Extended Duration Safety and Efficacy of Adjunctive Ganaxolone Treatment in Patients with CDKL5 Deficiency Disorder: 8-Month Minimum Open-Label Extension Follow-Up

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Introduction

CDKL5 deficiency disorder (CDD) is a rare inherited epileptic encephalopathy resulting from pathogenic loss-of-function variants in the CDKL5 gene. 2,3 Clinical presentations include early-onset refractory epilepsy and developmental and intellectual impairment, along with disabilities related to sleep, regulation, gastrointestinal function, and cardiac viability.4 Despite treatment with multiple current antiepileptic medications (AEMs), many patients with CD-related epilepsy are highly refractory and continue to experience seizures.6,7

• Improvements have been reported to often be short-lived (median, 4 months)8

The chronic refractory nature of seizures combined with severe comorbidities results in a heavy burden of care and diminished quality of life for the patients and their caregivers.9

In a recent placebo-controlled Phase 3 clinical study (Marigold Study, NCT03572933), ganaxolone, a neuroactive steroid, diminished quality of life for patients and their caregivers1,7

In the OLE group, improvements were reported to often be short-lived (median, 6 months)4

Baseline Characteristics

• Patients who completed the 17-week double-blind phase of the Marigold study were eligible to enroll in the OLE

• Key eligibility criteria:
  - Age, ≥1 year
  - CDKL5 deficiency disorder (CDD) is a rare X-linked epileptic encephalopathy resulting from pathogenic, loss-of-function

Conclusions

• Adverse events in the OLE are consistent with those observed in the double-blind phase as well as the known safety profile of ganaxolone

• Safety data in the OLE provide supportive evidence for maintenance of efficacy and diminishing major motor seizures associated with CD2O and approximately 6 months and up to 12 months in patients who continue ganaxolone treatment

• Results of the present study suggest that ganaxolone treatment in patients with CDD is safe and well tolerated

• The most common AEs (in the OLE [≥10% of patients) were sedation,omnia, gait unsteadiness, ataxia, and upper respiratory tract infections

Figure 1. Patient Disposition

Figure 2. Percent Reduction in 28-Day Median Major Motor Seizure Frequency of Various Time Points Within the OLE

Figure 3. Treatment-emergent Adverse Events (TEAEs)

Figure 4. Clinical Global Impression—Improvement Assessment by Clinicians and Caregivers at 34 Weeks

Table 1. Demographics

Table 2. Baseline Characteristics

Table 3. Table 3. Treatment-emergent Adverse Events (TEAEs)

Table 4. Table 4. Clinical Global Impression—Improvement Assessment by Clinicians and Caregivers at 34 Weeks

Methods

Patient Disposition

• In the OLE, patients who completed the double-blind phase were randomized to receive ganaxolone (GNX) or placebo (PBO) in an open-label fashion, remaining in the OLE study

• Of the 101 patients entering the double-blind phase, 88 (87.1%) continued into the OLE (43 were initially randomized to ganaxolone [GNX-GNX] and 45 to placebo [PBO-GNX]...