INTRODUCTION

- A retrospective chart review and small, prospective, observational study have suggested that fenfluramine has antiepileptic activity in patients with Dravet syndrome (DS).
- Based on data from these open-label investigations, Zogenix is initiating a Phase 3 development program for ZX008 (fenfluramine HCl oral suspension) as adjunctive treatment for uncontrolled seizures in children with DS.
- Here we present an outline of the Phase 3 clinical study program for ZX008 as adjunctive treatment of seizures in children with DS.

STUDIES 1501 AND 1502: PROPOSED PROTOCOL

Subjects

| Study 1501 | 14-week, randomized, double-blind, placebo-controlled study conducted in the United States and Canada |
| Study 1502 | 14-week, randomized, double-blind, placebo-controlled study conducted in Europe, Australia, and other countries |

Key Exclusion Criteria

- Pregnant or lactating females
- History of cardiovascular disease, pulmonary hypertension, anorexia nervosa, depression, or glaucoma
- Treatment with concomitant serotonergic medications
- Treatment with cytidine P540 206/3442/286 inhibitors or substrates
- Treatment with stiripentol in past 21 days before screening, or participation in an experimental protocol in past 30 days
- Current treatment with carabazepine, oxcarbazepine, phenobarbital, phenytoin, or any cannabindoid product, or treatment with any of these in the previous 30 days as maintenance therapy

Key Safety Assessments

- Vital signs
- Cardiac examination
- Laboratory safety parameters (hematology, chemistry, urinalysis)
- Treatment with concomitant serotonergic medications
- Treatment with cytidine P540 206/3442/286 inhibitors or substrates
- Treatment with stiripentol in past 21 days before screening, or participation in an experimental protocol in past 30 days
- Current treatment with carabazepine, oxcarbazepine, phenobarbital, phenytoin, or any cannabindoid product, or treatment with any of these in the previous 30 days as maintenance therapy

STUDY DESIGN FOR ACUTE PHASE 3 EFFICACY/SAFETY TRIALS

- Multicenter, randomized, double-blind, parallel-group, placebo-controlled
- Pediatric and young adult subjects with DS (N=105 in each study)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>N=105</th>
<th>12-week treatment</th>
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<tbody>
<tr>
<td>ZX008 0.8 mg/kg/day</td>
<td>0.8 mg/kg/day</td>
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<tr>
<td>ZX008 0.2 mg/kg/day</td>
<td>0.2 mg/kg/day</td>
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<tr>
<td>Placebo oral solution</td>
<td>Placebo oral solution</td>
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</tbody>
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SUMMARY

The proposed 2 randomized, double-blind studies of ZX008 oral solution at doses of 0.8 and 0.2 mg/kg/day compared with placebo, plus long-term, open-label safety extension are designed to provide adequate efficacy and safety information for registration for the indication of adjunctive treatment of uncontrolled seizures in pediatric patients with DS.

REFERENCES


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DISCLOSURE

The studies presented here were conducted by Zogenix, Inc. JS and LL have received honoraria as advisors and are investigators and LL has also received honoraria as a consultant from Brabant Pharma and Zogenix. RK is a contact employee and KR, AM, BG, and GF are full-time employees of Zogenix, Inc.