Long-Term Safety and Durability of Effect of Ecopipam in Pediatric Patients

With Tourette Syndrome: Results of a 12-Month Open-Label Extension Study

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**BACKGROUND**

- Tourette syndrome (TS) is a childhood-onset movement disorder characterized by motor and phonic tics that can disrupt function and affect mental and physical health.
- Medications currently prescribed for TS include dopamine D2 receptor antagonists, which have a safety profile that includes risk of weight gain and development of metabolic abnormalities and treatment-emergent disorders.
- Ecopipam is a first-in-class D2 receptor antagonist under investigation as a potential treatment for TS.

**OBJECTIVE**

- To evaluate the safety and tolerability of ecopipam in TS, and to inform the durability of effect for up to 12 months in pediatric patients with TS who completed the phase 2b placebo-controlled trial.

**METHODS**

- **Patients:** Patients aged 6 to 18 years with confirmed TS who completed the phase 2b placebo-controlled trial were eligible for the open-label extension (OLE) trial (NCT01904520).
- **Treatments:** All patients in the OLE trial were titrated over a 4-week period to an oral dose of ecopipam 2 mg/kg/day; patients received the last dose of ecopipam and a follow-up phone call was conducted 30 days after the last dose of ecopipam (Figure 1).
- **Assessments:** To evaluate the long-term safety and tolerability of ecopipam in pediatric patients with TS the following were completed:
  - Vital signs and orthostatic blood pressure, physical examination, electrocardiogram, and laboratory tests with monitoring of adverse events (AEs); and
  - The Abnormal Involuntary Movement Scale (AIMS), the Barnes Akathisia Rating Scale (BARS), the Children’s Depression Rating Scale-Revised (CDRS-R), the Columbia-Suicide Severity Rating Scale (C-SSRS).

**RESULTS**

- **Safety and Tolerability:** Ecopipam was generally well tolerated, with 69.4% (90/129) of patients reporting any AE and 15.0% (19/123) of patients discontinuing due to a potential AE (Figure 2).

**CONCLUSIONS**

- Significant improvements in measures of TS severity from baseline were noted in YGTSS-TTS, and in both motor and vocal subscases, in YGTSS-GS, and CGI-TS-S.
- **Side Effects:** AEs of special interest included:
  - Extrapyramidal side effect-related events including balance disorders, bruxism, and tongue biting (n=2, 1.7%)
  - Suicidal ideation (n=3, 2.5%)

- AEs of special interest included:
  - Adverse movement-related events including balance disorders, bruxism, and tongue biting (n=2, 1.7%)
  - Suicidal ideation (n=3, 2.5%)

- During the 12-month study period, p-scores for height, weight, and body mass index showed no apparent clinically significant change.

- Most common AEs (≥5%)
  - Nausea (14.0%), anxiety (9.1%), depression (including depression, depressed mood, major depression, and depressive symptoms)
  - Headache (7.4%), diarrhea (7.4%), and insomnia (7.4%)
  - Muscle spasm (5.0%), fatigue (4.7%), upper respiratory tract infection (URTI) (4.7%), and cystitis (4.7%)

- Safety profile that includes risk of weight gain and development of metabolic abnormalities and treatment-emergent disorders.

- Ecopipam had an acceptable safety and tolerability profile over this 12-month study.

- In a previously published phase 2b, randomized, double-blind, parallel-group, placebo-controlled trial (ecopipam [n=76]; placebo [n=77]), ecopipam tablets (2 mg/kg/day for 12 weeks) reduced the Yale Global Tic Severity Scale-Total Tic Score (YGTSS-TTS) by 30% from baseline, which was significant compared with placebo (p=0.03).

- Weight gain, metabolic syndrome, and drug-induced dyskinesias associated with antipsychotic agents were not observed in this study of up to 12 weeks duration.

**REFERENCES**


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**DISCLOSURE:** The authors report a clinical trial site investigator for Emales Biosciences, Inc., and PTC Therapeutics. DBK, HIPH, GDA, CIB, and FEH are employees of Emales Biosciences, Inc. DSM and TH are employees of Paragon Biosciences, LLC, a company that founded Emales Biosciences, Inc.

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