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

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Poster #213

KEY TAKEAWAYS

Pharmacodynamic (PD) results from our ongoing placebo-controlled phase 1/2 trial in healthy volunteers (HVs) and patients with active TED treated with 2 infusions of **VRDN-001**:

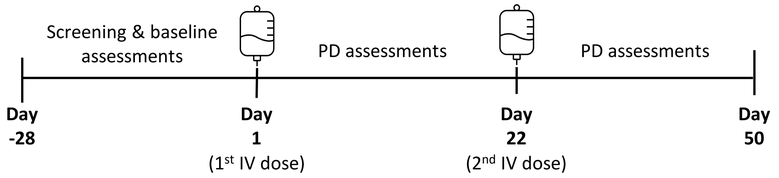
- **VRDN-001** elicited rapid and sustained increases in IGF-1 serum levels that were similar across groups, indicating maximal target engagement at all doses tested.
- All doses were well tolerated, with no severe or serious AEs or infusion reactions observed.
- In HVs receiving 3-20 mg/kg **VRDN-001**, mean IGF-1 serum levels increased 5-7-fold from baseline.
- In patients with TED receiving 3-20 mg/kg **VRDN-001**, mean IGF-1 serum levels increased 5-6-fold from baseline.

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

INTRODUCTION AND STUDY DESIGN

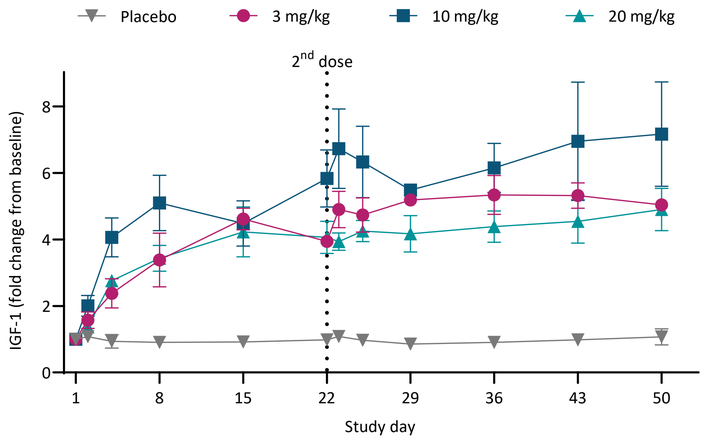
- **VRDN-001**, a full antagonist antibody to the IGF-1 receptor, is under development for the treatment of TED.
- Clinical and preclinical evidence suggest a central role for IGF-1 receptor antagonism in reducing the inflammation and proptosis that occur in TED.[1-4]
- We assessed the PD response (serum IGF-1 levels) to treatment with **VRDN-001** in HVs and patients with active TED through 50 days.

HVs	Randomized to **Placebo** (n=3), **VRDN-001 3 mg/kg** (n=3), **VRDN-001 10 mg/kg** (n=3), or **VRDN-001 20 mg/kg** (n=4)
Patients with active TED	Randomized to **Placebo** (n=6), **VRDN-001 3 mg/kg** (n=9), **VRDN-001 10 mg/kg** (n=6), or **VRDN-001 20 mg/kg** (n=6)



VRDN-001 INCREASES IGF-1 SERUM LEVELS

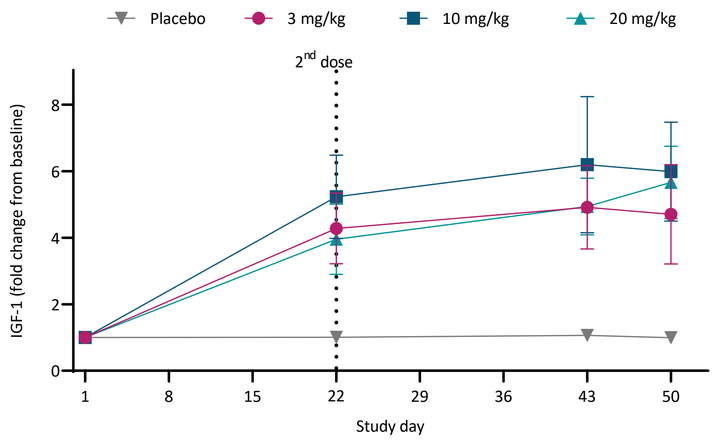
Healthy volunteers



Data are mean and SD. Missing baseline samples were normalized to population baseline average. Data from the withdrawn HV (20 mg/kg) are included for the 1st dose.

- 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



Data are mean and SD. Missing baseline samples were normalized to population baseline average. Data from the withdrawn patient (placebo) are included for the 1st dose.

- Mean IGF-1 levels in patients with TED across the **VRDN-001** groups increased from 138-156 ng/mL at baseline to 625-907 ng/mL after 2 infusions, representing a 5-6-fold increase.
- Increases occurred after the first infusion and were sustained through 50 days.

STUDY PARTICIPANTS

- Adult HVs and patients with active, moderate-to-severe TED were randomized to receive 2 intravenous infusions 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 personal reasons after the 1st infusion and was followed through Day 35. Mean age was 49 years; 8 were male and 5 were female.
- In the TED cohorts (n=27), 26 patients completed the trial; 1 in the placebo group was withdrawn prior to the 6-week visit because of protocol deviation and was followed through Day 26. For the 26 patients, mean age ranged from 39 to 51 years; 5 were male and 21 were female.

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[5] and indicate maximal target engagement, even at the lowest dose.
- In vitro data and 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 are presented in ATA 2023 Oral Presentation, Session #3.
- The safety and efficacy of **VRDN-001** will be further assessed in the ongoing THRIVE (active TED; NCT05176639) and planned THRIVE-2 (chronic TED; NCT06021054) phase 3 clinical trials.

Disclosures: This study was sponsored by Viridian Therapeutics, Inc. **VRDN-001** is an investigational therapy not approved for use in any country. Formatting and editorial assistance was provided by Keira Kim, an employee of Viridian Therapeutics, Inc. All authors met the ICMJE authorship criteria and had full access to relevant data. The authors would like to thank the study investigators, research teams, and study participants who make this research possible.

References: 1. Pritchard J et al. *J Immunol*; 170:6348–6354 (2003); **2.** Krieger CC et al. *J Clin Endocrinol Metabolism;* 100:1071–1077 (2015); **3.** Smith TJ et al. *NEJM*; 376:1748–1761 (2017); **4.** Douglas RS et al. *NEJM*; 382:4 (2020). **5.** Soria et al. *Eur J Cancer*; 49:1799–1807 (2013).

PDF of poster and additional information: Scan QR code

Abbreviations used in poster: IGF-1R, insulin-like growth factor 1 receptor; HV, healthy volunteer; PD, pharmacodynamic; IV; intravenous; SD, standard deviation

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Clinical Trial ID: NCT05176639

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