



Mechanism of Action of a Fully Human Anti-Thymocyte Globulin, SAB-142, for the Treatment of Type 1 Diabetes

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September 18, 2025



Forward-Looking Statements

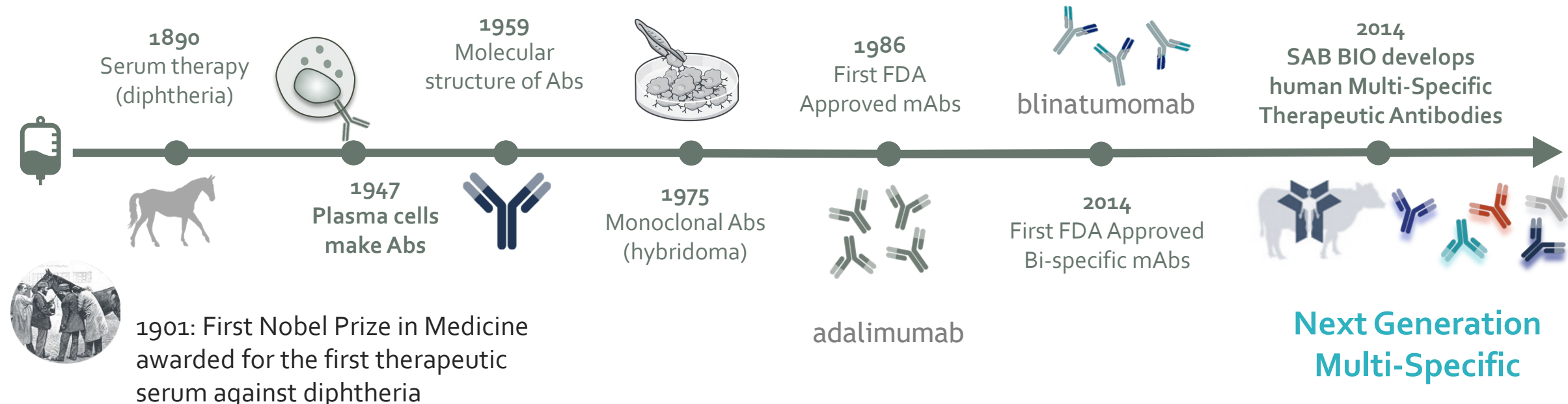
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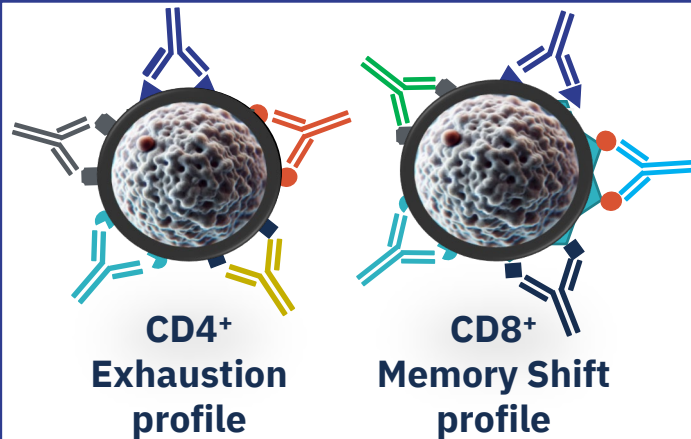
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Multi-Specifics: The Next Generation of Therapeutic Antibodies

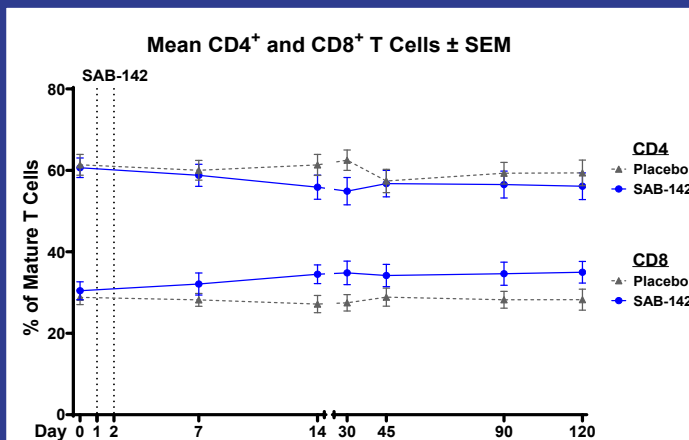


Multi-Specific Animal pAbs	Single & Bi-Specific mAbs	Multi-Specific Human pAbs
<ul style="list-style-type: none"> Multi-Specific Targets Causes Serum Sickness Single Dose Only 	<ul style="list-style-type: none"> Limited to Single or Dual Epitope Targeting Risk of escape mutations 	<ul style="list-style-type: none"> Multi-Specific Abs Multi-Epitope Targeting No Serum Sickness Repeat Dosing Possible

SAB-142 is a Fully Human, Multi-Specific, Targeted Anti-Thymocyte Globulin (hATG) for Delaying Onset and Progression of T1D



Mechanism of action (MOA) indicates **“exhaustion”** and **“memory shift”** profiles across multiple T-cells, strongly correlated with C-peptide preservation in rATG clinical studies



SAB-142 is positioned for safe and reliable re-dosing due to **no sustained lymphodepletion, no serum sickness and no/low immunogenicity**

✓ **Target dosing over 2 days vs. 12-14 days with teplizumab**

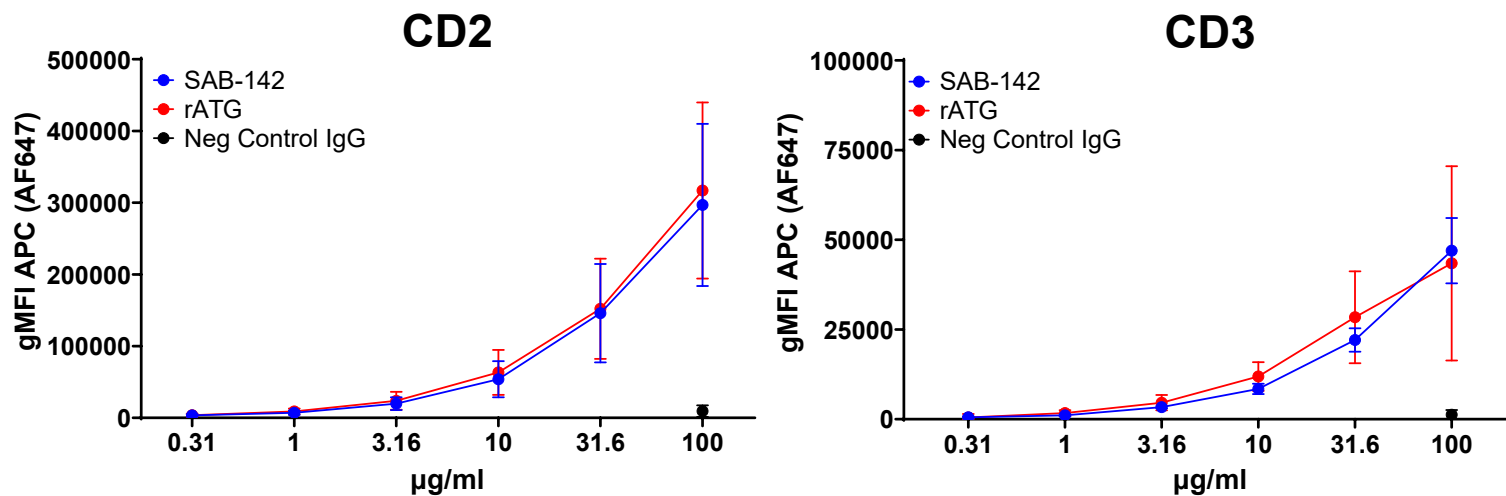
SAB-142 has a **competitive dosing regimen** in ambulatory setting

SAB-142

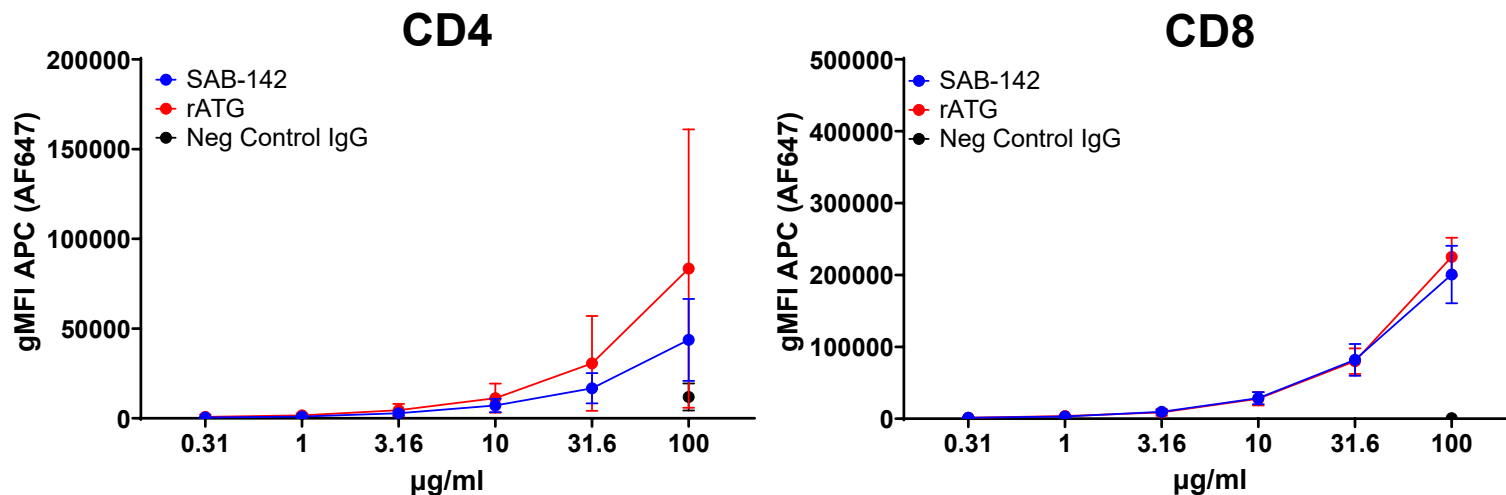
Pre-clinical data

SAB-142 binds to CD2, CD3, CD4, and CD8 receptor surface markers similar to rATG

SAB-142 binds to the same receptors as rATG



Binding of Directly Labeled SAB-142 and rATG to CD2, CD3, CD4 and CD8 Cell Lines



Data generated by Judith Leitner from the laboratory of Peter Steinberger lab based on published methodology.

American Journal of Transplantation 2013; 13: 3103-3113
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doi: 10.1111/ajt.12514

A Comprehensive and Quantitative Analysis of the Major Specificities in Rabbit Antithymocyte Globulin Preparations



CENTER FOR PATHOPHYSIOLOGY,
INFECTIOLOGY AND IMMUNOLOGY
MEDICAL UNIVERSITY OF VIENNA



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Phase 1 Study Design

Randomized, double-blind, placebo-controlled, single- and multiple ascending dose, adaptive design clinical study in healthy volunteers and patients with established T1D

Total n=68
subjects
Randomized:

HVs n=62
T1D patients n=6

Repeat dosing	n=8
4.5 mg/kg	n=8
2.5 mg/kg	N=22
1.5 mg/kg	n=8
0.5 mg/kg	n=16
0.1 mg/kg	n=8
0.03 mg/kg	n=6

SAB-142 demonstrated a multi-specific MOA clinically validated for preserving C-peptide and treating T1D



PD Highlights

Data demonstrate “MoA” signatures known to correlate with C-peptide preservation and delayed progression of T1D

- ✓ Transient cytokine increase likely activating T-cells
- ✓ Treg preservation
- ✓ Treg activation likely contributing to sustained T-cell immunomodulation
- ✓ Induced T-cell differentiation shift to a memory phenotype
- ✓ Sustained T-cell exhaustion profile

Shared MoA with effective T1D Immunomodulating drugs:
SAB-142 shares beneficial MoA signatures demonstrated for C-peptide preservation and clinical efficacy with rabbit ATG and teplizumab, both T1D T-cell targeting immunomodulatory drugs

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Phase 1 Top Line

SAB-142 CD4⁺ T conv Cell Single Exhaustion Markers

SAB-142 induced sustained expression of inhibitory receptors (PD-1 and TIGIT) on CD4⁺ T conv cells indicative of an exhausted phenotype.

SAB-142: combined 1.5 and 2.5mg/kg HV cohorts

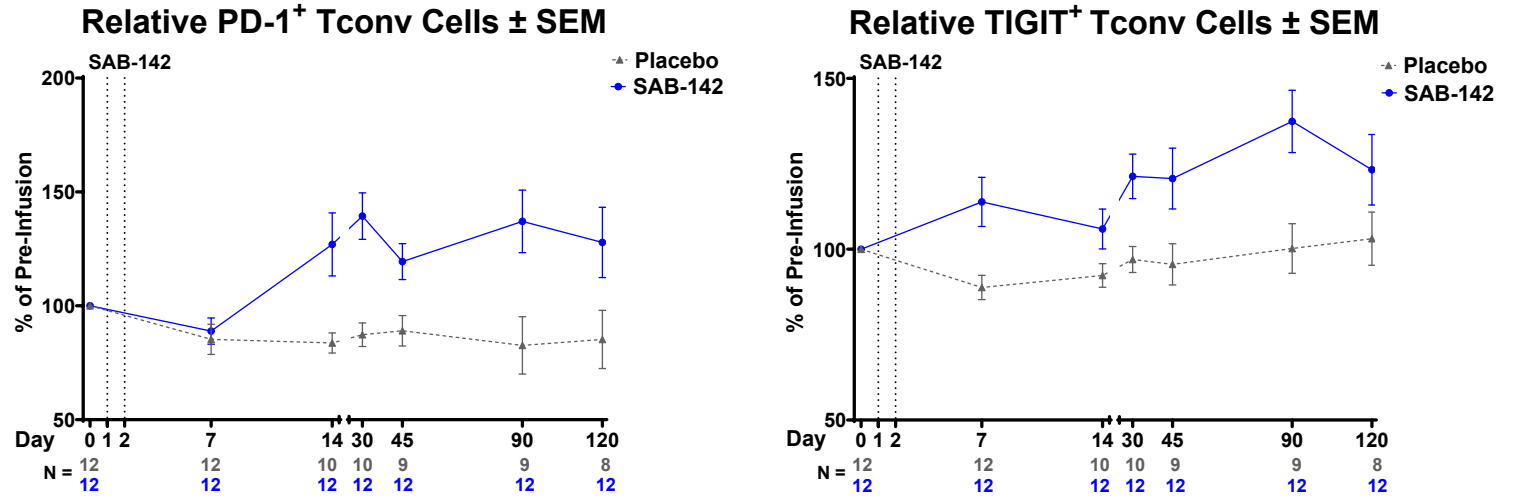
SAB-142 CD4⁺ T conv Cell Dual Exhaustion Markers

SAB-142 induced persistent expression of co-inhibitory receptors on CD4⁺ T conv cells.

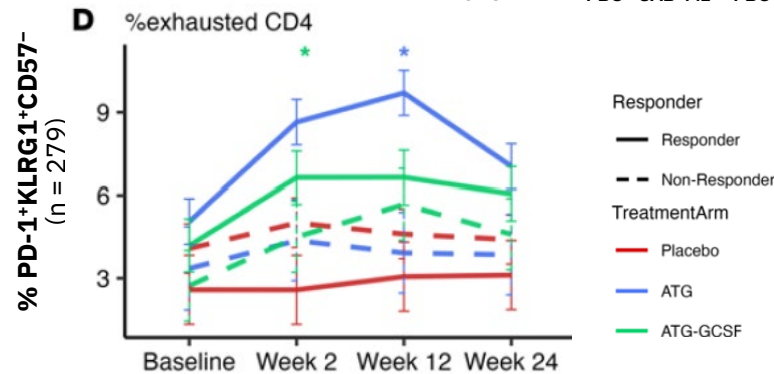
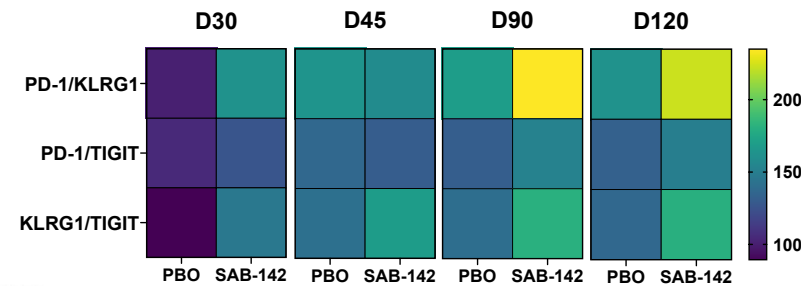
CD4⁺ Exhaustion is correlated with C-peptide preservation

Low-dose ATG induced sustained expression of co-inhibitory receptors (PD-1, KLRG1) on CD4⁺ cells indicating exhaustion-like phenotype which correlates with C-Peptide preservation.

SAB-142 demonstrates sustained CD4⁺ T conv cell exhaustion analogous to rATG



Tconv Median Percent Change from Pre-Infusion



JCI insight CLINICAL MEDICINE

Responders to low-dose ATG induce CD4⁺ T cell exhaustion in type 1 diabetes

Laura M. Jacobsen,^{1,2} Kirsten Diggins,¹ Lori Blanchfield,³ James McNichols,² Daniel J. Perry,² Jason Brant,² Xiaoru Dong,^{2,4} Rhonda Bacher,⁴ Vivian H. Gersuk,¹ Desmond A. Schatz,¹ Mark A. Atkinson,^{1,5} Clayton E. Mathews,^{1,2} Michael J. Haller,¹ S. Alice Long,¹ Peter S. Linsley,¹ and Todd M. Brusko^{1,2}

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Phase 1 Top Line

Treg preservation

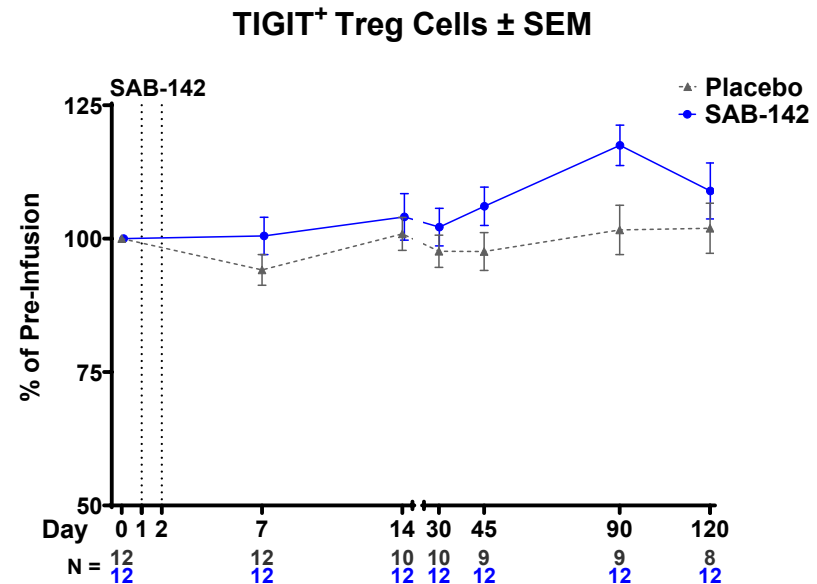
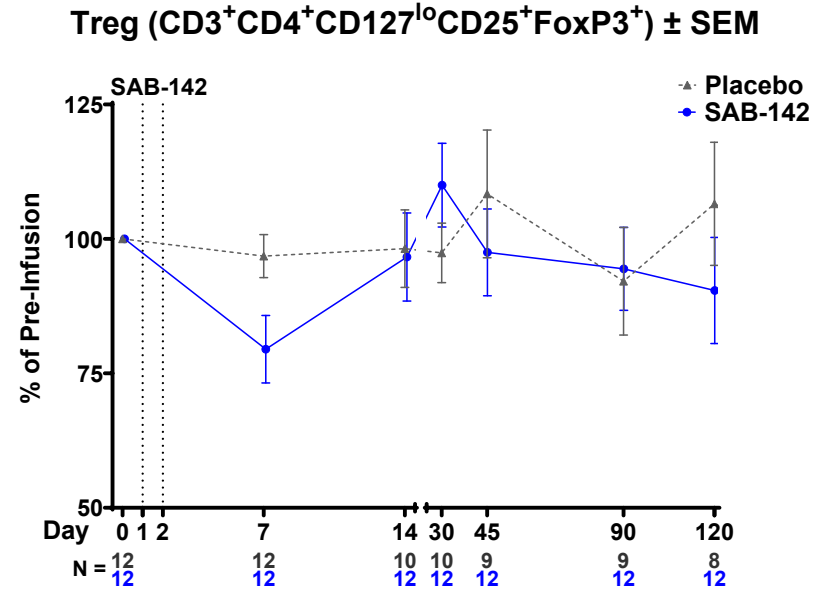
SAB-142 preserves Treg Cells maintaining regulatory immune function.

SAB-142: combined 1.5 and 2.5mg/kg HV cohorts

Treg activation

SAB-142 induced expression of inhibitory receptor (TIGIT) on Tregs indicative of potential activation possibly contributing to sustained immunomodulation.

SAB-142 Preserves and Activates T Regulatory Cells



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Phase 1 Top Line

T-cell populations stable

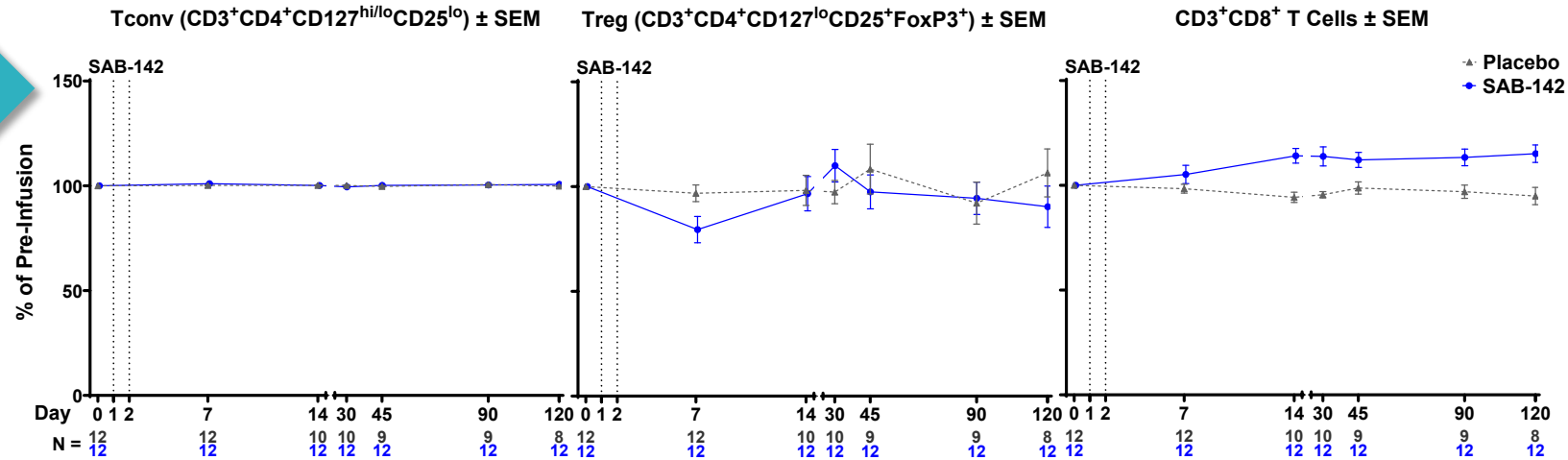
Mean subject normalized plots for CD4⁺ Tconv, Treg, and CD8⁺ T-cells indicate generally stable populations among treated subjects and a lack of depletion.

SAB-142: combined 1.5 and 2.5mg/kg HV cohorts

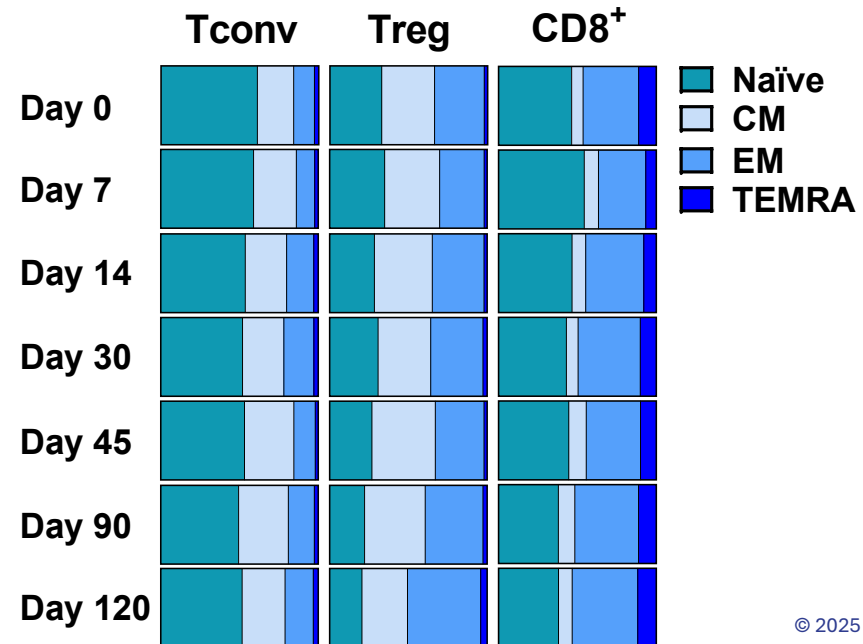
T-cells shifted to a memory phenotype

Mean frequencies for naïve, CM, EM, and TEMRA demonstrate phenotypic shifts toward various differentiated states with SAB-142 treatment in each cell type.

SAB-142 Induces Differentiation from Naïve to a Memory Phenotype

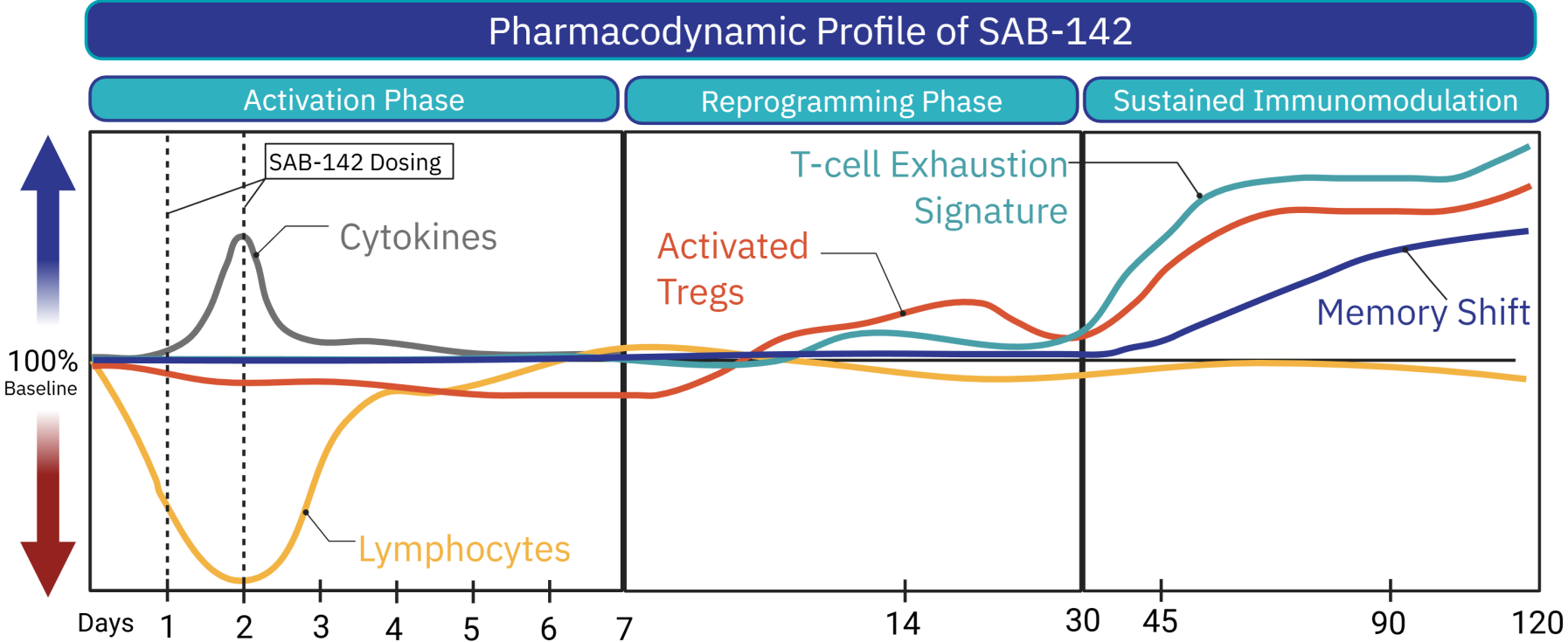


Mean T-Cell Subset Frequencies



SAB-142: The Next Generation of Beta Cell Guardians

Sustained Immunomodulation without Lymphodepletion



Mechanism of Action of SAB-142

- | | | |
|---|--|---|
| <ul style="list-style-type: none"> • Transient Cytokine Increase • Transient Lymphocyte Margination | <ul style="list-style-type: none"> • Treg preservation and activation • Initiation of Memory Phenotype Shift | <ul style="list-style-type: none"> • Sustained T-cell Exhaustion Signature • Supporting Restoration of Immune Tolerance |
|---|--|---|

SafeGUARD

SAFety and Efficacy of Human Antithymocyte ImmunoGlobUlin
SAB-142 ARresting Progression of Type 1 Diabetes



SAFEGUARD Trial has Launched

Global start-up activities are underway, with approvals already received in the U.S., Australia, and New Zealand, and submissions to the EMA and MHRA planned for September 2025.

SAB-142 Data in Depth at EASD

Thursday, Sep 18

Novel Pharmacokinetic Assay for measuring SAB-142, a fully human Anti-Thymocyte Globulin

- Session: SO 018 Clinical Tales from the T1D Trenches
- Presentation 391 | Station 03, Hall C
- 14:00 - 15:00

Specimen Quality for Multicenter Clinical Trials: Comparing Novel Blood Preservation Methods to Cryopreserved PBMC

- Session: SO 018 Clinical Tales from the T1D Trenches
- Presentation: 392 | Station 03, Hall C
- 14:00 - 15:00