Zogenix Announces Presentation of New Efficacy and Safety Data from its First Pivotal Phase 3 Clinical Trial of ZX008 in Dravet Syndrome

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Efficacy and Safety Data in Patients on ZX008 Who Previously Failed Stiripentol Treatment Prior to Entry into First Phase 3 Trial (Study 1) Comparable to Results from Full Study 1 Population

Patients on ZX008 Also Achieved Significant, Clinically Meaningful Reduction in Total Seizure Frequency Compared to Those on Placebo

Data Presented at 2018 American Academy of Neurology Annual Meeting

EMERYVILLE, Calif., April 25, 2018 (GLOBE NEWSWIRE) -- Zogenix, Inc. (NASDAQ:ZGNX), a pharmaceutical company developing therapies for the treatment of rare central nervous system (CNS) disorders, today announced additional data from analyses of its first Phase 3 trial (Study 1) of the Company's investigational drug, ZX008 (low-dose fenfluramine hydrochloride), for the adjunctive treatment of seizures associated with Dravet syndrome. Top-line results from Study 1 were previously reported in September 2017. The additional Study 1 results were presented in two late-breaker poster presentations at the Emerging Science session at the 2018 American Academy of Neurology (AAN) Annual Meeting being held April 21-27 in Los Angeles, California (see study data here and here).

As previously reported, Study 1 met its primary objective of demonstrating that ZX008, at a dose of 0.8 mg/kg/day, is superior to placebo as an adjunctive therapy in the treatment of Dravet syndrome in children and young adults based on change in the frequency of convulsive seizures between the 6-week baseline observation period and the 14-week treatment period (p<0.001).

The first poster, presented by Elaine C. Wirrell, M.D., Director of Pediatric Epilepsy at the Mayo Clinic, showed the results of a post-hoc analysis evaluating the effect of ZX008 in enrolled patients in Study 1 who had previously failed treatment with stiripentol, which is currently the only medication for adjunctive treatment of seizures in patients with Dravet syndrome, approved in Europe, Australia, Canada, and Japan, and available via compassionate use in the U.S. For purposes of this subgroup analysis, failed treatment included patients who discontinued for reasons of efficacy or tolerability, both efficacy and tolerability, or any other reason. A total of 58 subjects from Study 1 were included in this post-hoc analysis, consisting of the following treatment groups: ZX008 0.8 mg/kg/day (30 mg maximum daily dose; n=22), ZX008 0.2 mg/kg/day (n=20) and placebo (n=16).

“It is highly encouraging to see that the efficacy and tolerability in this subgroup of patients who had previously failed treatment with stiripentol was comparable to the full Study 1 population,” said Rima Nabbout, M.D., Ph.D., Department of Pediatric Neurology, Reference Center for Rare Epilepsies, and one of the poster’s authors. “As stiripentol is a commonly used antiepileptic drug, it is important to understand how tolerable and effective ZX008 is in this subgroup of patients.”

In this subgroup of patients, ZX008 demonstrated robust antiseizure activity in *patients who failed prior treatment with stiripentol.* The efficacy and tolerability results in this subgroup were comparable to those achieved in the full Study 1 population. In the post-hoc analysis, patients taking ZX008 0.8 mg/kg/day achieved a 60.8% greater reduction in mean monthly convulsive seizures compared to placebo (p=0.002). In the full Study 1 population, patients taking ZX008 0.8 mg/kg/day achieved a 63.9% greater reduction in mean monthly convulsive seizures compared to placebo (p<0.001). Other select endpoint comparisons are presented below.

	Subgroup Population: Subjects Who Failed Treatment with Stiripentol Prior to Study 1		Full Study 1 Population	
	ZX008 0.8 mg/kg/day	Placebo	ZX008 0.8 mg/kg/day	Placebo
	(N=22)	(N=16)	(N=40)	(N=40)
Patients with ≥50% reduction in monthly convulsive seizures	73% (p=0.006)	13%	70% (p<0.001)	7.5%
Patients with ≥75% reduction in monthly convulsive seizures	50% (p=0.036)	6.3%	45% (p=0.001)	2.5%
Longest seizure-free interval (median)	24.5 days (p=0.003)	9 days	20.5 days (p<0.001)	9 days
% rated as Much Improved or Very Much Improved on CGI-C* Rated by Parents / Caregivers	41% (p=0.012)	6%	55% (p<0.001)	10%
% rated as Much Improved or Very Much Improved on CGI-C* Rated by Investigator	64% (p<0.001)	6%	63% (p<0.001)	10%

** Clinical Global Impression (CGI-C) of Improvement indicates rating of very much improved or much Improved in overall condition.*

The post-hoc analysis showed a consistent safety and tolerability profile, as previously seen in the full Phase 3 trial population. The most common treatment emergent adverse events in this subgroup of patients included decreased appetite, lethargy, fatigue, diarrhea, upper respiratory tract infection, nasopharyngitis, pyrexia, and somnolence. The most common treatment emergent adverse events in the full Study 1 population included diarrhea, vomiting, fatigue, pyrexia, nasopharyngitis, upper respiratory tract infection, fall, weight decreased, decreased appetite, lethargy, seizure, and somnolence.

As reported for the full Study 1 population, there was no clinical and/or echocardiographic evidence of cardiac valvulopathy or pulmonary hypertension in any patient at any time during the study. No patient discontinued participation or required a change in monitoring in the study due to cardiac factors in this subgroup or the full Study 1 population.

A second poster presented by Joseph Sullivan, M.D., Director of the Pediatric Epilepsy Center at University California San Francisco, et al., highlighted the results of a prespecified secondary analysis evaluating the effect of ZX008 on total seizure (TS) frequency (i.e., includes all seizure types) in the full Study 1 population. A total of 119 patients were randomized to treatment (n=40, 0.8 mg/kg/day; n=39, 0.2 mg/kg/day; n=40, placebo) in Study 1. During baseline, the median monthly TS frequency ranged from 40.7 to 53.9 in the three groups. At endpoint, after the 14-week treatment period, median percent changes in TS frequency were -13.1% in placebo, -34.3% in ZX008 0.2 mg/kg/day (p=0.031), and -70.1% in ZX008 0.8 mg/kg/day (p<0.001).

“The efficacy and safety data generated from ZX008 in Study 1 continue to be extremely compelling,” said Bradley M. Galer, M.D., Executive Vice President and CMO. “All patients in

our second Phase 3 study in Dravet syndrome, Study 1504, are taking stiripentol as part of their baseline standard of care, which will provide prospective data on the efficacy and safety of ZX008 in this patient population. We anticipate the availability of top-line results from this study at the end of the second quarter of 2018."

ZX008 is designated as an orphan drug in both the U.S. and Europe, and has received Breakthrough Therapy designation in the U.S. for the treatment of Dravet syndrome.

About Study 1
The randomized, double blind, placebo controlled, Phase 3 study enrolled 119 patients across sites in the U.S., Canada, Europe and Australia. The median age of patients was 8 years (range, 2-18 years). Following a six-week baseline observation period, patients were randomized to one of three treatment groups: ZX008 0.8 mg/kg/day (30 mg maximum daily dose; n=40), ZX008 0.2 mg/kg/day (n=39) and placebo (n=40) in which ZX008 or placebo was added to current regimens of antiepileptic drugs. Patients were titrated to their target dose over two weeks and then remained at that fixed dose for 12 weeks. The mean baseline convulsive seizure frequency across the study groups was approximately 40 seizures per month.

About Zogenix
Zogenix (Nasdaq:ZGNX) is focused on developing therapies for patients with rare central nervous system (CNS) conditions that have limited or no treatment options but face a critical need. For more information, visit www.zogenix.com.

Forward Looking Statements
Zogenix cautions you that statements included in this press release or in the poster presentations that are not a description of historical facts are forward-looking statements. Words such as "believes," "anticipates," "plans," "expects," "indicates," "will," "intends," "potential," "suggests," "assuming," "designed" and similar expressions are intended to identify forward-looking statements. These forward-looking statements include statements regarding: ZX008's potential as a treatment for seizures associated with Dravet syndrome; and the timing of top-line results from Study 1504. These statements are based on Zogenix's current beliefs and expectations. The inclusion of forward-looking statements should not be regarded as a representation by Zogenix that any of its plans will be achieved. Actual results may differ from those set forth in this release or in any poster presentation due to the risks and uncertainties inherent in Zogenix's business, including, without limitation: the top-line data and post-hoc analysis data Zogenix has reported is based on preliminary analysis of key efficacy and safety data, and such data may change following a more comprehensive review of the data related to the clinical trial and such data may not accurately reflect the complete results of the trial, and the FDA may not agree with Zogenix's interpretation of such results;; the uncertainties associated with the clinical development and regulatory approval of product candidates such as ZX008, including potential delays in the enrollment and completion of clinical trials such as Study 1504; unexpected adverse side effects or inadequate therapeutic efficacy of ZX008 that could limit approval and/or commercialization, or that could result in recalls or product liability claims; the potential that earlier clinical trials and studies may not be predictive of future results; Zogenix's reliance on third parties to conduct its clinical trials, enroll patients, manufacture its preclinical and clinical drug supplies; and other risks described in Zogenix's prior press releases as well as in public periodic filings with the Securities and Exchange Commission. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof, and Zogenix undertakes no obligation to revise or update this press release to reflect events or circumstances after the date hereof. All forward-looking statements are qualified in their entirety by this cautionary statement. This caution is made under the safe harbor provisions of Section 21E of the Private Securities Litigation Reform Act of 1995.

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