Proof-of-Concept Phase-2a Clinical Trial of ANB020 (Anti-IL-33 Antibody) in the Treatment of Moderate-to-Severe Adult Atopic Dermatitis

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Conflicts of interest

Advisory boards, consultancies, research grants or equity with: AnaptysBio, Celgene, Eli Lilly, Novartis, Janssen, Orbit Discovery, UCB Pharma

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Travel/registration costs for AAD: AnaptysBio
IL-33: Central Mediator of Type 2 Diseases
Key Role in Pathogenesis of Atopic Dermatitis

- IL-33 is a key cytokine in type 2 inflammatory responses to allergen
  - Responsible for activation of Th2 and ILC2
  - Functions upstream of IL-4, IL-5 and IL-13
  - Modulates mast cell degranulation

- IL-33 is rapidly released by epithelium upon allergen exposure

- Genetic association of IL-33 pathway mutations with type 2 diseases\(^1\)

- IL-33 is highly expressed in skin of atopic dermatitis patients with active disease\(^2\)

1. Ramirez-Carrozzi et al. 2014
2. Savinko et al. 2012
ANB020: Anti-Human IL-33 Antibody

- ANB020 is humanized anti-human IL-33 monoclonal antibody
  - High affinity binding to human IL-33 with $K_d$ of approximately 1 pM
  - Potent neutralizing activity with an $IC_{50}$ of approximately 1.5 nM

- Healthy volunteer Phase 1 trial (n=96) reported safety, pharmacokinetics and pharmacodynamics
  - Subjects dosed with 10mg to 750mg of ANB020 in single dose cohorts (n=48), 40mg to 300mg of ANB020 weekly for 4 weeks in multiple dose cohorts (n=24) and placebo (n=24)
  - *In vivo* half-life of approximately 16 days for both intravenous and subcutaneous administration
  - Pharmacodynamic effect persisted for 85 days at certain single dose levels of ANB020
  - ANB020 was generally well tolerated and no dose-limiting toxicities were observed

Single dose ANB020 healthy volunteer Phase 1 pharmacodynamic *ex vivo* assay measuring inhibition of IL-33 induced Interferon-gamma (IFN-g) relative to pre-dose levels

% Inhibition of IFN-g

<table>
<thead>
<tr>
<th>Dose</th>
<th>0</th>
<th>7</th>
<th>14</th>
<th>21</th>
<th>28</th>
<th>35</th>
<th>42</th>
<th>49</th>
<th>56</th>
<th>63</th>
<th>70</th>
<th>77</th>
<th>84</th>
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<tbody>
<tr>
<td>10 mg SC</td>
<td>100</td>
<td>80</td>
<td>60</td>
<td>40</td>
<td>20</td>
<td>0</td>
<td>0</td>
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<td>100 mg SC</td>
<td>100</td>
<td>80</td>
<td>60</td>
<td>40</td>
<td>20</td>
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<td>0</td>
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<td>0</td>
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<td>0</td>
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</tr>
<tr>
<td>300 mg SC</td>
<td>100</td>
<td>80</td>
<td>60</td>
<td>40</td>
<td>20</td>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>300 mg IV</td>
<td>100</td>
<td>80</td>
<td>60</td>
<td>40</td>
<td>20</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>750 mg IV</td>
<td>100</td>
<td>80</td>
<td>60</td>
<td>40</td>
<td>20</td>
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<td>0</td>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Pooled Placebo</td>
<td>100</td>
<td>80</td>
<td>60</td>
<td>40</td>
<td>20</td>
<td>0</td>
<td>0</td>
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<td>0</td>
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</tbody>
</table>

Days Post-Dose 0 7 14 21 28 35 42 49 56 63 70 77 84
ANB020 Phase 2a Atopic Dermatitis
Proof-of-Concept Trial

- Study design:
  - Enrolled 12 moderate-to-severe adult atopic dermatitis patients inadequately controlled with topical corticosteroids
  - Single intravenous dose of placebo (Day -7) followed by a single 300 mg intravenous dose of ANB020 (Day 1)
  - EASI, 5-D pruritus, SCORAD, DLQI and IGA clinical scores determined at specific time points

- Study objective:
  - Demonstrate EASI-50 response in at least 50% of patients at Day 29 (primary endpoint)
## Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Average (n=12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>40.4 ± 13.5</td>
</tr>
<tr>
<td>Male, number (%)</td>
<td>11 (91.7%)</td>
</tr>
<tr>
<td>Caucasian race, number (%)</td>
<td>12 (100%)</td>
</tr>
<tr>
<td>Body-Mass Index</td>
<td>26.14 ± 4.145</td>
</tr>
<tr>
<td>EASI, score</td>
<td>32.25 ± 10.89</td>
</tr>
<tr>
<td>IGA, 0-5 scale</td>
<td>4 ± 0.74</td>
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<tr>
<td>SCORAD, score</td>
<td>64.79 ± 12.02</td>
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<tr>
<td>Pruritus, 5-D score</td>
<td>19.1 ± 4.85</td>
</tr>
<tr>
<td>DLQI, score</td>
<td>12.92 ± 6.54</td>
</tr>
</tbody>
</table>

All 12 patients were inadequately controlled on corticosteroids pre-study
7 of 12 enrolled patients were treated with systemic immuno-modulators pre-study and presented with a baseline EASI score of 36
5 of 12 patients were not treated with systemic immuno-modulators pre-study and presented with a baseline EASI score of 27
### EASI Scores Following Single ANB020 Dose

Rapid response and all patients achieved EASI-50 on or before Day 57

<table>
<thead>
<tr>
<th>Timepoint</th>
<th>Average % EASI Score Reduction*</th>
<th>% Patients Achieving EASI-50*</th>
<th>% Patients Achieving EASI-75*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day -21 (Baseline)</td>
<td>0%</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Day 1 (ANB020 Dosing)</td>
<td>4%</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Day 15</td>
<td>58%</td>
<td>9 of 12 (75%)</td>
<td>3 of 12 (25%)</td>
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<tr>
<td>Day 29</td>
<td>61%</td>
<td>10 of 12 (83%)</td>
<td>4 of 12 (33%)</td>
</tr>
<tr>
<td>Day 57</td>
<td>62%</td>
<td>9 of 12 (75%)</td>
<td>5 of 12 (42%)</td>
</tr>
<tr>
<td>Day 78</td>
<td>62%</td>
<td>9 of 12 (75%)</td>
<td>2 of 12 (17%)</td>
</tr>
<tr>
<td>Day 113</td>
<td>55%</td>
<td>8 of 12 (67%)</td>
<td>2 of 12 (17%)</td>
</tr>
<tr>
<td>Day 140</td>
<td>45%</td>
<td>5 of 12 (42%)</td>
<td>3 of 12 (25%)</td>
</tr>
</tbody>
</table>

*Relative to baseline upon enrollment at Day -21
Additional Efficacy Data
5-D Pruritus, SCORAD, DLQI and IGA Scores

IGA scores of zero or 1 (clear/almost clear skin) observed in 25% (3/12) of patients
Key Conclusions & Next Steps

• Rapid and persistent efficacy following single dose of ANB020
  - Rapid efficacy observed as early as Day 15
  - Efficacy was maximized between Day 29 and Day 57
  - All patients achieved at least EASI-50 response on or before Day 57
  - EASI responses consistent with 5-D pruritus, SCORAD, IGA and DLQI scores

• Disease severity does not limit ANB020 efficacy
  - ANB020 was similarly efficacious in patients with higher baseline EASI scores (treated with systemic immuno-modulators pre-study) versus lower baseline EASI score patients that did not require systemic therapy pre-study

• ANB020 was well-tolerated and no drug-related safety signals observed
  - Most frequent adverse event was dizziness in 17% of patients post-placebo versus headache in 25% of patients post-ANB020
  - A single serious adverse event of depression reported on Day 140 post-ANB020, which was consistent with the patient’s pre-trial history of depression, and was deemed not drug-related

• Next step: advance ANB020 into placebo-controlled, double-blind, randomized 200-300 adult moderate-to-severe atopic dermatitis Phase 2b trial
  - Assess different dose levels and dosing frequencies of subcutaneously-administered ANB020
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