VRDN-001, a Full Antagonist Antibody to IGF-1R: Proof-of-Concept Results in Chronic TED

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Disclosures

- This study was sponsored by Viridian Therapeutics, Inc. All data are proprietary.
- **VRDN-001** is an investigational therapy not approved in any country. All authors met the ICMJE authorship criteria and had full access to relevant data.
- All data from the chronic TED phase 2 proof-of-concept study are as of data cutoff of May 30, 2023.
- Presenting author: Roger E. Turbin is a clinical research investigator for Viridian Therapeutics, Inc. and a former investigator for Horizon Therapeutics and has received consulting fees from Viridian Therapeutics, Inc. and Horizon Therapeutics.
- Coauthors: Michael T. Yen, Kimberly Cockerham, Jody Abrams, Andrea Kossler, Raghu Mudumbai, Madhura Tamhankar, and Raymond S. Douglas have consulted for, conducted studies funded by, or received honoraria for services provided to Viridian Therapeutics, Inc. Cathy Michalsky and Barrett Katz are employees of Viridian Therapeutics, Inc.
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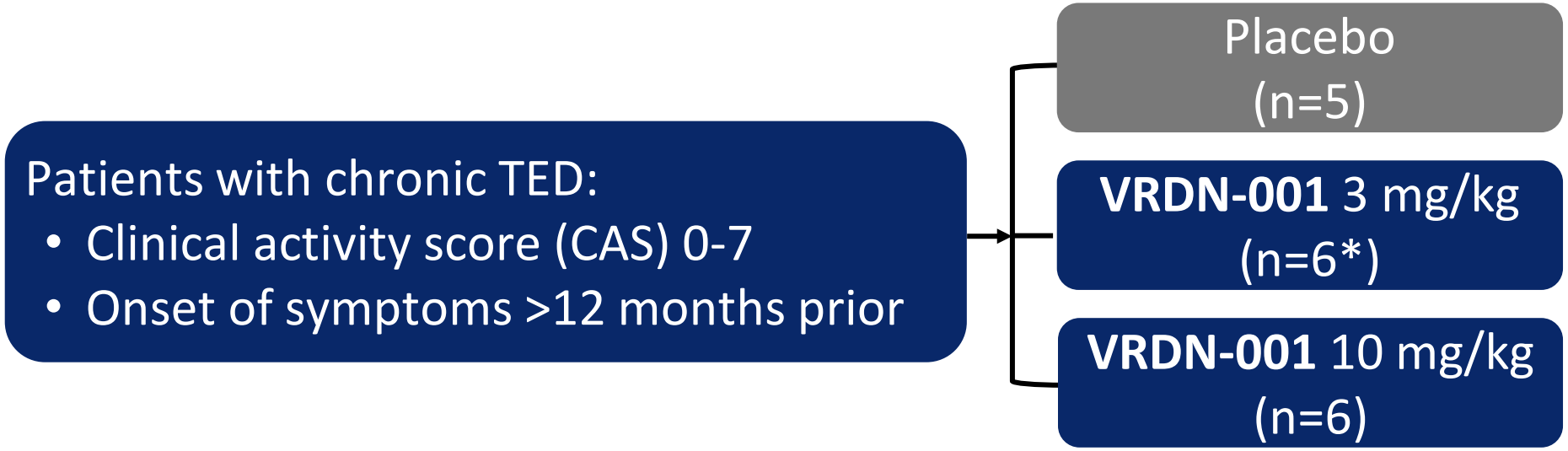
Proof-of-concept randomized, double-masked trial tested 2 doses in chronic TED

Patients received 2 infusions 3 weeks apart



*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, resulting in 6 patients treated with VRDN-001 3 mg/kg evaluable for the Week 6 clinical endpoint analyses.

Baseline patient characteristics

	VRDN-001 (3 & 10 mg/kg)	Placebo
n	**12**	5
Proptosis, mean (SEM)	**22.2 (1.2)**	25.0 (1.6)
CAS, mean (SEM)	**3.3 (0.8)**	2.8 (0.8)
Diplopia, n (%)	**5 (42%)**	2 (40%)
Gorman diplopia score, mean (SEM)	**0.9 (0.4)**	0.6 (0.4)
Months since onset of TED signs/symptoms, mean (SEM)	**94.0 (33.7)**	194.4 (81.2)
Age, mean years (SEM)	**50.7 (3.3)**	49.4 (4.4)
Female, n (%)	**10 (83%)**	5 (100%)

SEM = Standard error of the mean

Summary of VRDN-001 outcome measures

Preliminary data after 2 infusions (6 weeks)

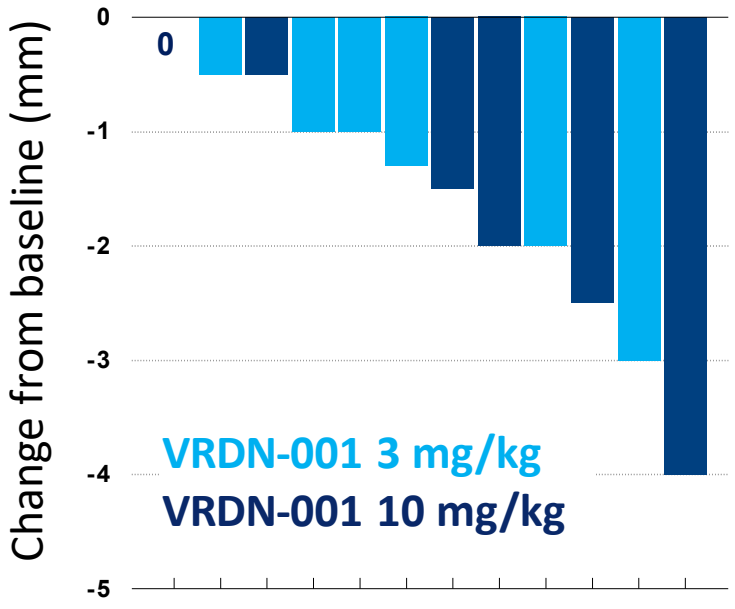
Week 6	Proptosis responder rate	Proptosis mean change by Hertel	Proptosis mean change by MRI/CT*	CAS score of 0 or 1**	CAS mean change**	Diplopia complete resolution***
VRDN-001 (3 and 10 mg/kg) n=12	**42%**	**-1.6 mm**	**-2.0 mm**	**40%**	**-2.3**	**0%**
10 mg/kg, n=6	50%	-1.8 mm	-1.5 mm	50%	-2.8	0%
3 mg/kg, n=6	33%	-1.5 mm	-2.6 mm	33%	-2.0	0%

Proptosis responder rate: % of patients with ≥2-mm reduction in proptosis measured by exophthalmometry
Clinical activity score (CAS): a composite 0-7 scale scoring signs and symptoms of TED
*MRI/CT available for 4 of 6 VRDN-001 10 mg/kg treated patients, 4 of 6 VRDN-001 3 mg/kg treated patients. **2 patients with CAS of 0 at baseline excluded from calculation. ***Includes only patients who had diplopia present at baseline. Diplopia was present at baseline in 5 of 12 VRDN-001 treated patients (mean Gorman score of 2.2): 2 were in 3 mg/kg cohort and 3 were in 10 mg/kg cohort.

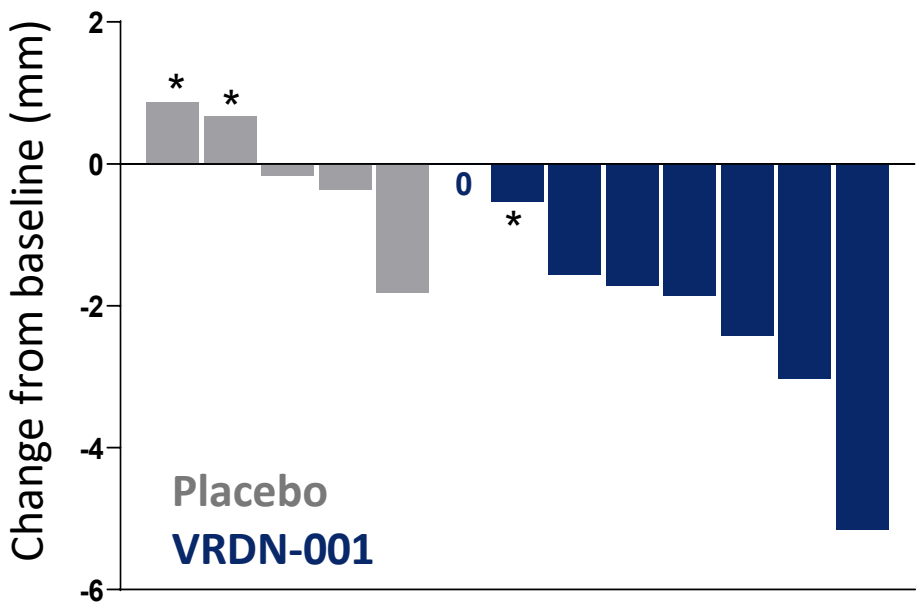
Proptosis reductions by exophthalmometer and MRI/CT

Preliminary data after 2 infusions (6 weeks)

Individual Hertel proptosis change (all VRDN-001 patients)

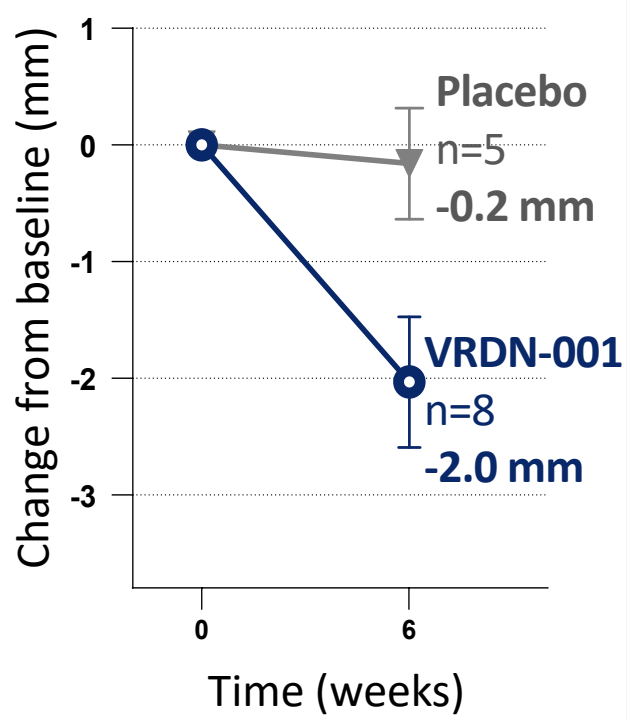


Individual MRI/CT proptosis change (all patients with scans**)



*2 placebo and 1 VRDN-001 treated patients were responders by exophthalmometer, but response was not confirmed by MRI/CT.

Mean MRI/CT proptosis change (all patients with scans**)



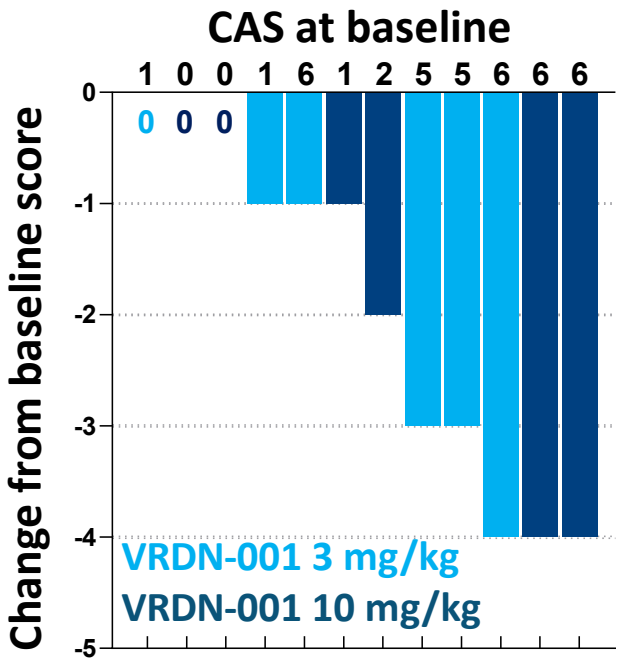
**Masked, centrally reviewed MRI/CT data were available for 5 of 5 placebo patients and 8 of 12 VRDN-001 patients. All MRI/CT images were reviewed centrally by 2 independent, masked readers.

Changes in clinical activity score (CAS)

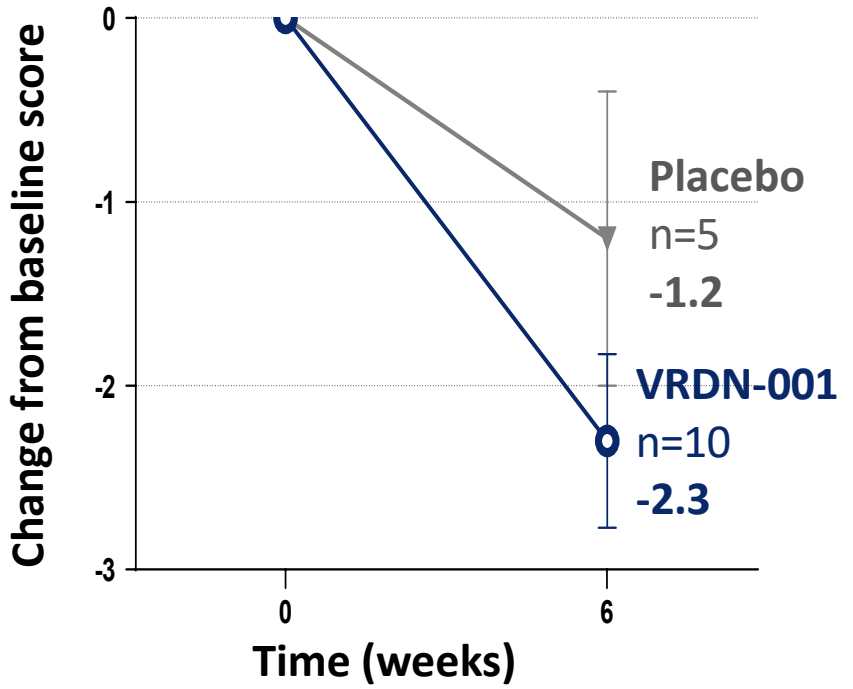
Preliminary data after 2 infusions (6 weeks)

Clinical activity score (CAS): a composite 0-7 scale scoring signs and symptoms of TED

Individual CAS change
(all VRDN-001 patients)



Mean change in CAS
(patients with CAS >0 at baseline)



Mean CAS at baseline was 3.9 for VRDN-001 patients (n=10) and 2.8 for placebo patients (n=5).

Safety profile

Preliminary data

No serious adverse events (SAEs); no hearing impairment or hyperglycemia events

Adverse events occurring in ≥10% of patients	**VRDN-001** 3 & 10 mg/kg (n=13*), n	Placebo (n=5), n
Back pain	2 (15%)	0 (0%)
Muscle spasms	2 (15%)	0 (0%)
Headache	1 (8%)	2 (40%)
Ear discomfort	0 (0%)	1 (20%)
Fatigue	0 (0%)	1 (20%)
Flatulence	0 (0%)	1 (20%)
Pruritus	0 (0%)	1 (20%)

Preliminary data are as of data cutoff of May 30, 2023.

*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.

Conclusions

- Both 3 and 10 mg/kg doses were well tolerated and showed clinical activity, with almost half of patients achieving ≥2 mm reduction in proptosis after just 2 infusions
- Two infusions of **VRDN-001** have demonstrated clinically meaningful results in both chronic and active TED (ESOPRS presentation)
- 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

Thank you!
Questions?

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