**INTRODUCTION**

- VRDN-002 is a next generation, half-life extended antagonist antibody to IGF-1R under development for the treatment of TED.
- TED is a debilitating autoimmune disorder associated with orbital inflammation, proptosis, diplopia, and soft tissue changes.¹
- Clinical and preclinical evidence indicates a central role for IGF-1R antagonism in reducing inflammation and proptosis that occur in TED.² ³
- We present safety and pharmacokinetic/pharmacodynamic (PK/PD) results from our phase 1 clinical trial evaluating VRDN-002 dosed at 3-20 mg/kg.

**STUDY DESIGN AND PARTICIPANTS**

12 adult HVs were randomized to a single IV infusion of placebo or VRDN-002, mean age was 55 years (range: 29 to 72); 7 were male and 5 female.

- One HV (20 mg/kg) was withdrawn because of their protocol noncompliance and was followed for safety through Day 29.
- Adverse events (AEs) and PK and PD (IGF-1 serum levels) parameters were assessed at regular intervals through 85 days.

**SAFETY RESULTS**

<table>
<thead>
<tr>
<th>All treatment-emergent AEs</th>
<th>Placebo (n=3)</th>
<th>VRDN-002 3 mg/kg (n=3)</th>
<th>VRDN-002 10 mg/kg (n=3)</th>
<th>VRDN-002 20 mg/kg (n=3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dizziness</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Headache</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Elevated blood pressure</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hypotension</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

- 4 HVs had 4 AEs, all transient and mild in severity.
- There were no withdrawals due to AEs.
- No serious AEs or hyperglycemia, muscle spasms, infusion reactions, or hearing impairment were observed.

**PHARMACOKINETIC RESULTS**

VRDN-002 has extended half-life up to 43 days in HVs

**PHARMACODYNAMIC RESPONSE**

VRDN-002 increased IGF-1 serum levels in HVs

- Mean IGF-1 serum levels across the VRDN-002 groups increased from 137-148 mg/mL at baseline to 350-429 mg/mL after 15 days following 1 infusion.
- IGF-1 serum levels started to increase within a day and reached 2-3-fold above baseline by Day 15 for all VRDN-002 doses; they remained elevated through Day 85 for the 10 mg/kg and 20 mg/kg groups.

**THERAPEUTIC IMPLICATIONS**

- The robust PD response with a favorable safety profile suggests VRDN-002 may be an effective anti-IGF-1 antibody for the treatment of TED.
- VRDN-002’s half-life extension (up to 43 days) could enable therapeutic concentrations to be achieved with low-volume SC dosing via a patient-controlled pen, decreasing the treatment burden for patients with TED.