ANB032, a novel BTLA agonist monoclonal antibody, inhibited T cell proliferation, reduced inflammatory cytokines, and down regulated BTLA expression on circulating T and B cells in Phase 1, progresses into a Phase 2 study in atopic dermatitis

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**ABSTRACT**

BTLA is a member of the CD28 superfamily that negatively regulates T cell, B cell, and DC cell-mediated inflammation. ANB032, a novel BTLA agonist monoclonal antibody, is being developed for the treatment of autoimmune and inflammatory diseases such as atopic dermatitis (AD). Because AD is not just a Th2 disease, but also has Th1 and Th17 involvement, immune modulators that downmodulated cellular immune responses to the pathology of AD, such as ANB032, have the potential to better treat the disease than with single cytokine targeted biologics. Preclinical data from AD patient-derived peripheral blood mononuclear cells (PBMCs) demonstrate ANB032 reduced T cell proliferation and secretion of inflammatory cytokines, including IFNγ, IL-5, IL-13 and IL-17A, which are mediators in chronic AD. ANB032 also downregulates BTLA expression during T cell stimulation. Phase 1 healthy subjects data demonstrated that ANB032 was well-tolerated with no dose limiting toxicities or serious adverse events (AEs). Most AEs were mild to moderate, resolved without sequelae, occurred sporadically and were dose independent. PK profile was favorable, including a 2-week half-life. ANB032 exhibited rapid and sustained target engagement on T and B cells. Full BTLA receptor occupancy (RO) occurred within hours and was maintained for more than 30 days after a single dose. Moderate reduction (~50%) of cell surface BTLA expression on T and B cells was observed. The duration of reduced BTLA expression dose-dependently correlated with RO and was also maintained for more than 30 days after a single dose. The phase 1 data demonstrated robust PK and target engagement in humans. These clinical data, in conjunction with preclinical translational data from AD patients, support progression of ANB032 into a phase 2 trial in AD.

**RESULTS**

- 96 healthy subjects were randomized into the SAD and MAD cohorts.
- Results between SAD and MAD cohorts were similar.

**Pharmacokinetics:**
- PK profile was favorable demonstrating ~2-week half-life with IV and SC dosing and dose proportionality in Cmax, and AUC.

**Pharmacodynamics (Figure 3):**
- Full BTLA RO was observed within hours and maintained for > 30 days following IV or SC dosing.
- Rapid and sustained target engagement on both T cells and B cells.
- Reduction of cell surface BTLA expression.
- Duration of reduced BTLA expression persisted in a dose-dependent manner.

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

**FUTURE DIRECTIONS**

- Global Phase 2b study initiated Q2 2023 in moderate to severe AD.
- All corer population; including subjects with/without dupilumab/L13-13 experience.

Phase 2 Study Design

<table>
<thead>
<tr>
<th>Dose</th>
<th>Treatment Period</th>
<th>Follow Up</th>
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<tbody>
<tr>
<td>ANB032 Dose 1 SC</td>
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<td></td>
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<tr>
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<tr>
<td>ANB032 Dose 3 SC</td>
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</tr>
<tr>
<td>Placebo SC</td>
<td>12-week Follow Up</td>
<td></td>
</tr>
</tbody>
</table>

Dosing is every 2 weeks or monthly

**REFERENCES**

2. Bekiaris et al. 2013
3. Bekiaris et al. 2013

**ACKNOWLEDGEMENTS**

The trial was conducted at Australia’s Southern Cross University. AD authors are current or previous employees of AnaptysBio, Inc.

**PRESENTED AT**

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