SAB BIO INNOVATION DAY

ACCELERATING DISEASE-MODIFYING TREATMENTS IN AUTOIMMUNITY

(Nasdaq: SABS)

January 28, 2025

Today's Speakers

Samuel Reich

Chairman and CEO

Alexandra Kropotova, MD

Chief Medical Officer & EVP

Michael Haller, MD

Professor and Chief
Pediatric Endocrinology
University of Florida

Forward-Looking Statements

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This presentation may contain forward-looking statements including statements regarding our intent, belief, or current expectations with respect to SAB’s businesses and operations, market conditions, results of operations and financial condition, capital adequacy, specific provisions, and risk management practices. These forward-looking statements include, but are not limited to, statements regarding future events, including, the data, development, clinical results, and efficacy of our T1D program and other discovery programs. Readers are cautioned not to place undue reliance on these forward-looking statements. SAB does not undertake any obligation to update any information herein for any reason or to publicly release the result of any revisions to these forward-looking statements to reflect events or circumstances after the date hereof to reflect the occurrence of unanticipated events unless required by law. While due care has been used in the preparation of forecast information, actual results may vary in a materially positive or negative manner and the presentation may contain errors or omissions. Forecasts and hypothetical examples are subject to uncertainty and contingencies outside SAB’s control. Past performance is not a reliable indication of future performance. The forward-looking statements contained or implied in this presentation are subject to other risks and uncertainties, including those discussed under the heading "Risk Factors" in SAB’s most recent Annual Report on Form 10-K with the Securities and Exchange Commission (the “SEC”) and in other filings that SAB makes with the SEC.

Unless otherwise specified, information is current at the date hereof.

Welcome and Opening Comments

Samuel J. Reich

Chairman and Chief Executive Officer

Today’s Agenda

Opening Comments	Samuel J. Reich
SAB-142: Phase 1 Study Design and Safety Profile	Alexandra Kropotova, MD
SAB-142: PD data, Phase 2 Plan and Overview	Michael Haller, MD
Q&A	All Speakers

Michael J. Haller, MD, Pediatric Endocrinologist

Division Chief of the Pediatric Endocrinology Division at the University of Florida

Silverstein Family Eminent Scholar Chair in Pediatric Endocrinology

Dr. Haller has been involved in type 1 diabetes research since the early 1990s and has published over 200 manuscripts and more than 20 reviews/book chapters on type 1 diabetes pathogenesis, prevention, and interdiction.

He is the principal investigator or co-investigator on numerous studies funded by the NIH, Breakthrough T1D, and the Helmsley Charitable Trust. Dr. Haller's research focuses on predicting, preventing, and ultimately reversing type 1 diabetes through the use of immunotherapeutics.

Dr. Haller is the Principal Investigator of the U. Florida TrialNet Clinical Center, chairs the TEDDY Clinical Implementation Committee, and was the PI of the UF/Stanford ECHO Collaborative. He has received the Mary Tyler Moore Excellence in Clinical Research Award and the University of Florida Outstanding Clinical Research Scientist award.

Type 1 Diabetes is One of the Greatest Health Challenges of Our Lifetime

~1.4M

People with T1D cases in the US[1]

~9.4M

People with T1D globally in 2024[2]

~16.4M

People with T1D globally by 2040[2]

35 years of healthy life lost, on average, per person

1. https://www.breakthrought1d.org/explore-research/research-strategy/
2. https://www.t1dindex.org/

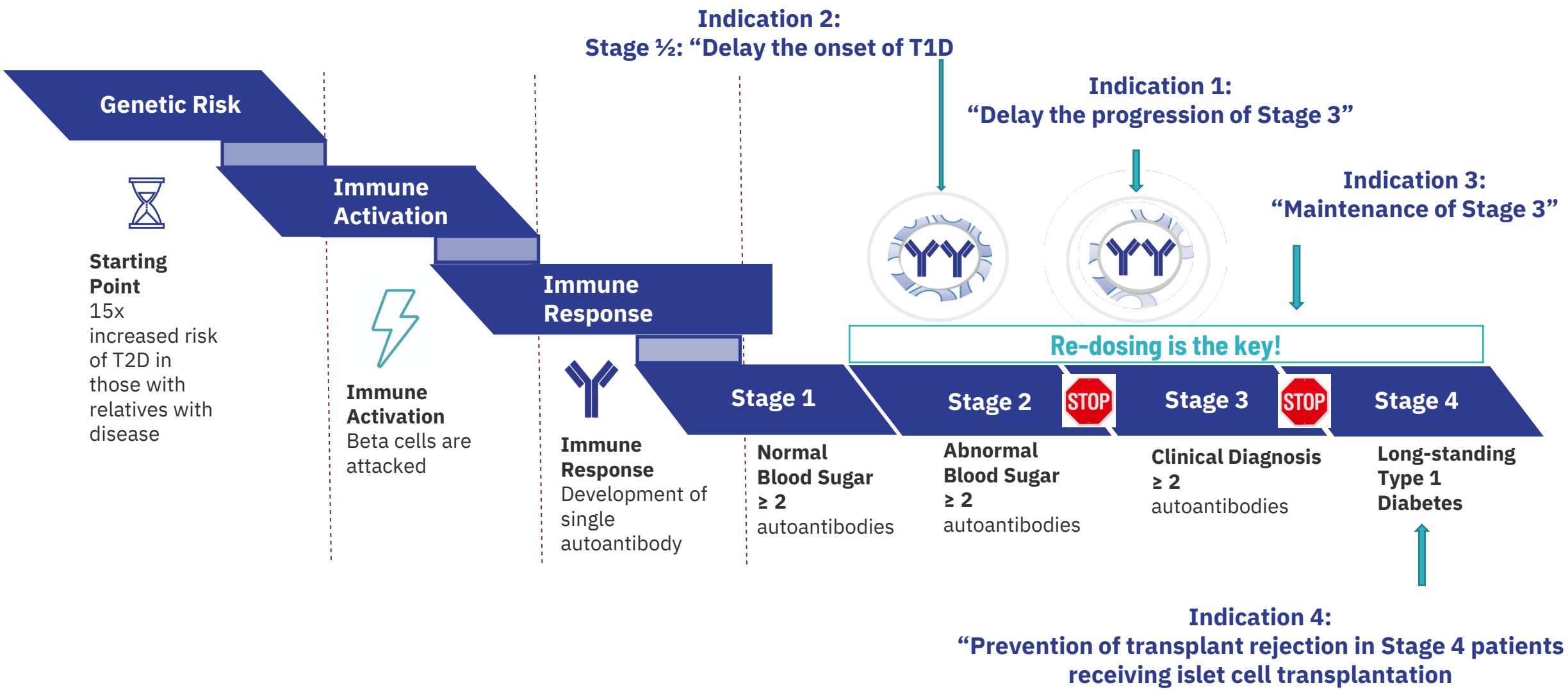
It’s time to change the story.

We can change the lives of the millions of people impacted by T1D through unique disease-modifying therapies like SAB-142.

SAB-142
Phase 1 Study Design and Safety Profile

Alexandra Kropotova, MD, MBA
Chief Medical Officer

SAB-142 has Established MOA to Potentially Control or Prevent T1D Over the Entire Life Span



SAB-142: Potential Best-In-Class T1D Immunotherapy

SAB-142 demonstrated clinically validated multi-target MOA with sustained immunomodulation in a Phase 1 trial

Phase 1 clinical data confirm SAB-142 is fully human and not immunogenic

- Doesn’t cause serum sickness
- Doesn’t cause anti-drug antibodies

Phase 1 clinical data demonstrate sustained “T-cell exhaustion” signature

- Clinically validated by rabbit ATG and other T1D immunomodulatory drugs
- Proven to correlate with C-peptide preservation

Phase 1 clinical data strongly position SAB-142 for potentially safe chronic dosing

Phase 1 topline results support advancement to Phase 2b SAFEGUARD study in adult and pediatric patients with new onset T1D

SAB-142-101 Study Design

Data generated for doses:

- 0.03, 0.1, 0.5, 1.5, and 2.5mg/kg IV

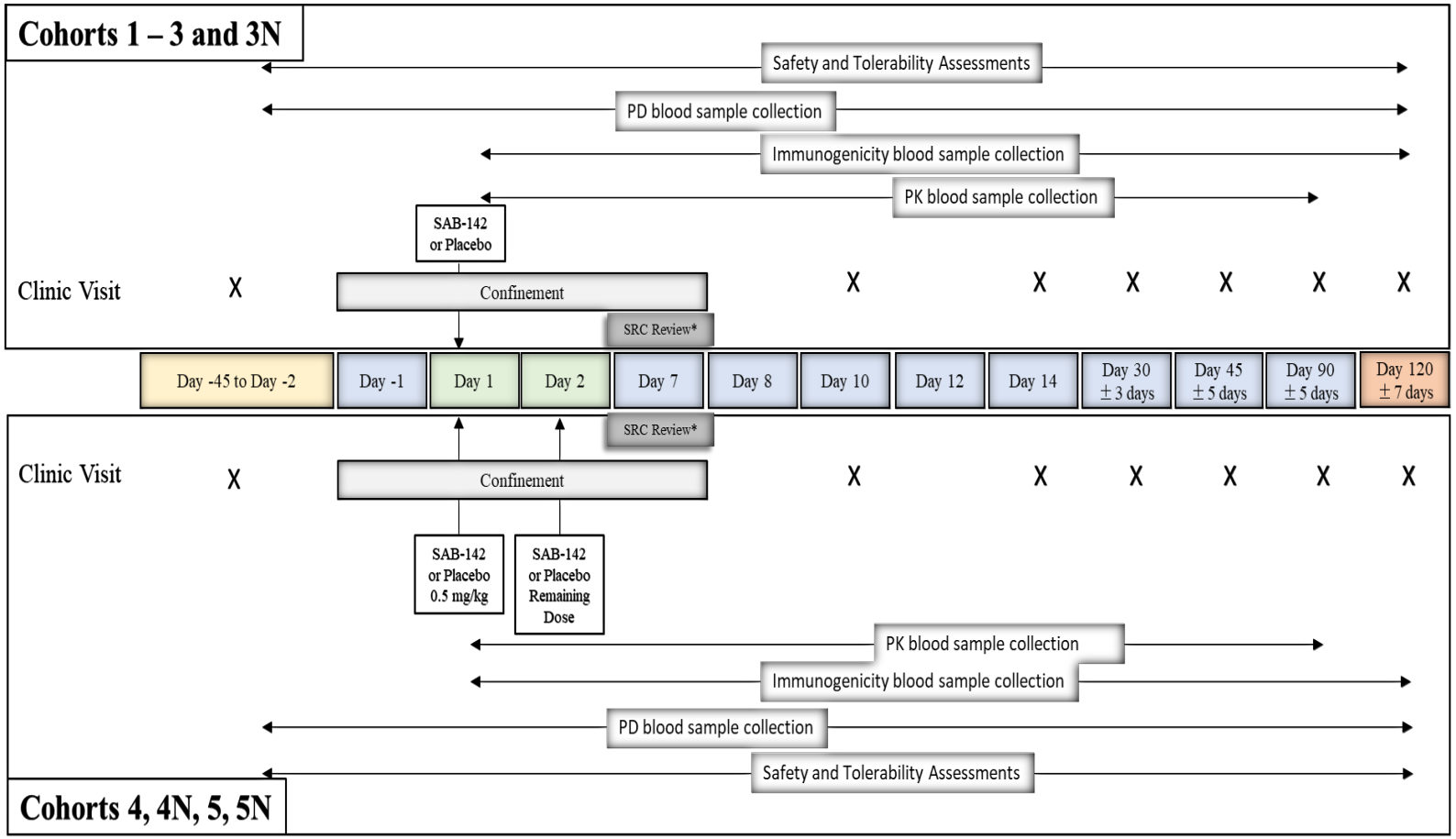
2 cohorts at 2.5mg/kg target dose
Dosing: IV infusion on Day 1 and 2

Safety & Tolerability

PK Data

Immunogenicity: ADA

Proof of Biological Activity: FACS and Cytokines



SAB-142 Safety Profile Enables Desired Ambulatory Dosing

Majority of adverse events (AEs) are mild, associated with Day 1-2 infusions and resolved by the end of the first week

Safety profile enables ambulatory dosing

- 7 Cohorts of Healthy Volunteers (HVs)
  - Total n=54, 40 HVs on SAB-142 and 14 on Placebo
- Most frequent AEs:
  - Headaches: typical for all T-cell engaging therapies, associated with Days 1-2
  - ***Transient asymptomatic lymphopenia: anticipated PD effect; rapidly self-resolves within 1-3 days**
    - **On target effect not observed past Day 8-180 (accounts for 100% Grade 4 ("Life-threatening") TEAEs by severity)**
    - **Defined as a lab value and not associated with clinical symptoms**
  - Infusion-related reactions (IRRs):
    - CRS: flu-like symptoms, Grade 1 (mild) only, Day 1-2 symptoms
    - Infusion-site reactions (ISR): erythema, tenderness, phlebitis
- No drug-related SAEs
- No serum sickness, no AEs associated with ADAs
- No decrease in RBCs, no neutropenia, no lymphopenia or thrombocytopenia from Day 7 on

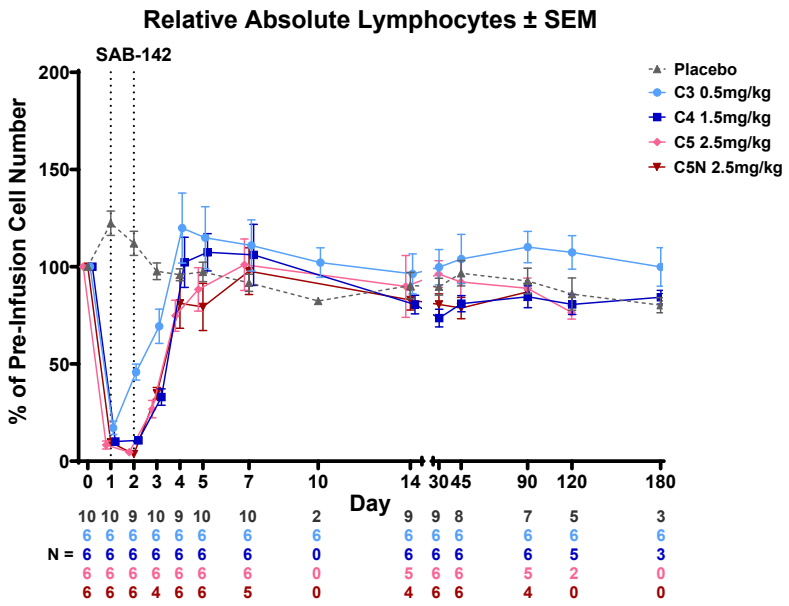
Overall summary of treatment emergent adverse events (safety analysis set)

	Day 1 to 7		Day 8-180	
Category	**Pooled Placebo HV (N=14) n (%)**	**Pooled SAB-142 HV (N=40) n (%)**	**Pooled Placebo HV (N=14) n (%)**	**Pooled SAB-142 HV (N=40) n (%)**
Number of participants with any:				
TEAEs	8 (57.1%)	36 (90.0%)	6 (42.9%)	18 (45.0%)
TEAEs by Severity:				
Grade 1	6 (42.9%)	2 (5.0%)	2 (14.3%)	13 (32.5%)
Grade 2	2 (14.3%)	3 (7.5%)	4 (28.6%)	4 (10.0%)
Grade 3	0	14 (35.0%) *	0	1 (2.5%)
Grade 4	0	17 (42.5%) *	0	0
Grade 5	0	0	0	0
Treatment-related TEAEs by Severity:				
Grade 1	3 (21.4%)	1 (2.5%)	0	4 (10.0%)
Grade 2	2 (14.3%)	3 (7.5%)	1 (7.1%)	1 (2.5%)
Grade 3	0	14 (35.0%)	0	0
Grade 4	0	17 (42.5%)	0	0
Grade 5	0	0	0	0

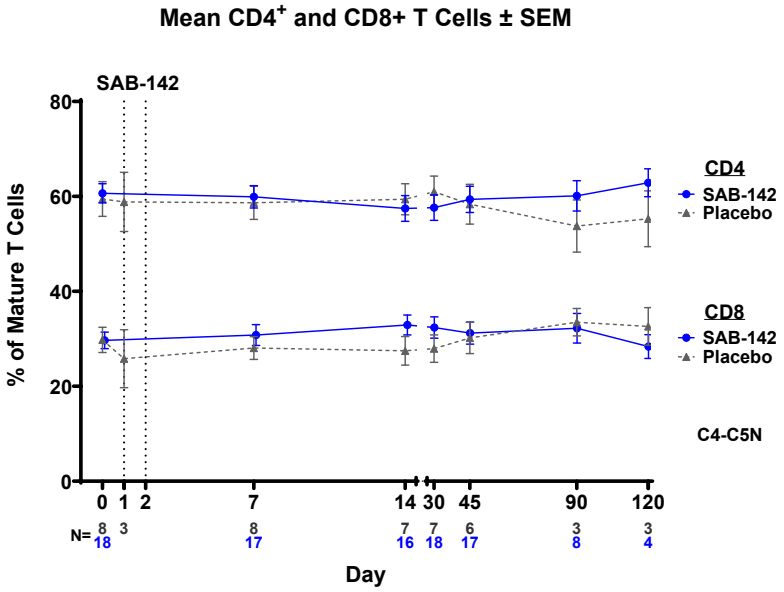
Transient asymptomatic lymphopenia: On target effect not observed past Day 8

SAB-142 Demonstrated MOA to Deliver Potentially Best-in-Class T1D Immunotherapy

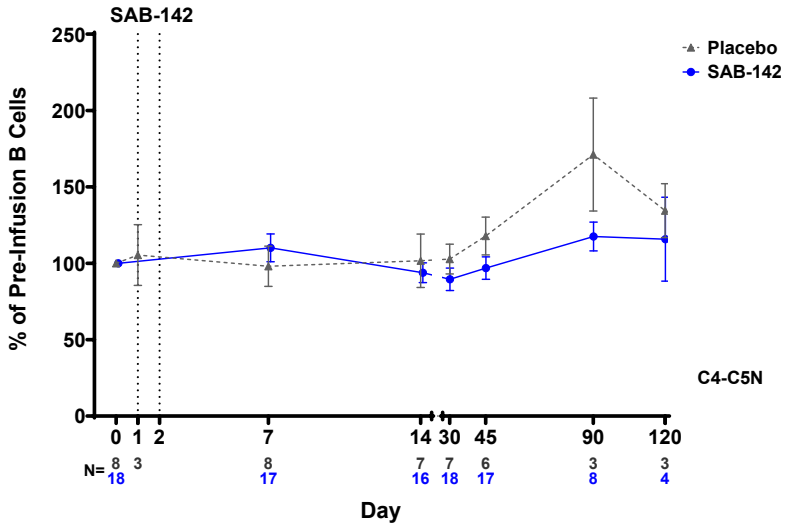
No sustained total lymphodepletion



No sustained CD4+ and CD8+ T-cell lymphodepletion



No sustained B-cell lymphodepletion

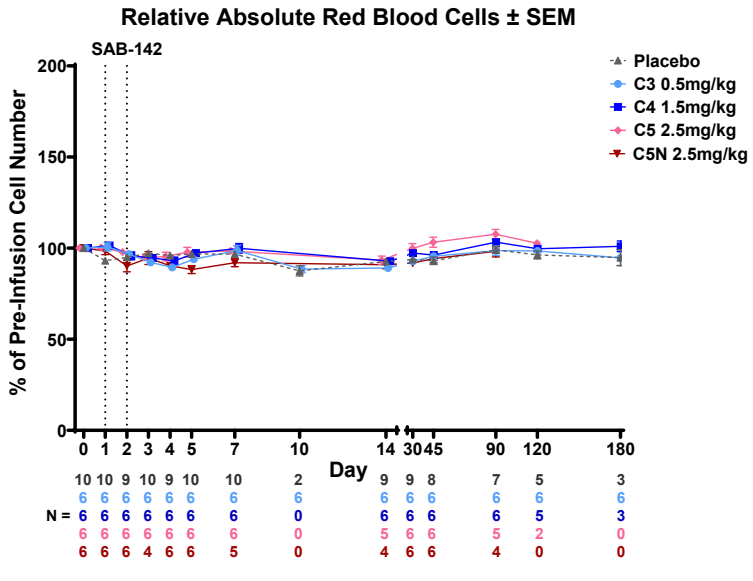


No sustained lymphodepletion

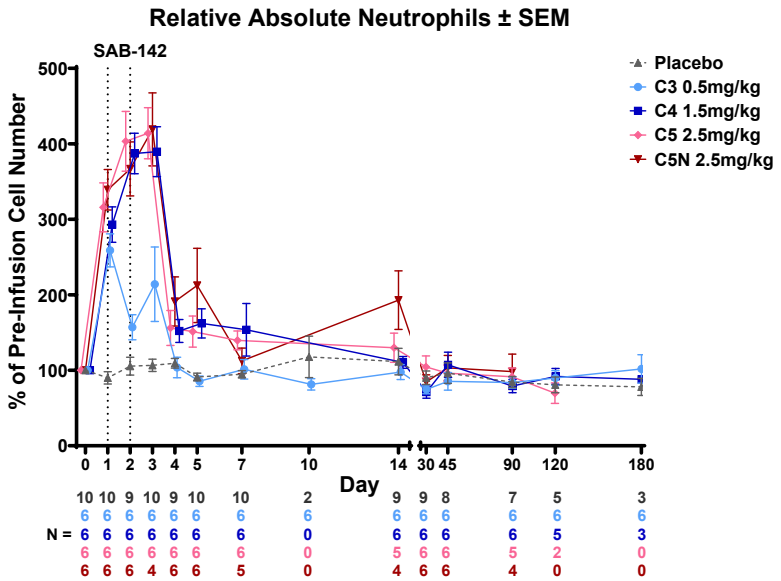
(Unlike rabbit ATG that causes decrease in CD4+ T-cells for up to 2 years)

SAB-142 Doesn't Deplete Any Cells: No Difference vs. PBO and Baseline From Day 7 Onward

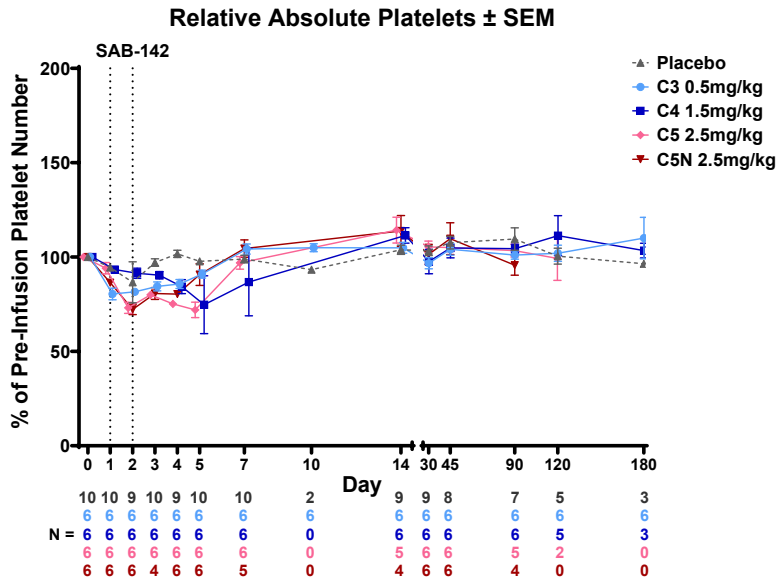
No RBC depletion



No neutropenia



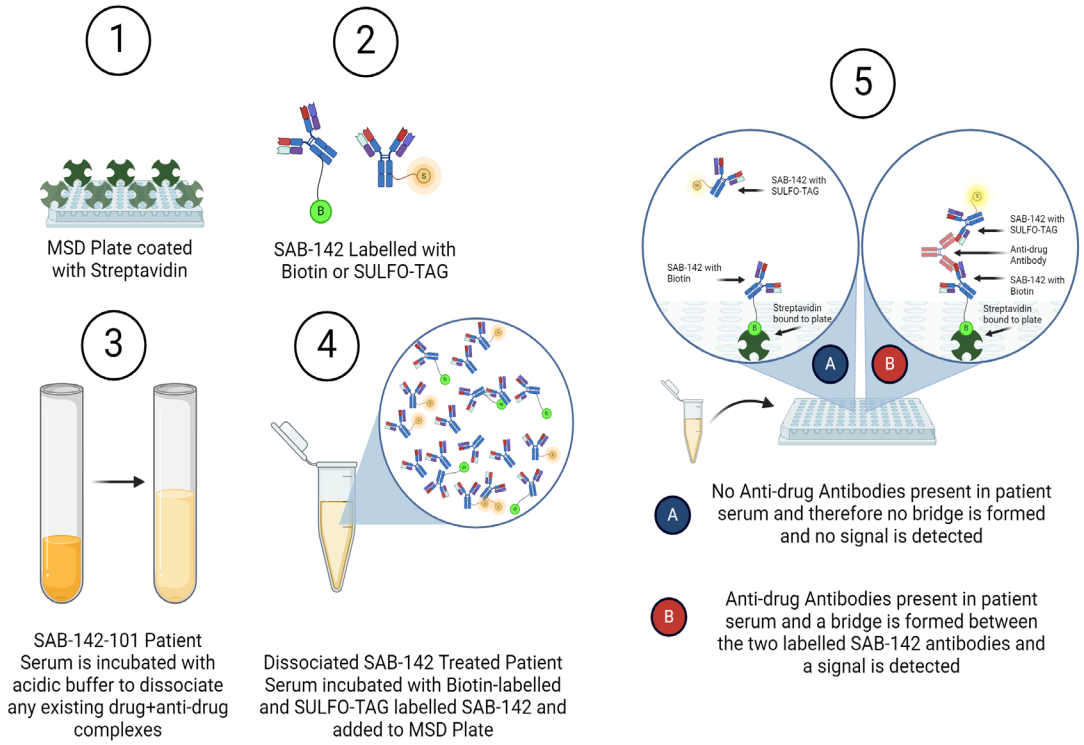
No thrombocytopenia



Sustained immunomodulation mostly through T-cell exhaustion without any sustained cell depletion

SAB-142 Shown Not to be Immunogenic

ADA Assay Design



No immunogenicity at target dose level

At the target dose (2.5mg/kg), both cohorts of SAB-142 didn't generate anti-SAB-142 antibodies in HVs

This demonstrated that SAB-142, fully human IgG pAbs, is less immunogenic than Thymoglobulin, rabbit IgG pAbs*

*MRD=1:10

CONCLUSION: Following a single IV infusion of SAB-142, there are no ADAs at target doses.

SAB-142-101 Topline Data Confirms Potential for Safe and Reliable Lifetime Dosing

No serum sickness in 100% randomized Healthy Volunteer subjects

Why is it important?

Serum sickness (SS) is a hypersensitivity reaction, a result of the formation of immune complexes between human proteins and heterologous (non-human) proteins

SS is observed in >70% adults and children treated with rATG; Grade 3-4 SS is observed in >50%; requires treatment with steroids[1]

Re-treating patients with treatments causing SS is likely to result in higher rate and severity of AEs

No ADAs in two 2.5mg/kg cohorts

Why is it important?

Biologics may trigger formation of antidrug antibodies (ADAs). ADAs may affect patient safety and treatment efficacy

Both rATG and teplizumab are highly immunogenic. 68% of patients treated with rATG develop ADA2. 57% of patients treated with teplizumab develop ADAs, 46% developed neutralizing ADAs

Re-treating patients is likely to cause increased ADA rates and impact on PK and consequently on efficacy

Topline data confirms competitive safety and advantageous immunogenicity profile

SAB-142 is a highly competitive biologic modality

01
Fully Human

Fully human biologic

Results in no serum sickness and low/no immunogenicity

+

02
Multi-target

Directly induces CD4+ and CD8+ exhaustion phenotype without lymphodepletion

High-titer, high-avidity multi-target modality directly targets multiple receptors on CD4+ and CD8+ cells

+

03
High responder rate

100% Immunological Response achieved

100% of subjects dosed with SAB-142 target dose 2.5mg/kg achieved nearly identical T-cell exhaustion profile

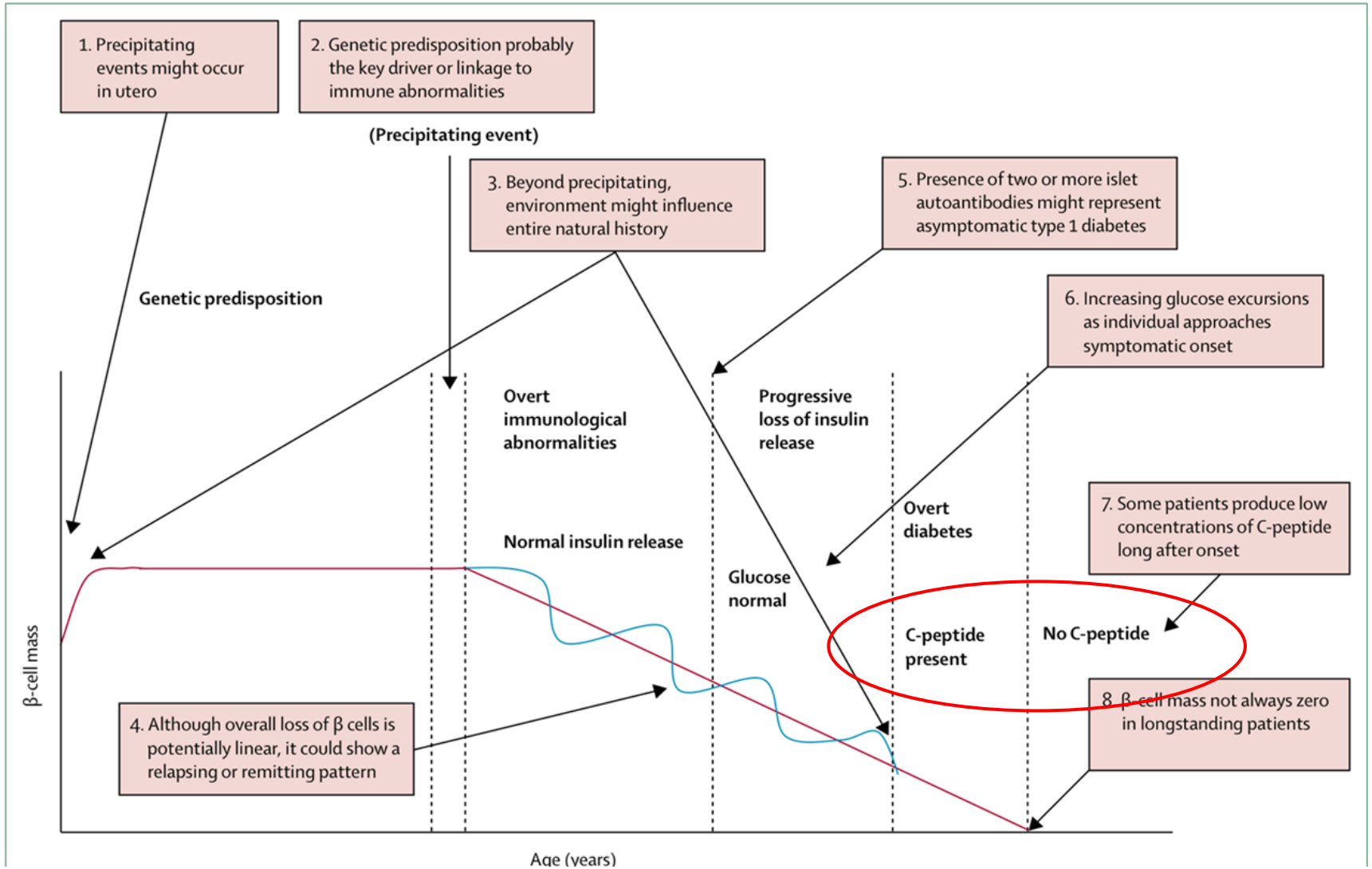
SAB-142
Overview, Phase 1 Topline Data, Phase 2 Design

Presented by:

Michael Haller, MD
Professor and Chief, Pediatric Endocrinology Silverstein Family Eminent Scholar Chair
University of Florida

SAFEGUARD Chief Investigator and Chair of the SAB-142 Advisory Board

Type 1 Diabetes Pathogenesis

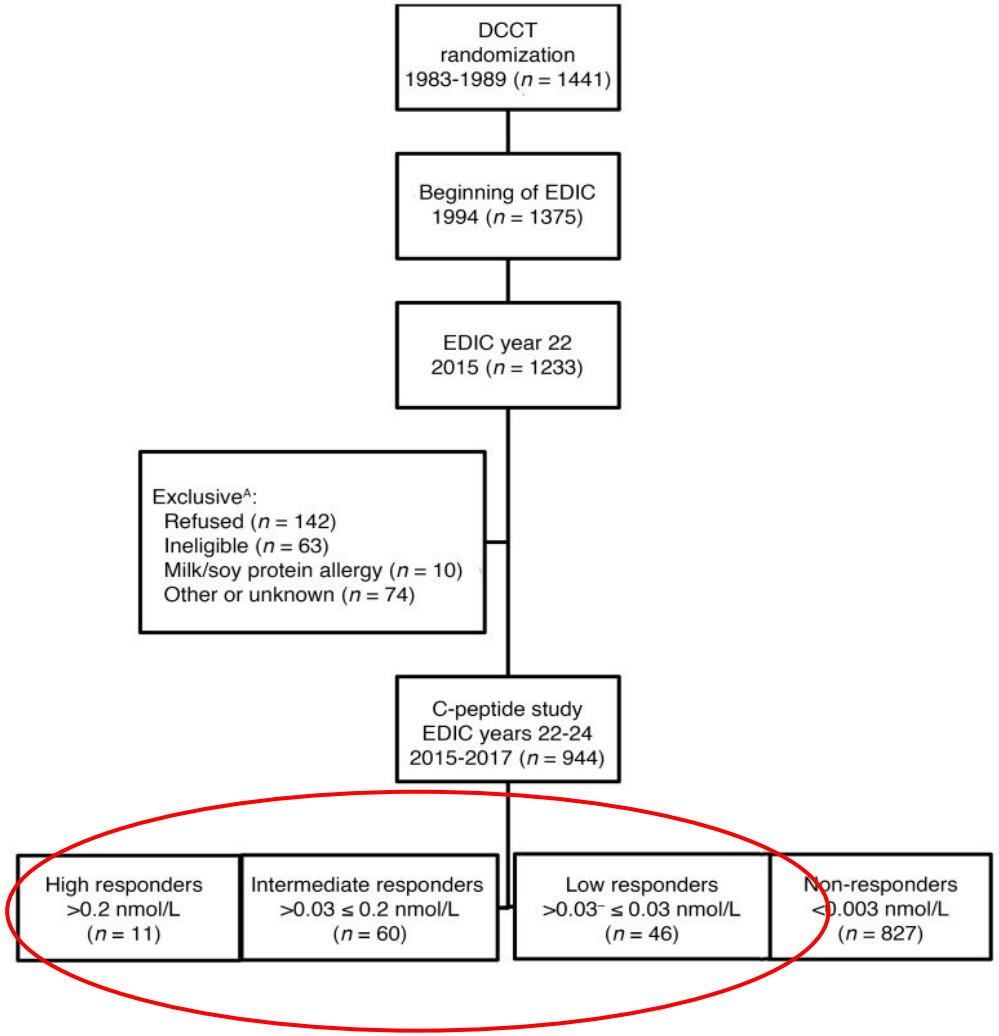


Atkinson, M; Eisenbarth, G.S.; Michels, A. *Lancet,* 2014

Why C-Peptide vs. A1c vs. Insulin Dose ?

- **C-peptide IS the ONLY true measure of Beta Cell Function**
- **LONG-TERM risk of complications REDUCED**
- **LONG-TERM complication free survival…C-Peptide**
- **DCCT / EDIC – C-pep > 0.03 nmol/L associated with reduced Severe Hypoglycemia**

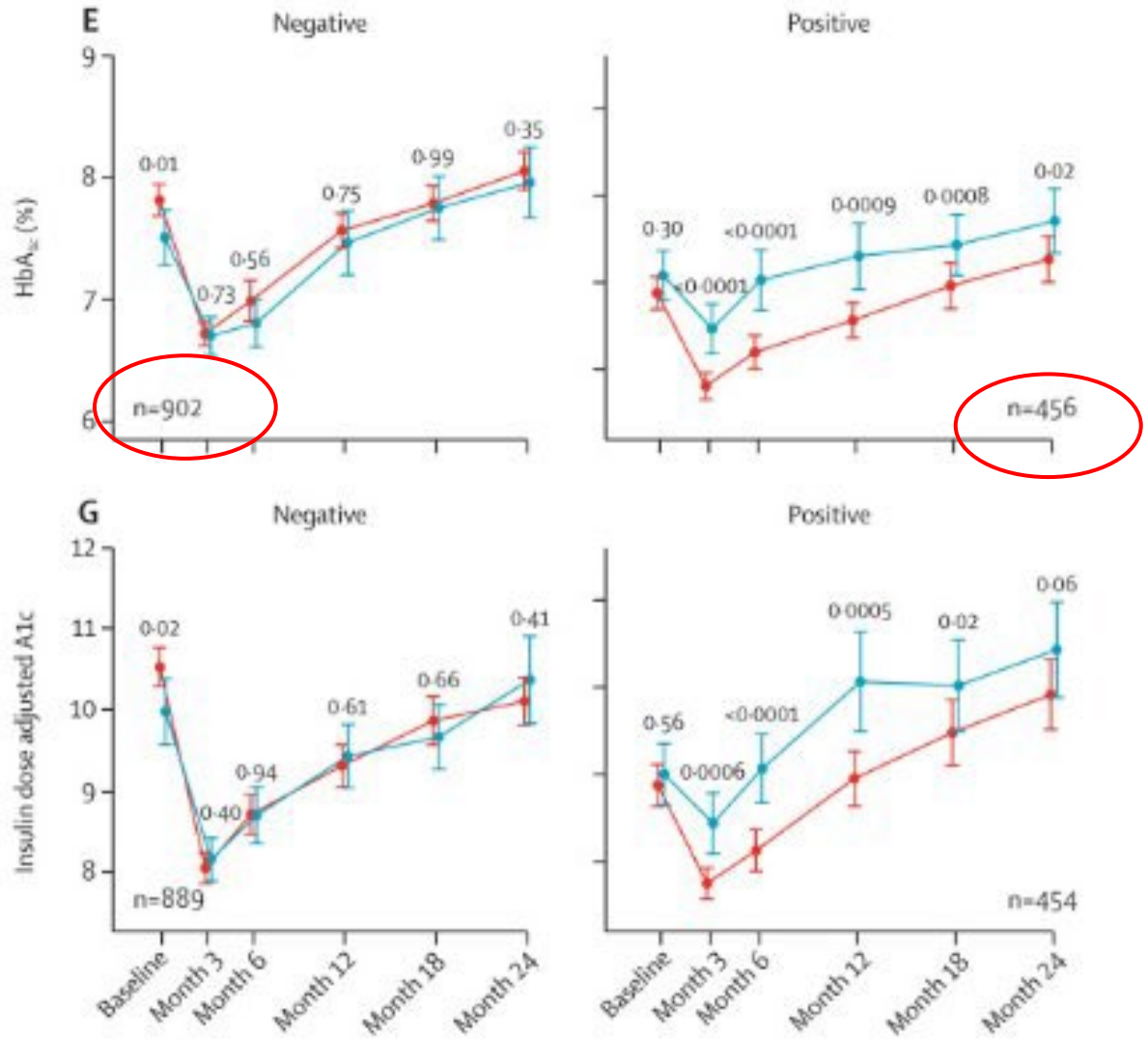
- **Automated Insulin - improves A1c . Insulin Use but:**
  - **Does not delay disease**
  - **Does not meet the needs / wants / desires of the T1D community**



J Clin Invest. 2021 Feb 1;131(3):e143011. doi: 10.1172/JCI143011

Why C-Peptide vs. A1c vs. Insulin Dose ?

- **Trial Outcome Markers Initiative (TOMI)**
- **Subjects from multiple positive/negative studies…Power**
- **Lancet - 2023**
- **Breakthrough T1D – Diabetes 2024**



THE LANCET DIABETES & ENDOCRINOLOGY, VOLUME 11, ISSUE 12, 2023, PAGES 915-925, 2023

Tzield/Teplizumab 1992 to 2022: 30 Years

FDA NEWS RELEASE

FDA Approves First Drug That Can Delay Onset of Type 1 Diabetes

Prevention of Autoimmune Diabetes With Nonactivating Anti-CD3 Monoclonal Antibody

KEVAN C. HEROLD, JEFFERY A. BLUESTONE, ANTHONY G. MONTAG, ASHU PARIHAR, AMY WIEGNER, RONALD E. GRESS, AND RAPHAEL HIRSCH

Proc. Natl. Acad. Sci. USA
Vol. 91, pp. 123–127, January 1994
Immunology

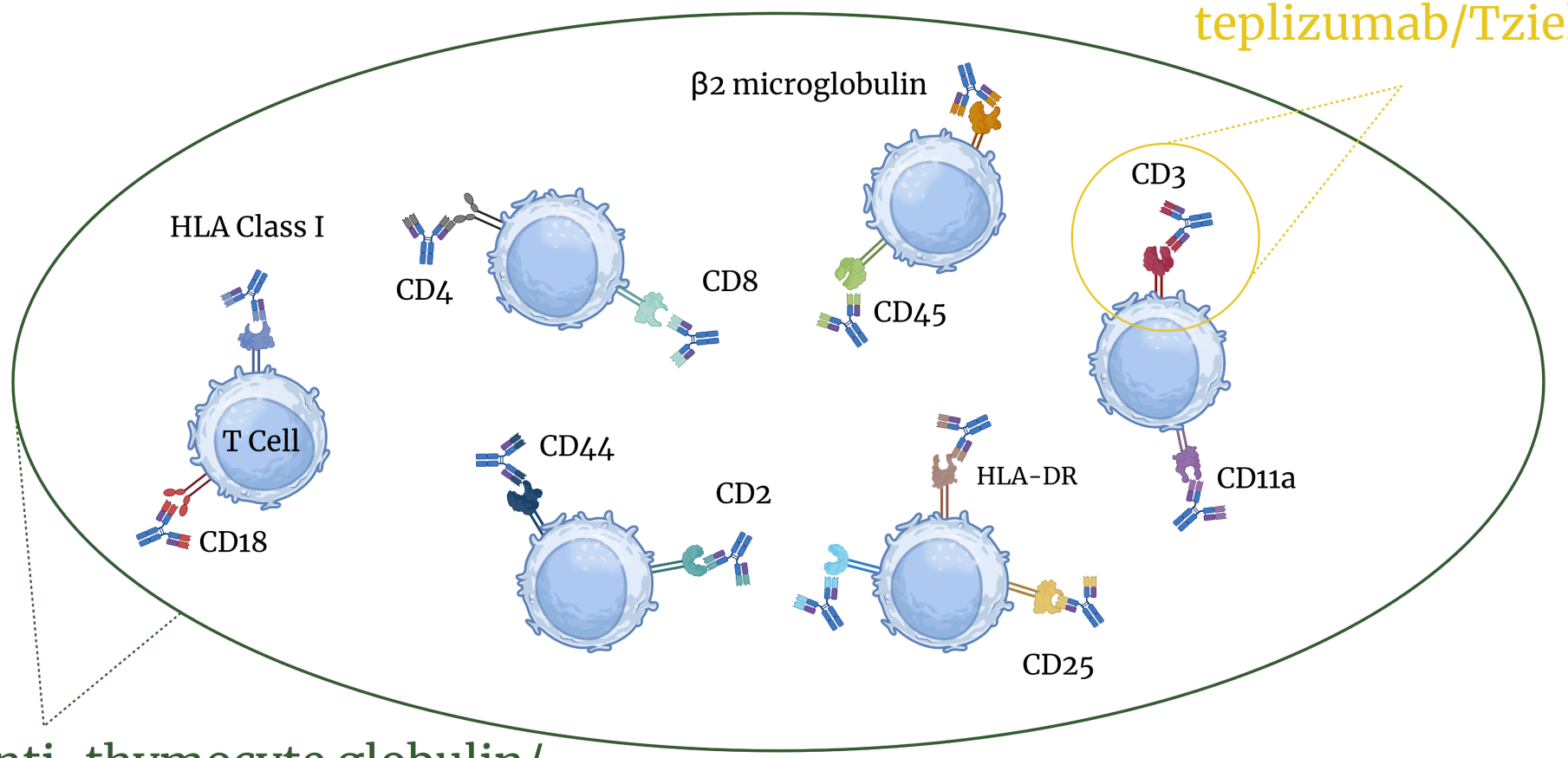
Anti-CD3 antibody induces long-term remission of overt autoimmunity in nonobese diabetic mice

(autoimmunity/diabetes)

LUCIENNE CHATENOUD, ERIC THERVET, JACQUELINE PRIMO, AND JEAN-FRANÇOIS BACH

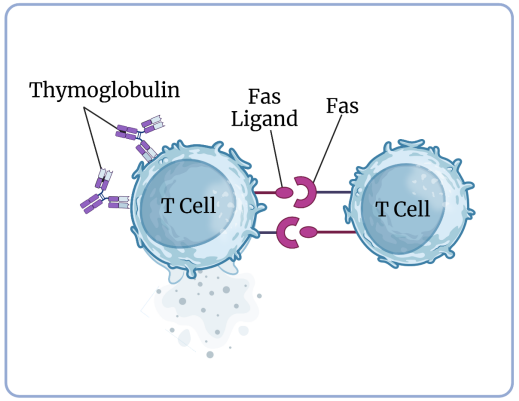
Institut National de la Santé et de la Recherche Médicale U 25, Hôpital Necker, 161 Rue de Sèvres, 75015 Paris, France

TZIELD® (teplizumab-mzwv) vs. Thymoglobulin (rabbit ATG)

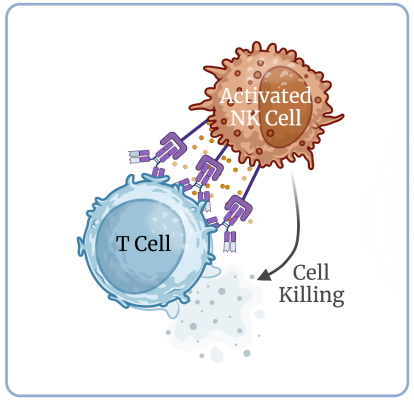


Thymoglobulin Depletes and Modulates

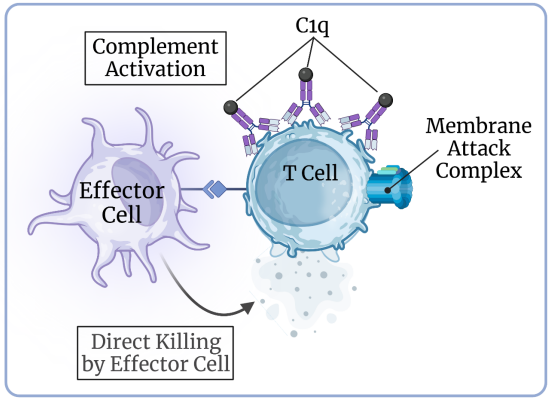
Apoptosis via Activation-Induced Cell Death



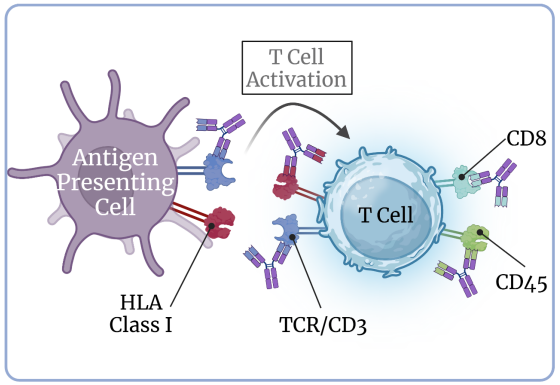
Antibody-Dependent Cell-Mediated Cytotoxicity



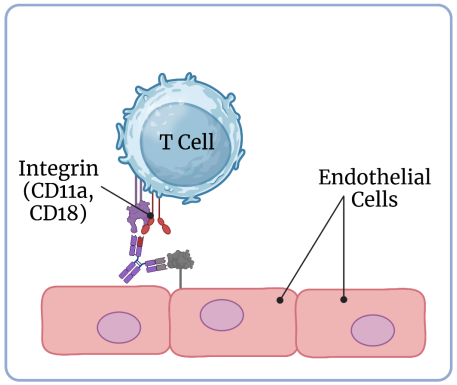
Complement-Mediated Cell Cytotoxicity



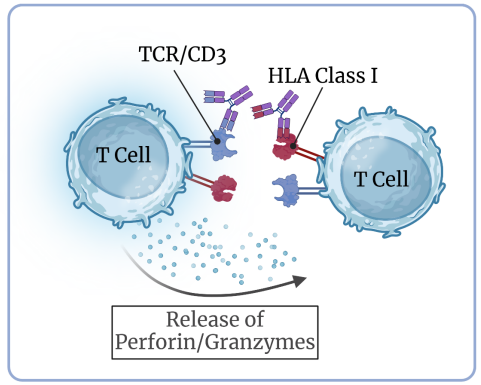
Modulation of T Cell Activation



Modulation of Homing

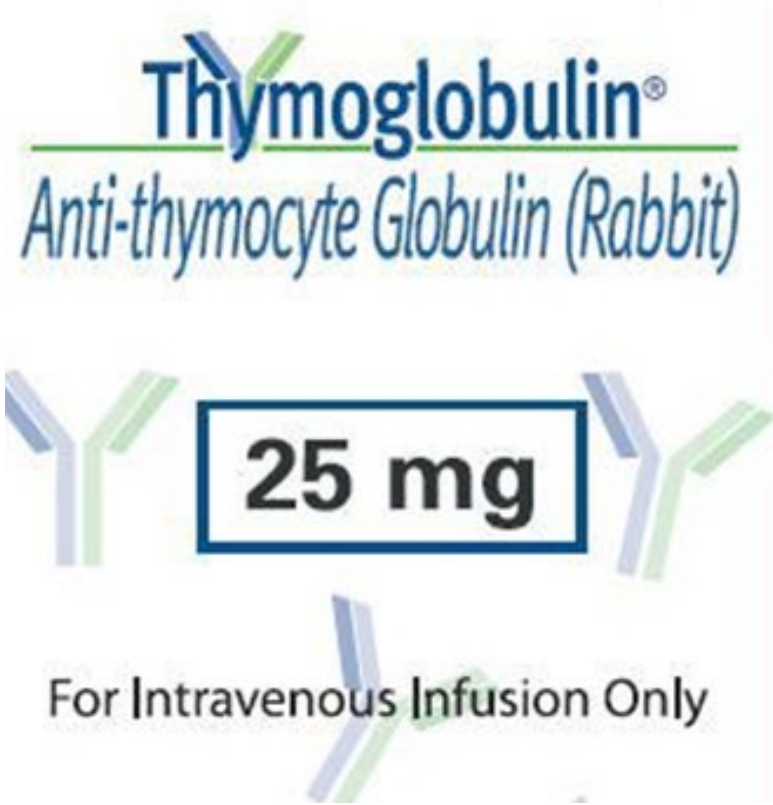


Modulation of Cytotoxic Activities



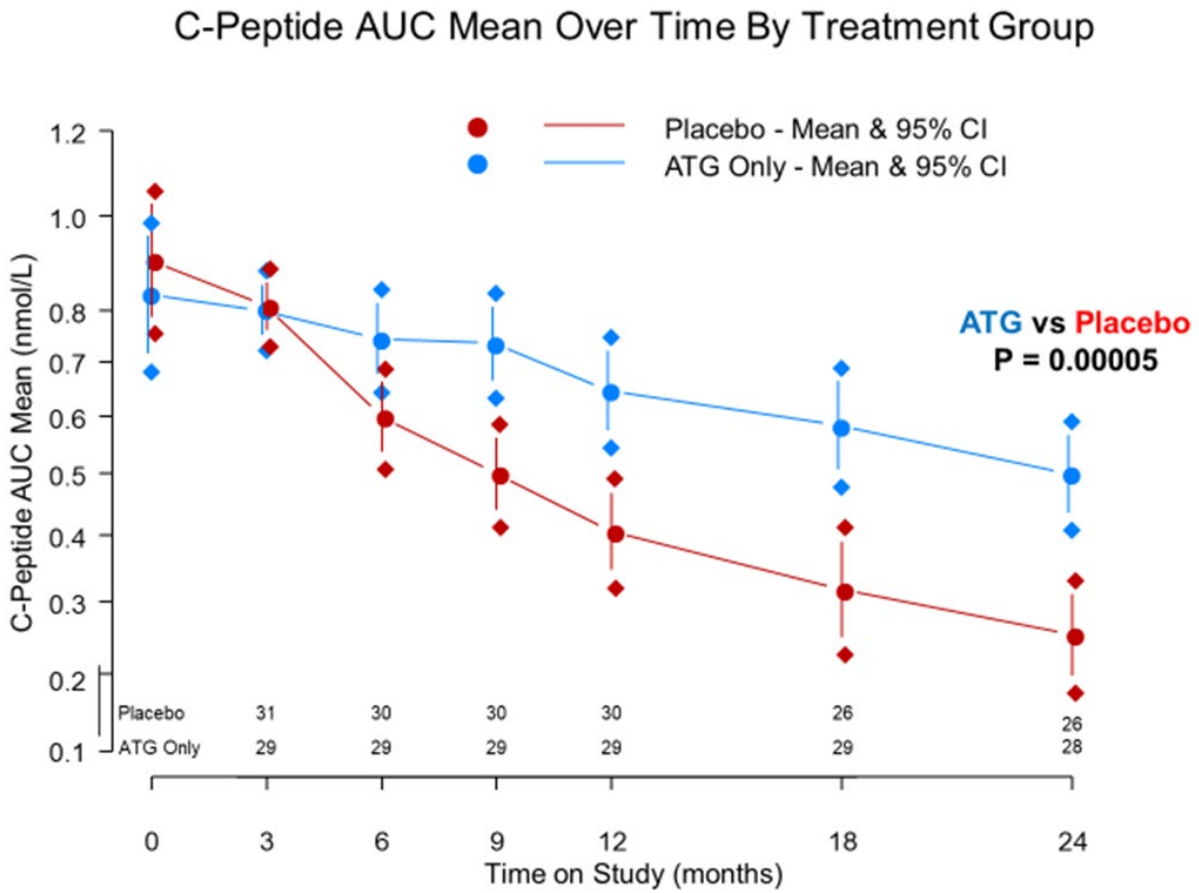
Thymoglobulin

- **Human Thymus / T-cells > Immunized Rabbit**
- **Polyclonal Mix of Rabbit Anti-Human Antibodies**
- **FDA approved ~30 years**
- **Standard in Renal Transplant – up to 10mg/kg**
- **Near complete depletion of Treg and Teff with slow recovery at Transplant dose**
- **What about lower dose?**



Thymoglobulin in Type 1 Diabetes

- **George Eisenbarth – 1985 – ATGAM**
- **START Trial - 2013 - 6.5mg/kg**
- **Low-Dose ATG - 2015 - 2.5mg/kg**
- **TrialNet Low-Dose ATG – 2018 – 2.5mg/kg**
- **Low-Dose ATG – 2024 - Stage 2 T1D**



Diabetes Care. 2024 Feb 1;47(2):285-289.
JCI Insight. 2023 Aug 22;8(16):e161812
Diabetes Technol Ther. 2020 Dec;22(12):948-953.
Diabetes. 2019 Jun;68(6):1267-1276.
Diabetes Care. 2018 Sep;41(9):1917-1925

T-cell Exhaustion Phenotype is Universally Linked to C-peptide Preservation

JCI insight

RESEARCH ARTICLE

Exhausted-like CD8+ T cell phenotypes linked to C-peptide preservation in alefacept-treated T1D subjects

Kirsten E. Diggins,[1] Elisavet Serti,[2] Virginia Muir,[1] Mario Rosasco,[1] TingTing Lu,[2] Elisa Balmas,[3] Gerald Nepom,[2] S. Alice Long,[3] and Peter S. Linsley[1]

[1]Systems Immunology, Benaroya Research Institute at Virginia Mason, Seattle, Washington, USA. [2]Immune Tolerance Network (ITN), Bethesda, Maryland, USA. [3]Translational Immunology, Benaroya Research Institute at Virginia Mason, Seattle, Washington, USA.

[Exhausted-like CD8+ T cell phenotypes linked to C-peptide preservation in alefacept-treated T1D subjects - PubMed]

Published in final edited form as:
Sci Immunol. 2016 November ; 1(5): . doi:10.1126/sciimmunol.aai7793.

Partial exhaustion of CD8 T cells and clinical response to teplizumab in new-onset type 1 diabetes

S. Alice Long[1], Jerill Thorpe[1], Hannah A. DeBerg[2], Vivian Gersuk[2], James Eddy[2], Kristina M. Harris[3], Mario Ehlers[4], Kevan C. Herold[5], Gerald T. Nepom[3], and Peter S. Linsley[2,*]

[Partial exhaustion of CD8 T cells and clinical response to teplizumab in new-onset type 1 diabetes - PubMed]

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

[1]Department of Pediatrics, College of Medicine, University of Florida, Gainesville, Florida, USA. [2]Department of Pathology, Immunology, and Laboratory Medicine, University of Florida Diabetes Institute, Gainesville, Florida, USA. [3]Benaroya Research Institute at Virginia Mason, Seattle, Washington, USA. [4]Department of Biostatistics, University of Florida, Gainesville, Florida, USA.

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

Published in final edited form as:
Cell Immunol. 2017 September ; 319: 3–9. doi:10.1016/j.cellimm.2017.07.007.

Remodeling T cell compartments during anti-CD3 immunotherapy of type 1 diabetes

S. Alice Long[a], Jerill Thorpe[a], Kevan C. Herold[b], Mario Ehlers[c], Srinath Sanda[c], Noha Lim[d], Peter S. Linsley[a], Gerald T. Nepom[a,d], and Kristina M. Harris[d,*]

[a]Benaroya Research Institute at Virginia Mason, Seattle, WA, USA

[b]Departments of Immunobiology and Internal Medicine, Yale University, New Haven, CT, USA

[c]Immune Tolerance Network, San Francisco, CA, USA

[d]Immune Tolerance Network, Bethesda, MD, USA

[Remodeling T cell compartments during anti-CD3 immunotherapy of type 1 diabetes - PubMed]

RESEARCH ARTICLE

The Journal of Clinical Investigation

Autoreactive CD8+ T cell exhaustion distinguishes subjects with slow type 1 diabetes progression

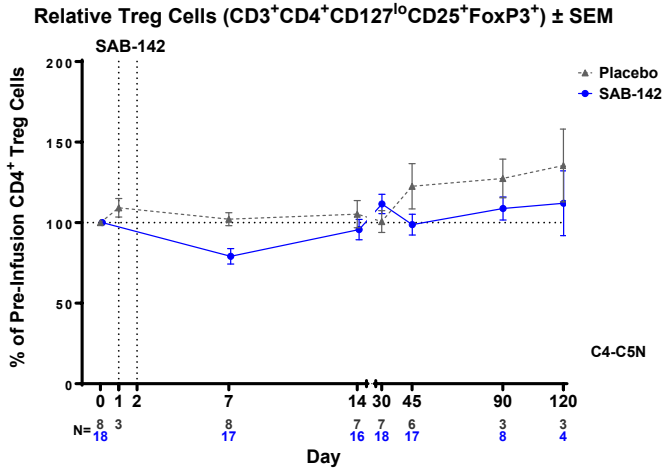
Alice E. Wiedeman,[1] Virginia S. Muir,[2] Mario G. Rosasco,[2] Hannah A. DeBerg,[2] Scott Presnell,[2] Bertrand Haas,[2] Matthew J. Dufort,[2] Cate Speake,[3] Carla J. Greenbaum,[3] Elisavet Serti,[4] Gerald T. Nepom,[1,4] Gabriele Blahnik,[1] Anna M. Kus,[1] Eddie A. James,[1] Peter S. Linsley,[2] and S. Alice Long[1]

[1]Translational Research Program, [2]Systems Immunology, and [3]Diabetes Program, Benaroya Research Institute (BRI) at Virginia Mason, Seattle, Washington, USA. [4]Immune Tolerance Network (ITN), Bethesda, Maryland, USA.

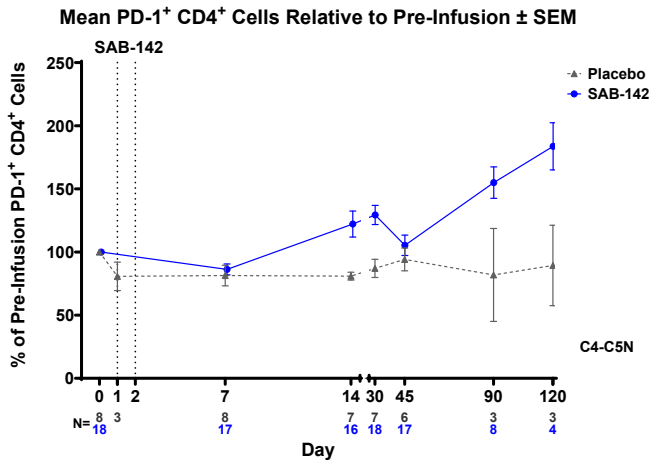
[Autoreactive CD8+ T cell exhaustion distinguishes subjects with slow type 1 diabetes progression - PubMed]

SAB-142 Demonstrates MOA Analogous to Rabbit ATG Key Parameters Correlative to C-peptide Preservation

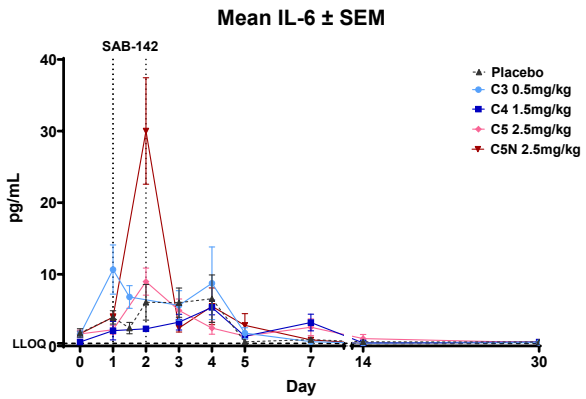
01 Treg preservation

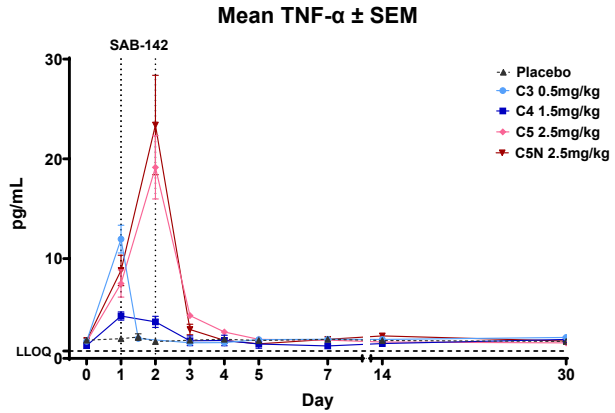


02 Durable CD4+ exhaustion phenotype



03 Transient increase in IL-6 and TNF-alpha





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

[1]Department of Pediatrics, College of Medicine, University of Florida, Gainesville, Florida, USA. [2]Department of Pathology, Immunology, and Laboratory Medicine, University of Florida Diabetes Institute, Gainesville, Florida, USA. [3]Benaroya Research Institute at Virginia Mason, Seattle, Washington, USA. [4]Department of Biostatistics, University of Florida, Gainesville, Florida, USA.

RESULTS. Treatment with low-dose ATG preserved regulatory T cells (Tregs), as measured by stable methylation of *FOXP3* Treg-specific demethylation region (*TSDR*) and increased proportions of CD4+FOXP3+ Tregs ($P < 0.001$) identified by flow cytometry. While treatment effects were consistent across participants, not all maintained C-peptide. Responders exhibited a transient rise in IL-6, IP-10, and TNF-α ($P < 0.05$ for all) 2 weeks after treatment and a durable CD4+ exhaustion phenotype (increased PD-1+KLRG1+CD57- on CD4+ T cells [$P = 0.011$] and PD1+CD4+ Temra MFI [$P < 0.001$] at 12 weeks, following ATG and ATG/G-CSF, respectively). ATG nonresponders displayed higher proportions of senescent T cells (at baseline and after treatment) and increased methylation of *EOMES* (i.e., less expression of this exhaustion marker).

CONCLUSION. Altogether in these exploratory analyses, Th1 inflammation-associated serum and CD4+ exhaustion transcript and cellular phenotyping profiles may be useful for identifying signatures of clinical response to ATG in T1D.

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

SAB-142 Topline Phase 1 Data from Healthy Volunteer Cohorts

SAB-142 demonstrated clinically validated multi-target MOA with sustained immunomodulation in Phase 1

Phase 1 data confirm SAB-142 is fully human and not immunogenic

- Doesn’t cause serum sickness
- Doesn’t cause anti-drug antibodies

Phase 1 data demonstrate sustained “T-cell exhaustion” signature

- Clinically validated by rabbit ATG and other T1D immunomodulatory drugs
- Proven to correlate with C-peptide preservation

Phase 1 data strongly position SAB-142 for potentially safe chronic dosing

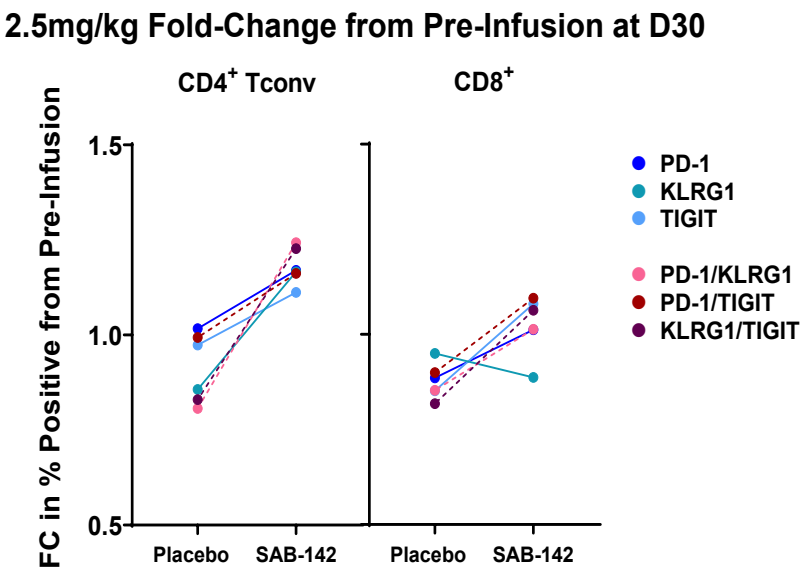
Phase 1 topline results support advancement to Phase 2b SAFEGUARD study in adult and pediatric patients with new onset T1D

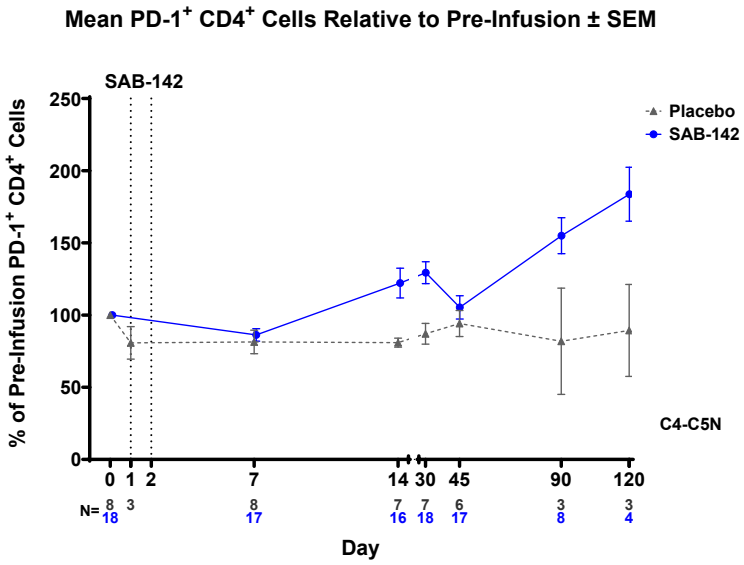
SAB-142 Induces a Sustained Cellular Exhaustion Profile on Both CD4+ and CD8+ T-cell Subsets Demonstrating Superior Multi-target Modality

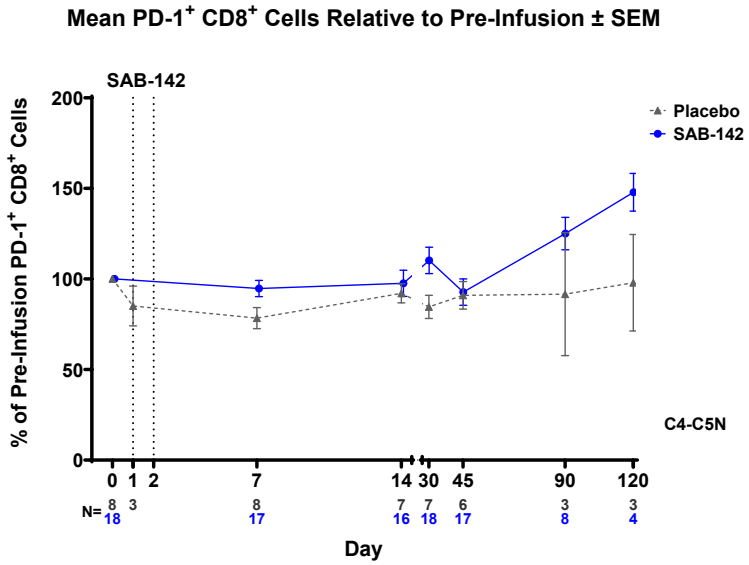
Shift towards exhaustion profile across multiple markers

Sustained CD4+ exhaustion profile

Sustained CD8+ exhaustion profile



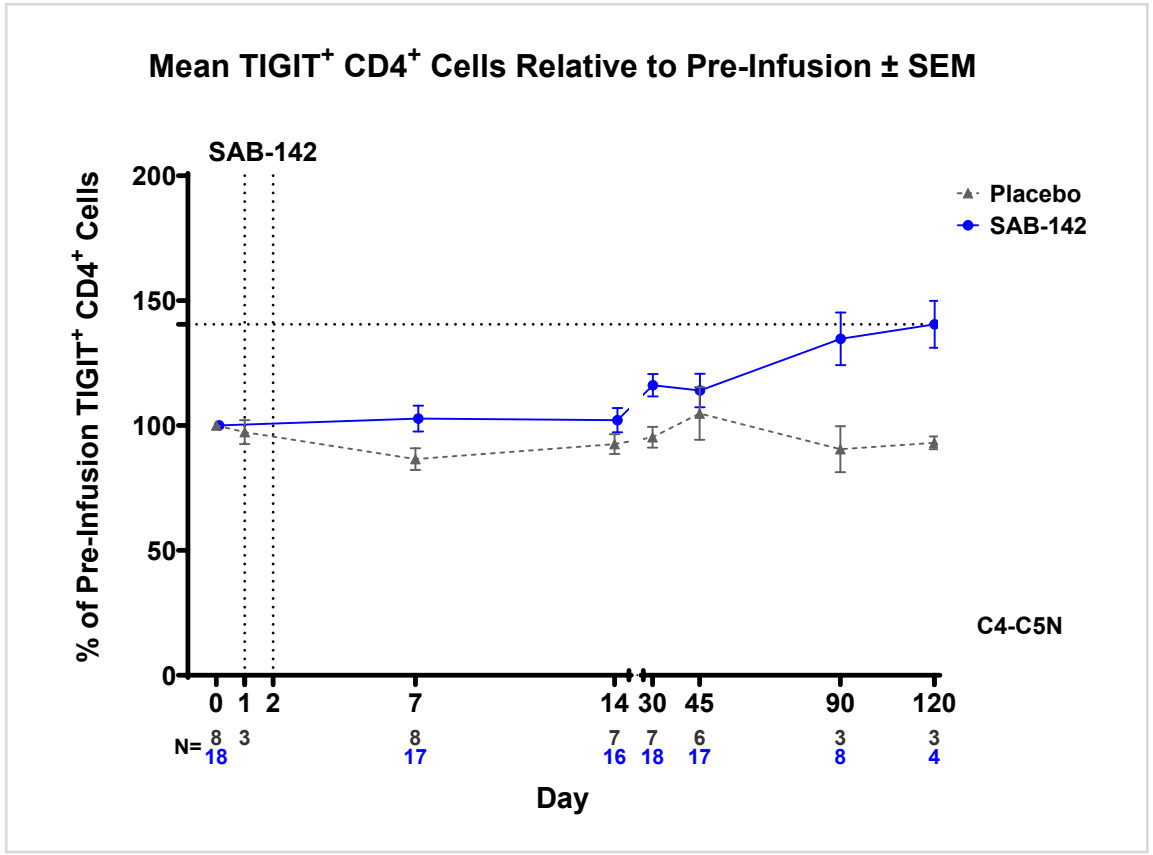


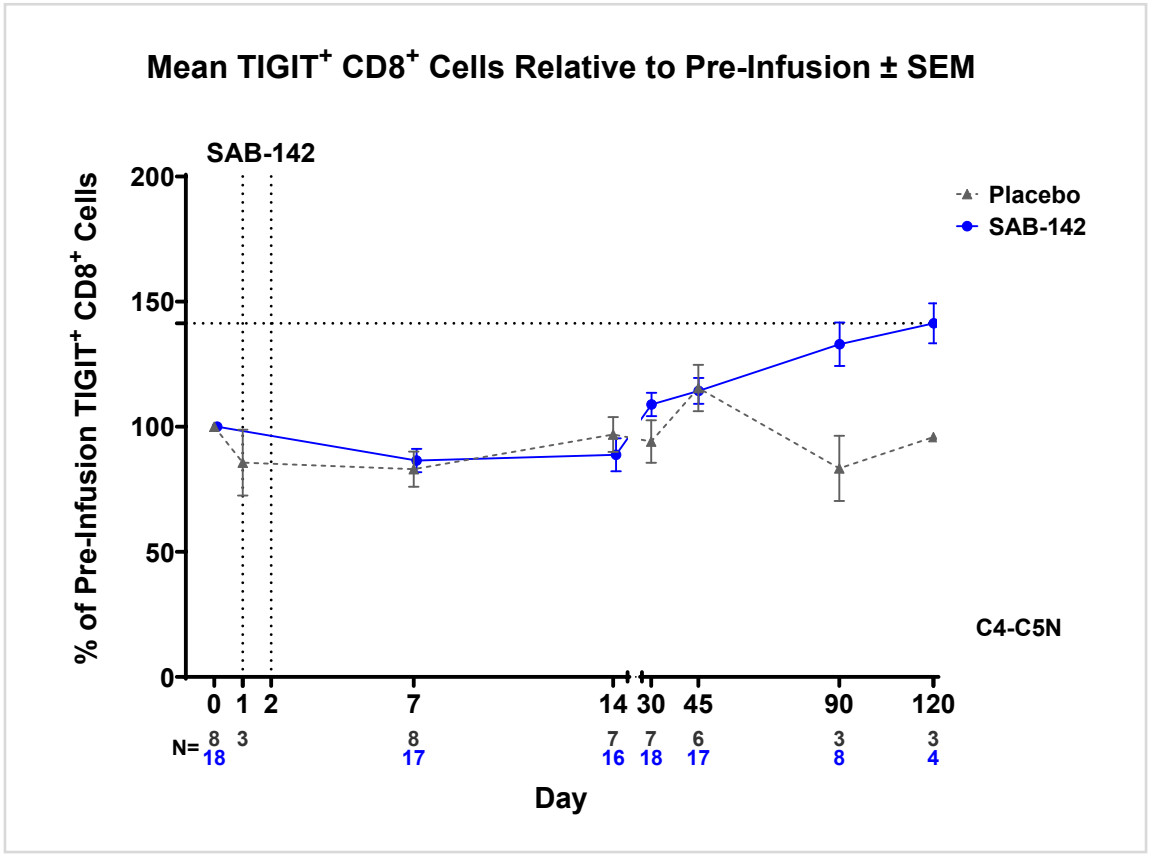


Both CD4 and CD8 T-cells expressing PD-1 and TIGIT notably increase at day 30 and continue to increase through day 120

SAB-142 Clearly Induces a Sustained Cellular Exhaustion Profile on Both CD4+ and CD8+ T-cell Subsets

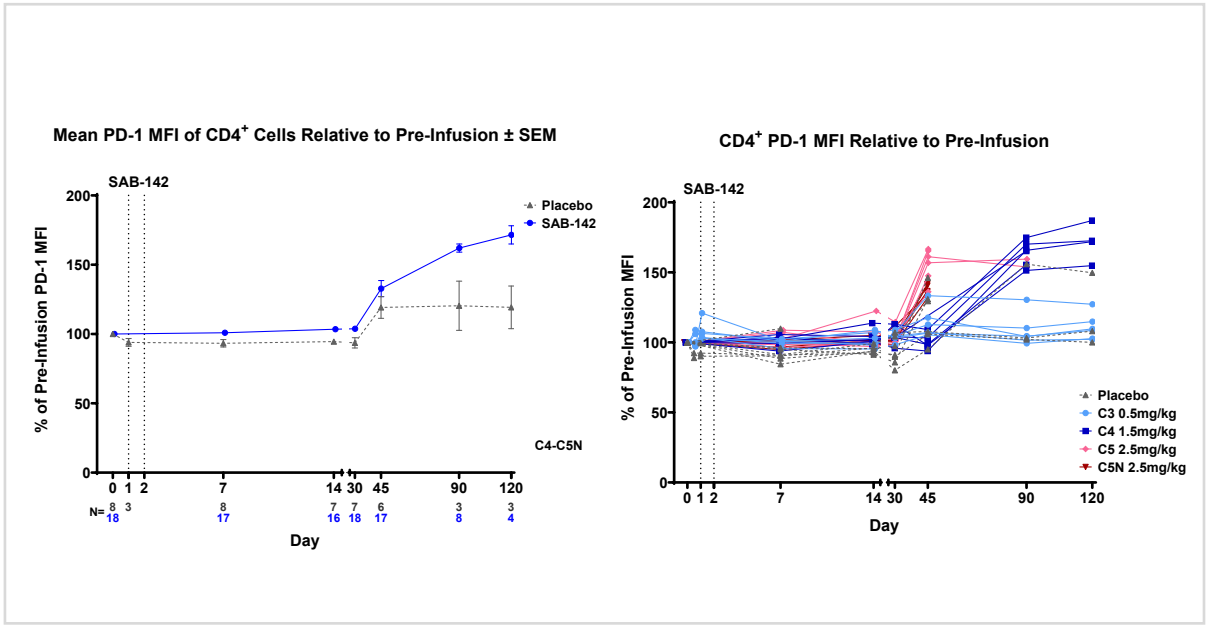
SAB-142 induces a sustained cellular exhaustion profile on both CD4+ and CD8+ T-cell subsets demonstrating superior multi-target modality

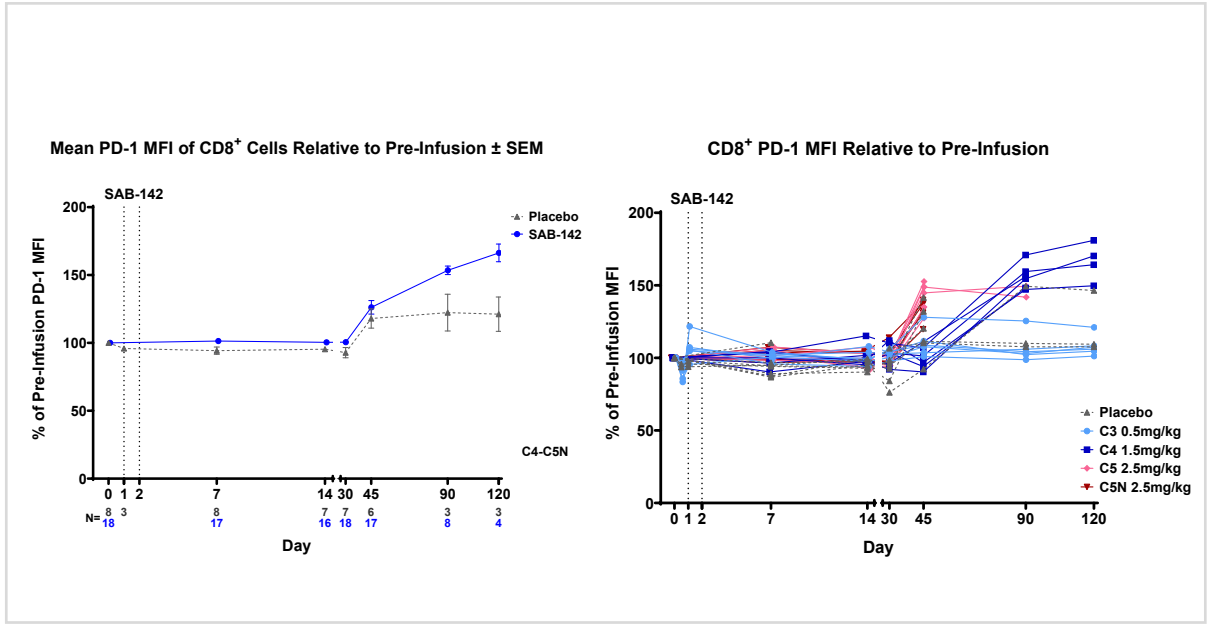




SAB-142 Produces Increasing PD-1 MFI Expression Levels on Both CD4+ and CD8+ T-cells Supporting Continued Reprogramming of These Targeted Cells

SAB-142 results in PD-1 MFI increase in notable dose-response manner

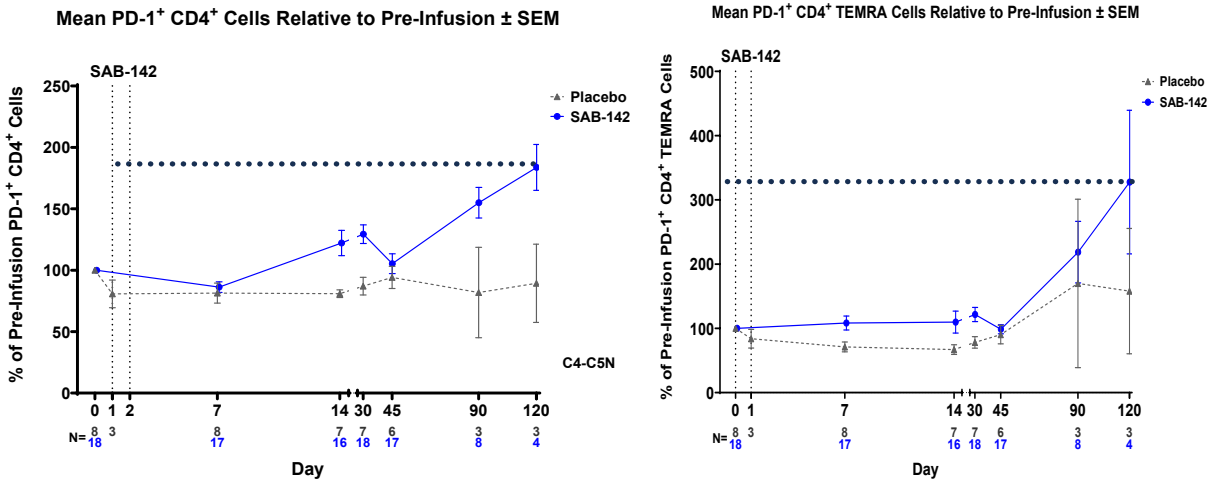




SAB-142 produces PD1 MFI with tight grouping of individual responders showing 100% of "immunological responders" in Cohorts 4, 5, and 5N

SAB-142 Demonstrates CD4+Tcell Exhaustion Analogous to Rabbit ATG

SAB-142 CD4+ T cell exhaustion



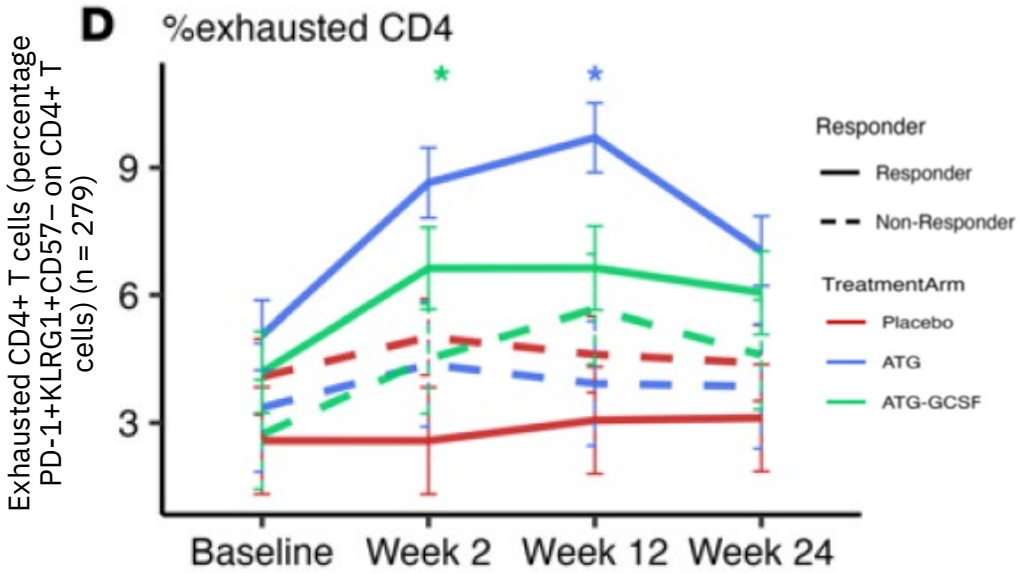
Cohorts C4, C5, & C5N Grouped (1.5mg/kg -2.5mg/kg)

Rabbit ATG CD4+ T cell exhaustion

JCI insight

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

Laura M. Jacobsen, … , Peter S. Linsley, Todd M. Brusko



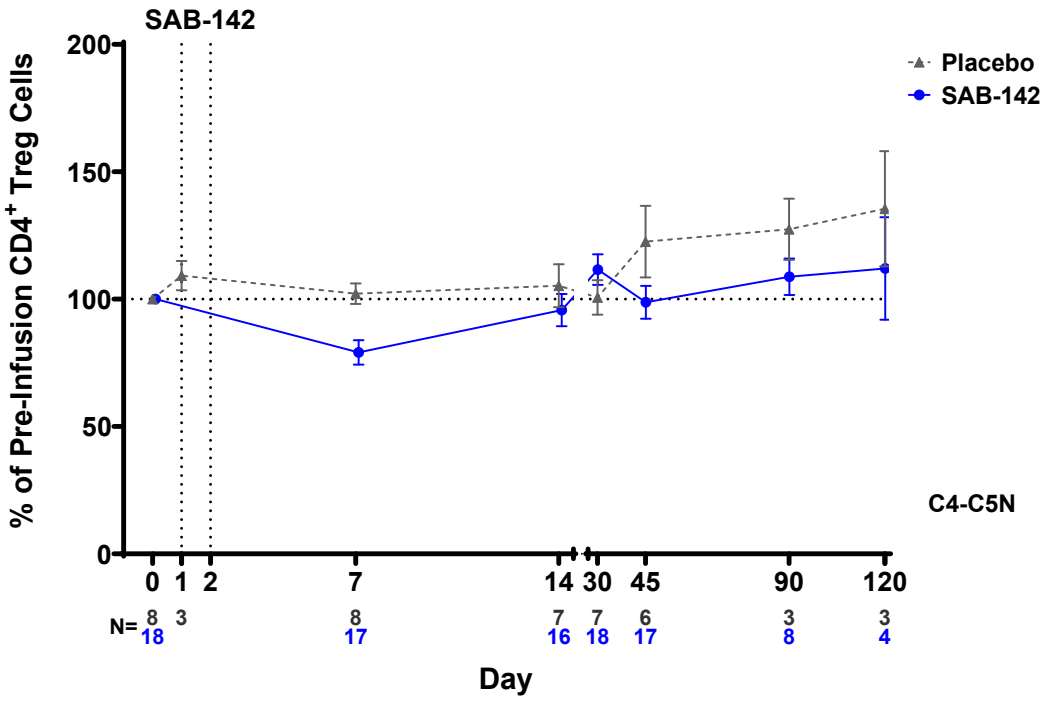
Low-dose ATG was found to persistently induce expression of coinhibitory receptors (PD-1, KLRG1) on T cells and, thus, exhaustion-like phenotypes in CD4+ T cell populations.

SAB-142 Not Only Preserves Tregs but Also Induces T-reg Activation State

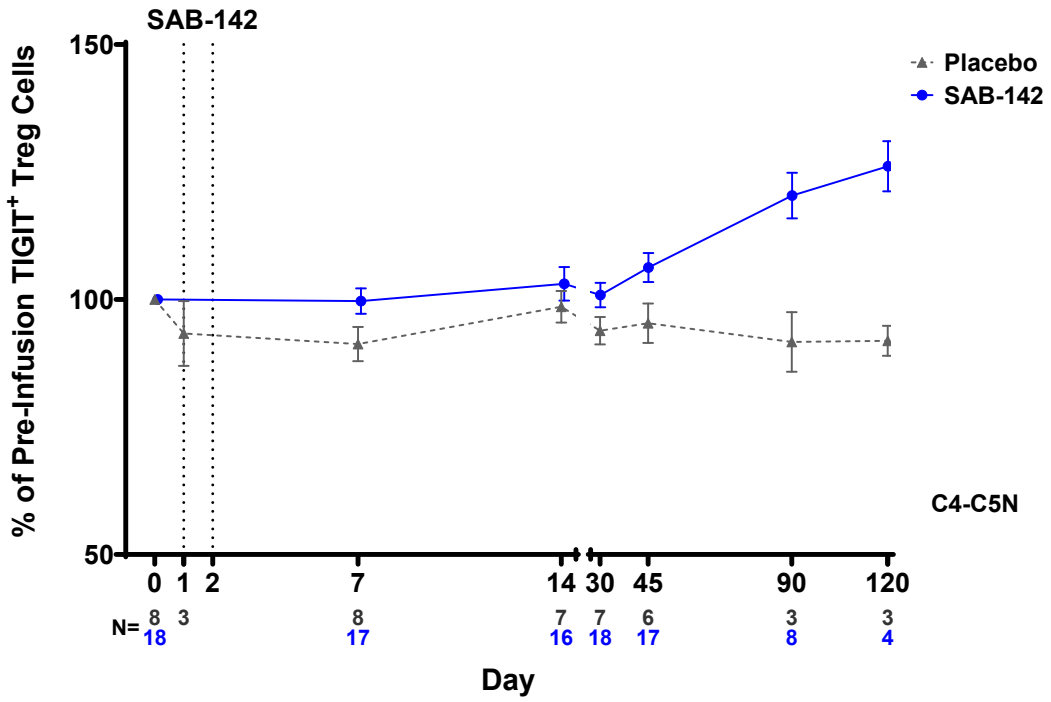
SAB-142 T-regulatory cells "sparing" effect demonstrated by no difference vs. baseline and PBO from Day 14 onwards

SAB-142 triggers activated state of T-regulatory cells demonstrated by increase in TIGIT+ Tregs by Day 45 that continues to increase through Day 120

Relative Treg Cells ($CD3^+CD4^+CD127^{lo}CD25^+FoxP3^+$) ± SEM

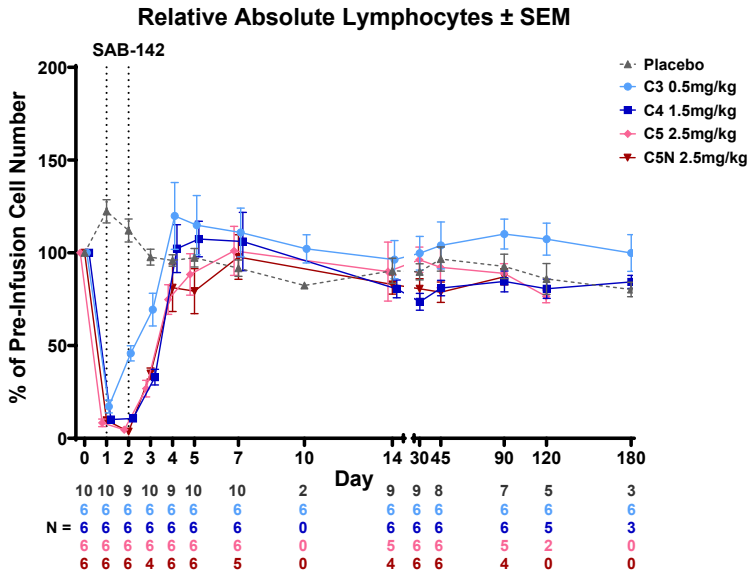


Relative TIGIT$^+$ Treg Cells ($CD3^+CD4^+CD127^{lo}CD25^+FoxP3^+$) ± SEM

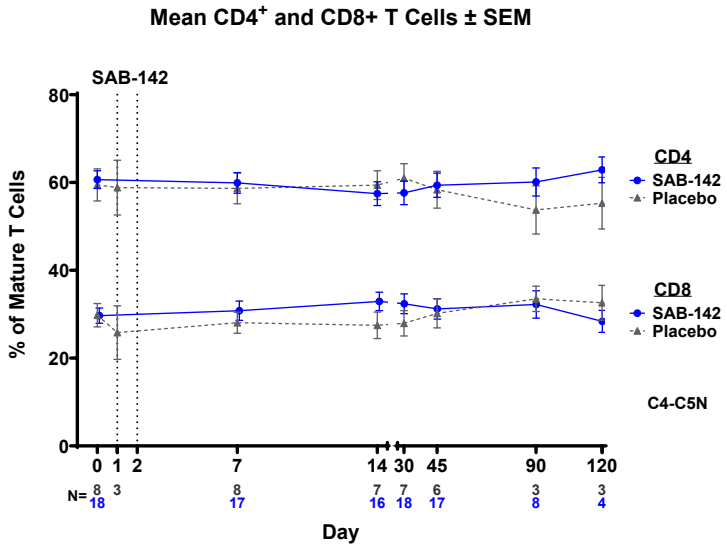


SAB-142 Doesn't Cause Sustained Total, T or B-cell Lymphodepletion

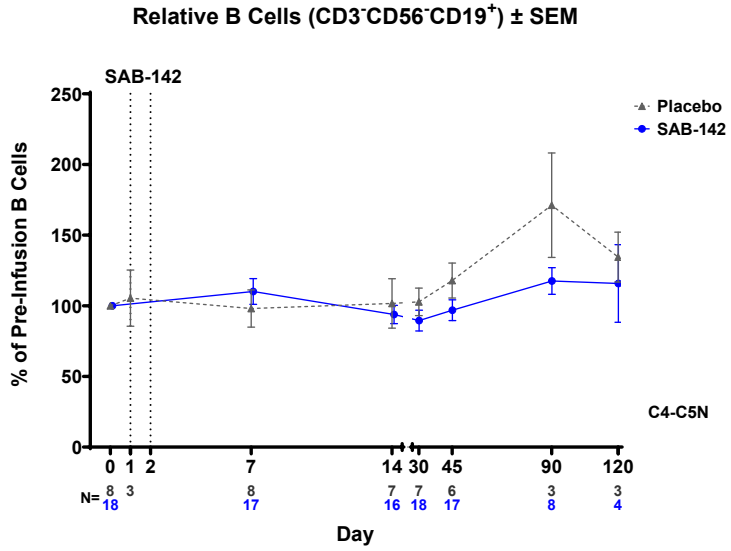
No sustained total lymphodepletion



No sustained CD4+ and CD8+ T-cell lymphodepletion

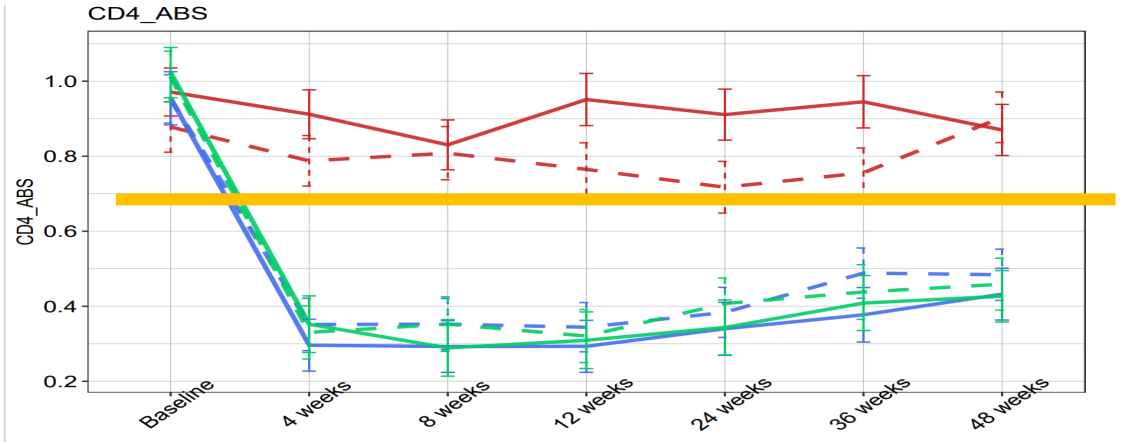


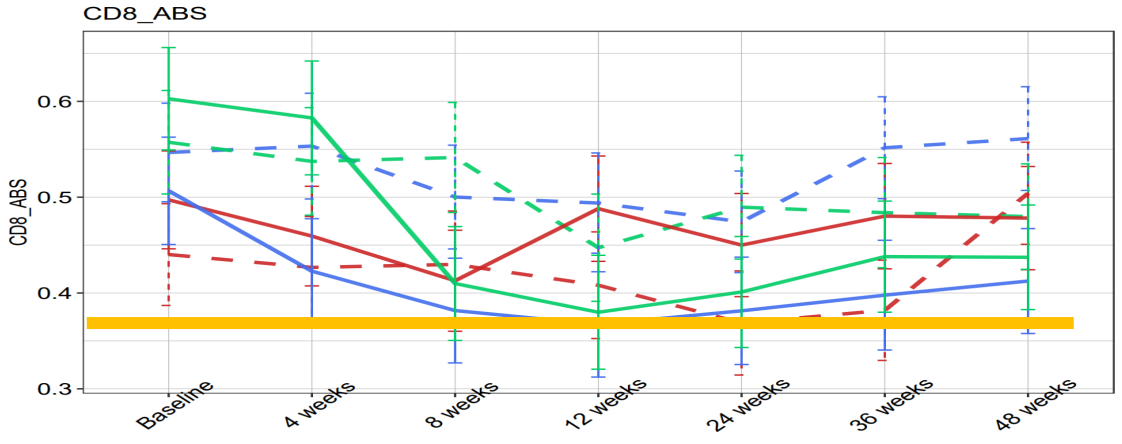
No sustained B-cell lymphodepletion



Efficacy of Rabbit ATG is Not Associated with the Degree of Lymphodepletion

Rabbit ATG results in sustained CD4+ decrease for up to 2 years





Response to ATG was not found to associate with the degree of serum sickness (9) or lymphocyte depletion. The immune features of responders we uncovered are unlikely to be a result of aging, as analyses were adjusted for age. Older participants (22–35 years old) in the high-dose ATG START trial (6, 44) also demonstrated C-peptide preservation, whereas the trial population as a whole did not. Other therapeutics — both B cell–directed (rituximab) and T cell–directed (teplizumab and abatacept) therapies — have demonstrated greater metabolic benefit in younger individuals (37, 43, 45, 46). Thus, there are inherent differences in how these therapies work in individuals with T1D that will allow for targeted treatment decisions.

Sustained decrease in CD4+ or CD8+ T-cells has not been shown to correlate with C-peptide preservation

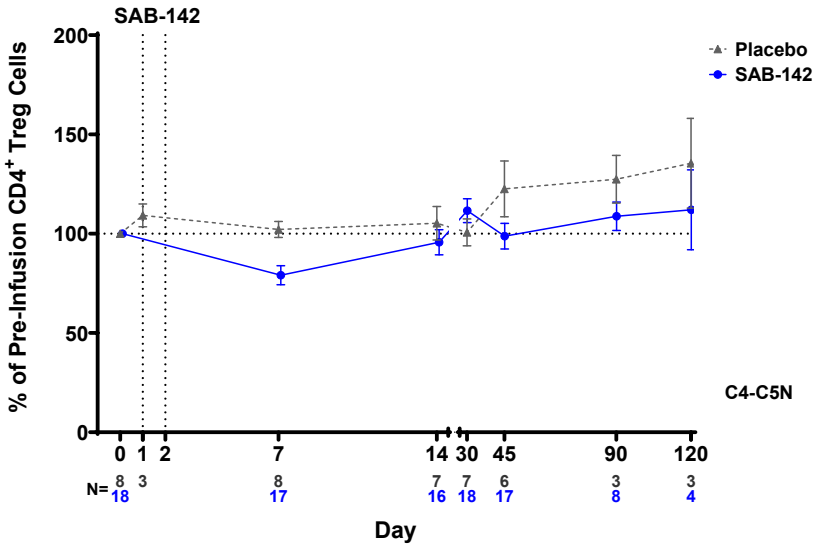
[Responders to low-dose ATG induce CD4+ T cell exhaustion in type 1 diabetes - PubMed]

SAB-142 Doesn't Lymphodeplete T Regulatory Cells, Unlike Teplizumab

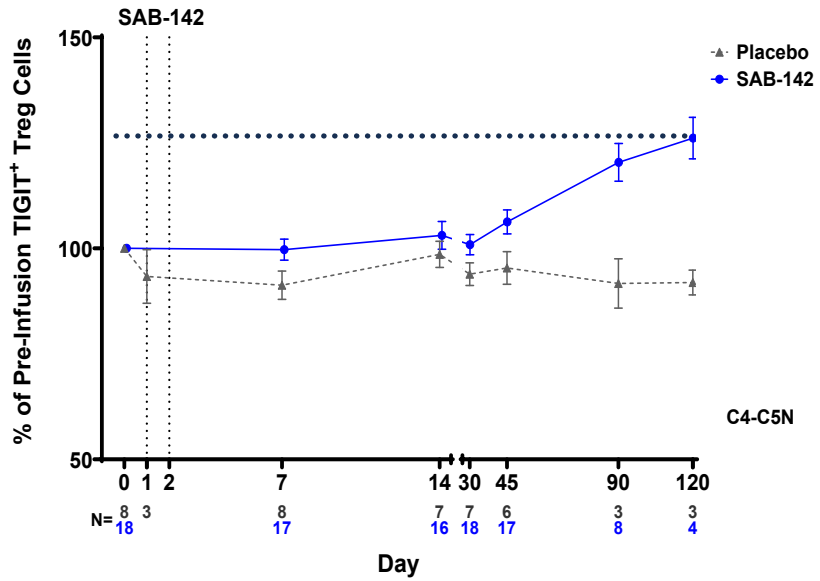
SAB-142 T-regulatory cells "sparing" effect demonstrated by no difference vs. baseline and PBO from Day 14 onwards

SAB-142 triggers activated state of T-regulatory cells demonstrated by increase in TIGIT+ Tregs by Day 45 that continues to increase through Day 120

Relative Treg Cells ($CD3^+CD4^+CD127^{lo}CD25^+FoxP3^+$) ± SEM



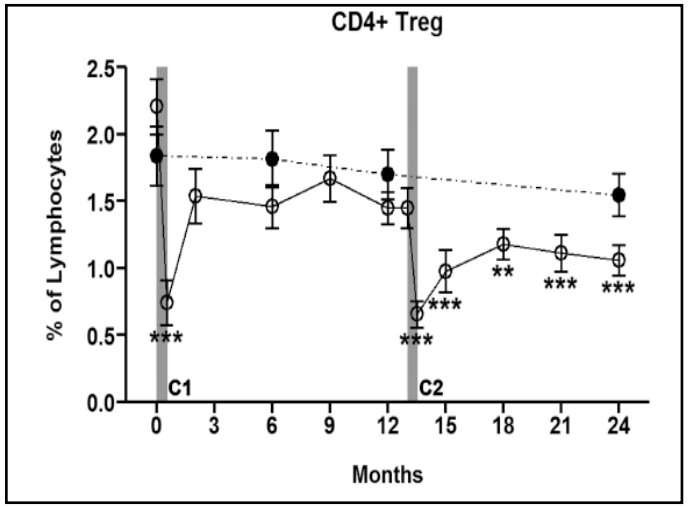
Relative TIGIT$^+$ Treg Cells ($CD3^+CD4^+CD127^{lo}CD25^+FoxP3^+$) ± SEM



Teplizumab

3. Results

3.1 Each course of teplizumab reduces the circulating pool of CD3-expressing lymphocytes



Within the pool of circulating CD4 T cells, teplizumab reduced Treg more than non-Treg **(~58%** vs. ~35% change from baseline, respectively)

https://pubmed.ncbi.nlm.nih.gov/28844471/

SAB-142 Demonstrated Competitive MOA with T-Cell Exhaustion Signature Correlated with C-peptide Preservation

	Thymoglobulin® Anti-thymocyte Globulin (Rabbit)	Tzield™ (teplizumab-mzwv)	SAB-142
CD4+ exhaustion signature	✓	✓	✓
CD8+ exhaustion signature	✗	✓	✓
Treg preservation	✓	✗	✓
No sustained lymphodepletion (Tconv and/or Tregs)	✗	✗	✓
No anti-drug antibodies	✗	✗	✓
No serum sickness	✗	✓	✓
C-peptide preservation	✓	✓	Primary endpoint SafeGUARD

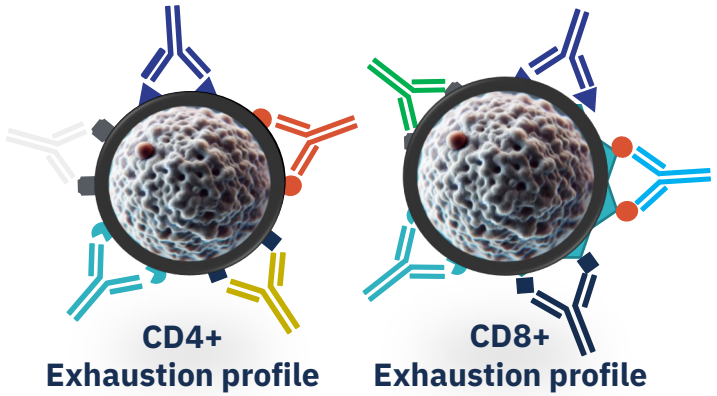
SAB-142 exhibits multi-target T-cell exhaustion profile and Treg-sparing without sustained lymphodepletion analogous to naturally occurring spontaneous partial remission known as honeymoon period

SAB-142 Topline Data Supports Potentially Best-in-Class T1D Immunotherapy

MOA indicates "exhaustion" profile across CD4+ and CD8+ T-cells, strongly correlated with C-peptide preservation

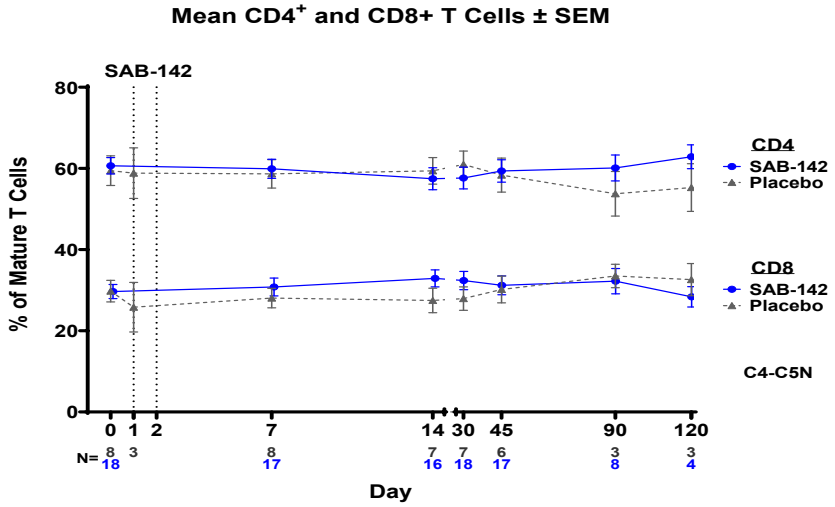
SAB-142 is positioned for chronic dosing due to no sustained lymphodepletion

SAB-142 has a competitive dosing regimen in ambulatory setting



CD4+ Exhaustion profile

CD8+ Exhaustion profile



- ✓ **Target dosing over 2-3 days vs. 12-14 days with teplizumab**
- ✓ **Infusion over ~6 hrs vs 12 hrs in MELD-ATG**

Combined Treg preservation and activation, cellular differentiation shift to a T-cell memory phenotype, and subsequent increase in CD4+ & CD8+ cellular exhaustion markers collectively contribute to the immune modulation MOA that could result in the sustained restoration of immune tolerance correlated with C-peptide preservation and delaying the onset of T1D.
(Jacobsen et al 2023; Riquelme et al, 2018; Yu et al, 2009)

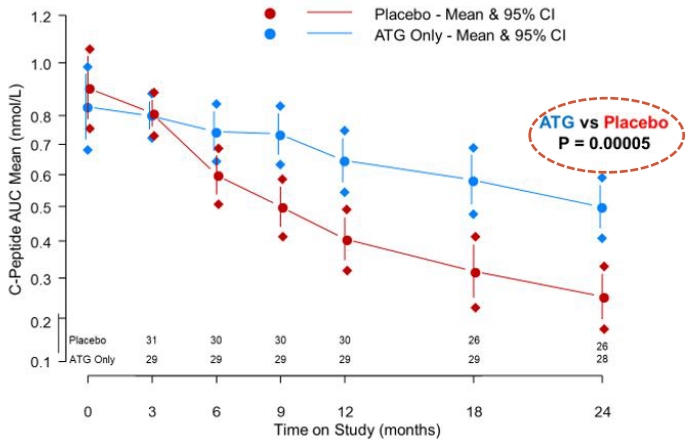
Robust Clinical Data Generated Across Multiple Clinical Studies of SAB-142 Supports Efficient Full Development

01 Low-Dose rabbit ATG Phase 2 Academic Study by Haller

Low-Dose rabbit ATG preserved C-Peptide vs. placebo in stage 3 T1D patients informing SAB to pursue SAB-142 in human clinical studies

Thymoglobulin
Anti-thymocyte Globulin (Rabbit)

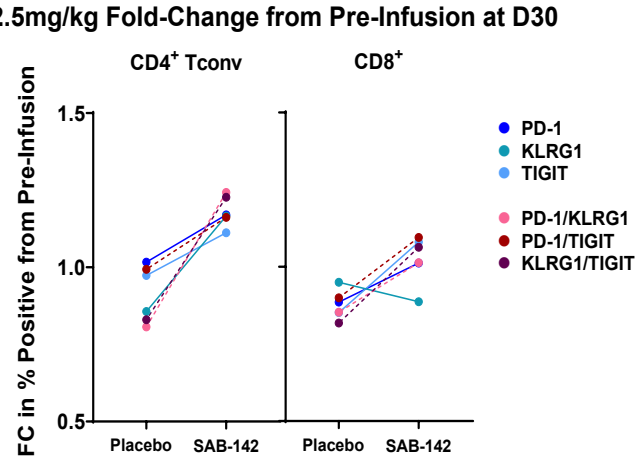
Decline in C-Peptide AUC Mean Over 2 Years



Haller et al. Diabetes. 2019. Jun;68(6):1267-1276

02 Phase 1 SAD HV Study

SAB-142 demonstrated clinically validated multi-target MOA inducing sustained T-cell exhaustion with no lymphodepletion, serum sickness or anti-drug antibodies



Phase 1 topline results support MOA competitive to rATG and teplizumab and advancement into a Phase 2B (SAFEGUARD) study

SafeGUARD

Potential registrational Phase 2b Study in Stage 3 T1D patients

Primary endpoint being C-peptide along with Time-In-Range (TIR) as the leading clinical end point

Global study expected to initiate mid 2025

Interim data expected mid 2026

SAB-142: Multicenter Global Phase 2b in Stage 3 Type 1 Diabetes Patients

SAFEGUARD study: SAFety and Efficacy of human anti-thymocyte immunoGlobUlin SAB-142 ARresting progression of type 1 Diabetes

Global study expected to initiate mid 2025

SafeGUARD

Trial design:

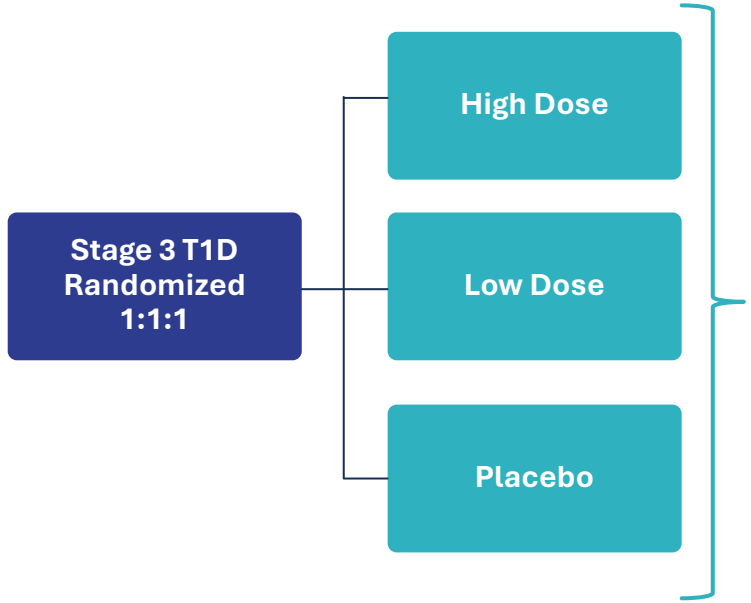
- 142 pediatric, adolescent, and adult patients (5-40 years)
- Randomized, double-blind, placebo-controlled, dose-ranging study

Inclusion criteria:

- New onset Stage 3 T1D: within 100 days of diagnosis
- Baseline C-peptide ≥200 pmol/L

Dosing regimen:

- Intravenous (IV)
- 0.5 mg/kg on Day 1 and remainder of dose Day 2/3



Endpoints

Primary:
Stimulated C-peptide following 2-hr MMTT at 12 months (detect at least 40% difference with 80% power)

Secondary:

- Lead Clinical end point: Time in Range
- Other Secondary end points:
  - Time in Tight Range, Time Below Range
  - Insulin use
  - HbA1c
  - Hypoglycemic episodes
  - Safety

United States (FDA)

Europe (EMA)

United Kingdom (MHRA)

Australia (TGA)

Q&A Session

Samuel Reich

Chairman and CEO

Alexandra Kropotova, MD

Chief Medical Officer & EVP

Michael Haller, MD

Professor and Chief
Pediatric Endocrinology
University of Florida