Major Depressive Disorder
Investigational medication

A clinical research study evaluating an investigational medication in major depressive disorder (MDD)

For more information about the Shoreline Study, or to refer a patient, please contact:

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Common symptoms of MDD:
- Feelings of hopelessness or guilt
- Changes in appetite or weight
- Fatigue or loss of energy
- Difficulty concentrating, remembering, or making decisions
- Feelings of worthlessness or of being unreasonable

Participating in this study could involve daily visits for 14 weeks. Your visit will include a physical exam, laboratory testing, and medication treatment. The study duration will consist of 3 visits, including the baseline visit, the follow-up visits, and the final study visit. Participants will be provided with medication as part of the study, and all study-related costs will be covered. This study is for adults ages 18 and older. If you are interested in participating, please contact ShorelineMDDstudy@sergerx.com or call (734) 323-0889.

If you have any questions or would like to learn more about the study, please feel free to call us. We are here to answer any questions you may have about the study and its potential benefits. Thank you for your interest in this important research study.
Shoreline Study
The Shoreline Study is a Phase 3, open-label, 1-year study of the safety and need for re-treatment with SAGE-217 in adults with major depressive disorder (MDD), as assessed by the Hamilton Depression Rating Scale (HAM-D).

Key Inclusion Criteria
- Men or women 18-75 years
- Current episode of MDD, with symptoms present for at least a 4-week period*
- MADRS total score of ≥ 28*
*As diagnosed by Structured Clinical Interview for Diagnostic and DSM-V Clinical Trial Version (SCID-I-CT).

Key Exclusion Criteria
- Active psychosis
- Attempted suicide associated with the current episode of MDD
- Medical history of seizures
- Psychiatric history of bipolar disorder, schizophrenia, and/or schizoaffective disorder
- Medical history of mild, moderate, or severe substance use disorder (including benzodiazepines) diagnosed using DSM-5 criteria in the 12 months prior to screening
- History of sleep apnea
- Treatment-resistant depression: defined as persistent depressive symptoms despite treatment with adequate doses of antidepressants within the current episode (excluding antipsychotics) from 2 different classes for at least 4 weeks of treatment.

NOTE: Other protocol-defined inclusion/exclusion criteria may apply.

Patient Involvement in the Shoreline Study
Study Duration: approximately 56 weeks

<table>
<thead>
<tr>
<th>Study Period</th>
<th>Purpose</th>
<th>Duration</th>
<th>Number of Visits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screening</td>
<td>Determines eligibility</td>
<td>Up to 28 days</td>
<td>1</td>
</tr>
<tr>
<td>Initial Treatment Period</td>
<td>Administer 14-day treatment with SAGE-217</td>
<td>14 days</td>
<td>3</td>
</tr>
<tr>
<td>Follow-up</td>
<td>Evaluate overall health and MDD symptoms</td>
<td>14 days</td>
<td>1</td>
</tr>
<tr>
<td>Observational Period</td>
<td>Assess MDD symptoms and the need for additional cycle(s) of treatment with SAGE-217</td>
<td>48 weeks  (approx. every 8 weeks)</td>
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</tbody>
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All study-related medication and medical care will be provided at no cost. Transportation may be available for those who require assistance.

Patients currently taking a stable antidepressant dosage may be able to stay on their medication during the study.

About SAGE-217
SAGE-217 is an oral compound that has been shown in vitro to be a possible allosteric modulator of synaptic and extrasynaptic GABA_A receptors. The GABAergic system is the major inhibitory-signaling pathway of the brain, and contributes to regulating CNS function.

The investigational medication is thought to target the brain in a new way. It is being studied as a 2-week treatment, with the option for additional 2-week treatment periods as needed during an observational period.

For more information about this trial, please visit: ClinicalTrials.gov/ct2/show/NCT03864614