Objective: VGL101: TREM2 Agonist (Figure 1)

VGL101 binds with high affinity to the extracellular domains of two TREM2 molecules, sequestering function mutations in the colony stimulating factor (CSF1R)-mediated signaling pathway and stimulating CSF1R, which is a central node in the post-activation profile of microglial cells. This interaction is critical for the restoration of microglial cell function and the promotion of beneficial microglial responses.

Study Design (Figures 2-3)

- Phase 2, multicenter, open-label study of VGL101 evaluating the safety, tolerability, PD, and PK of VGL101 in patients with ALSP.
- Screening Period (4 weeks)
- Treatment Period (24 weeks)
- Extension Period (24 weeks)
- Safety Follow-up Period (4 weeks)

Figure 2: IGNITE, Phase 2 Study of VGL101 in Patients with ALSP (NCT05677659): Study Design and Assessments

Participants (Table 1)

- 15 patients with a CSF1R mutation and findings consistent with ALSP

Study Objectives (Table 2)

- Primary: Safety and tolerability
- Secondary: Efficacy of VGL101 in imaging and fluid biomarkers
- Exploratory: Efficacy of VGL101 on clinical efficacy measures

Table 1: Key Eligibility Criteria

<table>
<thead>
<tr>
<th>Key Inclusion Criteria</th>
<th>Key Exclusion Criteria</th>
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<tbody>
<tr>
<td>Treatments are not applied in the 28 days prior to VGL101 initiation</td>
<td>Serious concurrent disease interfering with the ability to participate in study activities</td>
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<tr>
<td>Efficacy of VGL101 is not the primary objective</td>
<td>Any condition or situation that, in the opinion of the investigator, would interfere significantly with the participant’s participation in study activities</td>
</tr>
<tr>
<td>Cognitive or psychiatric impairment</td>
<td>Any condition or situation that, in the opinion of the investigator, would interfere significantly with the participants’ participation in study activities</td>
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Summary: ALSP is a rapidly progressive and debilitating neurodegenerative disorder associated with significant morbidity and mortality. Currently, there are no approved treatments for individuals with ALSP. VGL101 is a fully human monoclonal antibody that is currently in development for the potential treatment of ALSP. VGL101 was well-tolerated and demonstrated proof of target engagement and pharmacological activity in the Phase 1 healthy volunteer study at 20 and 40 mg/kg doses, which are being tested in the ongoing IGNITE study, a phase 2 proof-of-concept study in individuals with ALSP.

Enrollment in the IGNITE study is ongoing, and data are expected to inform on the safety, tolerability, and potential efficacy of VGL101 on MRI, other disease-related biomarkers, and clinical efficacy measures in patients with ALSP.