Zuranolone in Major Depressive Disorder: A Phase 3, Multicenter, Double-Blind, Randomized, Placebo-Controlled Trial

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Methods

- The study enrolled 581 adult (18–65 years old) patients with MDD and of qualifying severity by the 17-item Hamilton Rating Scale for Depression total score (HAM-D17; score ≥22) and the Montgomery-Asberg Depression Rating Scale total score (MADRS; score ≥32).
- Patients were stratified based on baseline antidepressant use and randomized 1:1:1:1 to receive zuranolone 20 mg, zuranolone 30 mg, or placebo. Blinded study drug was administered as identical gelatin capsules on an outpatient basis, daily, in the evening, for two weeks with follow-up through Day 42.

Exclusion criteria included attempted suicide associated with the current depressive episode, treatment-resistant depression, or medical history of bipolar disorder, schizophrenia, and/or suicidality disorder.

- Concomitant antidepressant medication was used when possible and evaluated up to a stable dose from 60 days prior to Day 1 and through Day 42.
- No changes in concomitant antidepressant medications were permitted at least 60 days prior to Day 1 through the Day 42 follow-up.

In the United States, 6.8% of adults (or 6.9 million people) have MDD, a common but often underdetected and undertreated depression.1,2 MDD is one of the largest contributors to disability in the United States.3 MDD is characterized by a period of depressed mood or loss of interest and pleasure lasting at least 2 weeks, as well as a sufficiently severe level of depressive symptoms associated with changes in affect, cognition, and function.4-6 Gamma-aminobutyric acid (GABA)-ergic neurotransmission regulates the activity of diverse brain networks that may be implicated in depression.7-9 Zuranolone (SAGE 217) is an investigational oral neurosteroid GABA-A positive allosteric modulator.10,11

Conclusion

- In the United States, 6.8% of adults (or 6.9 million people) have MDD, a common but often underdetected and undertreated depression.¾ MDD is one of the largest contributors to disability in the United States.¾ MDD is characterized by a period of depressed mood or loss of interest and pleasure lasting at least 2 weeks, as well as a sufficiently severe level of depressive symptoms associated with changes in affect, cognition, and function.¾ Gamma-aminobutyric acid (GABA)-ergic neurotransmission regulates the activity of diverse brain networks that may be implicated in depression.¾ Zuranolone (SAGE 217) is an investigational oral neurosteroid GABA-A positive allosteric modulator.¾

- There were no adverse events of loss of consciousness reported.

- More patients with an overall distribution of minor or severe anxiety symptoms were enrolled in this study compared to previous studies of zuranolone.12-13

- In a pivotal trial in MDD Treatment: Extended Naturalistic Follow-Up

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Safety and tolerability were evaluated throughout the study by adverse event reporting, the Columbia Suicide Severity Rating Scale (C-SSRS), the 20-item Physician Withdrawal Checklist, and standard clinical assessments.

- Post-hoc endpoints included change from baseline in HAMD-17 total score at each of all timepoints.

Results

Primary Endpoint: Reduction in HAMD-17

- Change from baseline in HAMD-17 total score at each of all timepoints.

- Secondary endpoints included the change from baseline in HAMD-17 total score at each of all timepoints.

- There were no adverse events of loss of consciousness reported.

- There was no signal for increased suicidal ideation or suicidal behavior compared to baseline.

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