ARGUS: A Phase II Study of EPX-100 (Clemizole Hydrochloride) as Adjunctive Therapy in Patients with Dravet Syndrome

Lekha M. Rao MD[1], Lorianne Masuoka MD[2], Mary Shatzoff MSc[2], Hahn-Jun Lee MSc PhD[2], Scott Baraban PhD[2]

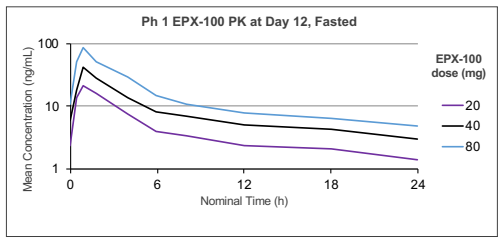
[1] *Department of Pediatrics, Division of Neurology, David Geffen School of Medicine at UCLA,* [2] *Epygenix Therapeutics*

Abstract

Dravet syndrome (DS) is a severe and progressive epileptic encephalopathy that begins in the first year of life and is characterized by high seizure frequency and severity, intellectual disability, and a risk of sudden unexpected death in epilepsy. Approximately 85% of DS cases are caused by de novo loss-of-function (LOF) mutations in a voltage-gated sodium channel gene, SCN1A[1]. Preclinical drug discovery using a LOF SNC1A zebrafish model for DS identified clemizole (EPX-100), a 1st generation antihistamine with serotonin-modulating properties, as a potential antiseizure medication (ASM) for these patients[2]. Here we describe results of a completed EPX-100 Phase 1 double-blind, placebo-controlled trial and the Phase 2 protocol for an on-going randomized, double-blind, placebo-controlled clinical trial in DS patients.

Phase 1 – Result Summary

- Completed Phase I study in 24 healthy adults
- No clinically significant adverse effects
- Good tolerability
- PK is proportional to dose (**Figure 1**)



Phase 2 - Study Design

Design	Randomized, double-blind, placebo-controlled
Duration	20 weeks
No. of patients	Up to 100 (1:1 randomization)
Locations	Multi-center and multi-country: U.S.A, Canada, UK, and Spain

- Study design **(Figure 2)** includes:
- Interim analysis will be set up when 60% of subjects have completed evaluation of primary endpoint at end of maintenance period

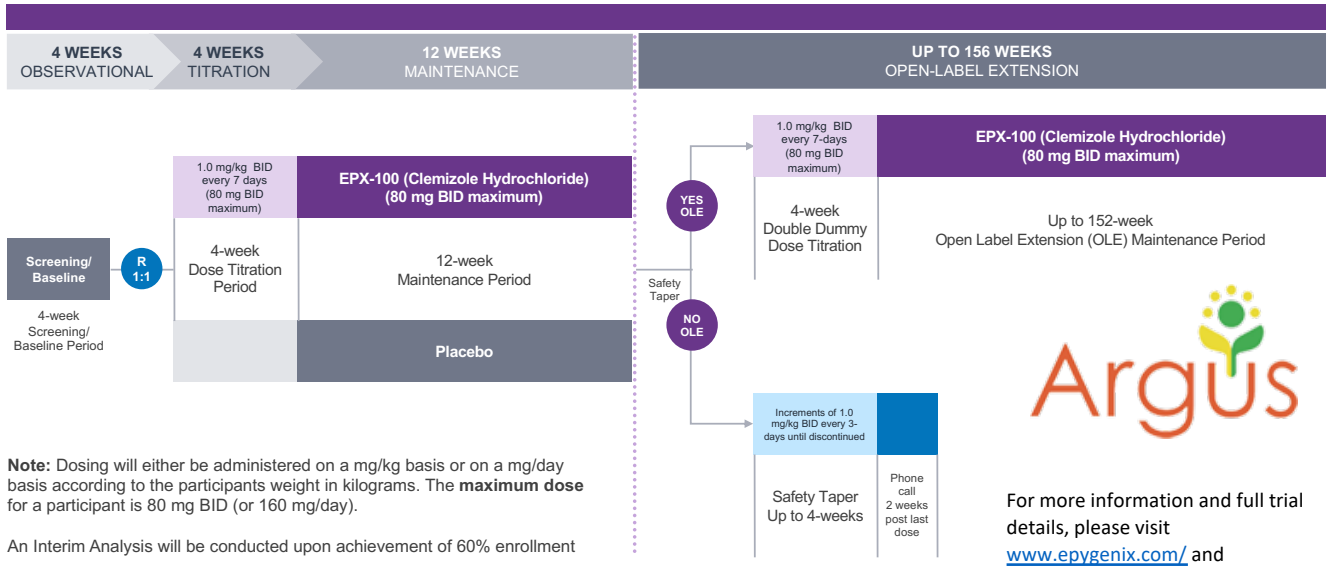
Inclusion Criteria

- Age 2 years or older
- Clinical diagnosis of DS
  - Seizures not completely controlled by AEDs
  - Onset of seizures prior to 18 months
  - *SCN1A* gene mutation
- ≥4 countable convulsive seizures per 4-week baseline period
- Stable regimen of AEDs ≥30 days prior to Visit 1

Exclusion Criteria

- Known sensitivity or previous exposure to EPX-100
- Recent exposure to or plans to participate in another drug or device trial
- Any medical conditions judged to potentially affect participant safety or study outcome
- Concurrent use of drugs known to interfere with EPX-100
- Suicidal thoughts

Figure 2



Note: Dosing will either be administered on a mg/kg basis or on a mg/day basis according to the participants weight in kilograms. The **maximum dose** for a participant is 80 mg BID (or 160 mg/day).

An Interim Analysis will be conducted upon achievement of 60% enrollment

Argus

For more information and full trial details, please visit www.epygenix.com/ and www.argustrial.com

Key Study Endpoints

Primary

- Mean percent change between EPX-100 vs placebo in countable convulsive seizure frequency (CCSF)

Secondary

- The number of countable convulsive seizure-free days in the Titration and Maintenance (T+M) period relative to baseline
- The proportion of participants with >50% reduction in the mean CCSF in the T+M period relative to baseline
- The total HASS (Hague Seizure Severity Scale) score in the T+M period relative to baseline
- The Clinical Global Impression (CGI) score, for each of the investigator and parent/caregiver assessments, in the T+M period
- The total score for the Quality of Life in Childhood Epilepsy (QOLCE-55) in the T+M period relative to baseline

Acknowledgements

This study is supported by Epygenix Therapeutics. We thank the patients, families, investigators, healthcare providers, and research staff involved in this work.

References

1. Akiyama M, Kobayashi K, Ohtsuka Y. Dravet syndrome: a genetic epileptic disorder. Acta Med Okayama. 2012.

2. Baraban SC, Dinday MT, Hortopan GA. Drug screening in Scn1a zebrafish mutant identifies clemizole as a potential Dravet syndrome treatment. Nat Commun. 2013.