THRIVE Phase 3 Trial of VRDN-001: A Full Antagonist Antibody to the IGF-1 Receptor for Thyroid Eye Disease (TED)

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KEY TAKEAWAYS

- THRIVE is a phase 3 randomized placebo-controlled trial to assess the efficacy and safety of VRDN-001, a full antagonist antibody to IGF-1R, in patients with TED.
- The trial is designed to identify a regimen that best balances efficacy, safety, and patient treatment burden.
- The study is currently enrolling patients with active, moderate-to-severe TED in North America and Europe, with topline results expected mid-2024.

INTRODUCTION

- VRDN-001 is a novel full antagonist monoclonal antibody targeting IGF-1R.
- Preclinical studies have shown VRDN-001 is a full antagonist of IGF-1R providing more complete receptor blockade than other anti-IGF-1R antibodies, including the only currently approved TED therapy.1
- Data from the VRDN-001 phase 2 proof-of-concept study in patients with active TED demonstrated marked improvements in proptosis, inflammation, and diplopia.2 (Presented in NANS platform session II)
- The THRIVE phase 3 study will assess the safety and efficacy of VRDN-001 treatment regimens in a larger population of patients with active TED (NCT05176639).

PATIENT POPULATION

- Sites
  - Approximately 50 sites across North America and Europe

- Patients
  - Female or male with active TED

Key inclusion criteria

- Active TED and CAS ≥4 in study eye
- Moderate-to-severe TED
- Recent onset of TED signs and symptoms

Key exclusion criteria

- Prior treatment with an IGF-1R antibody or any investigational agent for TED
- Systemic corticosteroids within 2 weeks or immunosuppressants within 60 days
- Compressive optic neuropathy requiring surgical decompression
- Clinically significant ear pathology, ear surgery, or hearing loss
- Inflammatory bowel disease

PROPOSED TRIAL DESIGN

Screening/Enrollment

- Patients with moderate-to-severe active TED, randomized 1:1:1

Double-Masked Treatment Period (24 weeks)

- VRDN-001 Q3W 8x
- VRDN-001 Q3W 5x + Placebo Q3W 3x
- Placebo Q3W 8x

Primary endpoint analysis

Double-Masked Observational Period (28 additional weeks)

- Monitor efficacy and safety

ENDPOINTS

- Primary efficacy endpoint in North America: proptosis responder rate (reduction ≥2 mm vs baseline).
- Primary efficacy endpoint in Europe: overall responder rate (combined proptosis reduction ≥2 mm and CAS reduction ≥2 points).
- Additional secondary endpoints: measures of diplopia, CAS, MRI/CT volumetric analyses, and quality of life.
- Safety and tolerability will be assessed throughout the full study period.

References:

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