Primary Results of A Phase 1 Multicenter Open-Label Study of Antolimab, An Anti-Siglec-8 Antibody, for the Treatment of Patients With Chronic Gastrointestinal Symptoms and Elevated Gastric and/or Duodenal Mast Cells

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Disclosures

- Dr. Adam Bledsoe is an investigator in the ENIGMA study

- Antolimab (AK002) is an investigational drug candidate and is not FDA/EMA approved
Mast Cells and Eosinophils: Effector Cells Central to Initiating and Maintaining Inflammatory Responses

- Found at the Internal/External Interface of the Body
  - In particular, in tissues and surrounding blood vessels and peripheral nerves
- Produce a Broad Range of Inflammatory Mediators
  - Vasoactive amines, lipid mediators, proteases, cytokines and chemokines
- Participate in Acute and Chronic Inflammation
  - Including both innate and adaptive immune responses
- Key Drivers in Many Serious Diseases
  - Including gastrointestinal, ophthalmic, dermatologic, respiratory, and proliferative diseases
Antolimab (AK002) Targets Siglec-8 on Eosinophils and Mast Cells

**Activation**
- Siglec-8
- Mast cell
- Eosinophil
- Inflammatory response

**Inhibition**
- Antolimab
- Mast cell
- Eosinophil
- ADCC/Apoptosis
ENIGMA Phase 2 Study in Eosinophilic Gastritis (EG) and/or Eosinophilic Duodenitis (EoD)

INCLUSION CRITERIA
- Patient-reported active moderate-to-severe symptoms per the EG/EoD Questionnaire®
  - Captures the symptoms of EG/EoD patients on a daily basis
  - Measures 8 symptoms each on a scale of 0-10; Total Symptom Score: (TSS) 80 points
    - Abdominal pain - Loss of appetite
    - Nausea - Abdominal cramping
    - Vomiting - Bloating
    - Early satiety - Diarrhea
  - Symptom criteria: weekly average ≥3 to 10 for abdominal pain, nausea, or diarrhea for at least 2 weeks
- Biopsy-confirmed EG and/or EoD
  - EG: ≥30 eos/hpf in 5 hpfs (stomach)
  - EoD: ≥30 eos/hpf in 3 hpfs (duodenum)

STUDY DESIGN
- Phase 2 multi-center, randomized, double-blind, placebo-controlled study
- 65 Patients – 3 arms, 4 monthly doses
  - 21 patients 0.3, 1.0, 3.0, 3.0 mg/kg antolimab
  - 22 patients 0.3, 1.0, 1.0, 1.0 mg/kg antolimab
  - 22 patients placebo
- Primary endpoint: Mean % reduction in tissue eosinophils from baseline to day 99
- Secondary endpoints
  - % Treatment responders (>75% reduction in tissue eosinophil counts AND >30% reduction in symptoms (TSS) from baseline to 2 weeks post-last dose)
  - Mean % reduction in TSS from baseline to 2 weeks post-last dose

RANDOMIZED STUDY RESULTS

<table>
<thead>
<tr>
<th>Prespecified Endpoints</th>
<th>Antolimab (n=39)</th>
<th>Placebo (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1° - Tissue Eosinophils</td>
<td>% Δ -95%</td>
<td>+10%</td>
</tr>
<tr>
<td></td>
<td>p-value &lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>2° - Treatment Responders</td>
<td>% 69%</td>
<td>5%</td>
</tr>
<tr>
<td></td>
<td>p-value 0.0008</td>
<td></td>
</tr>
<tr>
<td>2° - TSS</td>
<td>% Δ -53%</td>
<td>-24%</td>
</tr>
<tr>
<td></td>
<td>p-value 0.0012</td>
<td></td>
</tr>
</tbody>
</table>

- All primary and secondary endpoints met in the first randomized trial in patients with EG and EoD
- Generally well tolerated
ENIGMA Screening Identified Symptomatic Patients With Elevated Mast Cells Without Eosinophilia

16 of 88 symptomatic patients had elevated mast cells only. These patients were offered an open-label study of antolimab.

EG/EoD: ≥30 Eos & Mast Cells

MGID: ≥30 Mast Cells

1 65 met all enrollment criteria for ENIGMA; 1 patient had elevated eos only
2 ≥30 mast cells/hpf in 5 hpfs in the stomach and/or ≥30 mast cells/hpf in 3 hpfs in the duodenum
# Phase 1 Mast Cell GI Disease (MGID) Study

## Study Design

- Multi-center, open-label, multi-dose, Phase 1 study
- Active moderate to severe symptoms as measured by symptom questionnaire used in ENIGMA
- Biopsy confirmed elevated mast cells without tissue eosinophilia
  - Stomach: \( \geq 30 \) mast cells/high powered field (hpf) in \( 5 \) hpfs, and/or
  - Duodenum: \( \geq 30 \) mast cells/hpf in \( 3 \) hpfs
- 6 monthly doses
  - \( 0.3, 1.0, 3.0, 3.0, 3.0, 3.0 \) mg/kg antolimab
# Baseline Characteristics

<table>
<thead>
<tr>
<th>Mast Cell Gastritis Patients</th>
<th>n=7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, Mean (Range)</td>
<td>48 (19-79)</td>
</tr>
<tr>
<td>Female</td>
<td>100%</td>
</tr>
<tr>
<td>White</td>
<td>100%</td>
</tr>
<tr>
<td>Absolute Eosinophil Count /µL, Mean (Range)</td>
<td>127 (20-190)</td>
</tr>
<tr>
<td>Immunoglobulin-E (IU/mL)¹, Mean (Range)</td>
<td>28 (10-59)</td>
</tr>
<tr>
<td>Gastrointestinal² Eosinophils/hpf, Mean (Range)</td>
<td>17 (14-23)</td>
</tr>
<tr>
<td>Gastrointestinal² Mast Cells/hpf, Mean (Range)</td>
<td>55 (46-64)</td>
</tr>
<tr>
<td>Total Symptom Score (TSS) [0-80], Mean</td>
<td>27.1</td>
</tr>
</tbody>
</table>

¹ n=6
² Gastric or duodenum site with highest eosinophil or mast cell counts
Baseline Gastrointestinal Eosinophils and Mast Cell Counts

**MGID (n=7)**

- Eosinophils: 17
- Mast Cells: 55

**ENIGMA EG / EoD (n=65)**

- Eosinophils: 84
- Mast Cells: 64
EG/EoD and MGID Patients Have Similar Symptomatic Burden

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Reported Symptom Intensity During Screening (0-10)</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early Satiety</td>
<td>EG/EoD: 4.3</td>
<td>5.4</td>
</tr>
<tr>
<td></td>
<td>MGID: 4.3</td>
<td></td>
</tr>
<tr>
<td>Bloating</td>
<td>EG/EoD: 3.7</td>
<td>5.1</td>
</tr>
<tr>
<td></td>
<td>MGID: 3.7</td>
<td></td>
</tr>
<tr>
<td>Abdominal Pain</td>
<td>EG/EoD: 3.7</td>
<td>4.8</td>
</tr>
<tr>
<td></td>
<td>MGID: 3.7</td>
<td></td>
</tr>
<tr>
<td>Abdominal Cramping</td>
<td>EG/EoD: 3.4</td>
<td>4.6</td>
</tr>
<tr>
<td></td>
<td>MGID: 4.6</td>
<td></td>
</tr>
<tr>
<td>Loss of Appetite</td>
<td>EG/EoD: 3.7</td>
<td>4.5</td>
</tr>
<tr>
<td></td>
<td>MGID: 4.1</td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>EG/EoD: 4.0</td>
<td>4.0</td>
</tr>
<tr>
<td></td>
<td>MGID: 4.3</td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>EG/EoD: 1.9</td>
<td>2.8</td>
</tr>
<tr>
<td></td>
<td>MGID: 0.8</td>
<td></td>
</tr>
<tr>
<td>Vomiting</td>
<td>EG/EoD: 1.3</td>
<td>1.3</td>
</tr>
<tr>
<td></td>
<td>MGID: 1.3</td>
<td></td>
</tr>
</tbody>
</table>

EG/EoD Patients (n=65)  MGID Patients (n=7)
64% Improvement in Total Symptom Score

PRO TSS-8: Change from Baseline

MGID

Mean % Change from BL

-75%
-50%
-25%
0%

Antolimab 3.0 mg/kg
-64%

EG / EoD in ENIGMA

Mean % Change from BL

-75%
-50%
-25%
0%

Antolimab 3.0 mg/kg
-58%

Placebo
-24%
5 of 7 (71%) Patients with >50% Reduction in Symptoms

**PRO Total Symptom Score: >50% Reduction**

**MGID**

- **Antolimab 3.0 mg/kg**: 71% (5/7)

**EG / EoD in ENIGMA**

- **Antolimab 3.0 mg/kg**: 65% (13/20)
- **Placebo**: 15% (3/20)
Improvement Across All Symptoms Measured

MGID: PRO Symptom Score
Antolimab (n=7)

Median Score

- Abdominal Pain: -69%
- Nausea: -78%
- Vomiting: -100%
- Early Satiety: -90%
- Loss of Appetite: -91%
- Abdominal Cramping: -57%
- Bloating: -91%
- Diarrhea: -85%
MGID: Histologic Results

GI Eosinophils

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 22</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median GI(^a) Eosinophils Cells</td>
<td>16</td>
<td>0</td>
</tr>
</tbody>
</table>

\(-100\%\)

GI Mast Cells

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 22</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Mast Cells</td>
<td>57</td>
<td>47</td>
</tr>
<tr>
<td>(-18%))</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) Gastrointestinal; Gastric (5 hpfs) or duodenum (3 hpfs) site with highest eosinophils or mast cell counts at baseline.
• Generally well tolerated
• Most common AE was infusion related reactions (flushing, feeling of warmth, headache, nausea, dizziness), all of which were mild
• No drug-related SAEs
Conclusions

• A group of symptomatic patients suspected of EG/EoD were found to have elevated mast cell counts without blood or tissue eosinophilia (MGID)
• Antolimab treatment resulted in substantial symptom improvement in a prospective, open-label study of patients with MGID
• Antolimab treatment was generally well tolerated
• These results suggest that mast cells may be the primary driver of symptoms in this disease and could contribute to symptoms in other GI diseases such as EGIDs
• Antolimab may be a promising targeted therapy for EG/EoD and MGID
We thank the patients who participated in this study, investigators, and study staff.