BREAKING THE DEPLETION PARADIGM: IMMUNOMODULATION WITHOUT SUSTAINED LYMPHODEPLETION WITH SAB-142, A FULLY HUMAN, MULTI-SPECIFIC ANTI-THYMOCYTE GLOBULIN FOR T1D

Stan Stoyanov, MD

VP Clinical Development

March 14th, 2026

Forward-Looking Statements

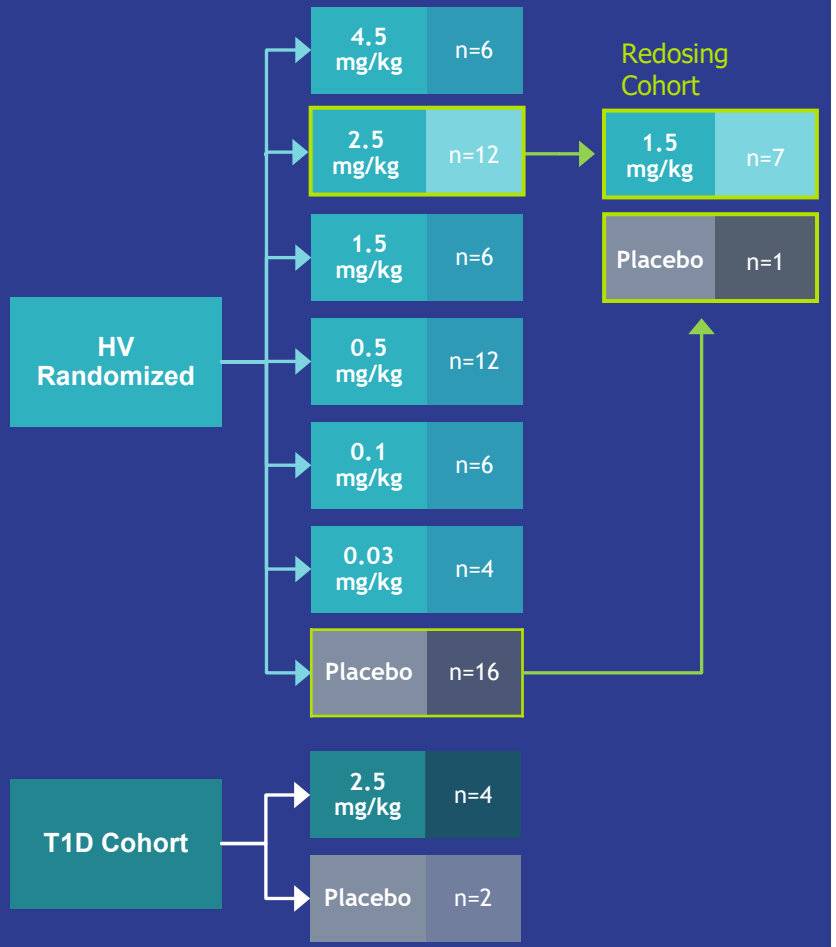
The material in this presentation has been prepared by SAB Biotherapeutics, Inc., doing business as SAB BIO ("SAB") and is general background information about SAB's activities current as of the date of this presentation. This information is given in summary form and is not intended to be complete. Information in this presentation, including financial forecasts, should not be considered advice or a recommendation to investors or potential investors in relation to holding, purchasing, or selling securities or other financial products or instruments and does not take into account any particular investment objectives, financial situation or needs.

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, the exercise of outstanding warrants for cash, results of operations and financial condition, capital adequacy, specific provisions, and risk management practices. 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 filed with the U.S. Securities and Exchange Commission (the "SEC") and in subsequent filings and reports that SAB makes with the SEC from time to time, including but not limited to SAB's Registration Statement on Form S-3 (File No. 333-289992) declared effective by the SEC on September 30, 2025, and the prospectus contained therein.

Unless otherwise specified, information is current at the date hereof. Except as otherwise required by law, SAB disclaims any intention or obligation to update or revise any forward-looking statements, which speak only as of the date they were made, whether as a result of new information, future events or circumstances or otherwise.

Phase 1: HUMAN* Trial Study Design

Randomized, double-blind, placebo-controlled, single- and multiple- ascending dose, adaptive design clinical study



SAB-142's Phase 1 Data Demonstrated Encouraging Efficacy Signals with Clinically Validated, Multi-specific MOA with Sustained Immunomodulation

Efficacy — Encouraging early signals of C-peptide preservation in established T1D patients

- Early C-peptide signal consistent with beta cell preservation

Immunogenicity — Confirm SAB-142 not immunogenic

- Does not cause anti-drug antibodies
- Enables safe and reliable redosing

PK/PD — Demonstrate sustained "T-cell exhaustion" signature

- Clinically validated by rATG and other T1D T-cell targeting biologics
- Demonstrated correlation with C-peptide preservation based on precedent rATG studies and natural course of T1D

Safety and Tolerability — Position SAB-142 for a convenient, potentially twice a year dosing regimen

- No sustained lymphodepletion leading to immuno-suppression; no neutropenia
- No serum sickness

*HUman anti-thymocyte biologic in first-in-MAN clinical study

SAB-142-101
Phase 1 Top Line

SAB-142 Does Not Cause Sustained Lymphodepletion

No sustained lymphodepletion

- SAB-142: Transient lymphopenia due to lymphocyte margination
- Lymphocytes recover back to baseline by Day 7 after Induction and Maintenance Doses of SAB-142

Rabbit ATG causes sustained lymphodepletion up to 2 years

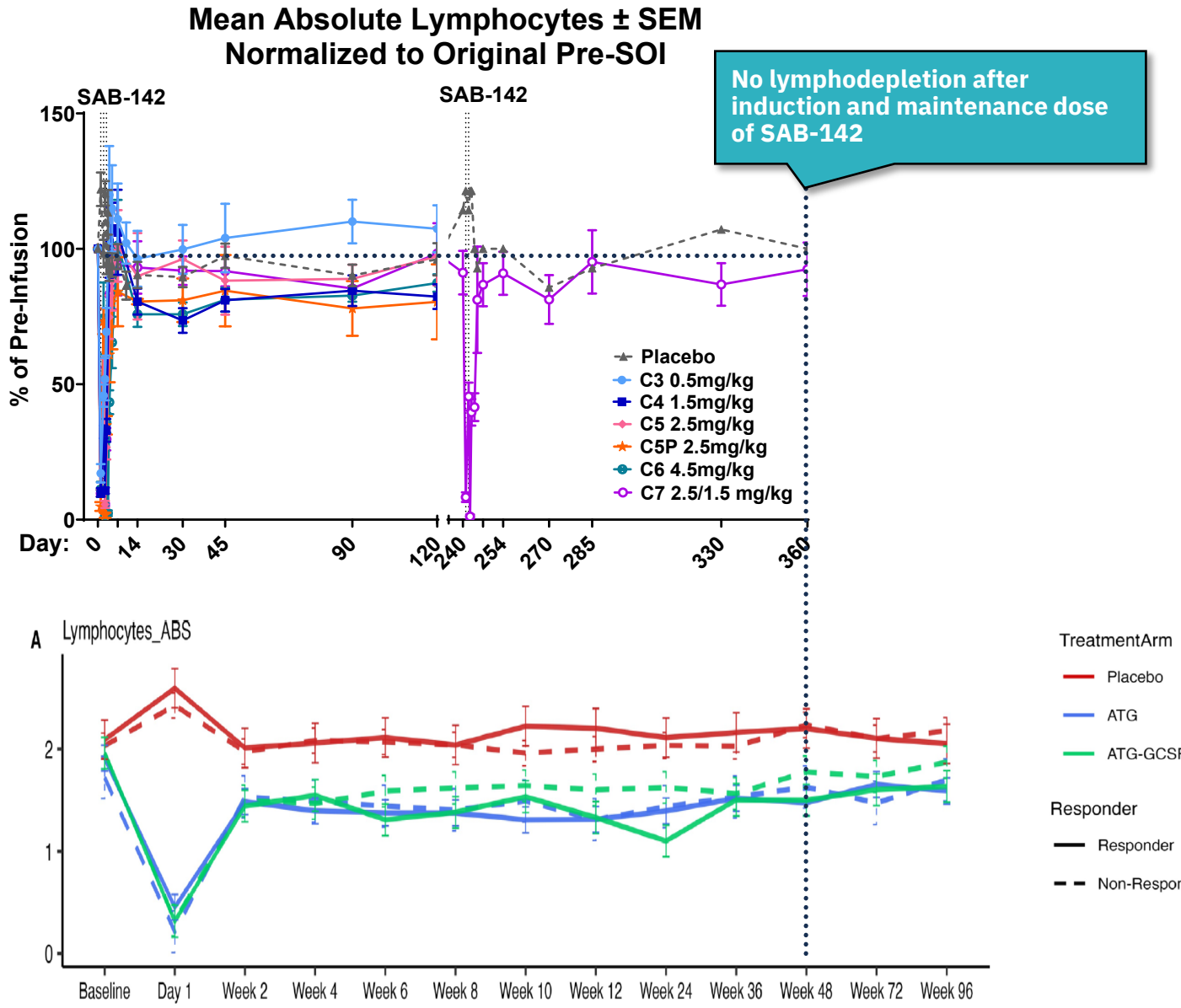

JCI insight

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,[1] 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.



SAB-142-101
Phase 1 Top Line

SAB-142 CD4+ T conv Cell Single Exhaustion Markers

SAB-142 induced sustained expression of inhibitory receptor PD-1 on CD4+ T conv cells indicative of an exhausted phenotype.

SAB-142 CD4+ T conv Cell Dual Exhaustion Markers

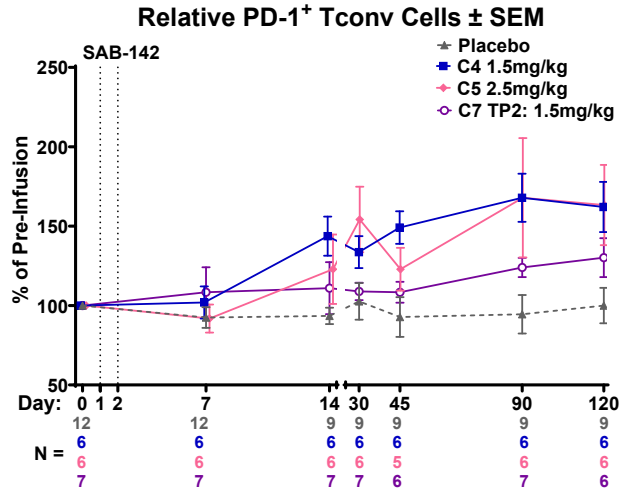
SAB-142 induced sustained expression of co-inhibitory receptors on CD4+ T conv cells.

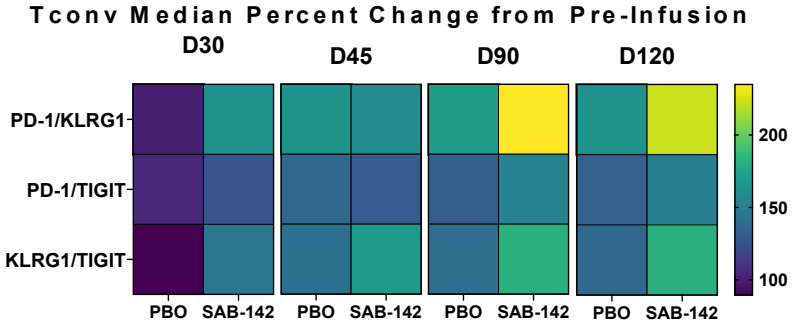
SAB-142: combined 1.5mg/kg and 2.5mg/kg dosed cohorts.

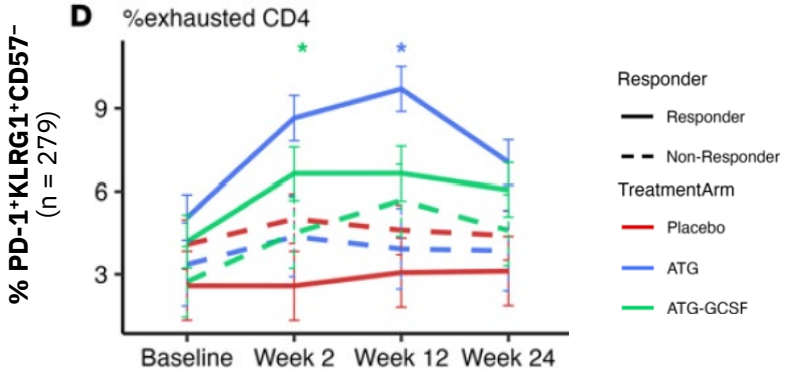
Rabbit ATG CD4+ T Cell Dual Exhaustion Markers

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 Conventional Cell Exhaustion Analogous to rATG







JCI insight CLINICAL MEDICINE

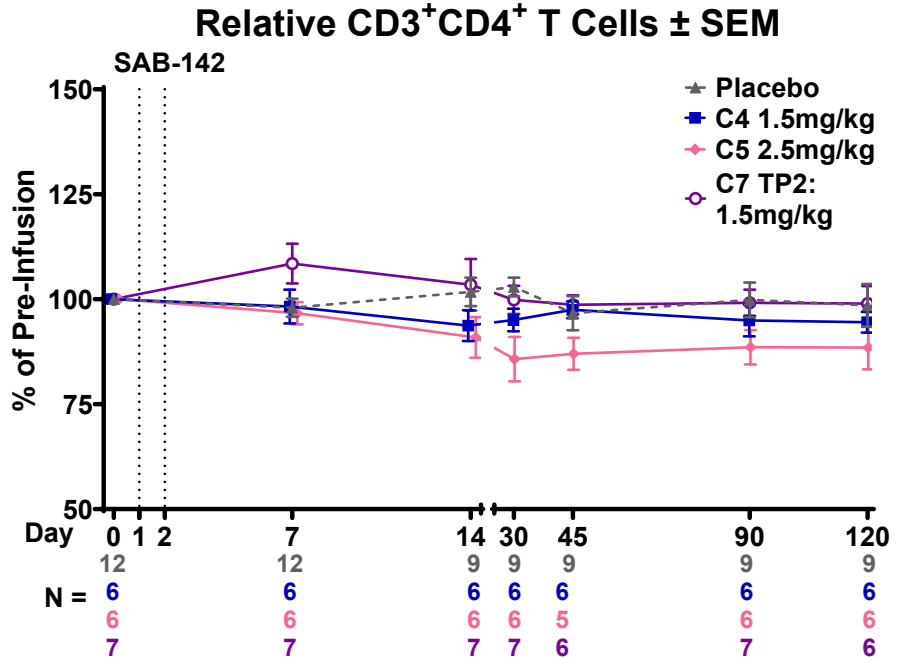
Responders to low-dose ATG induce CD4+ T cell exhaustion in type 1 diabetes

SAB-142-101
Phase 1 Top Line

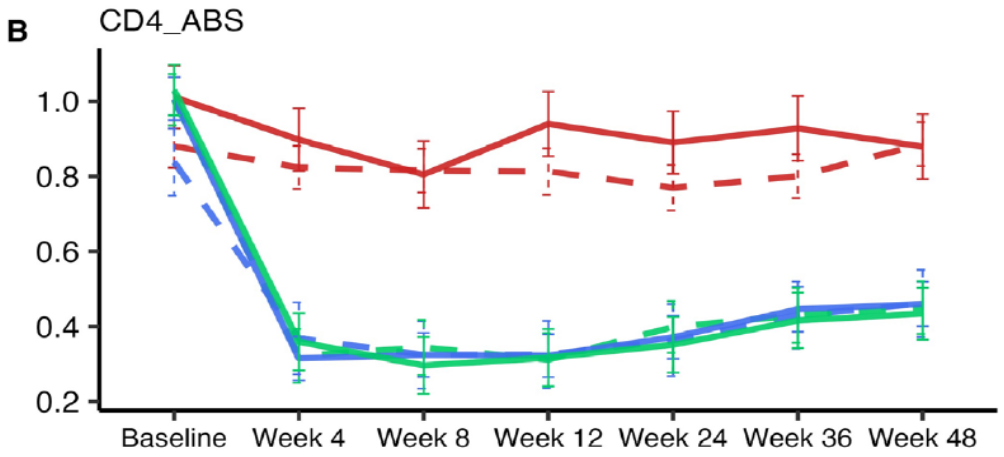
SAB-142 Does Not Cause Sustained Lymphodepletion

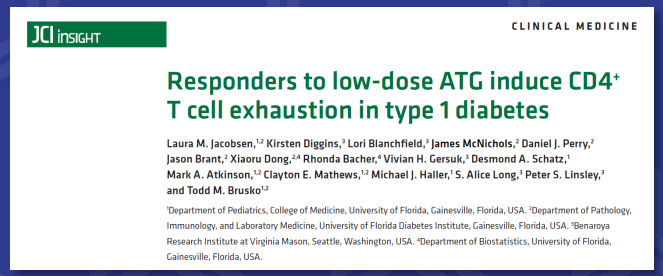
No loss of CD4⁺ T Cells

- SAB-142 results in immunomodulation with no depletion of CD4⁺ T cells
- SAB-142 demonstrated validated MOA to deliver potentially **Best-in-Class T1D immunotherapy**



Rabbit ATG causes sustained depletion of CD4⁺ T cells.




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.

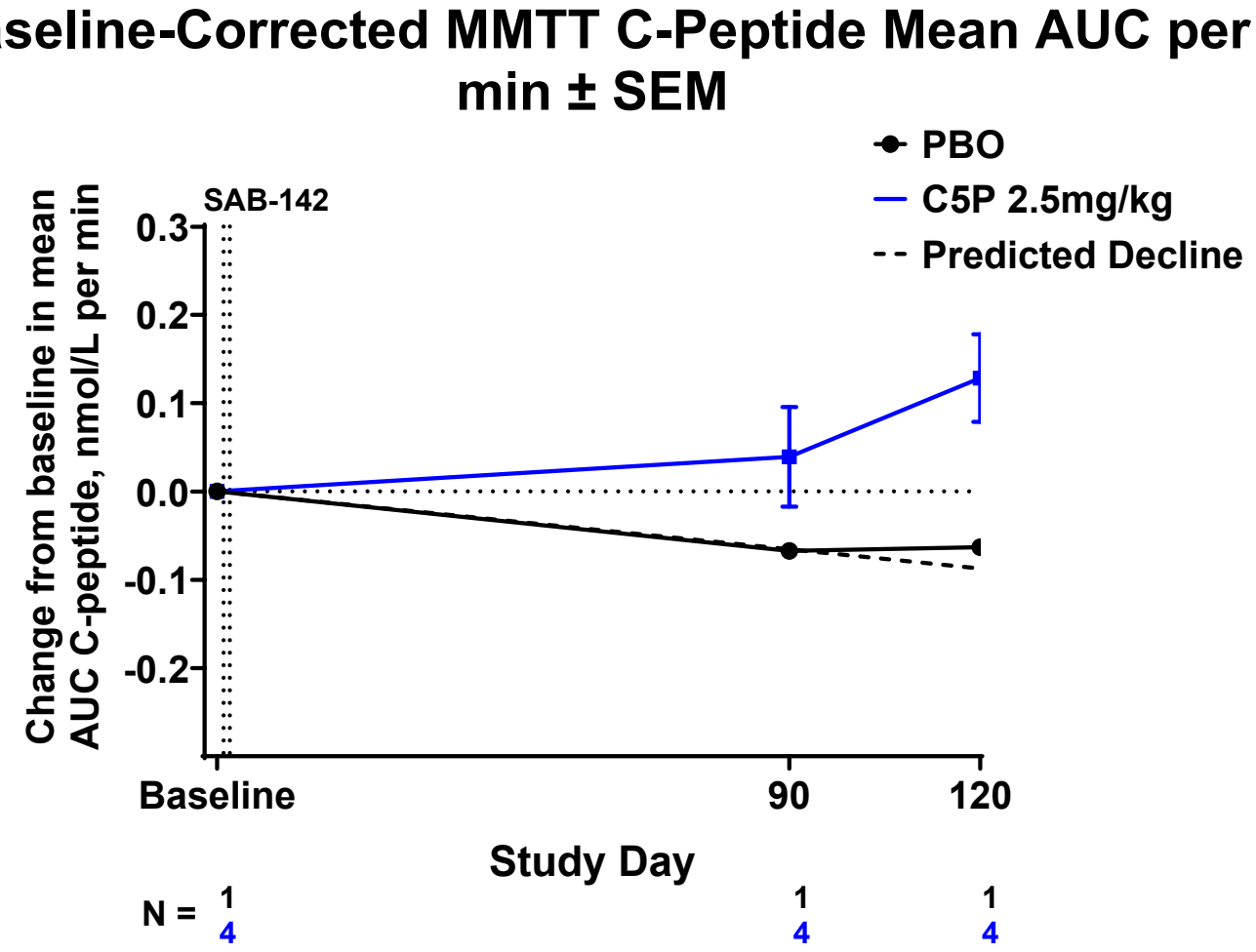
SAB BIO

SAB-142-101

T1D Cohort at 2.5mg/kg

SAB-142 effects on C-peptide are consistent with PD response

T1D Cohort: C-Peptide Response



Predicted Decline was estimated by first calculating the AUC of TN19 PBO subject C-peptide MMTT data (n=26) for Weeks 48-96 with post-2hr values masked. The linear slope was used to calculate the predicted rate of decline in days: AUC_{BL} – (-0.6108*(Study Day/7))

SAB-142
In Vitro Data

SAB-142 and rabbit ATG (rATG) Binding and Activation of FcγRIII Pathway (ADCC), FcRn and FcγRI

SAB-142 has less binding to FcγRIII and less ADCC activation than rATG

Binding to the FcγRIII on natural killer cells activates cellular pathways leading to antibody dependent cellular cytotoxicity (ADCC)

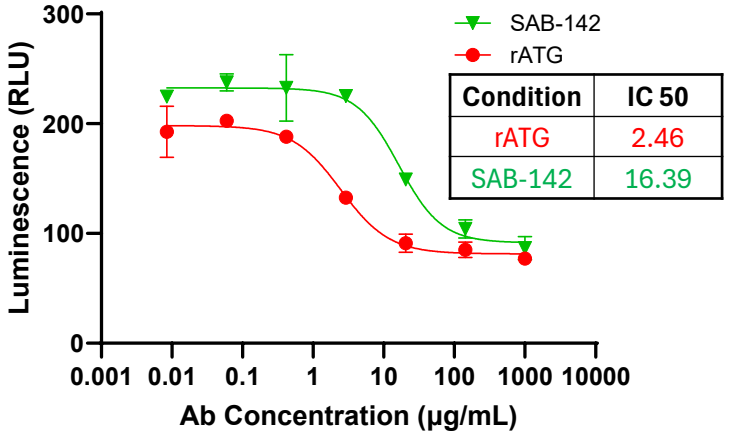
No ADCC at therapeutic doses of SAB-142 → no lymphodepletion

Similar or better binding to FcRn and FcγRI facilitates immune activation & exhaustion

The human FcRn transports IgG across endothelial barriers; facilitates movement of IgG in both directions

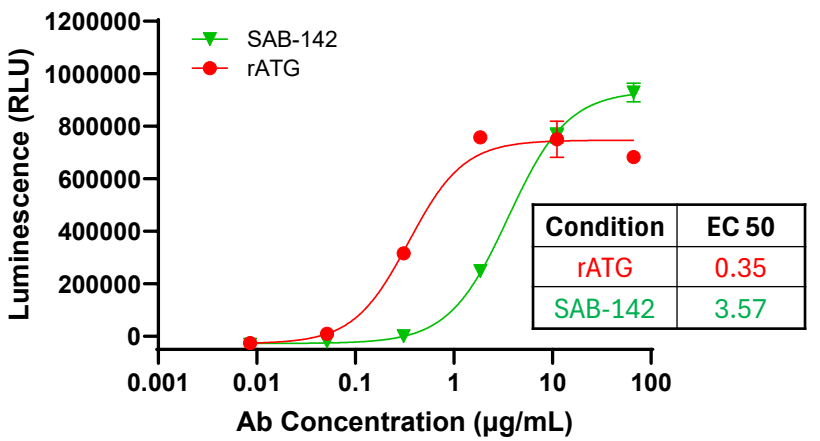
The human FcγRI increases immune activation in multiple immune cell types

Competitive Inhibition of FcγRIIIa(V158) Binding



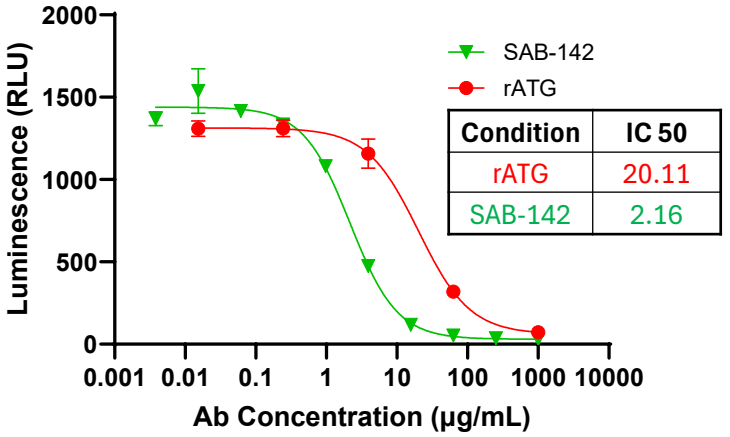
Condition	IC 50
rATG	2.46
SAB-142	16.39

ADCC Activation on Jurkat Cells



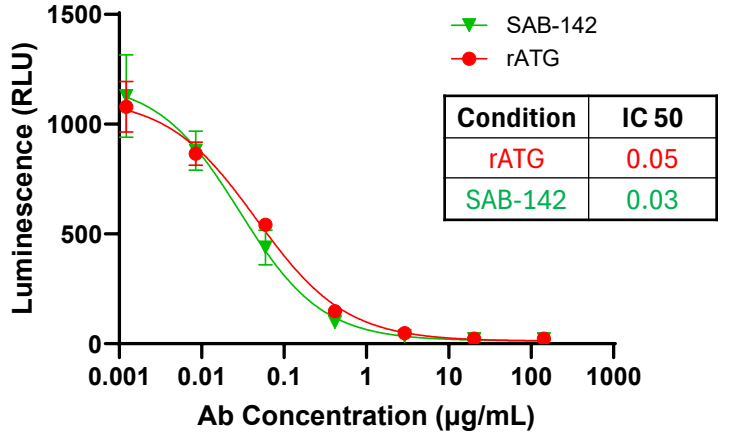
Condition	EC 50
rATG	0.35
SAB-142	3.57

Competitive Inhibition of FcRn Binding



Condition	IC 50
rATG	20.11
SAB-142	2.16

Competitive Inhibition of FcγRI Binding



Condition	IC 50
rATG	0.05
SAB-142	0.03

8

CONCLUSION

SAB-142 demonstrated a validated MOA with encouraging C-peptide preservation to deliver potentially Best-in-Class T1D immunotherapy

- Only transient lymphopenia due to margination was observed during dosing without sustained depletion
- SAB-142 has no ADCC activity at therapeutic concentrations

SAFEGUARD

Phase 2 Clinical Trial SAFEGUARD has Launched

USA, Australia, New Zealand, UK, and EMA countries are approved, with sites being initiated.

ATTD Advanced Technologies & Treatments for Diabetes 11-14 MARCH 2026 BARCELONA & ONLINE

SAB-142 data in depth at ATTD

March 11th-14th, 2026

BREAKING THE DEPLETION PARADIGM: IMMUNOMODULATION WITHOUT SUSTAINED LYMPHODEPLETION WITH SAB-142, A FULLY HUMAN, MULTI-SPECIFIC ANTI-THYMOCYTE GLOBULIN FOR T1D
CHARTING THE SAFETY LANDSCAPE OF MULTI-SPECIFIC MODALITIES: SAFETY PROFILE OF MULTI-SPECIFIC ANTI-THYMOCYTE GLOBULIN SAB-142
DECODING THE BINDING LANDSCAPE FOR MULTI-SPECIFIC T1D BIOLOGICS: TARGETED BINDING OF RABBIT VS HUMAN ANTI-THYMOCYTE GLOBULIN, SAB-142
BETA CELL GUARDIANS: MECHANISM OF ACTION OF SAB-142, AN EMERGING IMMUNOTHERAPY FOR NEW ONSET T1D
TRACKING MULTIPLICITY: IN VITRO AND CLINICAL PHARMACOKINETIC ASSAYS FOR MULTI-TARGET THERAPEUTICS
IMPROVING THE INTEGRITY OF CLINICAL SAMPLES: ASSESSING BLOOD PRESERVATION METHODS FOR ANAYLSYS BY FLOW CYTOMETRY

SAB BIO