ABSTRACT

ANB032, a BTLA agonist antibody, has the potential to modulate pathogenic inflammatory responses across diseases where the BTLA pathway is dysregulated. In preclinical studies, ANB032 inhibited activated T cell proliferation, reduced Type 2 cytokine secretion, and modulated dendritic cell function, including inducing Tregs. In Phase 1 healthy volunteer study, ANB032 was well-tolerated, had a favorable PK profile, demonstrated robust target engagement, and partial reduction in BTLA expression. Preclinical and Phase 1 results support advanced clinical development of ANB032. We describe the design of a global Phase 2 randomized, double-blind, placebo-controlled, multicenter trial to evaluate the safety, tolerability, and efficacy of ANB032 in subjects with moderate-to-severe atopic dermatitis (AD) (NCT05935085). Subjects meeting the following inclusion criteria are currently being enrolled: 18-65 years of age, clinical diagnosis of AD affecting at least 10% of total body surface area, an Eczema Area and Severity Index (EASI) score ≥ 16, and a validated investigator Global Assessment (IGA) for AD score ≥ 3. Subjects who are either dupilumab/L13 blocker-naïve or -experienced are eligible. The primary endpoint is change from baseline to Week 14 in EASI. Secondary endpoints include EASI75, IGA 0/1, PNS6, DLQI, SCORAD, and safety. This study of ANB032 will further the understanding of the biology of this heterogeneous disease.

INTRODUCTION

Unmet Need in Atopic Dermatitis (AD)

- AD is a systemic and heterogeneous disease, and its pathophysiology is not well understood.
- Although there has been an increase in effective treatment options, patient satisfaction with treatment is only partially or not met in more than 75% of patients surveyed with moderate to severe AD.
- Current treatment options do not target all the diverse immune cells and cytokines that contribute to the pathogenesis of this disease.

B and T Lymphocyte Attenuator (BTLA)

- BTLA is a co-inhibitory checkpoint receptor that is expressed across a range of immune cells, including T cells (Th1, Th2, Th17, Treg), B cells, and dendritic cells (DCs), which are key cell types contributing to inflammatory diseases such as AD.
- T cell activation requires antigen presentation in the context of MHC to the TCR, and co-stimulation via CD80/86 to CD28.
- BTLA engagement on DCs modulates maturation and function, by reducing both antigen presentation by MHC and expression of costimulatory molecules (Figure 1).

OBJECTIVE

ARISE-AD is evaluating the safety, tolerability, and efficacy of ANB032 in subjects with moderate to severe AD.

METHODS

Study Design and Subjects

- This global Phase 2b study is a randomized, double-blind, placebo-controlled, parallel-group, multicenter trial (Figure 3).
- Male and female subjects ≥ 18 years of age with ≥ 65 years of moderate to severe AD for at least 6 months, with a history of ≥50% response rate to topical AD medications or unable to tolerate topical treatment are included.
- At screening and randomization: EASI ≥ 16; ≥1A: ≥1B; ≥2A: ≥2B; ≥3A: ≥3B; ≥4A: ≥4B; ≥5A: ≥5B.
- Subjects who are both dupilumab/L13 blocker-naïve or -experienced are eligible for enrollment.

DISCUSSION

- Current treatment options in AD do not target all the diverse immune cells and cytokines that contribute to the pathogenesis of this disease.
- BTLA is a co-inhibitory checkpoint receptor that modulates activation of T cells, B cells, and DCs.
- The synergistic effect of ANB032's direct agonism of T cells and expression of costimulatory molecules by ANB032 and placebo. During screening and randomization, EASI ≥ 16, and a validated investigator Global Assessment (IGA) for AD score ≥ 3. Subjects who are either dupilumab/L13 blocker-naïve or -experienced are eligible. The primary endpoint is change from baseline to Week 14 in EASI. Secondary endpoints include EASI75, IGA 0/1, PNS6, DLQI, SCORAD, and safety. This study of ANB032 will further the understanding of the biology of this heterogeneous disease.

ACKNOWLEDGEMENTS

- This research is sponsored by AnaptysBio, Inc.
- Previously presented at EADV in Berlin, Germany, October 11-14, 2023.
- This global Phase 2b study is a randomized, double-blind, placebo-controlled, parallel-group, multicenter trial (Figure 3).
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- Subjects who are both dupilumab/L13 blocker-naïve or -experienced are eligible for enrollment.

REFERENCES


Figure 1. BTLA is an inhibitory checkpoint receptor

Figure 2. ANB032 Proposed Mechanism of Action

Figure 3. ARISE-AD Study Design