Clinical Activity and Safety of VRDN-001, a Full Antagonist Antibody to Insulin-like Growth Factor-1 Receptor, in Active and Chronic Thyroid Eye Disease

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Scan for presentation

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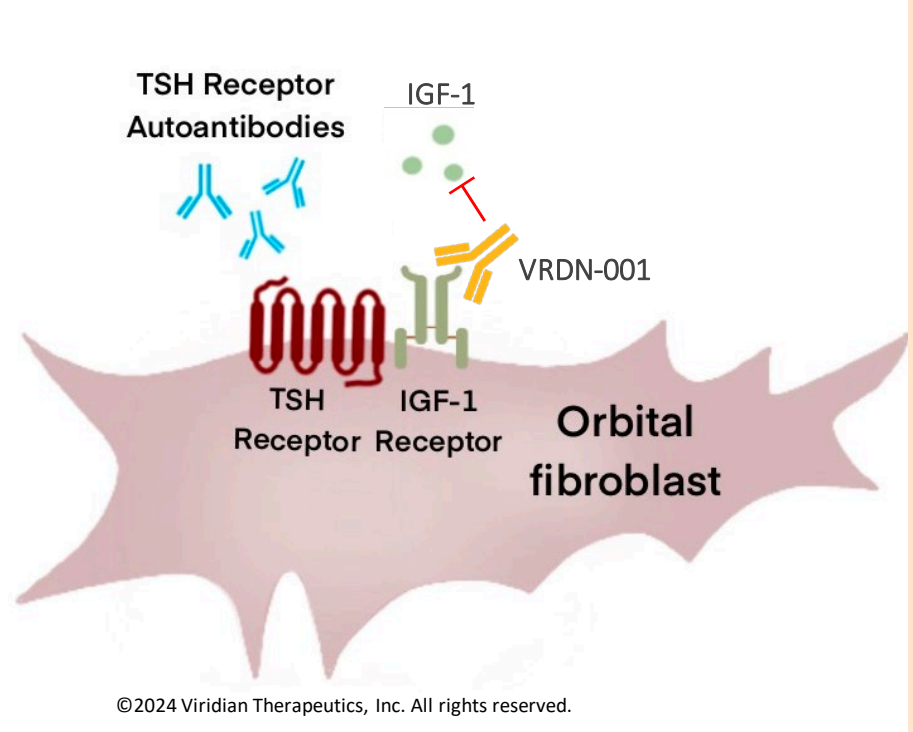
Disclosures

- These studies were sponsored by Viridian Therapeutics, Inc. All data are proprietary.
- Presenting author: **Kimberly Cockerham** is a clinical research investigator and consultant for Viridian Therapeutics, Inc., Amgen, Immunovant, Lassen, and Tourmaline.
- Coauthors: Roger E. Turbin, Michael T. Yen, Navdeep Nijhawan, Jody Abrams, Andrea Kossler, Rosa Tang, Chantal Boisvert, David Kaufman, Wendy W. Lee, Raghu Mudumbai, Madhura Tamhankar, Michael Yoon, and Shoaib Ugradar have consulted for, conducted studies funded by, or received honoraria for services provided to Viridian Therapeutics, Inc. Cathy Michalsky is an employee of Viridian Therapeutics, Inc., and Barrett Katz is a consultant for Viridian Therapeutics, Inc.
- The authors would like to thank the study investigators, research teams, and study participants who make this research possible.

VRDN-001, full antagonist antibody to IGF-1R, in development for the treatment of TED



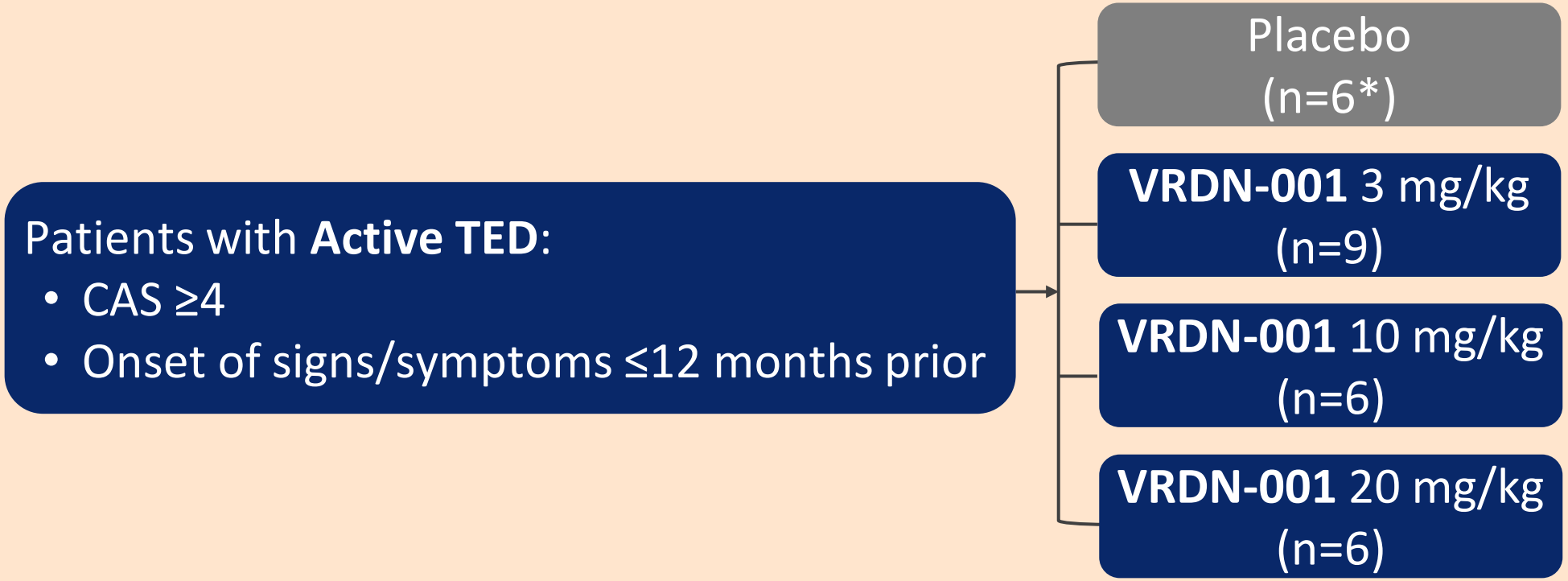
- **VRDN-001** is a monoclonal antagonist antibody against the IGF-1 receptor
- **VRDN-001** in preclinical studies:
  - Completely inhibits IGF-1 ligand binding to IGF-1R*
  - Completely antagonizes IGF-1R proximal & distal signaling*
- **VRDN-001** administration:
  - Intravenous formulation
  - Phase 2 proof-of-concept assessed 2 infusions
  - Phase 3 studies assessing 5 infusions

VRDN-001 is an investigational therapy not approved in any country.

*Zhao Y et al. VRDN-001, A Strong Antagonist Antibody to the Insulin-Like Growth Factor Receptor-1 (IGF-1R) in Development for Thyroid Eye Disease (TED), Binds to a Distinct Epitope From Teprotumumab. Late Breaking Highlighted Poster 132. *Thyroid.* 2022;32(1).

Proof-of-concept randomized, double-masked trial tested 3 different doses in Active TED

(Patients received 2 IV infusions 3 weeks apart)



CAS, clinical activity score

*One patient in the placebo arm discontinued the study before Week 6 and thus is not included in the efficacy analysis but is included in the safety analysis.

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Proof-of-concept randomized, double-masked trial tested 2 different doses in Chronic TED

(Patients received 2 IV infusions 3 weeks apart)

CAS, clinical activity score

*In the 3 mg/kg dose cohort, 7 patients were randomized to receive VRDN-001, 1 of whom discontinued the trial due to leaving the country for a family emergency prior to receiving the second dose of VRDN-001; 6 were available for efficacy outcomes, but all 7 were available for safety outcomes.

Rationale & objectives

- Preliminary phase 2 proof-of-concept results in **Active** and **Chronic TED** showed improvements in outcome measures across all doses tested
- Here we compare outcomes in **Active TED cohorts** with those in **Chronic TED cohorts** at 6 weeks following 2 IV infusions of **VRDN-001** of any dose

Baseline patient characteristics

	Active TED n=21	Chronic TED n=12
Proptosis, mean (SEM)	23.7 (0.7)	22.2 (1.2)
CAS, mean (SEM)	5.4 (0.2)	3.3 (0.8)
Diplopia, n (%)	13 (62%)	5 (42%)
Gorman diplopia score, mean (SEM)	1.3 (0.3)	0.9 (0.4)
Months since onset of TED signs/symptoms, mean (SEM)	7.4 (0.8)	94.0 (33.7)
Age, mean years (SEM)	47 (3.3)	50.7 (3.3)
Female, n (%)	19 (90%)	10 (83%)

SEM, standard error of the mean

CAS, clinical activity score, a composite 0-7 scale scoring signs/symptoms of TED

Preliminary clinical outcomes

After 2 IV infusions

	Active TED n=21	Chronic TED n=12
Proptosis responder rate by Hertel	71%	42%
Proptosis mean change by Hertel	-2.3 mm	-1.6 mm
Proptosis mean change by MRI/CT	-2.8 mm[1]	-2.0 mm[1]
Improvement in CAS to 0/1[2]	62%	40%
Mean change in CAS	-4.1	-2.3
Proptosis responder (Hertel) OR improvement in CAS to 0/1[3]	86%	67%
Improvement in diplopia[4]	85% (11/13)	20% (1/5)

[1] MRI/CT available for 16 of 21 Active patients and 8 of 12 Chronic patients.

[2] In patients with CAS>0.

[3] Either a reduction in proptosis of ≥2 mm OR CAS of 0/1 in patients with a CAS >0 at baseline AND a reduction in CAS of ≥1.

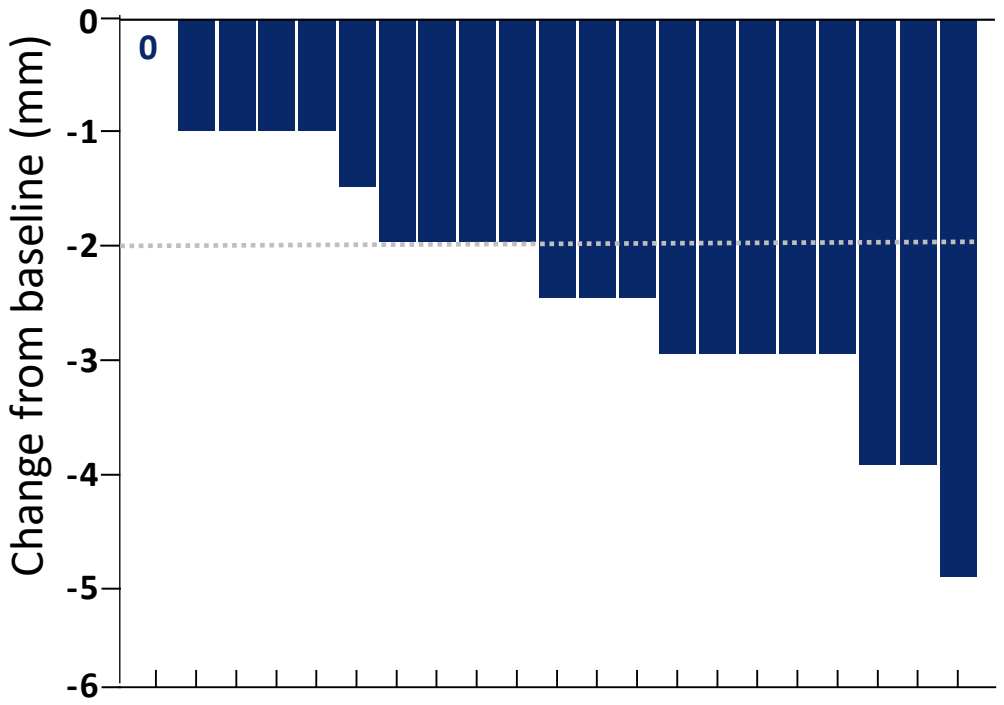
[4] Improvement in diplopia of ≥1 on Gorman score for patients who had diplopia at baseline: 13 of 21 Active patients (mean Gorman score of 2.2); and 5 of 12 Chronic patients (mean Gorman score of 2.2).

Proptosis reductions by exophthalmometer

(After 2 IV infusions)

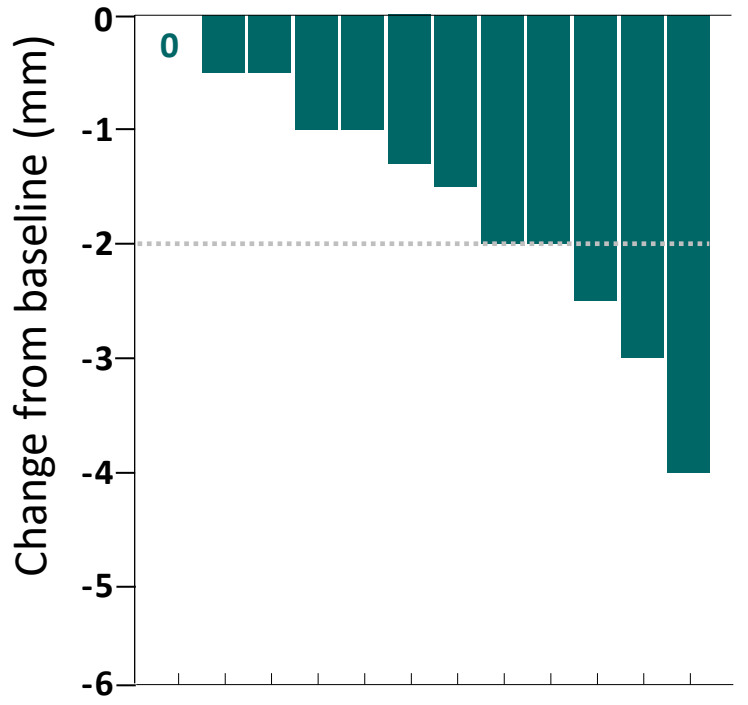
Active TED

Individual Hertel proptosis change
(all VRDN-001 patients)



Chronic TED

Individual Hertel proptosis change
(all VRDN-001 patients)



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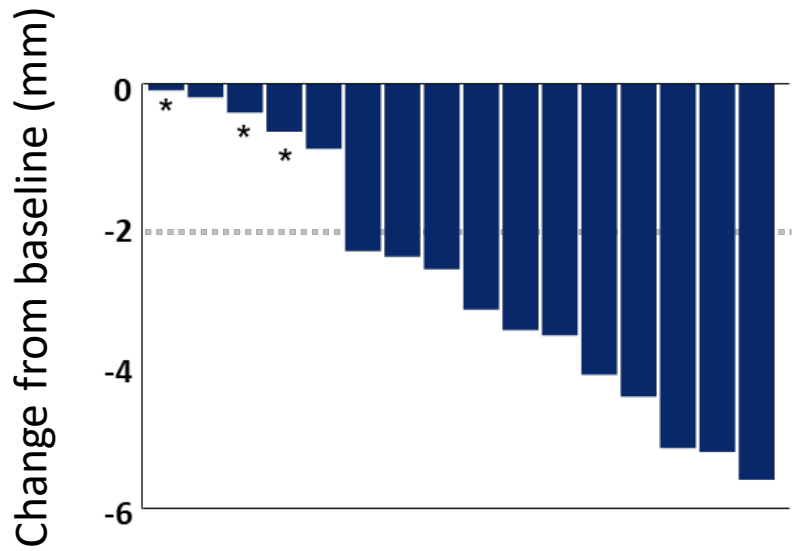
Proptosis reductions by MRI/CT

(After 2 IV infusions)

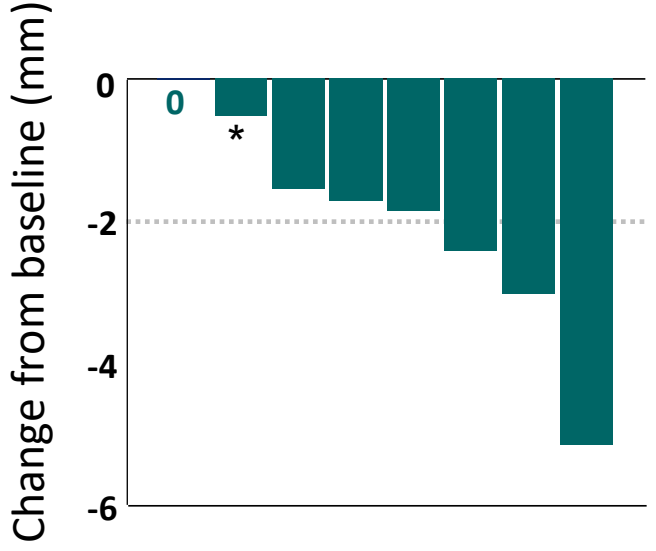
Active TED

Individual MRI/CT proptosis change
(all VRDN-001 patients with scans)



Chronic TED

Individual MRI/CT proptosis change
(all VRDN-001 patients with scans)



All MRI/CT images were reviewed centrally by 2 independent, masked readers.
MRI/CT data were available for 16 of 21 Active patients and 8 of 12 Chronic patients.
*Patients were proptosis responders by exophthalmometer, but response was not confirmed by MRI/CT.

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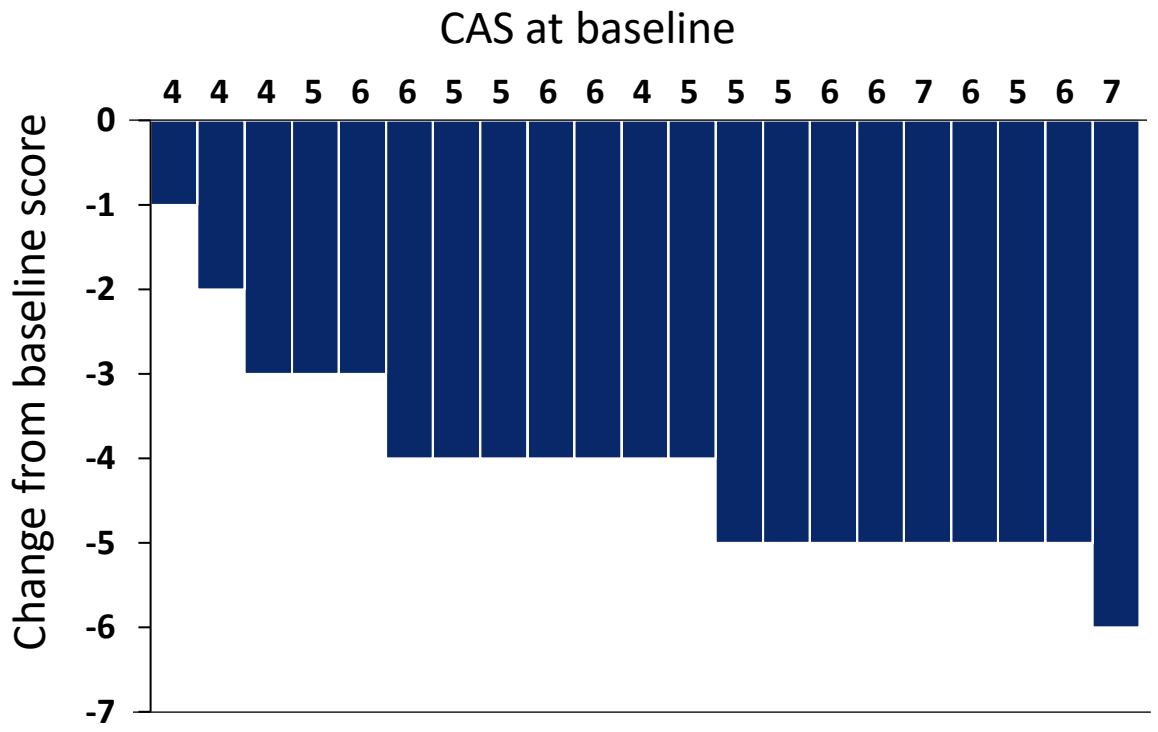
Changes in CAS

(After 2 IV infusions)

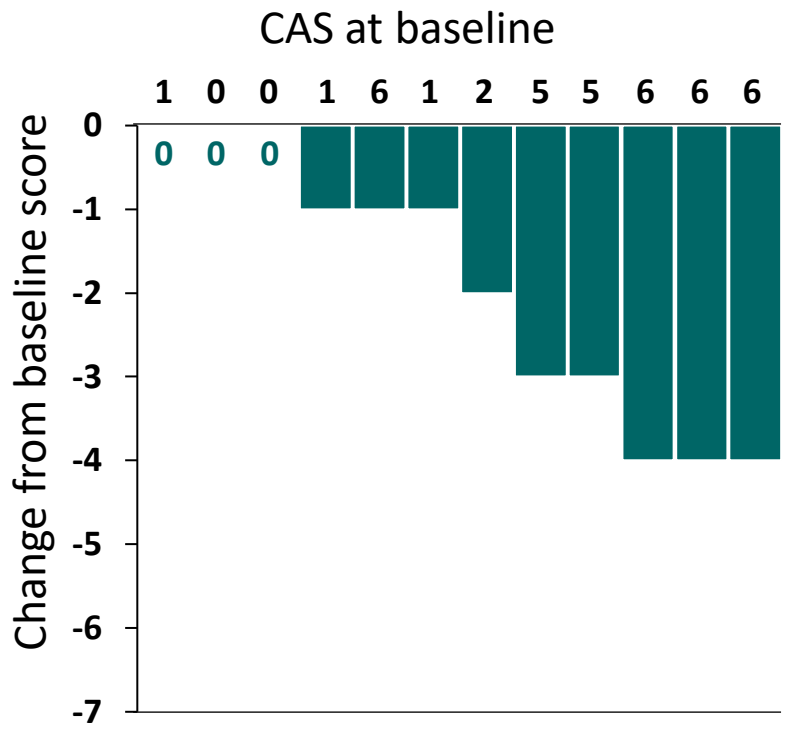
Active TED

Individual CAS change
(all VRDN-001 patients)



Chronic TED

Individual CAS change
(all VRDN-001 patients)



CAS, clinical activity score: a composite 0-7 scale scoring signs/symptoms of TED

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Preliminary safety profile of VRDN-001

After 2 IV infusions

AEs in ≥10% of either group	**Active TED** n=21	**Chronic TED** n=13*
Back pain	0	2 (15%)
Dry eye	4 (19%)	1 (8%)
Diarrhea	4 (19%)	1 (8%)
Fatigue	4 (19%)	0
Headache	4 (19%)	1 (8%)
Muscle spasms	6 (29%)	2 (15%)

- **No serious adverse events (SAEs)**
- **Additional AEs of interest:**
  - **Hearing impairment:** 2 (9.5%) in Active TED (hypoacusis and tinnitus, which returned to normal audiometry at follow-up); none in Chronic TED
  - **Hyperglycemia:** 2 (9.5%) in Active TED (1 related and 1 unrelated to study drug); none in Chronic TED

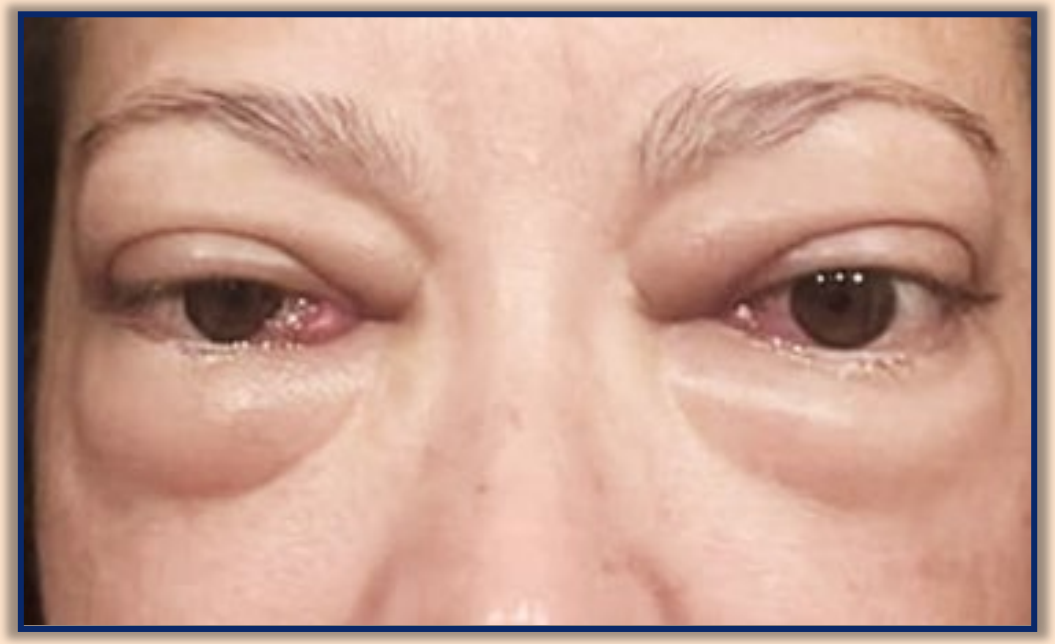
AE, treatment-emergent adverse event

Preliminary data as of December 19, 2022 for Active and May 30, 2023 for Chronic (all patients had reached 6-week visit)

*Though not evaluable at Week 6 for clinical activity, the 7th patient randomized in the 3 mg/kg cohort who discontinued the trial prior to Week 6 due to leaving the country for a family emergency was followed for safety until their discontinuation.

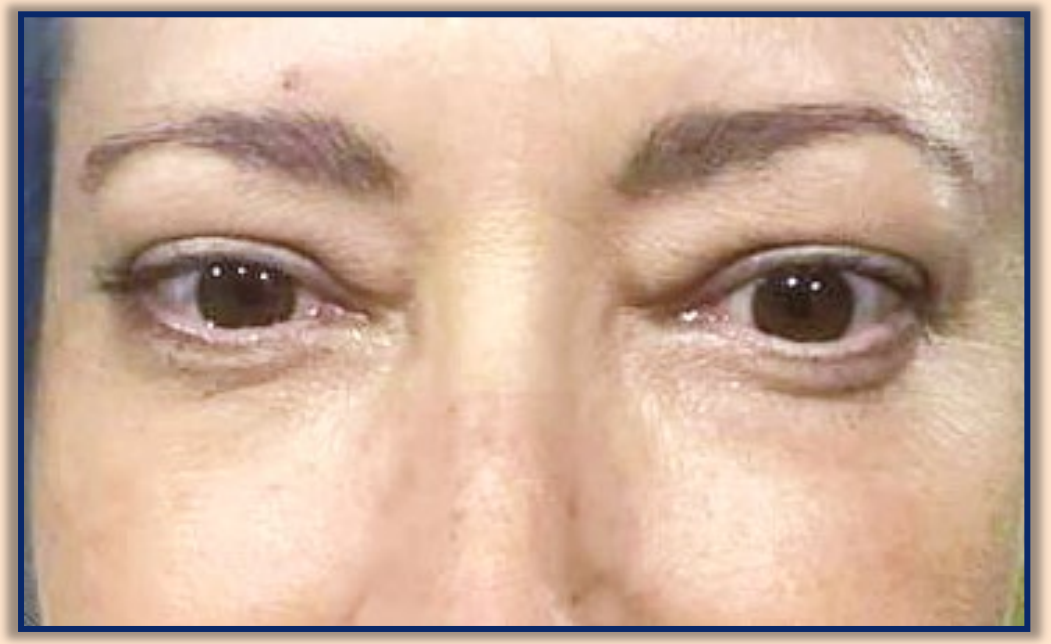
Active TED patient

Baseline at Week 0



2 days before 1st IV infusion of **VRDN-001**

Week 6

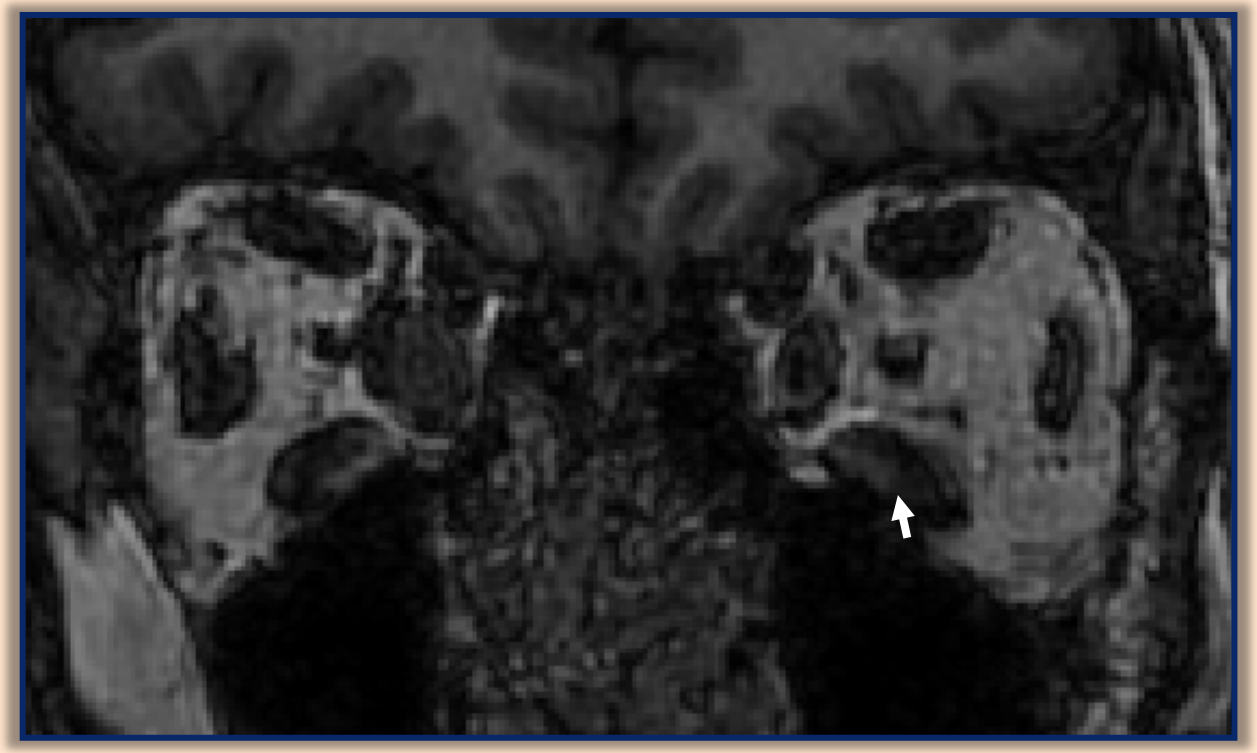


2 days following 2nd IV infusion of **VRDN-001**

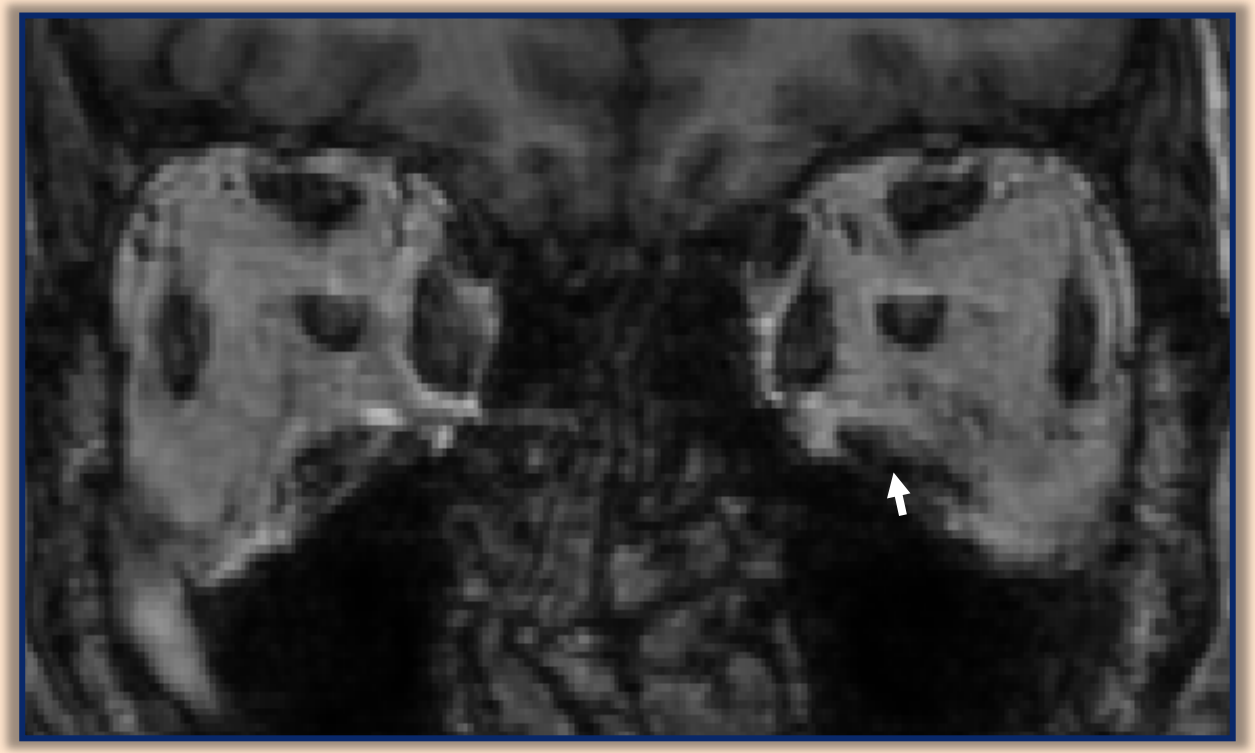
Patient photos taken by patient used with patient and investigator permission. Patient received 2 infusions in the study; in extended follow-up off treatment, TED symptoms have returned for this patient.

Active TED patient*

Baseline (Week 0)



After 2 **VRDN-001** IV infusions (Week 6)



White arrows highlight reduction in size of the inferior rectus muscle.

*Different patient from prior slide

Conclusions from phase 2 proof-of-concept data in Active and Chronic TED

- Preliminary phase 2 proof-of-concept results showed 2 IV infusions of **VRDN-001** were generally well tolerated and led to meaningful improvements in symptoms of both **Active TED** and **Chronic TED**, with larger magnitude of improvement in the **Active TED** cohort
- The safety and efficacy of **VRDN-001** for the treatment of TED are being further assessed in 2 ongoing phase 3 clinical trials (scan QR codes and see NANOS poster #467 for more details)

THRIVE
Active TED, NCT05176639

THRIVE-2
Chronic TED, NCT06021054

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Thank you! Questions?

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