

## **Inclusion Criteria**

1. Male or female  $\geq 18$  years of age.
2. A female participant is eligible to participate if she is of:
  - a. Non-childbearing potential defined as pre-menopausal females with a documented bilateral tubal ligation, bilateral oophorectomy (removal of the ovaries) or hysterectomy; hysteroscopic sterilization, or postmenopausal defined as 12 months of spontaneous amenorrhea [in questionable cases a blood sample with simultaneous follicle stimulating hormone (FSH) in the post-menopausal range is confirmatory].
  - b. Child-bearing potential and agrees to use one of the contraception methods for an appropriate period of time (as determined by the product label or Principal Investigator) prior to the start of dosing to sufficiently minimize the risk of pregnancy at that point. Female participants must agree to use contraception until 90 days after the last dose of study treatment.
3. Male participants must agree to use contraception. This criterion must be followed from the time of the first dose of study treatment until 90 days after the last dose of study treatment.
4. Clinical diagnosis of Graves' disease with hyperthyroidism associated with active, moderate to severe GO with a CAS $\geq$ 4 for the most severely affected eye at Screening and Baseline.
5. Onset of active GO within 9 months of screening.
6. Documented evidence at Screening of detectable anti-TSHR-Ab.
7. Participant does not require immediate surgical intervention and is not planning corrective surgery/irradiation or medical therapy for GO during the course of the study.
8. Moderate-to-severe active GO (not sight-threatening but has an appreciable impact on daily life), usually associated with one or more of the following: lid retraction  $\geq$ 2 mm, moderate or severe soft tissue involvement, proptosis $\geq$ 3 mm above normal for race and gender, and/or inconstant or constant diplopia.
9. Stable medical regimen; unlikely to require adjustment of thyroid medications during the 12-week treatment period.
10. Participants must be euthyroid with the baseline disease under control or have mild hypo- or hyperthyroidism (defined as free thyroxine [FT4] and free triiodothyronine [FT3] levels  $<$ 50% above or below the normal limits) at Screening. Every effort should be made to correct the mild hypo- or hyperthyroidism promptly and to maintain the euthyroid state for the entire duration of the clinical trial.

11. Stable dose of allowed concomitant medications (e.g. antidepressants) for 3 months from Baseline.
12. Participants who are rendered euthyroid by the block-and-replace regimen e.g., methimazole + adding levothyroxine) when FT4 and T3 have become normal are allowed.
13. Participants who have received radioactive iodine treatment for Graves' hyperthyroidism >6 months from Screening are allowed.
14. Willing and capable of giving written informed consent, which includes compliance with the requirements and restrictions listed in the consent form.

### **6.3.Exclusion Criteria**

1. Use of any steroid (IV, oral, steroid eye drops) for the treatment of GO or other conditions within 3 weeks prior to Screening. Steroids cannot be initiated during the trial. Exceptions include topical and inhaled steroids which are allowed.
2. Use of rituximab, tocilizumab, or any monoclonal antibody/Fc-fusion biologic for immunomodulation within the past 9 months prior to Baseline.
3. Use of selenium within 3 weeks prior to Baseline and use during the clinical trial (multivitamins that include selenium are allowed).
4. Use of biotin within 48 hours prior to any laboratory collection (this includes multivitamins that include biotin).
5. Participants with at least a 2-point decrease in CAS or 2 mm decrease in proptosis between screen & baseline assessments.
6. Total IgG level < 6 g/L at Screening.
7. Absolute neutrophil count <1500 cells/mm<sup>3</sup> at Screening.
8. Albumin level <3.5 g/dL at Screening.
9. Known advanced liver disease including any diagnosis of cirrhosis of any stage.

Non- alcoholic fatty liver disease (NAFLD) including non-alcoholic steatohepatitis (NASH) is allowable if there has been a recent (within 6 months) normal ultrasound, CT, or MRI. If the ultrasound, CT, or MRI demonstrate fatty changes alone, the participant may be enrolled if s/he has a normal range fibroscan for liver fibrosis.

10. AST or ALT  $\geq 1.5$ x ULN at Screening. The participant may only be enrolled if s/he has a recent (within 6 months) normal ultrasound, CT, or MRI. If the ultrasound, CT, or MRI demonstrate fatty changes alone, the participant may be enrolled if s/he has a normal range fibroscan for liver fibrosis.

11. Participants with decreased best corrected visual acuity due to optic neuropathy as defined by a decrease in vision of 2 lines on the Snellen chart, new visual field defect, or color defect secondary to optic nerve involvement within the last 6 months at Screening.

12. Previous orbital irradiation or surgery for GO.

13. Participant has any laboratory abnormality (at screening) that, in the opinion of the investigator, is clinically significant, has not resolved at baseline, and could jeopardize or would compromise the participant's ability to participate in this study.

14. Have known autoimmune disease other than GO, that would in the opinion of the Investigator and Medical Monitor, that would interfere with the course and conduct of the study.

15. Medical history of primary immunodeficiency, T-cell or humoral, including common variable immunodeficiency.

16. Have an active infection, a recent serious infection (i.e., requiring injectable antimicrobial therapy or hospitalization) within the 8 weeks prior to Screening.

17. History of or known infection with human immunodeficiency virus (HIV), hepatitis B virus (HBV), or Mycobacterium tuberculosis:

- Participants must have negative test results for HBV surface antigen, HBV core antibody, HIV 1 and 2 antibodies, and a negative QuantiFERON-TB Gold test at Screening.

- Participants with an indeterminate QuantiFERON-TB Gold test result will be allowed one retest; if not negative on retesting, the participant will be excluded.

18. Hepatitis C virus (HCV):

- Participants must have a negative test result for HCV antibody

or

- Participants with a known history of HCV must have documented evidence of sustained virologic response that is consistent with cure of hepatitis C infection. This is defined as undetectable or unquantifiable HCV RNA at least 12 weeks after stopping HCV treatment (HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C; 2014-2018, AASLD and IDSA). This should be confirmed with a negative HCV RNA test at Screening.

19. Participant has any clinically significant history of allergic conditions (including drug allergies, anaphylactic reactions), that would in the opinion of the Investigator, contraindicates their participation.
20. Participant has any medical condition (acute or chronic illness) or psychiatric condition that, in the opinion of the investigator, could jeopardize or would compromise the participant's ability to participate in this study
21. Body Mass Index (BMI) at Screening  $\geq 40$  kg/m<sup>2</sup>.
22. Enrollment in a previous RVT-1401 clinical trial.
23. Use of investigational drug within 3 months or 5 half-lives of the drug (whichever is longer) before Screening.
24. Currently participating or has participated in another GO clinical study within 28 days prior to signing the informed consent form.
25. Participant has received a live vaccination within 8 weeks prior to the Baseline Visit; or intends to have a live vaccination during the course of the study or within 7 weeks following the final dose of study treatment.
26. Participant has received a transfusion of any blood or blood products within 60 days or donated plasma within 7 days prior to baseline and during the treatment period.
27. History of sensitivity to any of the study treatments, or components thereof or a history of drug or other allergy that, in the opinion of the Investigator or Medical Monitor, contraindicates their participation.
28. Pregnant or lactating females as determined by positive serum or urine human chorionic gonadotropin test at screening or baseline.
29. Participant has had their spleen removed.
30. QTcF interval  $>450$  milliseconds for males and  $>470$  milliseconds for females at Screening (a single repeat is allowed for eligibility determination). QTcF  $>480$  msec in participants with Bundle Branch Block.