Veligrotug (VRDN-001), a Full Antagonist Monoclonal Antibody to IGF-1R, in Active Thyroid Eye Disease (TED): THRIVE Phase 3 Efficacy and Safety Topline Results

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KEY TAKEAWAYS

- Primary results from THRIVE in active TED showed **veligrotug** led to significant and clinically meaningful improvements in proptosis, diplopia, and clinical activity score at 15 weeks.
  - Primary endpoint and all secondary endpoints were statistically significant
  - In post hoc analysis, rapid onset of treatment effect was observed at 3 weeks
- **Veligrotug** was generally well tolerated, with mostly mild AEs and 96% of patients completing the treatment course.
- Results highlight **veligrotug** as a potential promising new treatment option in active TED.

INTRODUCTION

- TED remains a condition with significant unmet need.
- **Veligrotug**, a full antagonist humanized mAb to the IGF-1R, is being assessed in 2 ongoing phase 3 RCTs in active TED (THRIVE) and chronic TED (THRIVE-2).
- Here we present primary efficacy and safety data of 5 IV infusions of **veligrotug** (10 mg/kg) given Q3W from THRIVE (NCT05176639) in patients with active moderate-to-severe TED (symptoms for ≤15 months, proptosis ≥3 mm above normal, and CAS ≥3).
- THRIVE trial design and specifics are available via poster QR code.

BASELINE CHARACTERISTICS AND PATIENT DISPOSITION

	Veligrotug (n=75)	Placebo (n=38)
Age, mean years (SD)	48.9 (12.4)	49.1 (12.5)
Female, n (%)	56 (75%)	31 (82%)
Proptosis (Hertel), mean mm (SD)	23.2 (3.1)	23.2 (3.3)
CAS, mean (SD)	4.5 (1.0)	4.8 (1.1)
Diplopia at baseline, n (%)	50 (67%)	26 (68%)
Diplopia, mean Gorman score (SD)[1]	2.0 (0.8)	2.0 (0.7)
Time since TED onset, mean months (SD)	7.9 (3.7)	7.2 (3.8)

[1] In patients with diplopia at baseline

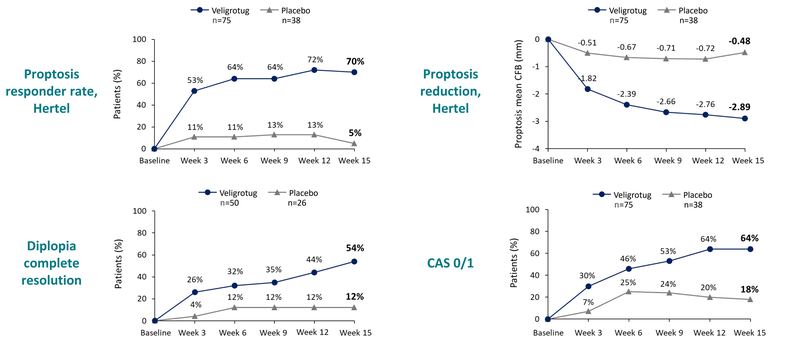
- 113 patients with active TED were randomized to **veligrotug** (n=75) or placebo (n=38) and all were included in the intent-to-treat population.
- Discontinued treatment: 4% **veligrotug** and 0% placebo

EFFICACY AT 15 WEEKS

		Veligrotug (n=75)	Placebo (n=38)	p-value
Overall Response	Overall responder rate (Hertel)[1]	67%	5%	p < 0.0001
Proptosis (Hertel)	Proptosis responder rate[1]	70%	5%	p < 0.0001
	Proptosis mean CFB, mm	-2.89	-0.48	p < 0.0001
Proptosis (MRI/CT)	Proptosis responder rate	69%	9%	p < 0.0001
	Proptosis mean CFB, mm	-2.91	-0.58	p < 0.0001
Diplopia	Diplopia complete resolution[2]	54%	12%	p < 0.0001
	Diplopia responder rate[3]	63%	20%	p < 0.0001
CAS	CAS reduction to 0/1 point	64%	18%	p < 0.0001
	CAS mean CFB	-3.4	-1.7	p < 0.0001

Missing values were imputed using prespecified imputation methodology. Results were obtained from a GEE model with an unstructured covariance matrix.
[1] Primary endpoints vary by region as follows: in Europe, Australia, UK, and Turkey: overall responder rate; percentage of participants with ≥2-mm reduction in proptosis (by Hertel) AND ≥2-point improvement in CAS from baseline in the study eye, without corresponding deterioration (≥2-mm/point increase) in proptosis or CAS in the fellow eye; in North America: proptosis responder rate; percentage of participants with ≥2-mm reduction in proptosis from baseline in the study eye, without deterioration in the fellow eye (≥2-mm increase). Other endpoints shown are secondary endpoints in at least one region. [2] Percentage of participants reporting baseline diplopia (Gorman Score >0) and a score of 0 at Week 15. [3] Percentage of participants reporting a reduction of at least 1 on the Gorman subjective diplopia scale, among patients with diplopia at baseline.

TIME COURSE OF TREATMENT EFFECT (POST HOC ANALYSIS)



SAFETY AT 15 WEEKS

Patients, n (%)	Veligrotug (n=75)	Placebo (n=38)
Any AEs	66 (88%)	24 (63%)
AEs occurring at ≥10% frequency in either group		
Muscle spasms	32 (43%)	2 (5%)
Headache	16 (21%)	5 (13%)
Infusion related reaction	13 (17%)	1 (3%)
Hearing impairment[1]	12 (16%)	4 (11%)
Hyperglycemia[1]	11 (15%)	2 (5%)
Fatigue[1]	10 (13%)	6 (16%)
Nausea	10 (13%)	3 (8%)
Ear discomfort	9 (12%)	1 (3%)
Diarrhea	8 (11%)	1 (3%)
Alopecia	6 (8%)	4 (11%)
Menstrual disorders[1,2]	8/34 (24%)	1/12 (8%)

[1] Includes multiple terms aggregated using standard sets of MedDRA terms. [2] Reported as percentage of menstruating women.

- The majority of AEs were mild (74% for **veligrotug** and 81% for placebo).
- 4 patients (**veligrotug**) had serious AEs (all unrelated to treatment).

UPDATE on THRIVE-2 in CHRONIC TED

- THRIVE-2 (NCT06021054) is evaluating the efficacy and safety of 5 IV infusions of **veligrotug** (10 mg/kg) given Q3W in patients with chronic moderate-to-severe TED (symptoms for >15 months, proptosis ≥3 mm above normal, and any CAS).
- Primary results showed the following:
  - At 15 weeks, primary and all secondary endpoints were statistically significant.
  - Veligrotug improved TED symptoms as early as 3 weeks after the first infusion.
  - **Veligrotug** was generally well tolerated, with mostly mild AEs and 94% of patients completing the treatment course.
- THRIVE-2 is the first RCT of IGF-1R inhibition in chronic TED to show significant improvement not only in proptosis but also in diplopia.

Disclosures: **Veligrotug** (VRDN-001) is investigational only; its safety and efficacy have not been established by any regulatory authority. Formatting and editorial assistance was provided by Keira Kim, MS, and funded by Viridian Therapeutics, Inc. All authors met the ICMJE authorship criteria and had full access to relevant data. VL, AMGH, MS, JBPR, EB, EE, MPL, MSS, PR, and PS are study investigators for Viridian Therapeutics, Inc. AP and AN are employees of Viridian Therapeutics, Inc.

PDF of poster and additional information: Scan QR code.

Abbreviations used in poster: AE, adverse event; CAS, clinical activity score; CFB, change from baseline; GEE, generalized estimating equations; IGF-1R, insulin-like growth factor-1 receptor; IV, intravenous; mAb, monoclonal antibody; MedDRA, Medical Dictionary for Regulatory Activities; Q3W, every 3 weeks; SD, standard deviation; TED, thyroid eye disease.

Clinical trial ID: THRIVE, NCT05176639. **Contact Information:** medinfo@viridiantherapeutics.com

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