TEAE)	Placebo (n=8)	2.4 mg (n=6)	8 mg (n=6)	24 mg (n=6)	80 mg (n=6)
Any TEAE, n (%)	6 (75%)	5 (83%)	5 (83%)	5 (83%)	6 (100%)
Severity: Mild, n (%)	5 (63%)	4 (67%)	5 (83%)	5 (83%)	6 (100%)
Severity: Moderate, n (%)	2 (25%)	1 (17%)	1 (17%)	2 (33%)	1 (17%)
Severity: Severe, n	0	0	0	0	0
SAEs, n	0	0	0	0	0

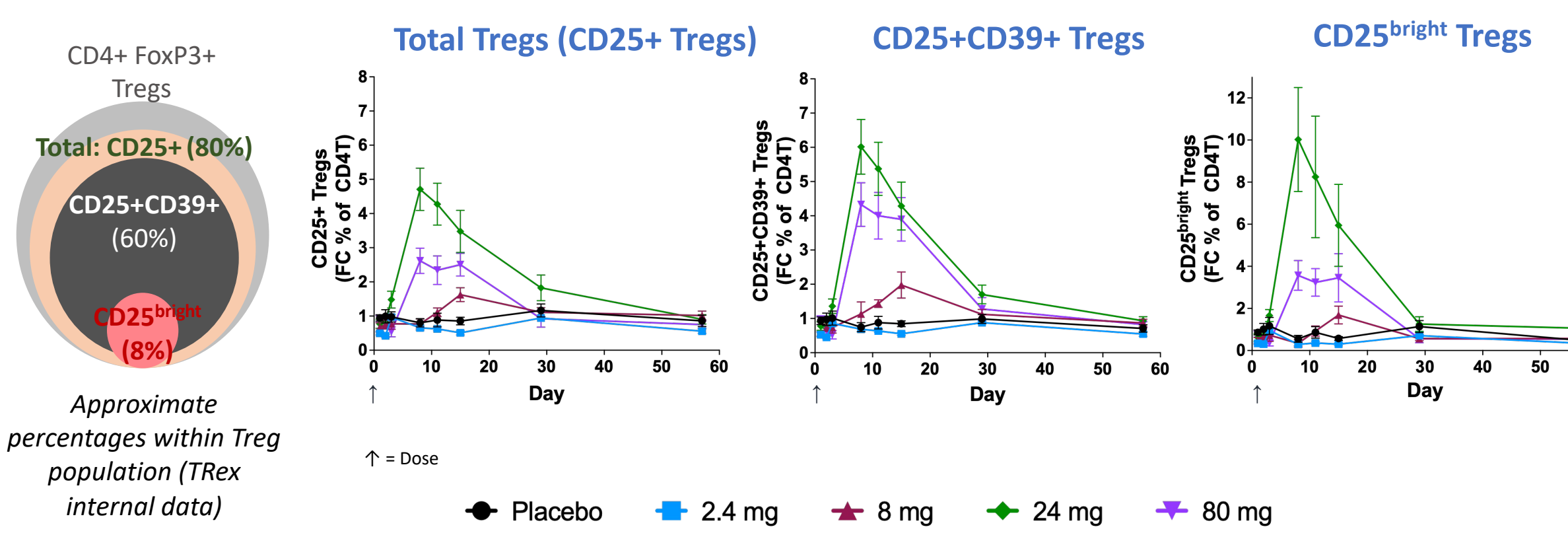
n; number of subjects
The most frequently reported TEAEs (≥ 10% of participants) included: upper respiratory tract infection, vascular access site bruising, contact dermatitis, back pain and headache

Dose proportional PK



- TRB-061 concentrations are shown over time following a single TRB-061 SC dose as mean (± standard deviation). LLOQ = lower limit of quantification
- C_{max} and AUC increased in a more than dose proportional manner, and the half-life of TRB-061 was up to 12 days.

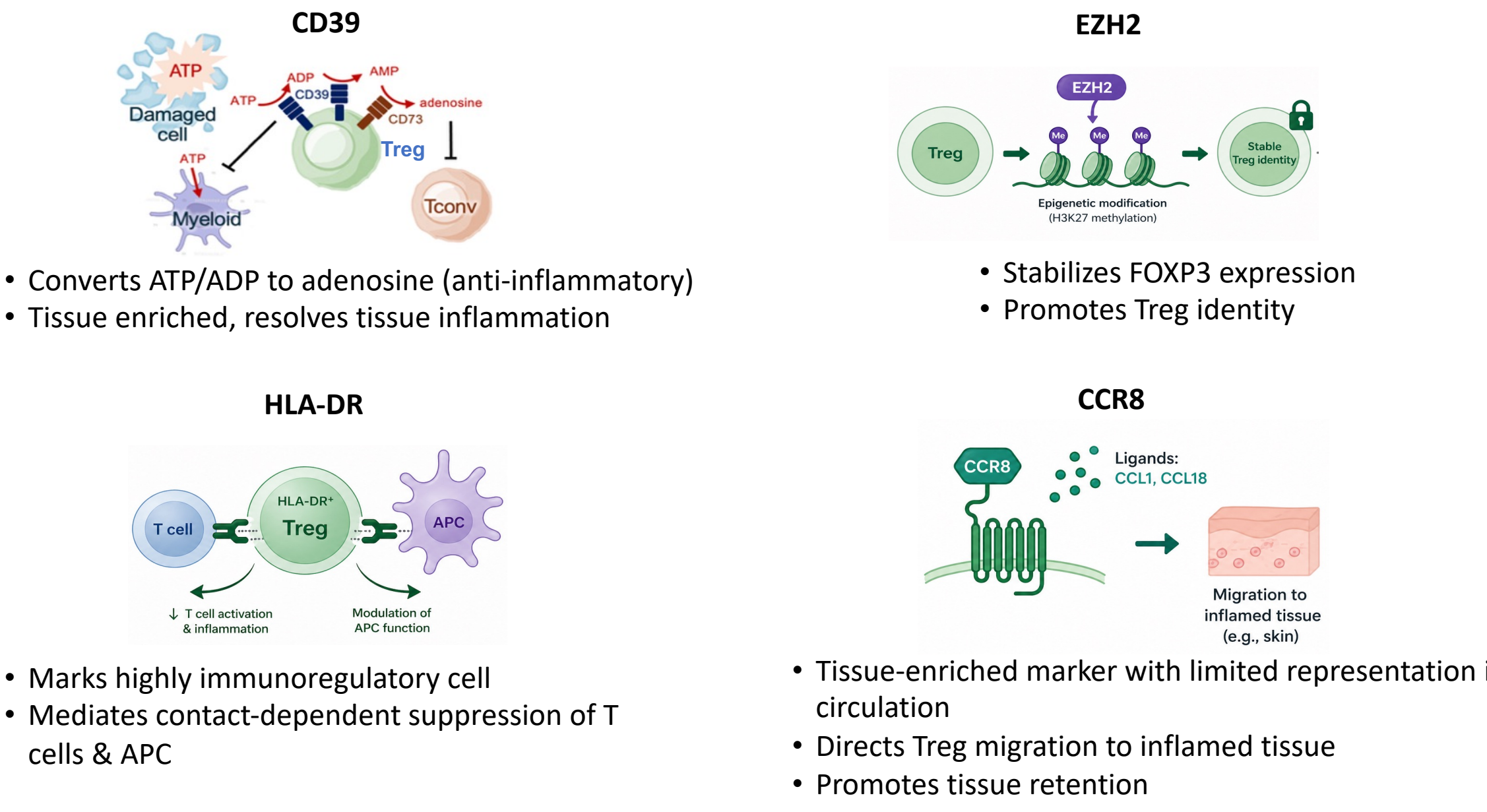
TRB-061 expanded FoxP3+ CD25+ Treg lineages



- Robust expansion of total FoxP3+CD25+ Tregs, CD39+ Tregs and CD25^{bright} Tregs was observed with Treg expansion approaching a plateau at higher doses, consistent with maximal PD activity.
- CD39+ Tregs are highly regulatory, associated with clinical remission, stable in the context of inflammation and highly enriched in the tissue^{3,4}.
- Fold changes from baseline of cell frequencies are shown as % of CD4+ T cells vs pre-dose baseline mean, and shown as mean ± SEM.

TRB-061 induced expression of activation and functional markers on total FoxP3+CD25+ Tregs

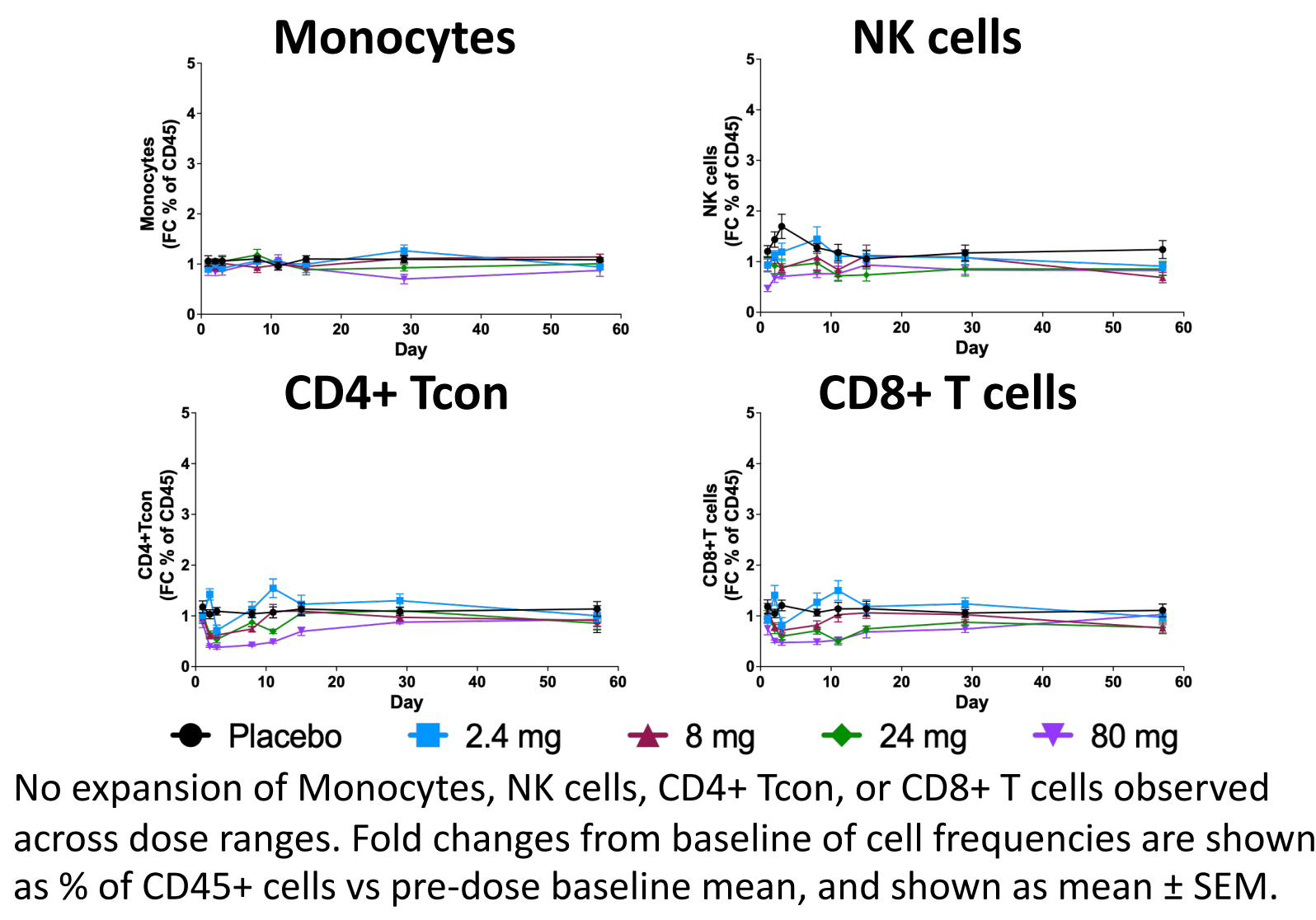
Biomarker Expression (Mean Fluorescence Intensity)	Description	Fold change from baseline
CD39	Regulatory	↑ 2-4x
EZH2	Stability	↑ 2-5x
HLA-DR	Activation	↑ 3-6x
CCR8	Tissue-homing	↑ 2-5x



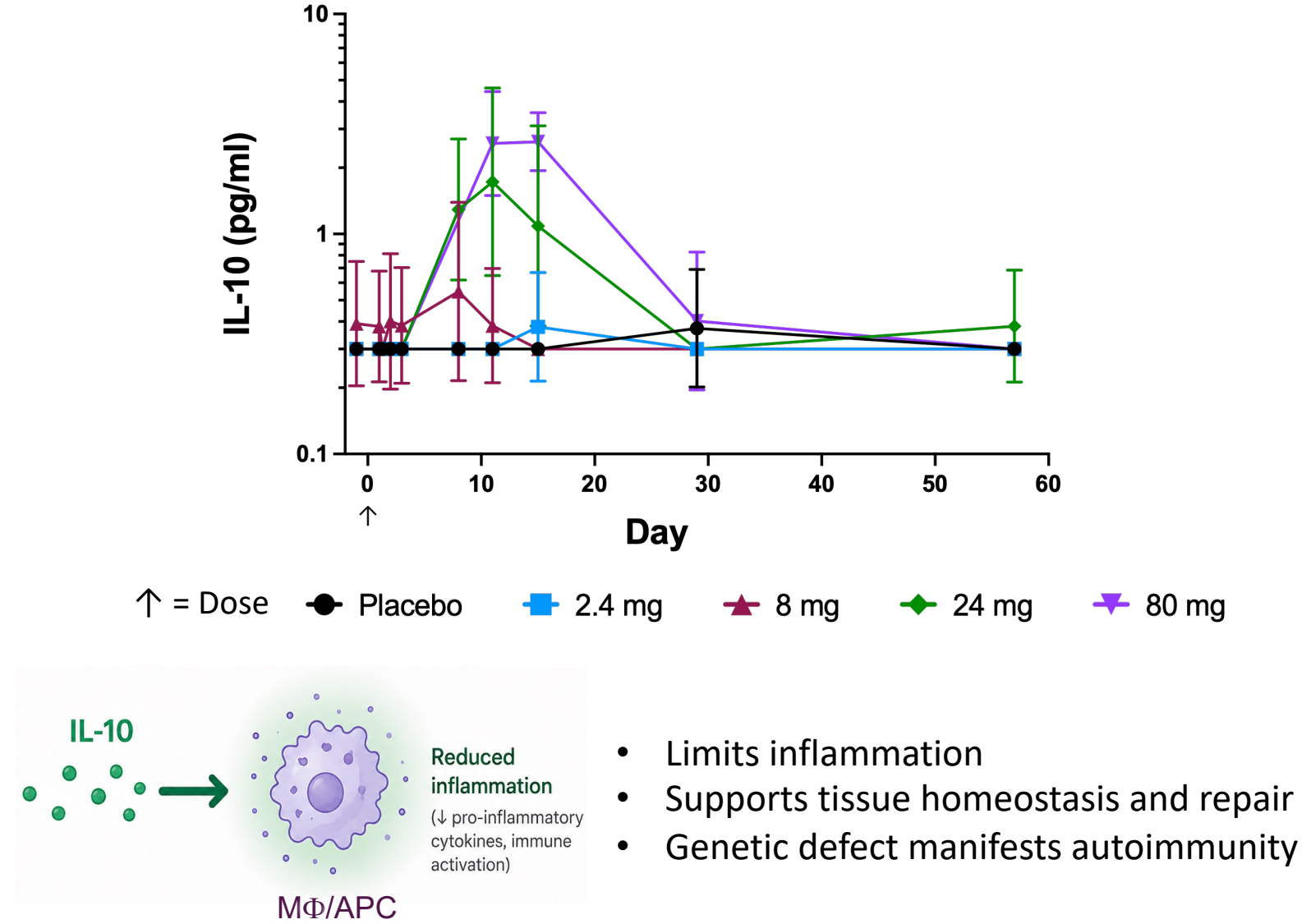
Acknowledgements: We thank Dr. Michael Rosenblum for helpful discussions during analysis of data from this study. All authors are employees of TRex Bio, Inc., South San Francisco CA, which also funded the study.

References:
1. McKay *et al.* (2026) Front. Immunol. 17:1870050. doi: 10.3389/fimmu.2026.1870050
2. Zarrin *et al.* (2021) Nat Rev Drug Disc 20:39–63. doi: 10.1038/s41573-020-0082-8
3. Gibson *et al.* (2015) Inflamm Bowel Dis 21:2806-2814. doi: 10.1097/mib.0000000000000566
4. Hamed *et al.* (2019) PLoS ONE 14(7): e0210308. doi: 10.1371/journal.pone.0210308

Treg selectivity maintained across dose range



TRB-061 induced serum IL-10 in a dose dependent manner



DISCUSSION

- The coordinated expansion of multiple FOXP3+ Treg populations suggests that TRB-061 augments the Treg compartment broadly.
- The apparent plateau in Treg expansion at higher doses may indicate that substantial pharmacodynamic activity is achieved within the tested dose range and informed dose selection for follow up MAD studies.
- Increased CD39, HLA-DR, EZH2, CCR8, and serum IL-10 suggest that TRB-061 enhances attributes associated with regulatory function, activation, stability, and tissue homing.
- The lack of expansion of major non-Treg immune lineages distinguishes the pharmacology from approaches that can simultaneously stimulate regulatory and effector immune compartments.

CONCLUSIONS

- TRB-061 was generally well tolerated in healthy volunteers.
- PK supports low volume SC dosing in early clinical trials
- Robust and selective Treg expansion was observed across multiple Treg populations, including total CD25+ Tregs, CD25+CD39+ Tregs, and CD25^{bright} Tregs.
- TRB-061 enhances multiple complementary features of Treg biology, including regulatory function and activation (HLADR, CD39, IL10), stability (EZH2), and tissue homing (CCR8).
- Sustained PD activity supports the potential for durable immune regulation beyond expansion of Tregs
- Together, these first-in-human data demonstrating coordinated pharmacodynamic effects establish clinical proof of mechanism of TRB-061 and supports its potential as a broadly applicable and differentiated Treg-directed therapy across multiple immune mediated diseases.
- A study in patients with moderate to severe AD is ongoing.

TRB-061 proposed MOA: Drive Treg-mediated immune regulation and tissue repair upstream of multiple inflammatory pathways in AD

