Treatment of Severe Allergic Conjunctivitis with AK002 Indicated Improvement of Ocular Signs and Symptoms and Reduction of Severity of Comorbid Atopic Diseases in a Phase 1b Open-Label Study

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Disclosures

- No financial conflicts to disclose

- AK002 is an investigational drug in clinical development as it is not FDA or EMA approved
AKC, PAC, & VKC Are Severe and Chronic Forms of Allergic Conjunctivitis

<table>
<thead>
<tr>
<th>CLINICAL FEATURES</th>
<th>IMPACT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms</td>
<td></td>
</tr>
<tr>
<td>Extreme Itching, Photophobia, Pain, Sensation</td>
<td>Poor Quality of Life</td>
</tr>
<tr>
<td>of Foreign Body, Burning, Watering, Mucous</td>
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<tr>
<td>Discharge</td>
<td></td>
</tr>
<tr>
<td>Signs</td>
<td></td>
</tr>
<tr>
<td>Redness (Hyperemia), Swelling (Chemosis,</td>
<td>Vision Loss, Poor Quality of</td>
</tr>
<tr>
<td>Periorbital Edema), Tarsal Papillae, Cicatricial</td>
<td>Life</td>
</tr>
<tr>
<td>Changes, Corneal Damage (Keratitis, Epithelial</td>
<td></td>
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<tr>
<td>Erosion, Ulcers)</td>
<td></td>
</tr>
<tr>
<td>Atopic Comorbidities</td>
<td></td>
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<tr>
<td>Common Atopic Comorbidities Include Atopic</td>
<td>High Systemic Disease Burden,</td>
</tr>
<tr>
<td>Dermatitis, Asthma, and Rhinitis</td>
<td>Poor Quality of Life</td>
</tr>
</tbody>
</table>
Severe Allergic Conjunctivitis

Redness, Chemosis

Photophobia, Watering, Periorbital Swelling

Giant Papillae

Corneal Ulcer (Vision Loss)
Mast Cells and Eosinophils are Key Effector Cells in Allergic Conjunctivitis


<table>
<thead>
<tr>
<th>Mast Cells</th>
<th>Perennial Allergic Conjunctivitis (PAC)</th>
<th>Vernal Keratoconjunctivitis (VKC)</th>
<th>Atopic Keratoconjunctivitis (AKC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eosinophils</td>
<td>++</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>T and B cells</td>
<td>+</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>Fibroblasts</td>
<td></td>
<td>++</td>
<td>++</td>
</tr>
</tbody>
</table>
Mast Cells and Eosinophils Are Key Drivers of Inflammatory Disease

SENSITIZATION

- Activated B Cell
- IgE
- T Cell

ACTIVATION AND RECRUITMENT OF OTHER IMMUNE CELLS AND TISSUE INFLAMMATION

- Mast Cell
  - Histamine, LTC₄, PGD₂ and proteases
- Neuron
  - Sub P
- Smooth Muscle
  - ECP, MBP, elastase, MMP, TNFα, IL-1β, TGFβ
- Eosinophil
- Neutrophil
- Macrophage

IL-4, IL-13

ACUTE AND CHRONIC INFLAMMATION

- Tissue damage, fibrosis
- Bronchoconstriction, increased GI motility, pain, itch

Histamine, NGF, Histamine

IL-5, IL-8, IL-6, TNFα

Epithelium

Allergens

- IL-33
- TSLP
- IL-4, IL-13

T Cell

B Cell

Activated B Cell
AK002 Targets Siglec-8 on Eosinophils and Mast Cells

Activating Receptors

Siglec-8

Cell Membrane

Activation

Inhibiting

Mast cell

Eosinophil

Inflammatory response

AK002

Inhibition

Mast cell

Eosinophil

ADCC/Apoptosis
KRONOS: Phase 1b Study

**Screening**
2 – 4 weeks

- Daily ACS questionnaire completion
- Baseline OSS assessment
- Screening and baseline assessments

**Treatment Period**
6 monthly doses of AK002 (mg/kg)

<table>
<thead>
<tr>
<th>0.3 mg/kg</th>
<th>1.0 mg/kg</th>
<th>1 or 3 mg/kg</th>
<th>1 or 3 mg/kg</th>
<th>1 or 3 mg/kg</th>
<th>1 or 3 mg/kg</th>
</tr>
</thead>
</table>

**Primary Objective – Safety and Tolerability:**
- Vital signs, physical exam, safety labs, ADA, and collection of adverse events

**Secondary Objectives:**
- Daily ACS questionnaire (Patient reported-outcome)
  - Itching, photophobia, foreign body sensation, ocular pain, and lacrimation
- Monthly OSS (Investigator assessment)
  - Itching, redness, tearing, and chemosis
- Atopic comorbidities assessment:
  - Asthma, Atopic dermatitis, Rhinitis

**Follow-Up**
5 months

- Monthly visits
- Safety and tolerability are assessed

**Pre-Treatment**

**Post-Treatment**
AK002 Clinical Activity Measured by PRO & Investigator Assessments

**ALLERGIC CONJUNCTIVITIS SYMPTOM (ACS)**

- Daily patient questionnaire
- Total ACS (0 – 50 point scale):
  - Itching (0-10)
  - Light sensitivity (0-10)
  - Eye pain (0-10)
  - Foreign body sensation (0-10)
  - Watering eyes (0-10)

**OCULAR SYMPTOM SCORE (OSS)**

- Monthly investigator assessment
- Total OSS (0 – 13 point scale):
  - Itching (0-4)
  - Redness (0-3)
  - Tearing (0-3)
  - Chemosis (0-3)

**COMORBID ATOPIC DISEASE ASSESSMENTS**

- Daily patient questionnaire for patients with comorbid atopic dermatitis, asthma and/or rhinitis
- 0 – 10 point scale grading global disease severity
## Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>AKC  (N=13)</th>
<th>VKC  (N=1)</th>
<th>PAC  (N=15)</th>
<th>Total (N=29)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, Median (Range)</td>
<td>50 (23-72)</td>
<td>25</td>
<td>53 (29-66)</td>
<td>51 (23-72)</td>
</tr>
<tr>
<td>Female</td>
<td>38%</td>
<td>0</td>
<td>67%</td>
<td>52%</td>
</tr>
<tr>
<td>Weight (kg), Median (Range)</td>
<td>81 (50-107)</td>
<td>68</td>
<td>84 (52-108)</td>
<td>81 (50-108)</td>
</tr>
<tr>
<td>BMI (kg/m²), Median (Range)</td>
<td>26 (20-43)</td>
<td>21</td>
<td>29 (19-40)</td>
<td>27 (19-43)</td>
</tr>
<tr>
<td>Total Symptom Score¹</td>
<td>ACS, Median</td>
<td>26.2</td>
<td>25.7</td>
<td>17.7</td>
</tr>
<tr>
<td></td>
<td>OSS, Median</td>
<td>7.0</td>
<td>7.0</td>
<td>6.0</td>
</tr>
<tr>
<td></td>
<td>≥1 Comorbidity</td>
<td>85%</td>
<td>100%</td>
<td>87%</td>
</tr>
<tr>
<td></td>
<td>Atopic Dermatitis</td>
<td>85%</td>
<td>0</td>
<td>40%</td>
</tr>
<tr>
<td></td>
<td>Asthma</td>
<td>54%</td>
<td>100%</td>
<td>27%</td>
</tr>
<tr>
<td></td>
<td>Rhinitis</td>
<td>54%</td>
<td>100%</td>
<td>73%</td>
</tr>
</tbody>
</table>
Improvements in Allergic Conjunctivitis Signs & Symptoms

**Patient Reported**

- **Baseline:** 23.0
- **Weeks 21-22:** 5.1
- **Improvement:** -78%

**Investigator Assessment**

- **Baseline:** 7.0
- **Day 140:** 2.0
- **Improvement:** -71%

*All Subjects (n=29)*
Patient Reported Improvements in Multiple Forms of Severe AC

**AKC (n=13)**
- Median Total ACS: 26.2
- Baseline: 6.9
- Wks 21-22: -74%

**VKC (n=1)**
- Median Total ACS: 25.7
- Baseline: 3.3
- Wks 21-22: -87%

**PAC (n=15)**
- Median Total ACS: 17.7
- Baseline: 5.1
- Wks 21-22: -71%
Physician Assessed Improvements in Multiple Forms of Severe AC

**AKC (n=13)**
- Baseline: 7.0
- Day 140: 2.0
- Improvement: -71%

**VKC (n=1)**
- Baseline: 7.0
- Day 140: 1.0
- Improvement: -86%

**PAC (n=15)**
- Baseline: 6.0
- Day 140: 1.0
- Improvement: -83%
### Allergic Conjunctivitis Symptom (ACS)
Patient Reported - Daily

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Median % Δ from BL to Wk 21-22</th>
</tr>
</thead>
<tbody>
<tr>
<td>Itching</td>
<td>-74%</td>
</tr>
<tr>
<td>Light Sensitivity</td>
<td>-57%</td>
</tr>
<tr>
<td>Eye Pain</td>
<td>-75%</td>
</tr>
<tr>
<td>Foreign Body Sensation</td>
<td>-80%</td>
</tr>
<tr>
<td>Watering Eyes</td>
<td>-76%</td>
</tr>
</tbody>
</table>

### Ocular Symptom Score (OSS)
Investigator Assessment - Monthly

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Median % Δ from BL to Day 140</th>
</tr>
</thead>
<tbody>
<tr>
<td>Itching</td>
<td>-67%</td>
</tr>
<tr>
<td>Redness</td>
<td>-67%</td>
</tr>
<tr>
<td>Tearing</td>
<td>-50%</td>
</tr>
<tr>
<td>Chemosis</td>
<td>-100%</td>
</tr>
</tbody>
</table>
Substantial Improvement in Atopic Comorbidities

Atopic Dermatitis (n=11)
- Baseline Symptom Score: 6.3
- Wks 21-22 Median Symptom Score: 2.2
- Improvement: -65%

Asthma (n=9)
- Baseline Symptom Score: 3.9
- Wks 21-22 Median Symptom Score: 1.1
- Improvement: -72%

Rhinitis (n=11)
- Baseline Symptom Score: 4.8
- Wks 21-22 Median Symptom Score: 1.5
- Improvement: -69%
Absolute Blood Eosinophil Counts

[Graph showing absolute blood eosinophil counts over time with median and interquartile range (IQR) for all subjects (n=29).]
Safety Summary

- Generally well-tolerated
- No drug-related Serious Adverse Events
- Most common adverse event was mild to moderate infusion-related reactions (IRRs; flushing, feeling of warmth, headache, nausea, or dizziness)
Case Study 1: Reversal of Neovascular and Inflammatory Changes

AKC with Comorbid Atopic Dermatitis & Rhinitis

Demographics
- 27 year-old male with severe AKC, atopic dermatitis, and rhinitis
- Baseline normal peripheral blood eosinophils (190 eos/µL)

Symptoms
- Itching, foreign body sensation, and watering
- Hyperemia (redness) and palpebral papillae
- Moderate comorbid atopic dermatitis & rhinitis

Treatment History
- AKC: topical antihistamines, topical corticosteroids
- Atopic Dermatitis: oral antihistamines
- Rhinitis: oral antihistamines
Case Study 1: Resolution of Ocular Symptoms

Month 1  Month 2  Month 3  Month 4  Month 5  Weeks 21-22

Watering  Foreign Body  Eye Pain  Light Sensitivity  Itching  Total ACS

99% reduction in Total ACS
Case Study 1: Reversal of Neovascular and Inflammatory Changes

Prior to AK002

Upper tarsal papillae

After 3 Doses of AK002

Resolution of papillae
Case Study 2: Improvement in AKC and Atopic Comorbidities

AKC with Comorbid Atopic Dermatitis, Asthma & Rhinitis

**Demographics**
- 53 year-old male with AKC, atopic dermatitis, asthma, and rhinitis
- Baseline normal peripheral blood eosinophils (120 eos/µL)

**Symptoms**
- Itching, photophobia, foreign body sensation, redness, & chemosis
- Severe comorbid atopic dermatitis & asthma

**Treatment History**
- AKC: topical antihistamines, topical corticosteroids
- Atopic Dermatitis: dupilumab, topical corticosteroids
- Asthma: daily ICS/LABA, albuterol
- Rhinitis: oral antihistamines
Case Study 2: Improvements in Ocular Signs and Symptoms and Comorbid Atopic Dermatitis, Asthma, and Rhinitis

**Total ACS**
- BL: 33.3
- Wks 21-22: 4.0
- Improvement: -88%

**Atopic Dermatitis**
- BL: 6.5
- Wks 21-22: 2.2
- Improvement: -67%

**Asthma**
- BL: 5.9
- Wks 21-22: 1.1
- Improvement: -82%

**Rhinitis**
- BL: 7.1
- Wks 21-22: 0.3
- Improvement: -96%
Conclusions/Discussion

• Mast cells and eosinophils are key effector cells in the pathogenesis and perpetuation of allergic conjunctivitis

• AK002 is a novel anti-Siglec-8 antibody that has demonstrated selective and rapid depletion of eosinophils and inhibition of mast cells in preclinical and clinical studies

• Substantial and consistent improvements reported in symptoms by patients and investigators in multiple forms of severe AC

• Clinical activity observed in atopic comorbidities

• AK002 was generally well-tolerated

• AK002 may be a promising treatment for severe AC as well as atopic dermatitis, asthma and other atopic conditions
Thank you