Working to Change the Lives of People Impacted by Type 1 Diabetes Through Unique Disease-Modifying Therapy

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Forward-Looking Statements

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

POTENTIAL DISEASE MODIFICATION

Lead candidate SAB-142 has the **potential to deliver disease modification in newly diagnosed Stage 3 T1D with convenient twice-yearly dosing,** supported by clinical data and a de-risked mechanism of action

POSITIVE PHASE 1 DATA SUPPORTS DE-RISKED MOA

Phase 1 data show SAB-142 has an MOA comparable to rabbit ATG, **with improved safety and potential for repeat dosing**, supporting advancement into the Phase 2b SAFEGUARD study

UNIQUE MULTI-SPECIFIC ANTIBODY PLATFORM

First-ever platform that can generate a diverse repertoire of **multi-specific, targeted, anti-thymocyte human IgG**

SAB BIO

SAB-142-101
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 clinically validated multi-specific MOA with sustained immunomodulation

Safety & Tolerability

Data strongly position SAB-142 for potentially safe & reliable chronic dosing

- Does not cause lymphodepletion
- Does not cause neutropenia, sustained decrease in RBCs or thrombocytes

PK/PD

Data demonstrate sustained "T-cell exhaustion" signature

- Clinically validated by rabbit ATG and other T1D T-cell targeting immunomodulatory drugs
- Proven to correlate with C-peptide preservation based on clinical studies in new onset T1D

No serum sickness & low/no immunogenicity

Data confirm SAB-142 is not immunogenic

- Does not cause serum sickness
- Does not induce anti-drug antibodies

SAB-142
Pre-clinical data

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

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

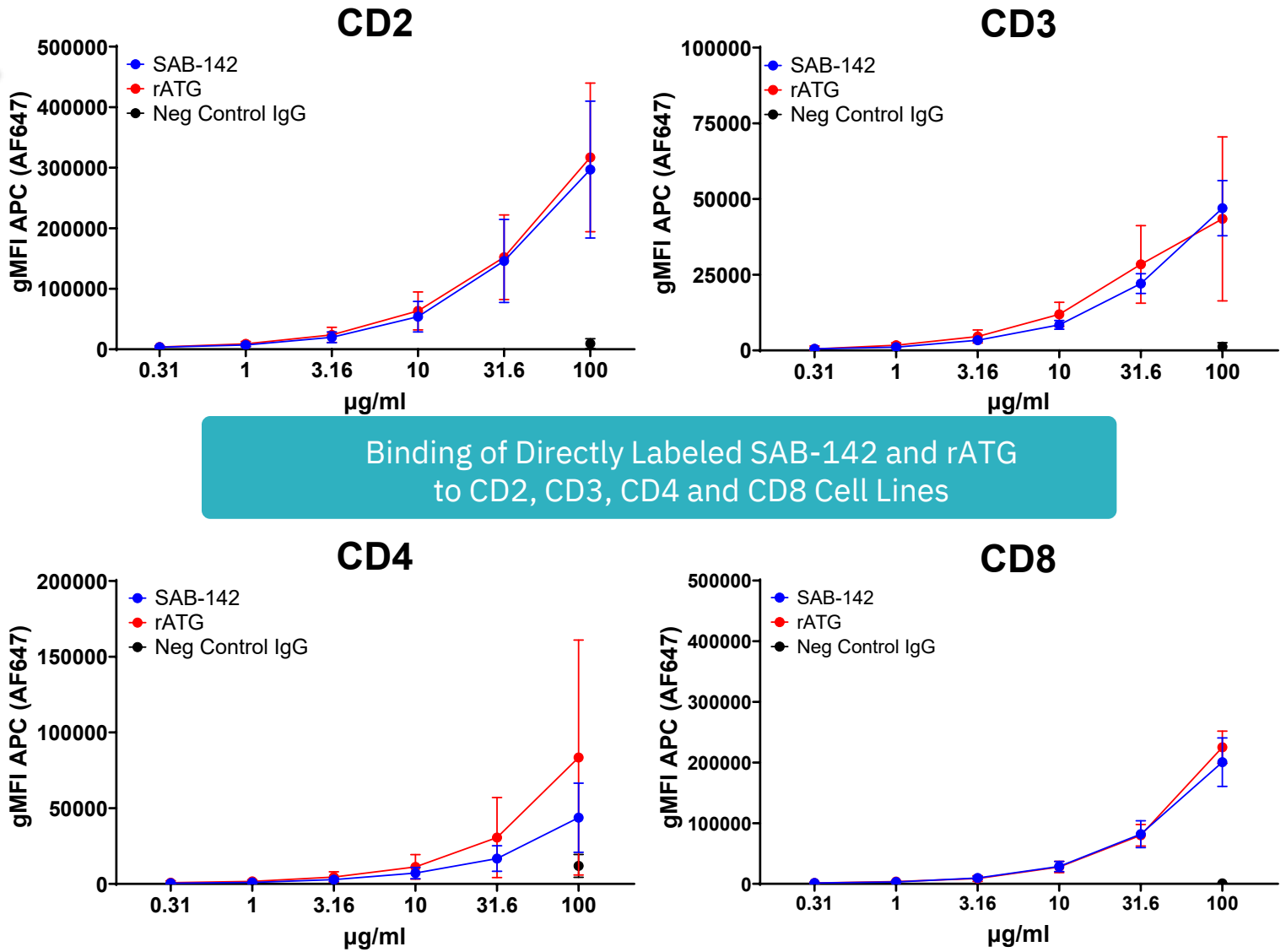
American Journal of Transplantation 2013; 13: 3103–3113
Wiley Periodicals Inc.

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

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

SAB-142-101
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 1.5mg/kg and 2.5mg/kg dosed cohorts

SAB-142 CD4+ T conv Cell Dual Exhaustion Markers

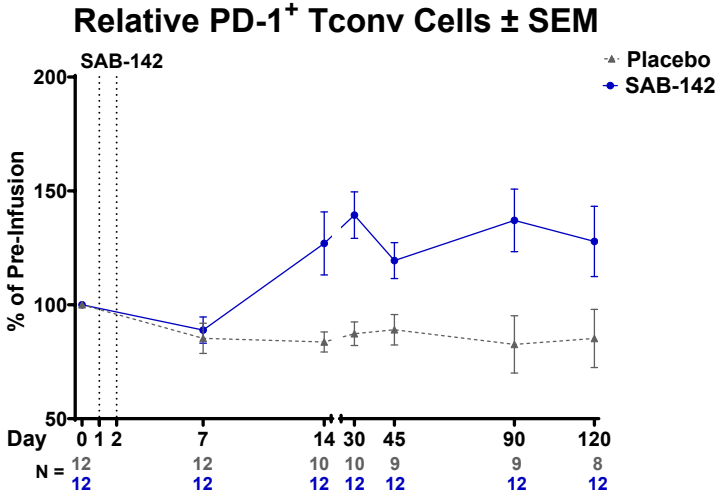
SAB-142 induced persistent expression of co-inhibitory receptors on CD4+ T conv cells.

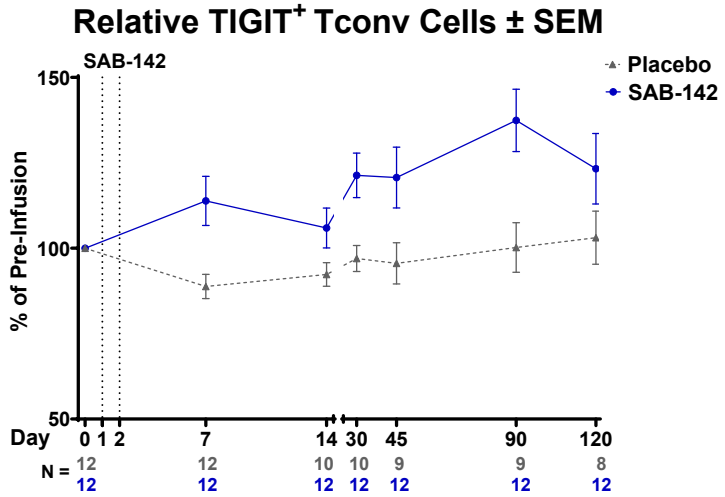
SAB-142: combined 1.5mg/kg and 2.5mg/kg dosed cohorts

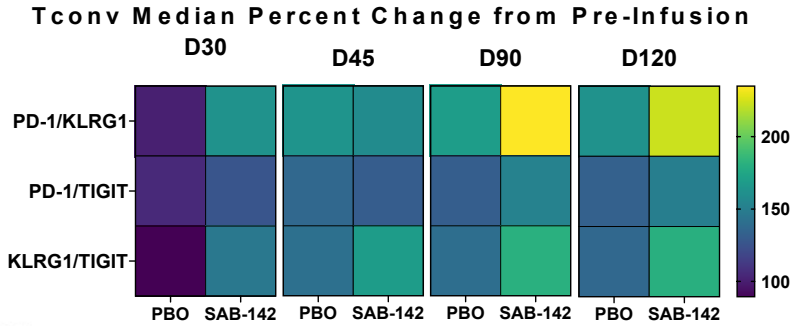
Rabbit ATG CD4+ T Cell Dual Exhaustion Markers

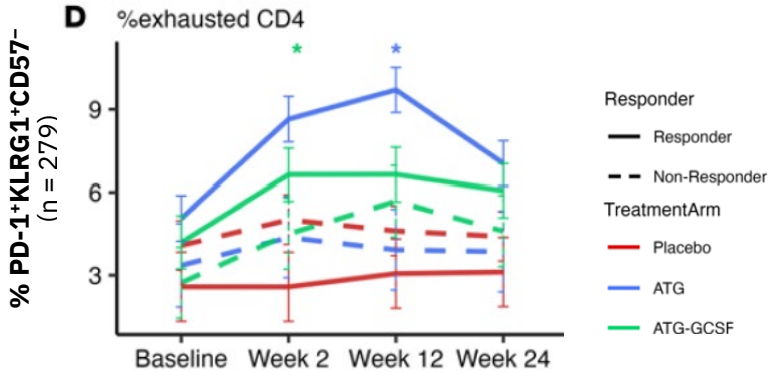
Low-dose ATG induced persistent expression of co-inhibitory receptors (PD-1, KLRG1) on CD4+ cells indicating exhaustion-like phenotype which correlates with C-Peptide preservation.

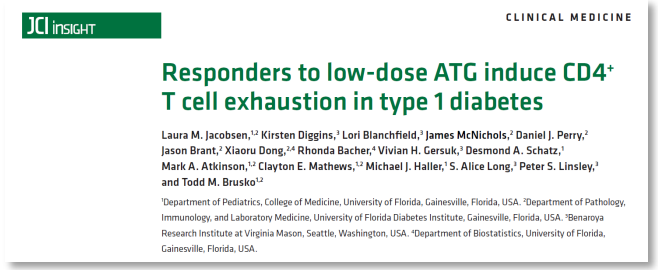
SAB-142 demonstrates sustained CD4+ T conv cell exhaustion analogous to rATG










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,[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.

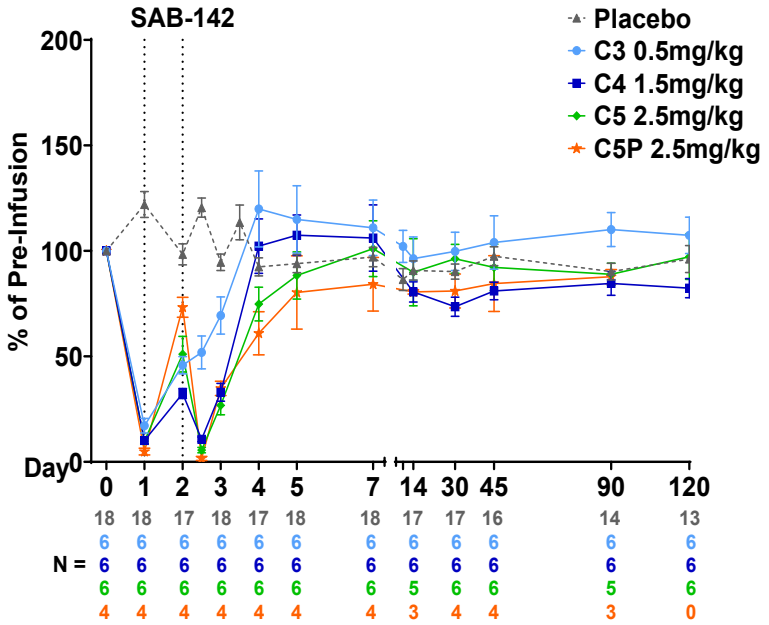
SAB-142-101
Phase 1 Top Line

No sustained lymphodepletion

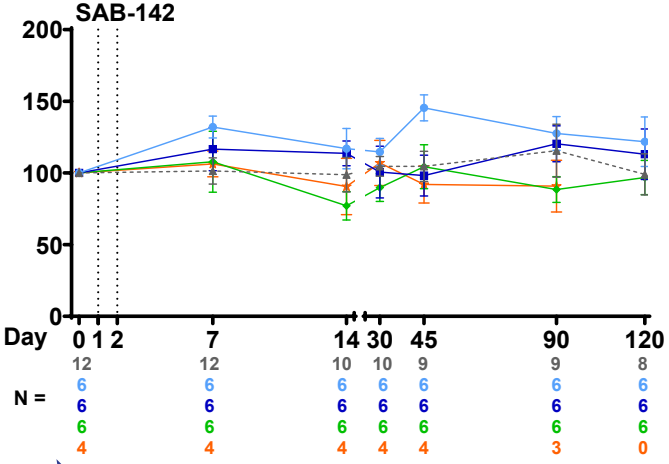
- SAB-142: Lymphocytes recover back to baseline by Day 7.
- SAB-142 results in immunomodulation with no sustained lymphodepletion, unlike rabbit ATG that causes decrease in CD4⁺ T-cells for up to 2 years.
- SAB-142 demonstrated validated MOA to deliver potentially **Best-in-Class T1D immunotherapy.**

SAB-142 does not cause sustained lymphodepletion

Relative Absolute Lymphocytes ± SEM

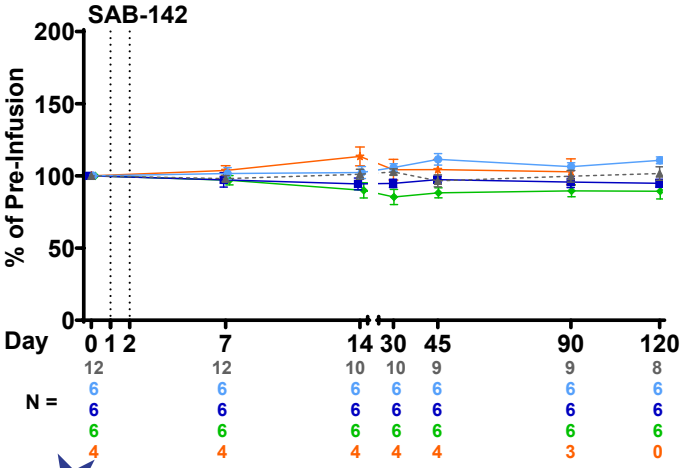


Relative B Cells ($CD3^-CD56^-CD19^+$) ± SEM



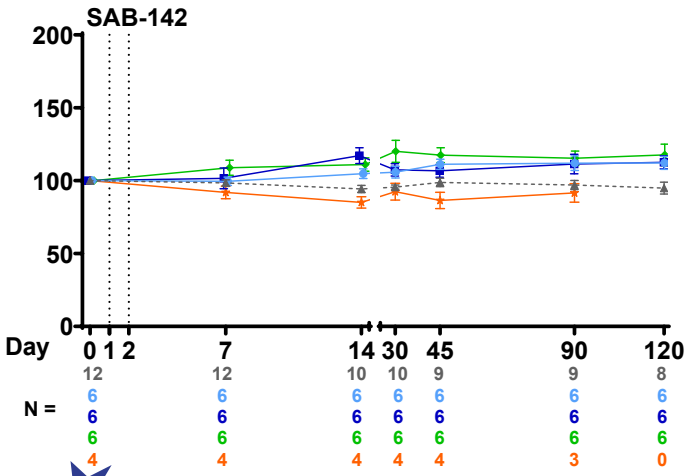
No B-cell lymphodepletion

Relative $CD3^+CD4^+$ T Cells ± SEM



No $CD4^+$ T-cell lymphodepletion

Relative $CD3^+CD8^+$ T Cells ± SEM



No $CD8^+$ T-cell lymphodepletion

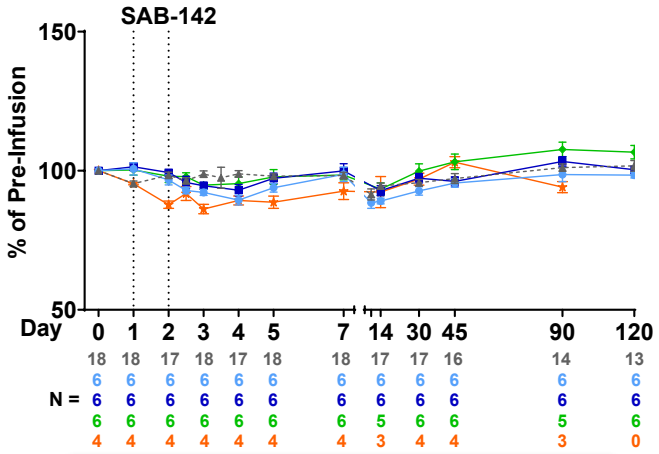
SAB-142-101
Phase 1 Top Line

SAB-142 does not deplete RBCs, Neutrophils or Platelets.
All cells recover back to baseline by Day 7.

SAB-142 demonstrated validated MOA to deliver potentially **Best-in-Class T1D immunotherapy**

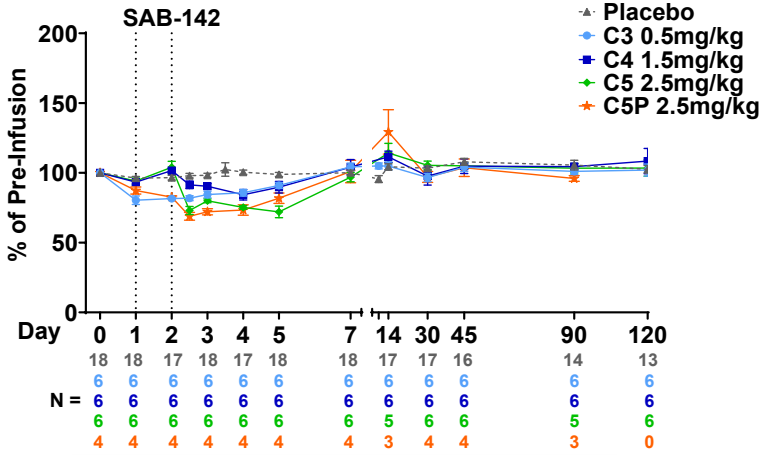
SAB-142 does not cause sustained depletion of other cells

Relative Absolute Red Blood Cells ± SEM



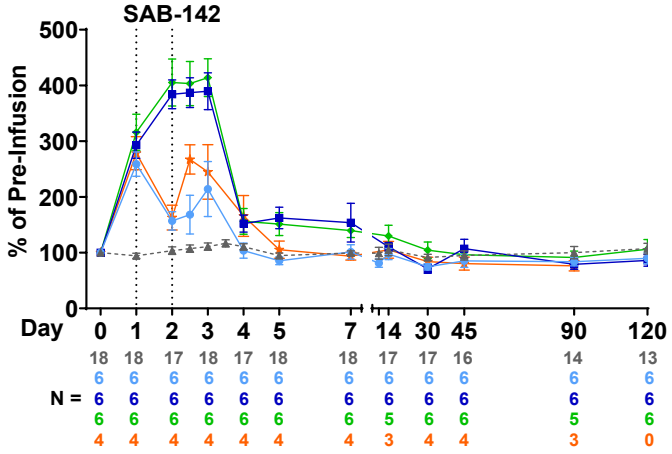
No RBC Depletion

Relative Absolute Platelets ± SEM



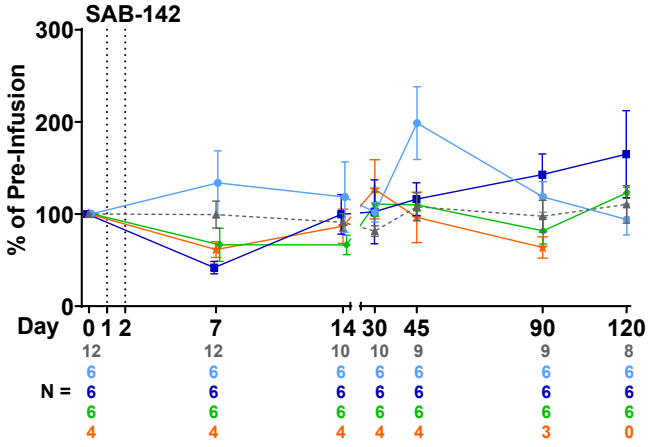
No Thrombocytopenia

Relative Absolute Neutrophils ± SEM



No Neutropenia

Relative NK ($CD3^{-}CD56^{+}$) Cells ± SEM



No NK Cell Depletion

SAB-142: Multicenter Global Phase 2b in Patients with New Onset Stage 3 T1D

SAFEGUARD Phase 2b Study

SAFety and **E**fficacy of human anti-thymocyte immuno**G**lob**U**lin SAB-142 **AR**resting progression of Type 1 **D**iabetes

Trial design:

- 159 pediatric, adolescent, and adult patients 5-40 years of age
- Part B is Randomized, double-blind, placebo-controlled, dose-ranging study

Inclusion criteria:

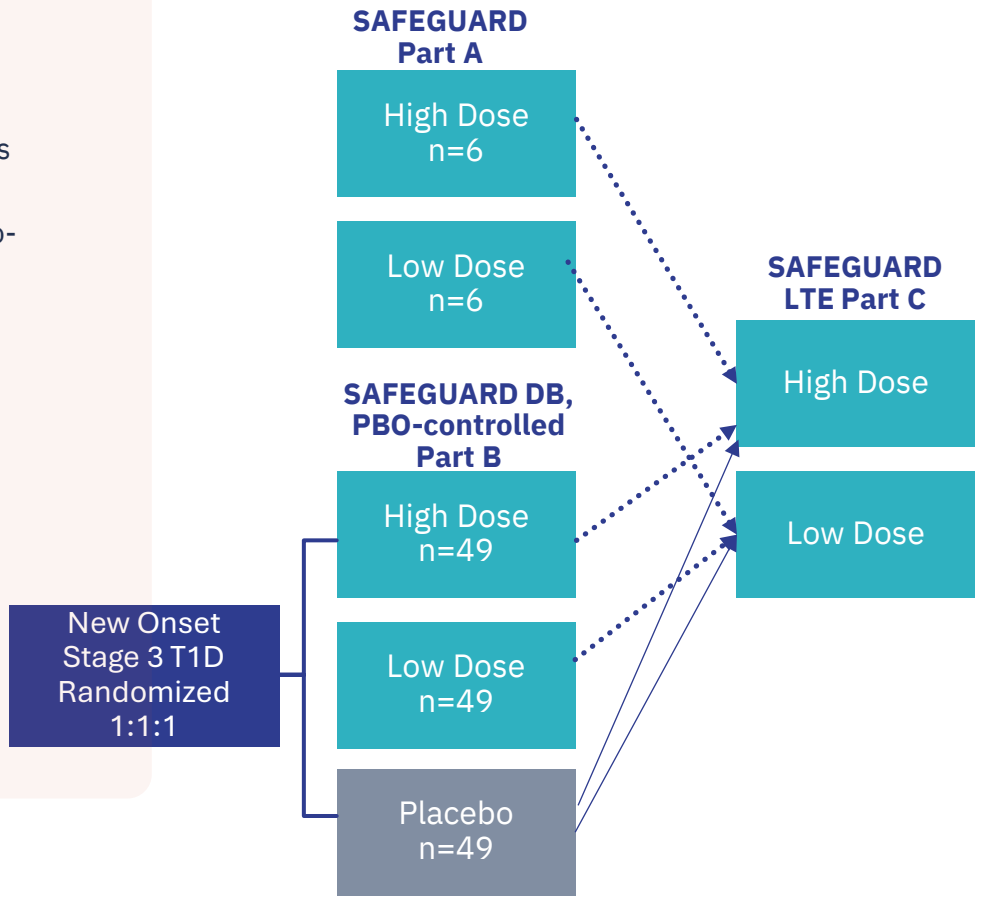
- New onset Stage 3 T1D: within 100 days of diagnosis
- Baseline C-peptide ≥200 pmol/L

Dosing regimen:

- High dose: 2.5mg/kg; Low dose: 1.5mg/kg
- Intravenous (IV) split two-day ambulatory dosing
- Administered every 6-month

Global study to initiate H2 2025 LPO expected H2 2027

SAFEGUARD Phase 2b Study Design



Primary Endpoint:

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

Secondary Endpoint:

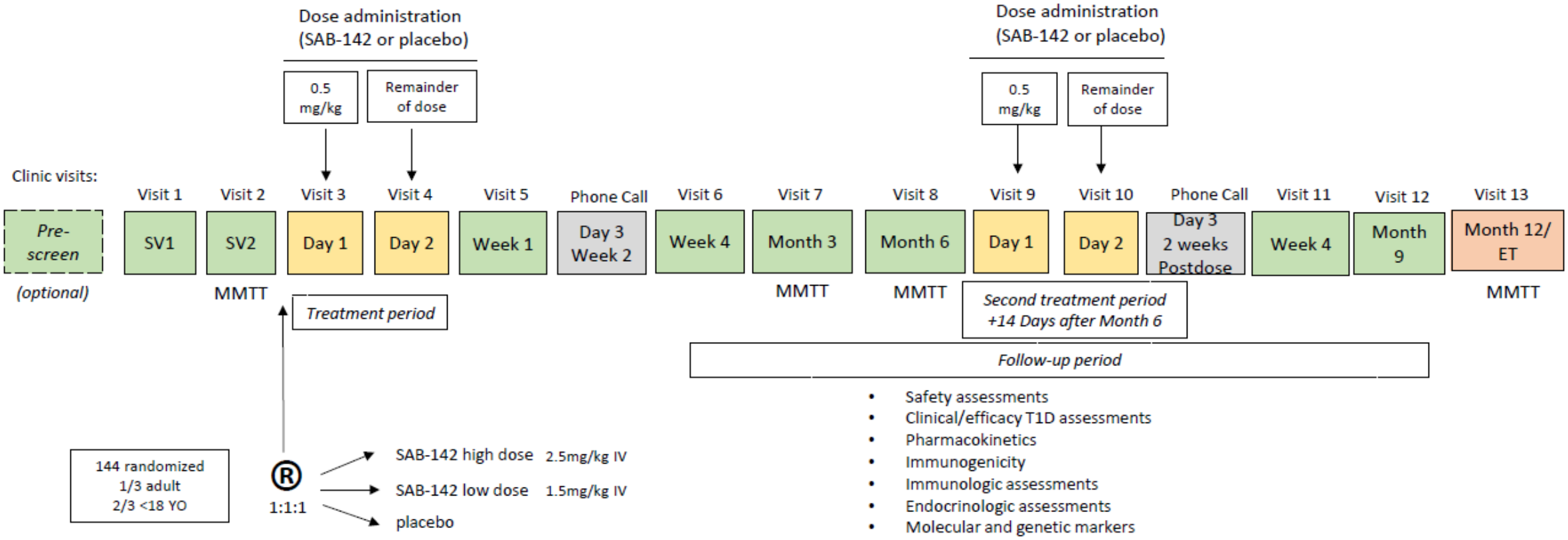
Leading Clinical Endpoint:
Time in Tight Range

Other secondary Endpoints:

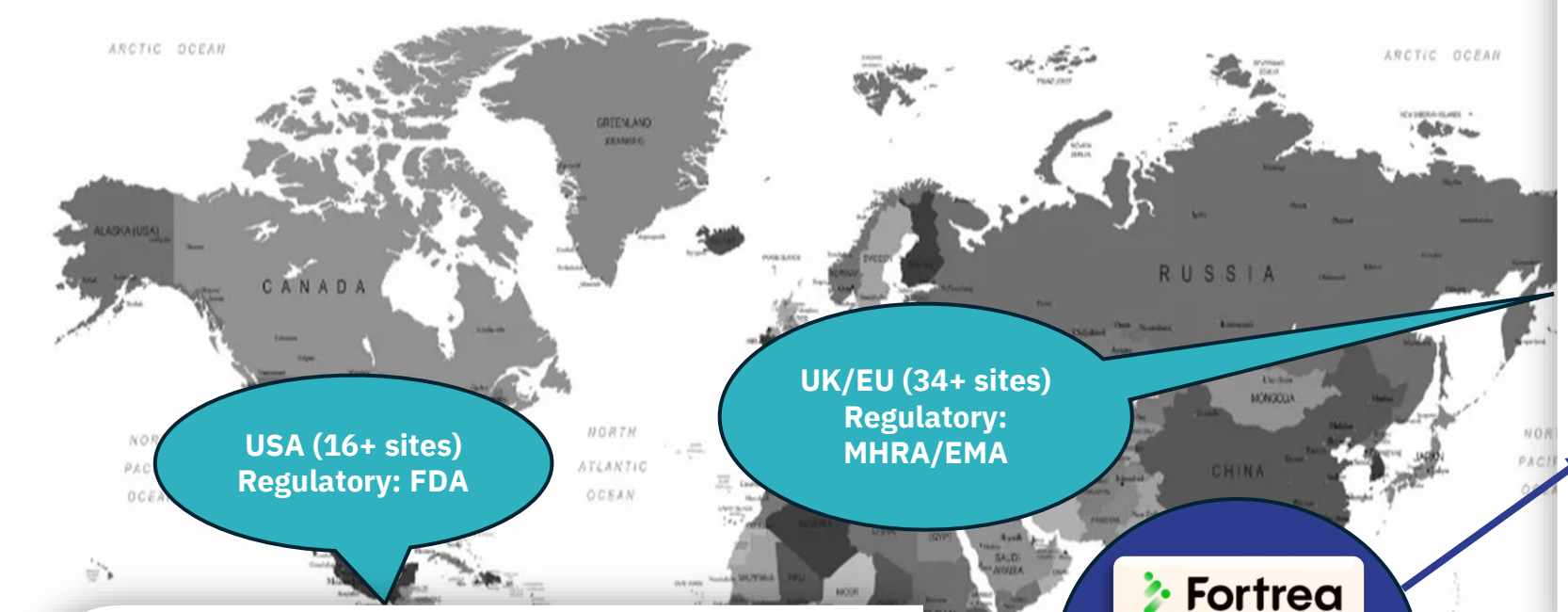
- → TITR, TIR, TBR
- → Insulin use
- → HbA1c
- → Hypoglycemic episodes
- → Safety

SAFEGUARD Study Design: Part B

A Phase 2B, Randomized, Double-Blind, Placebo-Controlled, Dose-Ranging Study Evaluating the Efficacy and Safety of SAB-142 for the delay of progression of Type 1 Diabetes in new/recent onset Stage 3 T1D patients



SAFEGUARD: Shared Journey



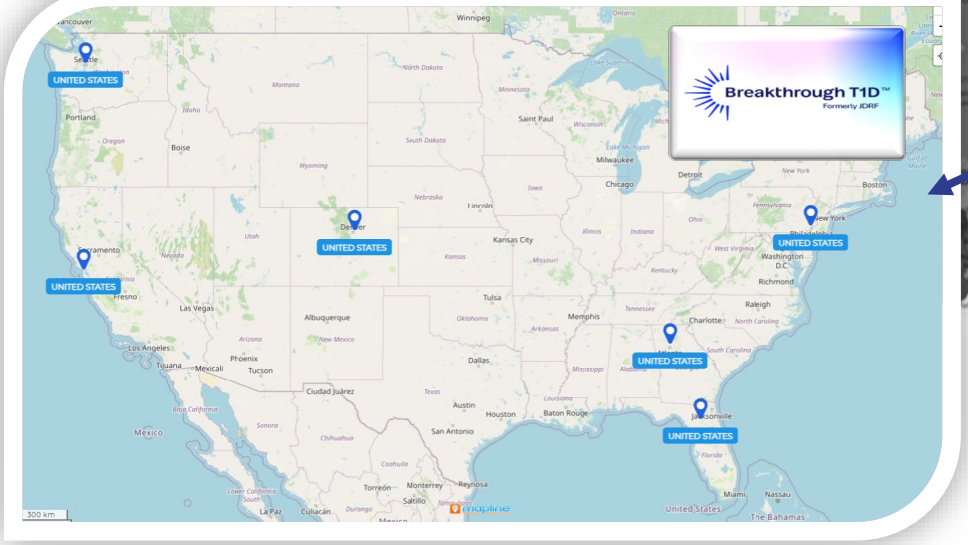
USA (16+ sites)
Regulatory: FDA

UK/EU (34+ sites)
Regulatory:
MHRA/EMA

AUS/NZ (9+ sites)
Regulatory:
TGA / MedSafe

Fortrea

SAB BIO



SAB-142 data in depth at EASD

Tuesday Sep 16

Immunomodulation Without Sustained Lymphodepletion: SAB-142, a Fully Human Anti-Thymocyte Globulin

- Session: OP 04 Behind the Screens: Adventures in T1D Clinical Trials
- Presentation number: 19 | Mumbia Hall
- 10:00 - 11:30

Thursday Sep 18

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

- Session: OP 28 Guardians of the Islet Galaxy: Protect and Replace
- Presentation number: 163 | Sofia Hall
- 10:45-12:15

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

