Preliminary Data from the Ongoing Open-Label XmAb5871 Phase 2 Pilot Study in IgG4-Related Disease Presented at American College of Rheumatology (ACR) 2016 Annual Meeting

John H. Stone¹
Zachary S. Wallace²
Cory A. Perugino²
Ana D. Fernandes²
Payal Patel²
Paul A. Foster³
Debra J. Zack³

¹Massachusetts General Hospital Rheumatology Unit
Harvard Medical School,
²Massachusetts General Hospital,
³Xencor, Inc.
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Conflicts of Interest

- Dr. Stone has received research funding from Xencor on the subject of IgG4-related disease.

- Drs. Zack and Foster are full-time employees of Xencor, Inc. and hold stock and stock options.
Mimicker of Sjögren’s syndrome, granulomatosis with polyangiitis, lupus, Takayasu’s arteritis, sarcoidosis, lymphoma, idiopathic membranous glomerulonephropathy
**XmAb®5871 Enhances Natural Regulatory Role of FcγRIIb**

**Natural:**
Ag + αAg Immune Complex

**XmAb5871:**
anti-CD19 with Immune Inhibitor Fc domain

- Inhibits many activation pathways in both healthy and diseased B cells
- Potent suppression of B-cell responses without destroying B cells
XmAb5871-03: Phase 2 Pilot Trial in IgG4-RD

• **Design:**
  Phase 2, open-label, multiple-dose trial

• **Study Population:**
  Histopathologically-proven, active disease:
  • Disease activity in one or more organ systems AND
  • IgG4-RD RI of ≥ 3

• **Numbers:**
  Target 15 patients (12 enrolled)

• **Study Drug Dose:**
  5 mg/kg of XmAb5871 IV q 14 days (12 doses)
Primary Objective

- To evaluate the effect of XmAb5871 on the IgG4-RD Responder Index (RI) in patients with active IgG4-RD.

- **Primary endpoint:**
  Proportion of patients on Day 169 with decrease in IgG4-RD RI of ≥ 2 points from Day 1 pre-dose disease activity score.

Secondary Objectives

- Safety, tolerability
- Pharmacokinetics, immunogenicity

Exploratory Objectives

- Mechanistic studies
- PET scans
This Trial Is Still In Progress

- Presentation is based on a data cut-off as of October 31, 2016.
- Exposure per patient (n = 12) shown below:

<table>
<thead>
<tr>
<th>Patient</th>
<th>Median Number of Infusions: 7 (range 1-12)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2 4 6 8 10 12</td>
</tr>
</tbody>
</table>

- Completed
- Early Termination
- Ongoing Patient

# of Infusions
### Demographics and Disease Characteristics

**Demographics (N=12)**

<table>
<thead>
<tr>
<th>Age</th>
<th>Years, median (range)</th>
<th>58 (43 - 78)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>Male</td>
<td>8 (67%)</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>4 (33%)</td>
</tr>
<tr>
<td>Race</td>
<td>White</td>
<td>10 (84%)</td>
</tr>
<tr>
<td></td>
<td>Black</td>
<td>1 (8%)</td>
</tr>
<tr>
<td></td>
<td>Asian</td>
<td>1 (8%)</td>
</tr>
</tbody>
</table>

**Baseline disease characteristics (N=12)**

| IgG4-RD Responder Index – median (range) | 10 (2 - 30) |
| IgG4 level (normal 3.9 - 86.4 mg/dl) – median (range) | 181 (25 - 2415) |
| Previously treated – n (%) | 8 (67%) |
Active Organs At Baseline

- Lymph Nodes: 75%
- Parotid Glands: 67%
- Lacrimal Glands: 58%
- Constitutional Symptom: 50%
- Other: 42%
- Kidney: 42%
- Heart / Pericardium: 33%
- Orbital Lesion: 25%
- Nasal Cavity Lesions: 17%
- Lungs: 17%
- Bile Ducts: 17%
- Other Salivary Gland: 17%
- Sinusitis: 8%
- Other ENT Lesion: 8%
- Retroperitoneal Fibrosis: 8%
- Pancreas: 8%
Number of Organs Involved At Baseline

| Median (Range) | 4 (1-10) |

- Median (Range): 4 (1-10)
No SAEs have been reported. TEAEs occurred in 58% of patients and were of mild to moderate severity.

<table>
<thead>
<tr>
<th>MedDRA preferred term</th>
<th>All TEAE</th>
<th>Related TEAE*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal Pain/Discomfort</td>
<td>4 (33%)</td>
<td>3 (25%)</td>
</tr>
<tr>
<td>Headache</td>
<td>2 (16.7%)</td>
<td>2 (16.7%)</td>
</tr>
</tbody>
</table>

* Related is possibly, probably or definitely related to drug as per the investigator.

One patient developed a rash and arthritis after her 5th infusion (Day 57). Anti-drug antibodies were positive and the self-limiting event was consistent with serum sickness.
Preliminary Efficacy

- 9 of 11 patients (82%) demonstrated treatment response
  - At least a 3 point decrease in the IgG4-RD RI within two weeks of first dose.

- 5 patients have achieved an IgG4-RD RI of 0.

- 2 patients who were on steroids at baseline were tapered and discontinued successfully.

- One patient with an atypical presentation (single organ, larynx) did not respond.

- A second patient responded initially but lost response on Day 85.
  - Both failed subsequent rituximab, too.
IgG4-RD Responder Index Over Time
Preliminary Conclusions

• XmAb5871 in active IgG4-RD was tolerated well.

• Treatment responses (decrease of IgG4-RD RI of ≥ 2) observed in 9 of 11 patients (82%).

• Initial response to therapy occurred quickly, within two weeks.

• Remission (IgG4-RD RI of 0) attained in 5 patients.

• Steroids tapered and discontinued in two of the patients that were on steroids at entry.

• Enrollment continues.
Thank you!

We thank the patients participating in this trial.