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

Jody Abrams[1], Steven Leibowitz[2], Michael T. Yen[3], Raghu Mudumbai[4], Kimberly Cockerham[5], Roger E. Turbin[6], Navdeep Nijhawan[7], Sandy Zhang-Nunes[8], Andrea Kossler[9], Ashley Pajak[10], Abhijit Narvekar[10], on behalf of the THRIVE Study Group

[1]Sarasota Retina Institute, Sarasota, FL; [2]UCLA Stein Eye Institute, Los Angeles, CA; [3]Baylor College of Medicine, Alkek Eye Center, Houston, TX; [4]UW Medicine, Seattle, WA; [5]Senta Clinic, San Diego, CA; [6]Rutgers NJ Medical School, Newark, NJ; [7]Oshawa Clinic, Ontario, Canada; [8]Keck School of Medicine, USC Roski Eye Institute, Los Angeles, CA; [9]Stanford University, Byers Eye Institute, Palo Alto, CA; [10]Viridian Therapeutics, Inc., Waltham, MA.

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Disclosures & acknowledgments

- **Veligrotug** is investigational only; its safety and efficacy have not been established by any regulatory authority
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- **Presenting author JA** is a research investigator, advisory board member, and consultant for Viridian Therapeutics, Inc and a research investigator, advisory board member, consultant, and speaker for Horizon Therapeutics/Amgen
- Contact information: MedInfo@viridiantherapeutics.com

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THRIVE study investigator group: Antonio Manuel Garrido Hermosilla, Mariola Méndez Muros, Steven Leibowitz, Michael T. Yen, Peerooz Saeed, Raghu Mudumbai, Michael Schittkowski, Kimberly Cockerham, Jody Abrams, Vickie Lee, Roger E. Turbin, Julian Bermúdez Pío-Rendón, Eckart Bertelmann, Edwina Eade, Navdeep Nijhawan, Marta Pérez-López, Marco Sales Sanz, Sandy Zhang-Nunes, Chantal Boisvert, Steven Couch, Mays Dairi, Laura Gil Arribas, Andrea Kossler, Raymond Douglas, Delphine Drui, John Mandeville, Yves-Marie Pers, Patrice Rodien, Angel Romo López, Dirk Sander, Madhura Tamhankar.

Introduction

- **TED is a debilitating disease**, with significant impact through all phases on:
  - Visual function
  - Quality of life
  - Mental health
- **More treatment options needed**
  - Currently only 1 FDA-approved treatment exists
  - Need to improve convenience, efficacy, and/or safety
- **Veligrotug**, a full antagonist humanized monoclonal antibody to the IGF-1R, is being assessed in 2 ongoing phase 3 RCTs:
  - THRIVE (active TED) and THRIVE-2 (chronic TED)
- 15-week **THRIVE** data are presented here, follow-up through 52 weeks is ongoing

Key inclusion criteria

THRIVE Clinical Trial

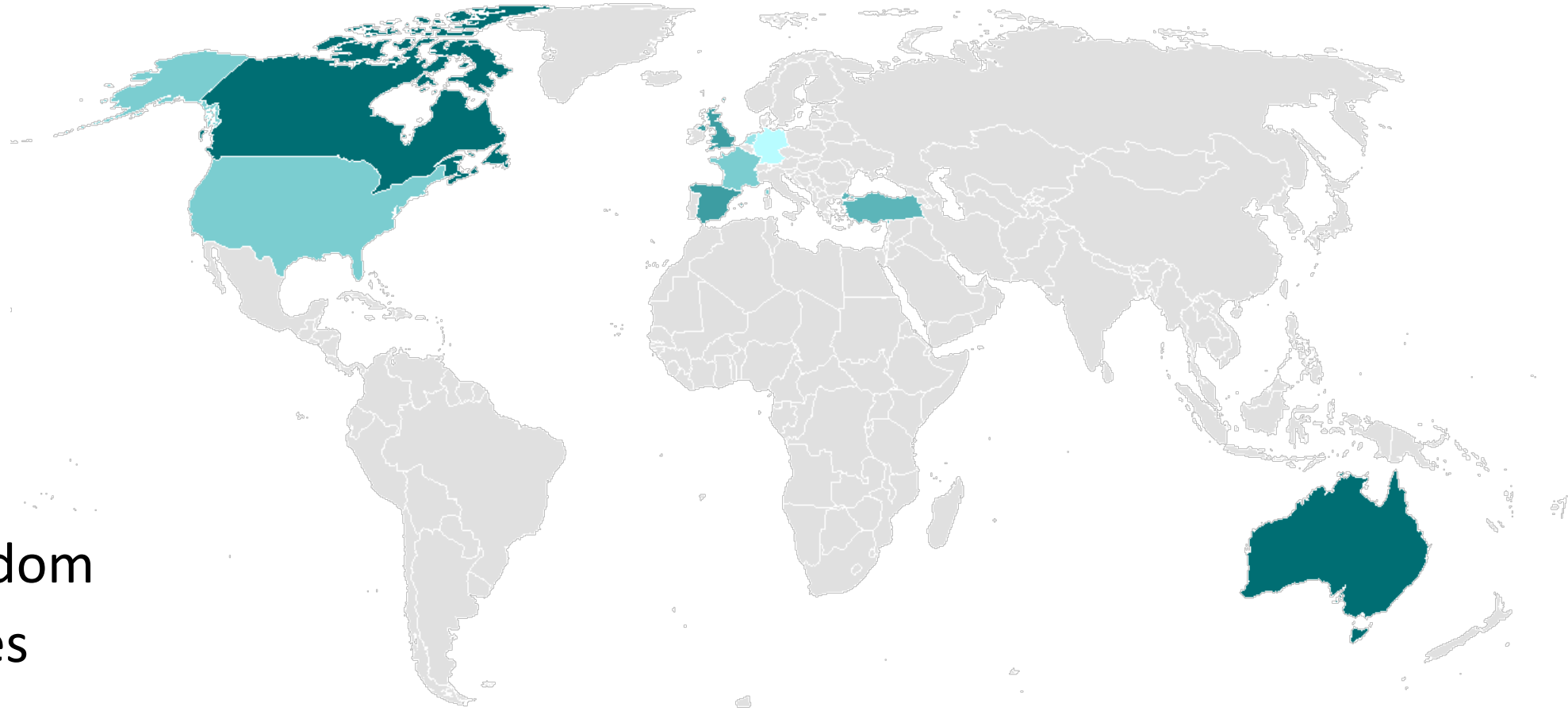
- Moderate-to-severe **active TED** with proptosis ≥3 mm above normal
- CAS ≥3 in study eye
- ≤15 months — Recent onset of TED signs and symptoms

NCT05176639

CAS = clinical activity score

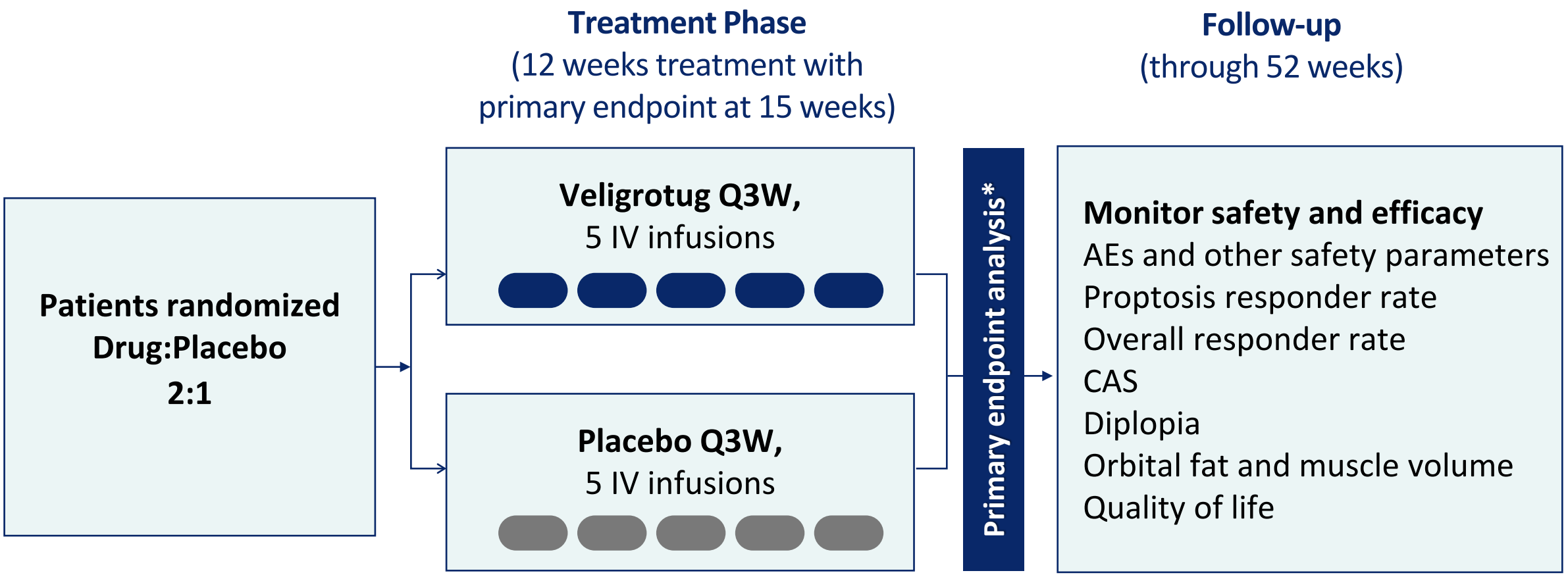
Global trial

- Australia
- Canada
- France
- Germany
- Netherlands
- Spain
- Turkey
- United Kingdom
- United States



Phase 3 trial design

THRIVE Clinical Trial



*Patients without a response (≥2-mm reduction in proptosis) at 15 weeks may enter a separate open-label study to receive a full course of **veligrotug**

THRIVE primary efficacy endpoints vary by region as follows:

- In North America: Proptosis responder rate, percentage of participants with ≥2-mm reduction in proptosis from baseline in the study eye (by Hertel), without deterioration in the fellow eye (≥2-mm increase).
- In Europe, Australia, 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.

IV = intravenous, CAS = clinical activity score, Q3W = every 3 weeks

Baseline characteristics

	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)

CAS, clinical activity score; SD, standard deviation. [1] In patients with diplopia at baseline.

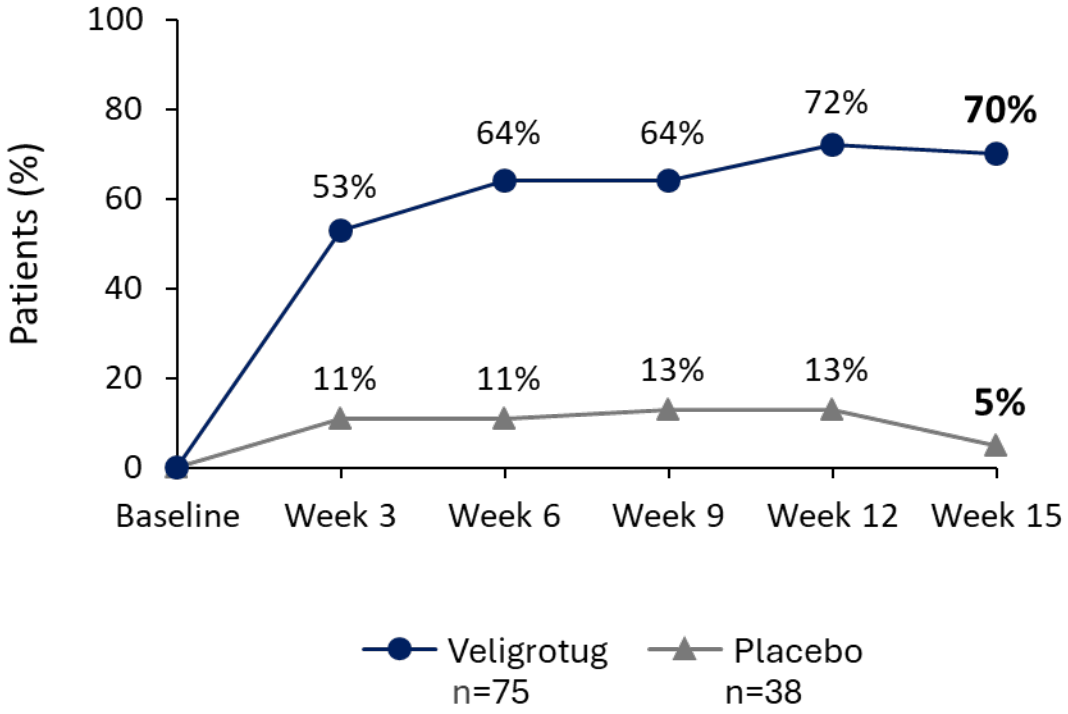
Primary analysis efficacy results at 15 weeks

		Veligrotug (n=75)	Placebo (n=38)	p-value
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
Overall Response	Overall responder rate (Hertel)[1]	67%	5%	p < 0.0001

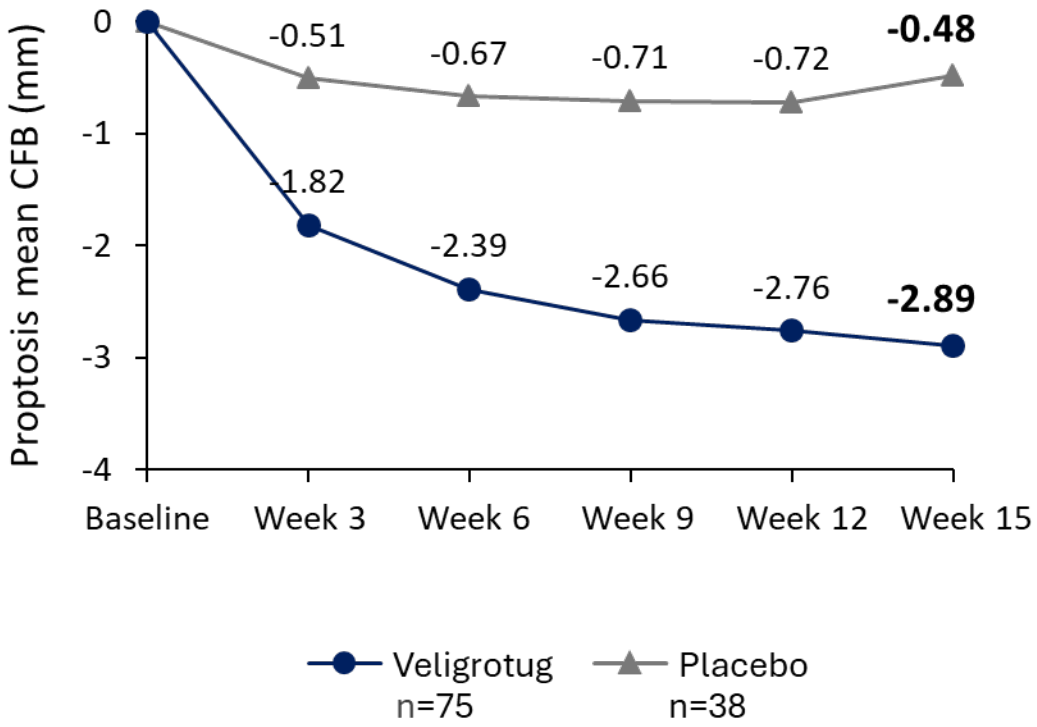
Missing values were imputed using prespecified imputation methodology. Results were obtained from a GEE model with an unstructured covariance matrix. CAS, clinical activity score; CFB, change from baseline.[1] Primary endpoints vary by region as follows: in North America: PRR, percentage of participants with ≥2-mm reduction in proptosis from baseline in the study eye (by Hertel), without deterioration in the fellow eye (≥2-mm increase); in Europe, Australia, 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. 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)

Proptosis responder rate, Hertel

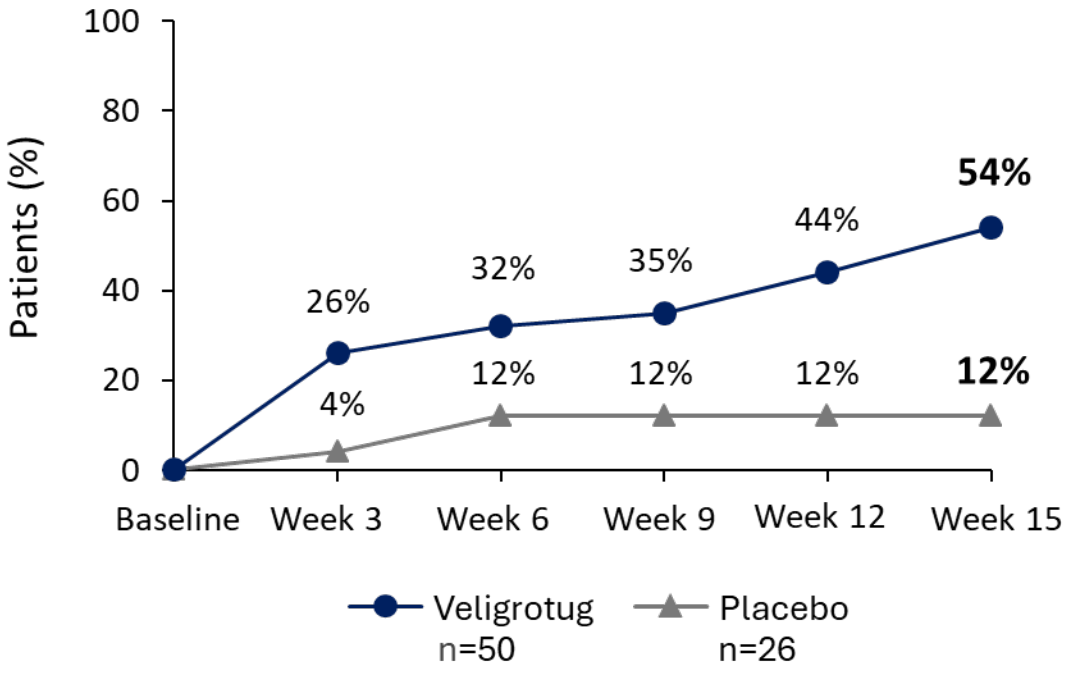


Proptosis reduction, Hertel

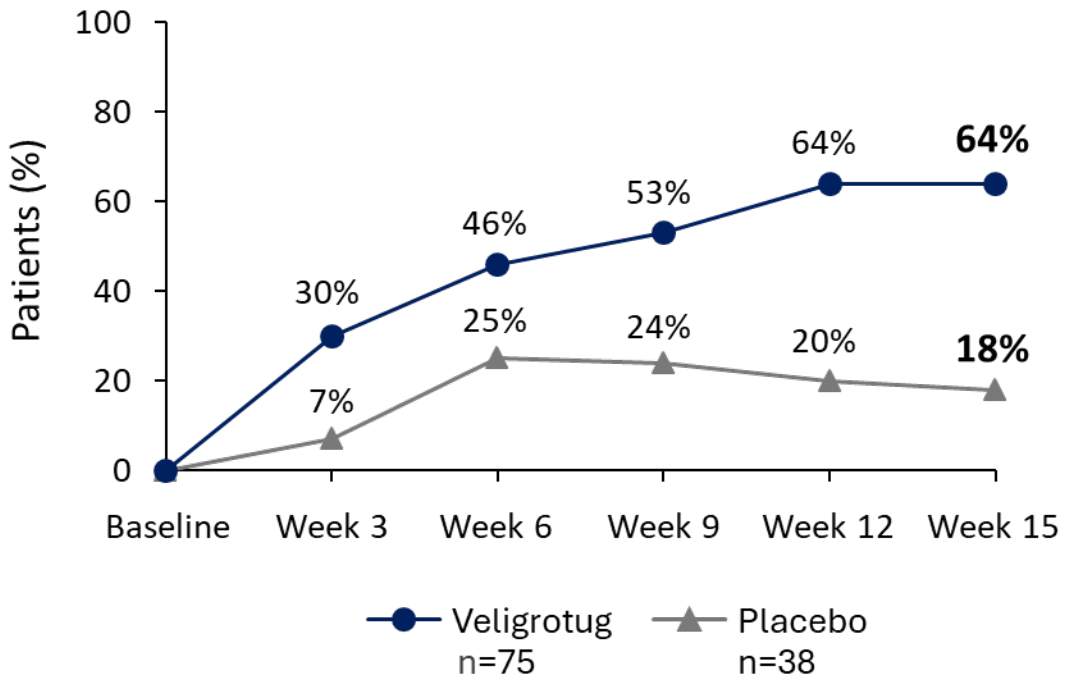


Time course of treatment effect (post hoc analysis)

Diplopia complete resolution*



CAS 0/1



*In patients with diplopia at baseline (score >0 on Gorman subjective diplopia scale)

Primary analysis safety results at 15 weeks

- Majority of AEs in both arms were mild
- Low treatment discontinuation rate of 4% in **veligrotug** arm
- Serious AEs (SAEs) occurred in 4 (5%) **veligrotug** and 0 placebo patients; none were treatment-related[1]

AEs occurring at ≥10% frequency in either arm	Veligrotug N=75, *n* (%)	Placebo N=38, *n* (%)
Muscle spasms	32 (43%)	2 (5%)
Headache	16 (21%)	5 (13%)
Infusion related reaction (IRR)	13 (17%)	1 (3%)
Hearing impairment[2]	12 (16%)	4 (11%)
Hyperglycemia[2]	11 (15%)	2 (5%)
Fatigue[2]	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[2,3]	8/34 (24%)	1/12 (8%)

Source: Viridian THRIVE data on file.
[1] 6 unrelated SAEs in 4 participants: cellulitis, appendicitis, dyspnea, hyperthyroidism, aortic dissection (planned surgery for known Type B aortic dissection), depression (diagnosed prior to 1st dose). [2] Includes multiple terms aggregated using standard sets of MedDRA terms. [3] Reported as percentage of menstruating women. AE = treatment-emergent adverse event

Conclusions

THRIVE Clinical Trial

- **Five** infusions of **10 mg/kg veligrotug** Q3W led to significant improvements at 15 weeks in:
  - Proptosis (Hertel & MRI/CT, with similar results)
  - Diplopia
  - Clinical activity score
- TED symptoms improved as early as 3 weeks after the 1st infusion
- Generally well tolerated, with mostly mild AEs, and 96% of patients completing the treatment course

Veligrotug is a potential promising new treatment option in active TED

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 1st infusion
  - **Veligrotug** was generally well tolerated, with mostly mild AEs and 94% of patients completing the treatment course
- Full primary data presented in AACE 2025 oral presentation SESS-1698

THRIVE-2 is the first RCT of IGF-1R inhibition in chronic TED to show significant improvement not only in proptosis but also in subjective diplopia

Next steps

Veligrotug (IV infusions)

- THRIVE and THRIVE-2 are ongoing; assess 52-week data
- Pursue FDA regulatory approval (targeted in 2H of 2026)

VRDN-003 (SC injections)

- REVEAL-1 (active TED) and REVEAL-2 (chronic TED) pivotal trials are **currently enrolling**
  - Scan QR code for study design (NANOS 2025 poster)

REVEAL-1 & REVEAL-2 study design

Thank you!
Questions?

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Jody Abrams, Sarasota Retina Institute, Sarasota, FL

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