ANB032, a Novel BTLA Agonist Monoclonal Antibody, Inhibits T Cell Proliferation, Reduces Inflammatory Cytokines, and Down Modulates BTLA Expression on Circulating T and B Cells:

Results from a First-in-Human Phase 1 Study

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Disclosures

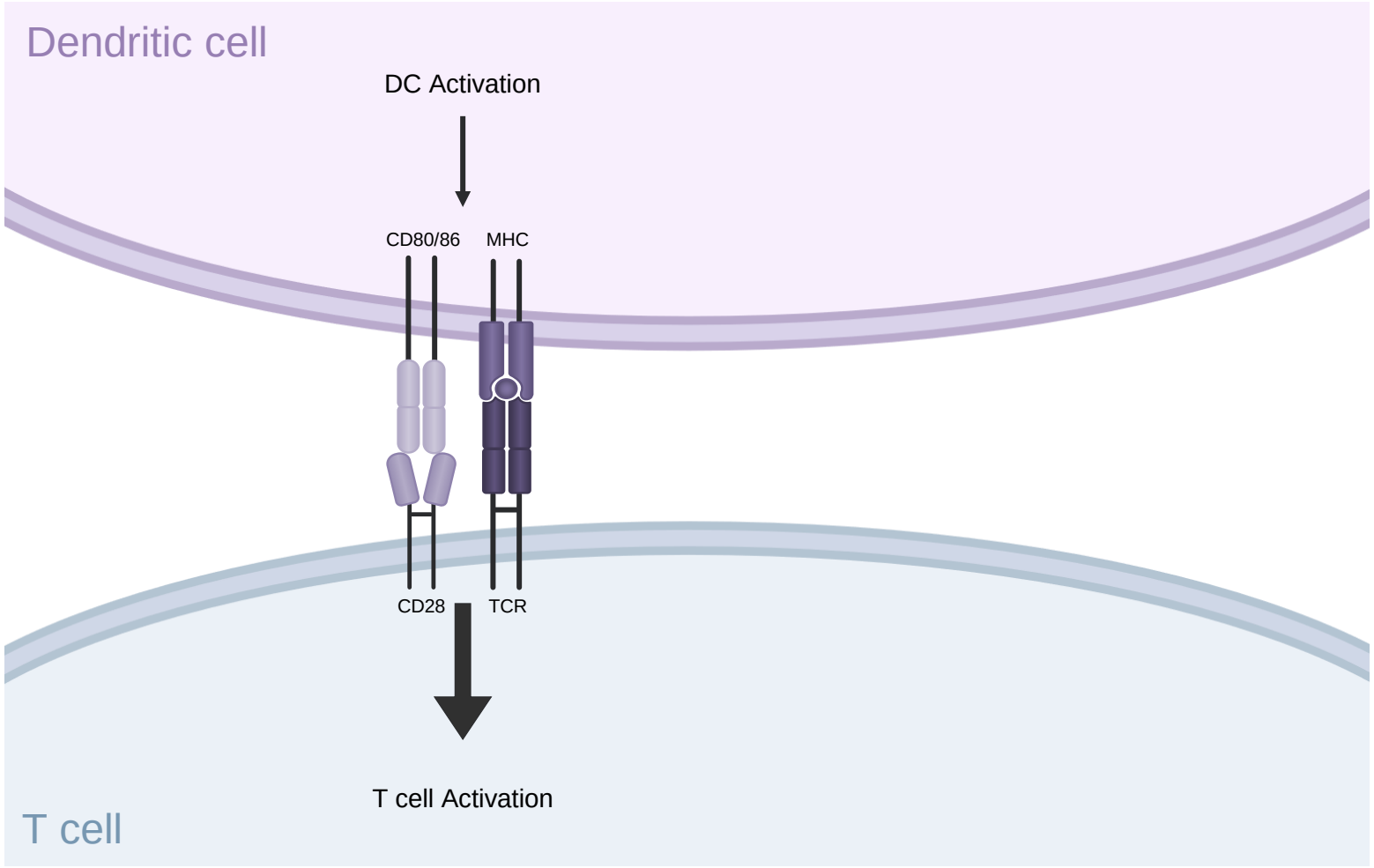
- All authors are employees of AnaptysBio, Inc., San Diego, CA, USA

Background & Introduction

- B and T cell lymphocyte attenuator (BTLA) is a co-inhibitory checkpoint receptor expressed on T cells (Th1, Th2, Th17 and Th22), B cells and dendritic cells (DC), key contributors to inflammatory diseases such as atopic dermatitis (AD)
- BTLA-deficient mice showed increased T cell proliferation and susceptibility to spontaneous development of autoimmune diseases, including dermatitis, demonstrating that BTLA negatively regulates T cell activation and proliferation[1,2]
- ANB032 is a humanized IgG4/κ monoclonal antibody to BTLA that modulates BTLA activity in a non-competitive fashion with its ligand, herpesvirus entry mediator (HVEM)
- In preclinical studies, ANB032 reduced cytokine secretion (Th1, Th2, Th17 and Th22) in AD patient-derived PBMCs[4] and reduced dendritic cell maturation[5]
- ANB032 has potential broad applicability to inflammatory diseases due to breadth of BTLA expression across immune cell types[3]

1. Nakagomi et al. J Invest Dermatol 2013;133:702-11.
2. Bekiaris et al Immunity 2013;39:1082-94
3. Murphy KM, Stockinger B. Nat Immunol 2010;11:674-80.
4. Luu, et al. ISID 2023;
5. Data on file. AnaptysBio, Inc.; abstract submitted.

B and T Lymphocyte Attenuator (BTLA) Checkpoint Receptor



T cell activation requires both:

1. Antigen presentation via MHC and TCR
2. Co-stimulation via CD80/86 and CD28

HVEM, Herpes Virus Entry Mediator; MHC, major histocompatibility complex; TCR, T cell receptor

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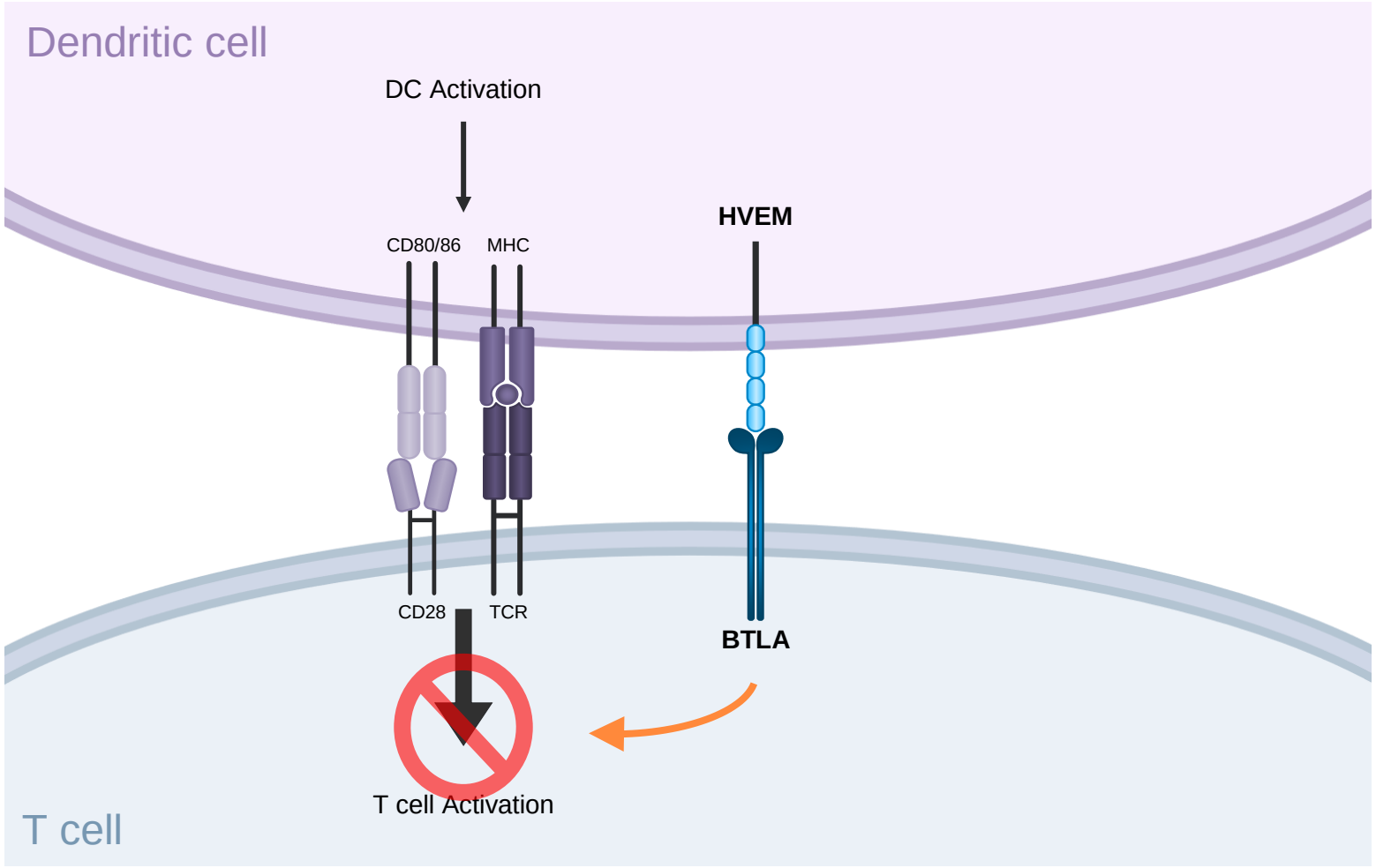

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BTLA on T cell inhibits priming, activation, and expansion of inflammatory T cells

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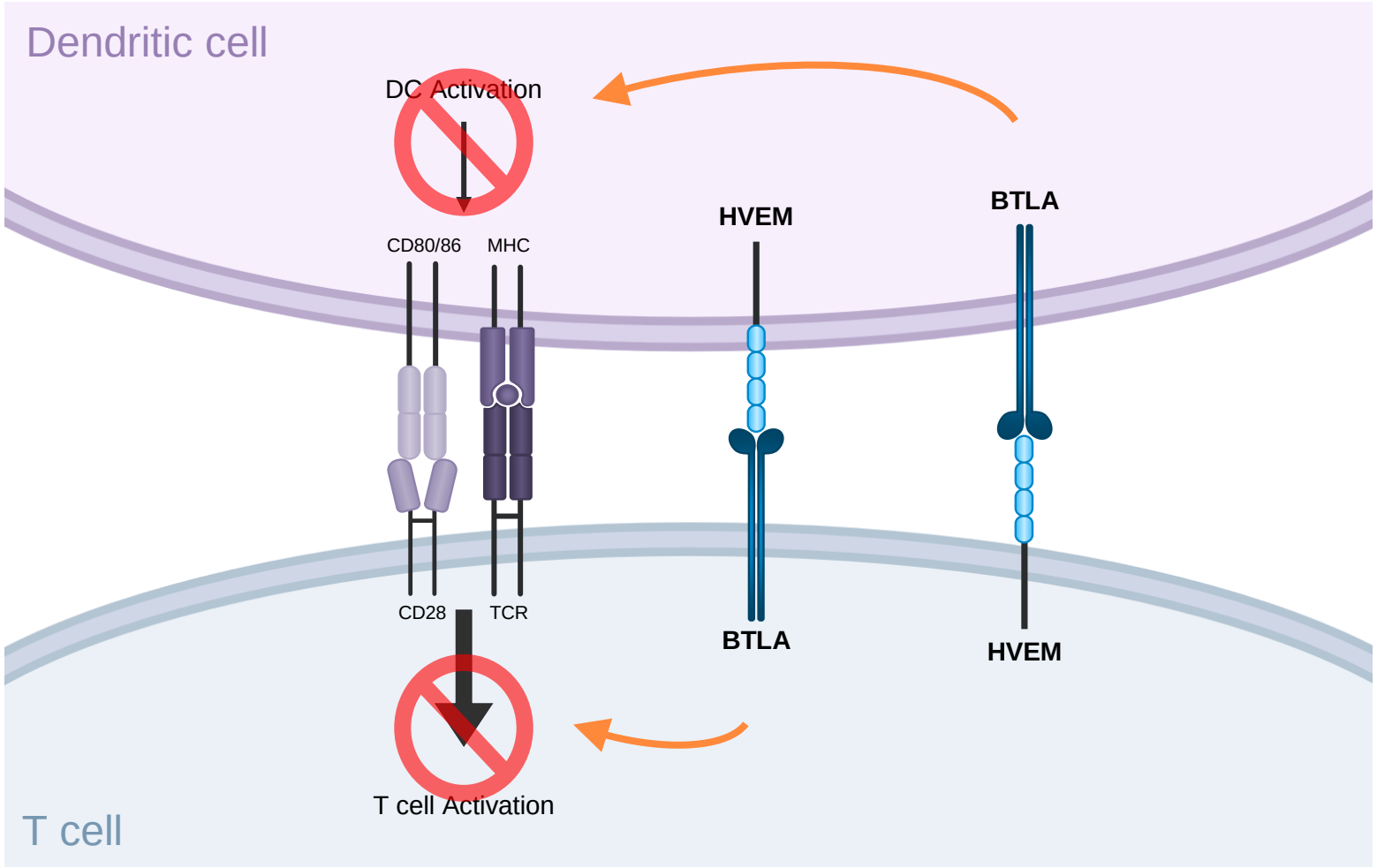

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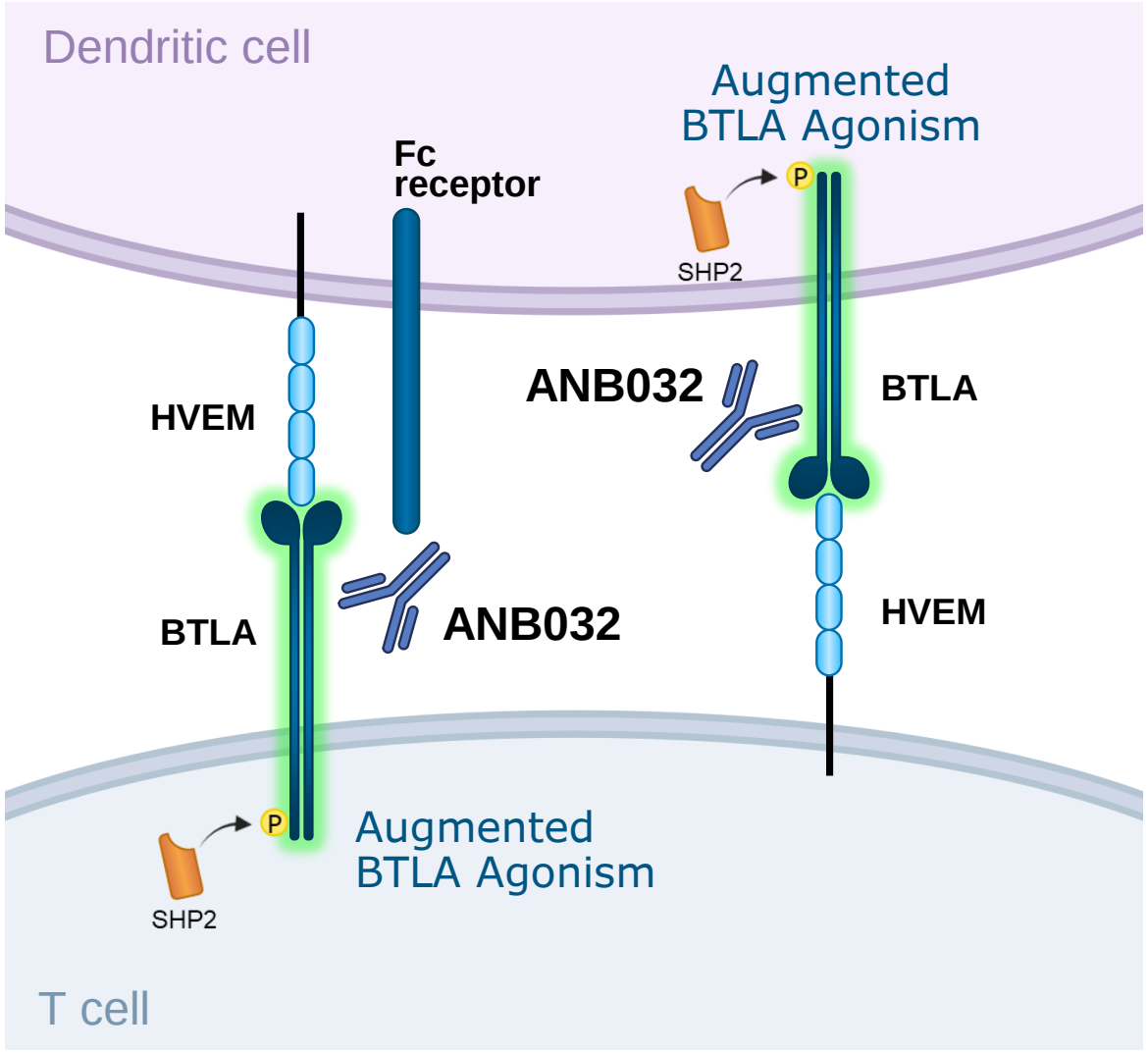
BTLA on T cell inhibits priming, activation, and expansion of inflammatory T cells

BTLA on dendritic cells modulates maturation and function, reducing both antigen presentation by MHC and expression of costimulatory molecules

HVEM, Herpes Virus Entry Mediator; MHC, major histocompatibility complex; TCR, T cell receptor

Proposed Mechanism of Action for ANB032



ANB032 binds to BTLA epitope on Th1, Th2, Th17 and Th22 T cells and dendritic cells

- Direct agonism of BTLA
- Does not block engagement of native ligand HVEM allowing endogenous inhibitory pathway to remain active
- Fc receptor binding profile contributes to differentiated potency

BTLA agonism augmented and potentiated by ANB032

ANB032 Phase 1 Study Objectives

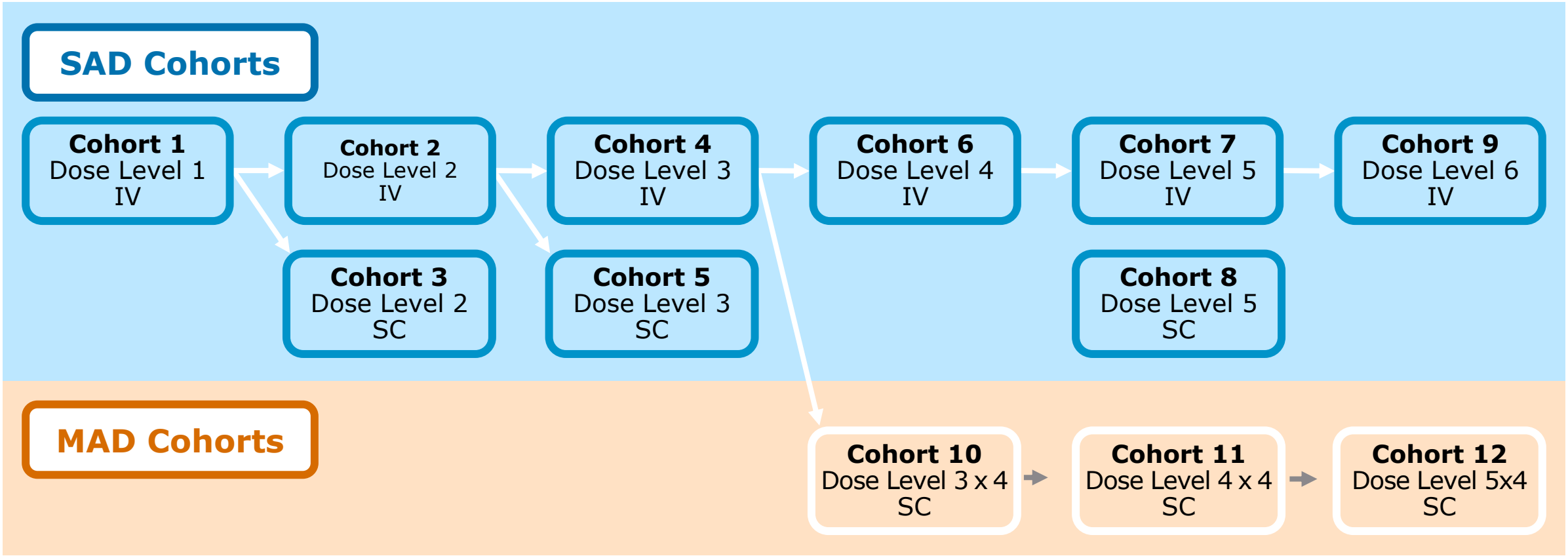
Primary:

- Assess safety and tolerability of single and multiple doses of ANB032 in healthy participants

Key Secondary & Exploratory:

- Characterize pharmacokinetics after single and multiple doses of ANB032
- Assess percent BLTA receptor occupancy following ANB032 administration
- Assess BTLA expression following ANB032 administration

ANB032 Phase 1 Study Design



- 96 healthy volunteers enrolled
- 8 participants in each cohort: 6 dosed with ANB032 and 2 with placebo IV or SC
- MAD cohorts dosed with ANB032 or placebo SC weekly for 4 weeks

Results

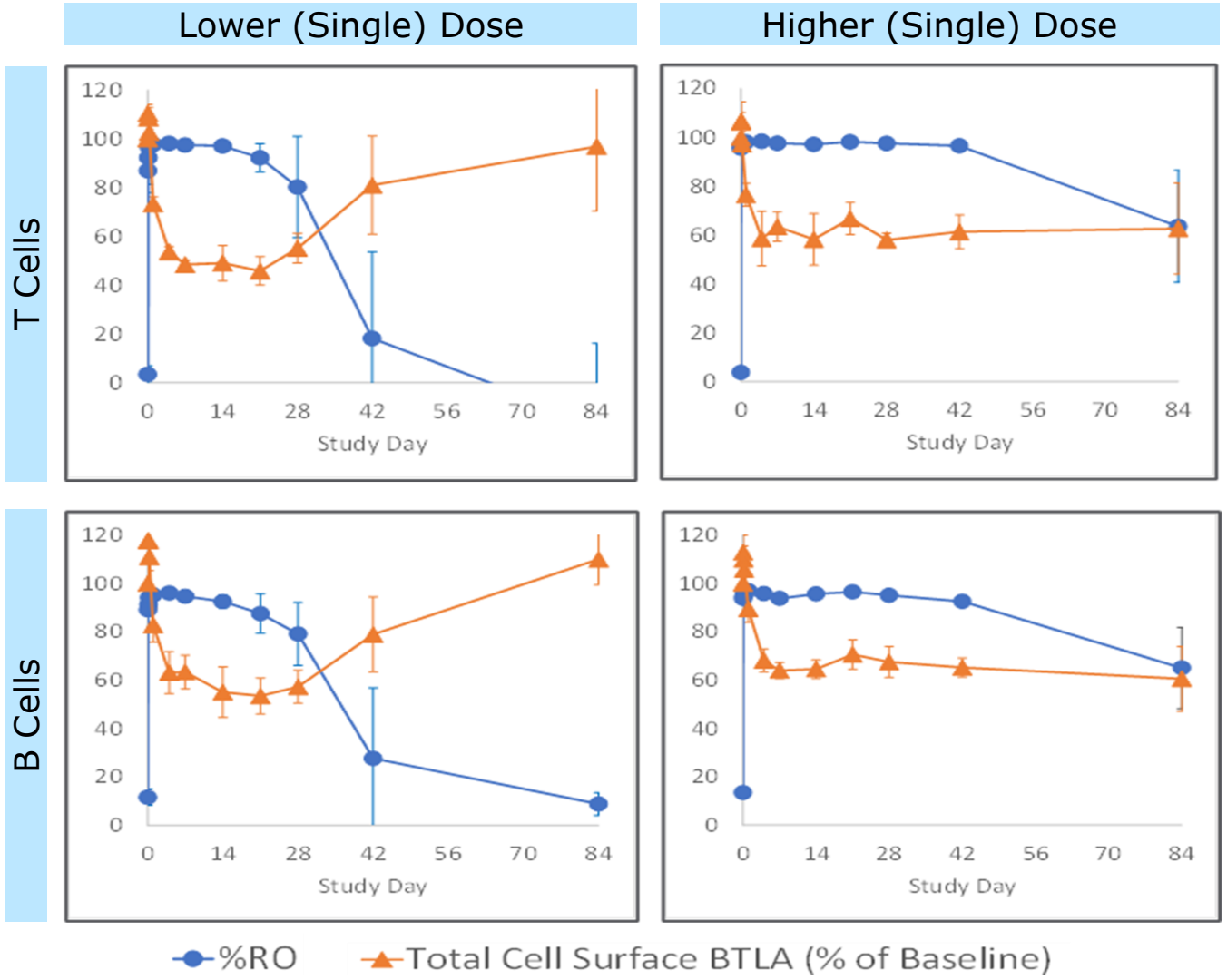
Safety and Tolerability

- ANB032 was well-tolerated with no dose-limiting toxicities
- Most adverse events were mild-to-moderate, of short duration, dose and timing from dose independent and resolved without sequelae
  - No serious adverse events were observed

Pharmacokinetics

- PK profile was favorable demonstrating approximately 2-week half-life with IV and SC dosing and dose proportionality in C_{max} and AUC

ANB032: Rapid and Sustained Pharmacodynamic Activity



- Rapid and sustained target engagement on both T cells and B cells
- Full BTLA RO was observed within hours and maintained for >30 days following IV or SC dosing
- Moderate reduction (50%) of cell surface BTLA expression
- Duration of reduced BTLA expression persisted in a dose-dependent manner

Summary of Phase 1 and Beyond

ANB032 Phase 1:

- Well-tolerated after single and multiple doses
- Favorable PK profile
- Demonstrated robust target engagement in healthy participants

Beyond:

- Atopic Dermatitis pathophysiology includes dysregulation of multiple proinflammatory pathways driven by Th1, Th2, Th17 and Th22 T cells and dendritic cells
- Based on a strong rationale and these Phase 1 data, ANB032 has progressed into a phase 2b trial for patients with moderate to severe atopic dermatitis
  - ARISE AD (NCT05935085) commenced Q2 2023 and topline data are expected end of year 2024 (see poster #P0558)