VRDN-001, a Full Antagonist Antibody to IGF-1 Receptor in Development for Thyroid Eye Disease (TED): Pharmacodynamic Responses in Healthy Volunteers and Patients with Active TED

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INTRODUCTION AND STUDY DESIGN

- **VRDN-001**, a full antagonist antibody to the IGF-1 receptor, is under development for the treatment of TED.
- Clinical and preclinical evidence suggest a central role for IGF-1 receptor antagonism in reducing the inflammation and proptosis that occur in TED.\(^1\)\(^-\)\(^3\)

We assessed the PD response (serum IGF-1 levels) to treatment with VRDN-001 in HVs and patients with active TED through 50 days.

STUDY PARTICIPANTS

- Adult HVs and patients with active, moderate-to-severe TED were randomized to receive 2 infusions of VRDN-001 3 weeks apart of either placebo or VRDN-001.
- In the HV cohorts (n=13), 12 HVs completed the trial; 1 in the 20 mg/kg group withdrew for reactions observed.
- In patients with TED receiving 10 or 20 mg/kg VRDN-001, mean IGF-1 serum levels increased 6-fold from baseline.

VRDN-001 INCREASES IGF-1 SERUM LEVELS

**Healthy volunteers**

- Mean IGF-1 levels across the VRDN-001 groups increased from 95-143 ng/mL at baseline to 655-685 ng/mL after 2 infusions, representing a 5-7-fold increase.
- Increases occurred within a day of the first infusion and were sustained through 50 days.

**Patients with active TED**

- Mean IGF-1 levels in patients with TED across the VRDN-001 groups increased from 139-156 ng/mL at baseline to 853-907 ng/mL after 2 infusions, representing a 6-fold increase.
- Increases occurred after the first infusion and were sustained through 50 days.

THERAPEUTIC IMPLICATIONS

- Increased serum levels of IGF-1 induced by VRDN-001 in HVs and patients with TED are consistent with the 6-fold IGF-1 increases induced by VRDN-001 in oncology patients\(^4\) and indicate maximal target engagement at the lowest dose.
- Preliminary results from a phase 2 proof-of-concept study of 2 infusions of either 3, 10, or 20 mg/kg VRDN-001 in patients with active TED is presented in Poster FRI-545.
- The efficacy and safety of VRDN-001 for the treatment of TED will be further assessed in the ongoing THRIVE phase 3 clinical trial (NCT05176639).

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KEY TAKEAWAYS

- Pharmacodynamic (PD) results from our ongoing placebo-controlled phase 1/2 trial in healthy volunteers (n=65) and patients with active TED treated with 2 infusions of VRDN-001.
- VRDN-001 elicited rapid and sustained increases in IGF-1 serum levels that were similar across groups, indicating maximal target engagement at all doses tested.
- All doses were generally well tolerated, with no severe or serious AEs or infusion reactions observed.
- In HVs receiving 3-20 mg/kg VRDN-001, mean IGF-1 serum levels increased 5-7-fold from baseline.
- In patients with TED receiving 10 or 20 mg/kg VRDN-001, mean IGF-1 serum levels increased 6-fold from baseline.

The efficacy and safety of VRDN-001 for the treatment of TED will be further assessed in the ongoing THRIVE phase 3 clinical trial (NCT05176639).

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