Long-Term Soticlestat Treatment in Patients with Developmental and/or Epileptic Encephalopathies in the ENDYMION Ongoing Open-Label Extension Study

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Objective:

To report interim safety and efficacy outcomes following ≤9 months of soticlestat (TAK-935/OV935) as adjunctive therapy in patients with developmental and epileptic encephalopathies (DEEs) in ENDYMION (NCT03635073).

Background:

DEEs typically start in childhood with treatment-resistant seizures, and are associated with progressive cognitive decline. In phase 2 studies, soticlestat was associated with reductions in seizure frequency in patients with Dravet syndrome (DS), Lennox-Gastaut syndrome (LGS) and CDKL5 deficiency disorder.

Design/Methods:

ENDYMION is a phase 2, multicenter, open-label extension study of soticlestat (≤600 mg/day; mg/kg dosing for <60 kg body weight) in pediatric and adult patients with DEEs who completed a previous soticlestat clinical study, or received treatment for ≥10 weeks. ENDYMION comprises a dose-optimization period, a maintenance period of <5 years, and a 4-week safety follow-up period. Safety endpoints include incidence of treatment-emergent adverse events (TEAEs) and efficacy endpoints include change from baseline in seizure frequency.

Results:

At the time of analysis, 83 of 116 patients (71.6%) with DEEs experienced ≥1 TEAE (mild, n=71 [61.2%]; moderate, n=31 [26.7%]; severe, n=8 [6.9%]). Twelve patients (10.3%) experienced ≥1 serious TEAE; none were considered to be drug-related. TEAEs occuring in ≥5% of patients were constipation, diarrhea, decreased appetite, insomnia, nasopharyngitis, pyrexia, seizure, somnolence, and upper respiratory tract infection. Six patients (5.2%) discontinued due to TEAEs.

At weeks 1–12, 13–24, 25–36, median changes in seizure frequency from baseline (of antecedent study) in DS patients were –36.11% (n=36), –48.45% (n=31), and –20.35% (n=14), respectively, and in LGS patients were –30.00% (n=57), –12.12% (n=48) and –21.64% (n=28), respectively.

Conclusions:

Interim results from ENDYMION suggest long-term administration of soticlestat is generally well-tolerated in the study population, with a safety profile consistent with findings from previous studies. Soticlestat reduced seizure frequency in patients with DEEs in this study population.

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