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Next Generation TED Therapy in Clinical Development

VRDN-001, a Full Antagonist Antibody to IGF-1 Receptor in Development for Thyroid Eye Disease (TED): Interim Phase 1/2 Pharmacodynamic Results

Kelly Foster, Brent Dickinson, Rochelle Summerfelt, Angela She, Vahe Bedian, Barrett Katz | Viridian Therapeutics Inc, Waltham, MA

KEY TAKEAWAYS

Pharmacodynamic (PD) results from our ongoing placebo-controlled phase 1/2 trial in healthy volunteers (HVs) and patients with 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.
- In HVs receiving 3-20 mg/kg **VRDN-001**, mean IGF-1 serum levels increased 5-7-fold from baseline.
- In TED patients receiving 10 mg/kg **VRDN-001**, mean IGF-1 serum levels increased 6-fold from baseline.

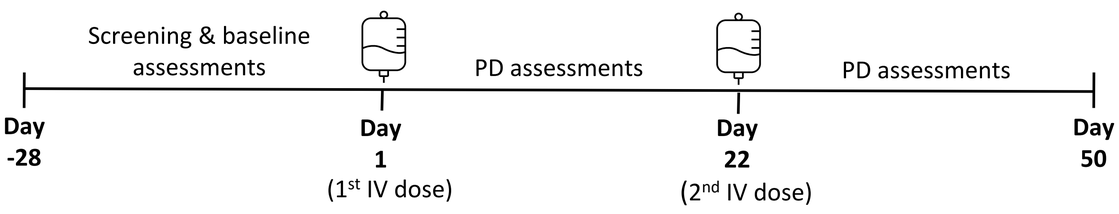
Results from the ongoing THRIVE phase 3 trial (NCT05176639, Poster #296) will further inform **VRDN-001** potential treatment regimens that balance efficacy and treatment burden in TED.

INTRODUCTION

- **VRDN-001**, a potent and full antagonist antibody to IGF-1R, is 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.[2-4]
- We assessed the PD response of **VRDN-001** administered intravenously to HVs at 3, 10, or 20 mg/kg and TED patients at 10 mg/kg.

STUDY DESIGN AND PARTICIPANTS

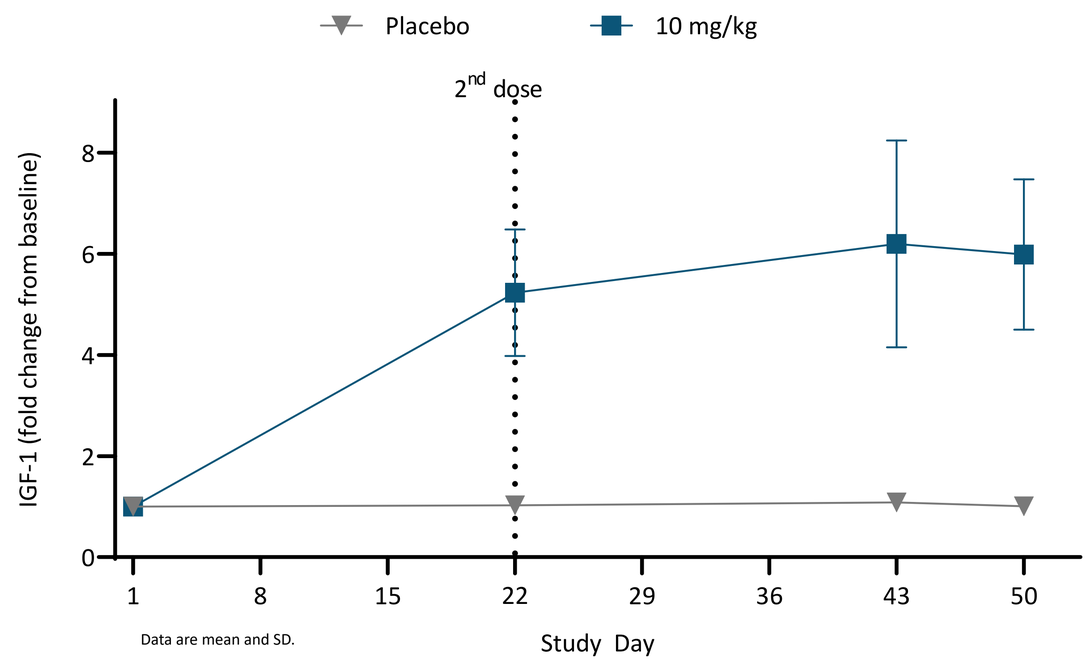
HVs	Randomized to **Placebo** (n=3), **VRDN-001 3 mg/kg** (n=3), **VRDN-001 10 mg/kg** (n=3), or **VRDN-001 20 mg/kg** (n=4)
Patients with TED	Randomized to **Placebo** (n=2) or **VRDN-001 10 mg/kg** (n=6)



- 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**. PD parameters (IGF-1 serum levels) were assessed through 50 days.
- 13 HVs were randomized; mean age of 49 years (range: 25 to 73), 8 male and 5 female. 12 completed the trial; 1 in the 20 mg/kg group withdrew for personal reasons after the 1st infusion and was followed through Day 35.
- 8 TED patients were randomized; mean age of 41 years (range: 27 to 59), 3 male and 5 female. The trial is ongoing and no patients in the 10 mg/kg cohort have withdrawn to date.

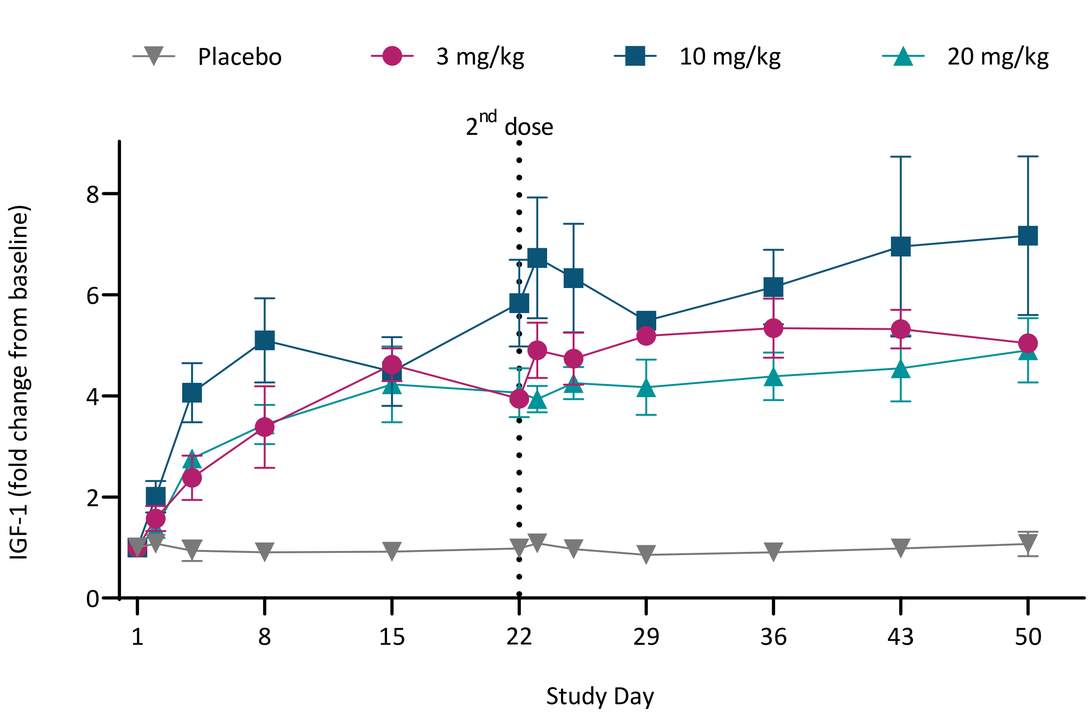
PHARMACODYNAMIC RESPONSE

VRDN-001 increased IGF-1 serum levels in TED patients



- Mean IGF-1 levels in TED patients receiving 10 mg/kg **VRDN-001** increased from 139 ng/mL at baseline to 853 ng/mL after 2 infusions, representing a 6-fold increase.
- Increases occurred after the first infusion and were sustained through 50 days.

VRDN-001 increased IGF-1 serum levels in HVs



Data are mean and SD. Missing baseline samples were normalized to population baseline average. Data from the withdrawn participant (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.

THERAPEUTIC IMPLICATIONS

- Increased serum levels of IGF-1 induced by **VRDN-001** in HVs and TED patients 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.
- The robust in vivo PD response observed with **VRDN-001** is consistent with in vitro data demonstrating **VRDN-001** more completely inhibits ligand binding to IGF-1R and more completely antagonizes IGF-1R signaling than is seen with teprotumumab (Poster #297).
- In TED patients, rapid and clinically meaningful improvement was seen in proptosis, inflammation, and diplopia at 6 weeks, following only 2 infusions of 3, 10, or 20 mg/kg **VRDN-001** (NANOS Platform Session II).

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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

Contact Information: info@viridiantherapeutics.com

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