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

December 4, 2017

ZX008 Patients More Likely to Achieve Clinically Meaningful Reduction in Seizure Frequency Compared to Those on Placebo

Parents/Caregivers and Investigators Rated Patients Treated with ZX008 as Very Much Improved or Much Improved in Overall Condition Compared to Placebo

Company to Host Callwith Pediatric Epilepsy Expert Joseph Sullivan, M.D.,
on Dravet Syndrome and ZX008, Today at 4:30 PM ET

EMERYVILLE, Calif., Dec. 04, 2017 (GLOBE NEWSWIRE) -- Zogenix, Inc. (NASDAQ:ZGNX), a pharmaceutical company developing therapies for the treatment of rare central nervous system (CNS) disorders, today announced new data from its first Phase 3 trial (Study 1) of its investigational drug, ZX008 (low-dose fenfluramine hydrochloride), for the treatment of Dravet syndrome. Top-line results from Study 1 were previously reported in September 2017. The updated Study 1 results, as well as additional data supporting the further investigation of ZX008 in refractory epilepsies, were presented at the 71stAmerican Epilepsy Society (AES) Annual Meeting, taking place this week in Washington, D.C. (see study data here).

The new Study 1 results presented at AES showed the odds of achieving a clinically meaningful (≥50%) or substantial (≥75%) reduction in convulsive seizure frequency were 29 and 50 times higher, respectively, among patients treated with ZX008 0.8 mg/kg/day than in patients treated with placebo. The study also measured improvement on the Clinical Global Impression (CGI-C) rating. Fifty-five percent of patients treated with ZX008 0.8 mg/kg/day were rated by parents/caregivers as very much improved or much improved in overall condition on the CGI-C compared to 10% of the placebo group (p=0.001) and 62.5% of patients treated with ZX008 0.8 mg/kg/day were rated by investigators as very much improved or much improved in overall condition on the CGI-C compared to 10% of the placebo group (p=0.001).

“Dravet syndrome is a rare form of intractable epilepsy for which a significant unmet medical need currently exists,” said Lieven Lagae, M.D., Ph.D., Professor at the University of Leuven, Belgium, Head of the Pediatric Neurology Department and Director of the Childhood Epilepsy Program at the University of Leuven Hospitals, and Principal Investigator of Study 1 in Europe. “These new data demonstrate Dravet syndrome patients treated with ZX008 achieved a clinically meaningful reduction in seizure frequency. If approved, ZX008 could play an important role in changing the treatment paradigm for patients and their families whose lives have been greatly impacted by the lack of effective seizure control provided by current treatment options.”

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 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). Patients taking ZX008 0.8 mg/kg/day achieved a 63.9% reduction in mean monthly convulsive seizures compared to placebo (p<0.001). The median percent reduction in monthly convulsive seizure frequency was 72.4% among ZX008 0.8 mg/kg/day patients, compared to 17.4% in placebo patients.

A key secondary endpoint was the same analysis for a comparison of ZX008 0.2 mg/kg/day and placebo. Patients taking ZX008 0.2 mg/kg/day achieved a reduction in mean monthly convulsive seizures of 33.7% compared to placebo (p=0.019). ZX008 0.8 mg/kg/day and ZX008 0.2 mg/kg/day also demonstrated statistically significant improvements versus placebo in additional key secondary measures, including the proportion of patients with clinically meaningful reductions in seizure frequency and longest seizure-free interval.

The most common treatment emergent adverse events (>10% in any treatment group) in Study 1 include diarrhea, vomiting, fatigue, pyrexia, nasopharyngitis, upper respiratory tract infection, fall, weight decreased, decreased appetite, lethargy, seizure and somnolence. Prospective cardiac safety monitoring throughout the study demonstrated trace regurgitation on mitral or aortic valves were recorded on at least one echocardiogram in >10% of subjects among all three treatment groups, placebo included. There was no clinical or echocardiographic evidence of cardiac valvulopathy or pulmonary hypertension. No patient discontinued participation or required a change in monitoring in the study due to cardiac factors.

“Our confidence in the potential of ZX008 as an effective treatment for seizures associated with Dravet syndrome continues to strengthen with the new data showing that both caregivers and clinicians perceived patients’ overall condition to be very much or much improved following treatment with ZX008,” said Stephen J. Farr, Ph.D., President and CEO. “The overall data to date reinforce the potential of ZX008 to be an important new treatment for seizure control in children and young adults with Dravet syndrome, and we look forward to sharing top-line results from our second pivotal Phase 3 trial, Study 1504, in the second quarter of 2018.”

Additional posters supporting the continued investigation of ZX008 in refractory epilepsies were also presented in the main exhibit hall at the AES meeting. One poster outlined findings from an ongoing prospective study of ZX008 in people with refractory Dravet syndrome, which found that low-dose fenfluramine provided clinically meaningful reductions in major motor seizure frequency with sustained benefit noted for up to 6.5 years, without any development of cardiac valvulopathy or pulmonary hypertension. Another poster showed that ZX008 provided sustained, clinically meaningful seizure reduction in a cohort of refractory Lennox-Gastaut syndrome (LGS) patients enrolled in a core and long-term extension study, treated for up to 15 months with no echocardiographic signs of cardiac valvulopathy or pulmonary hypertension. An additional poster focused on mechanism of action demonstrated that fenfluramine acts as a positive modulator on the Sigma-1 receptor, and of note, a recent publication found that positive modulators of the Sigma-1 receptor have antiepileptic activity in standard mouse seizure models. A further poster presented pre-clinical data suggesting that there may be a protective effect of fenfluramine in an accepted pre-clinical animal model of Sudden Unexpected Death in Epilepsy (SUDEP).

Data were also presented from a drug-drug interaction study assessing the pharmacokinetics (PK) and safety of ZX008 administered with and without a combination regimen of stiripentol, clobazam and valproic acid. Lastly, three posters were presented from studies on the caregiver burden and pharmacoeconomic impact related to severe childhood epilepsies. These data demonstrated that Dravet syndrome caregivers face substantial physical, emotional and time burdens, including elevated levels of anxiety/depression and financial burden.

The entire set of posters sponsored by Zogenix is available for review here at www.zogenix.com.

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

Conference Call Details
To access the call with pediatric epilepsy expert Joseph Sullivan, M.D., on Dravet Syndrome and ZX008, on Monday, December 4, 2017, 4:30pm ET/1:30pm PT, please see below:

Toll-Free: 800-289-0438

International: 323-794-2423
Conference ID: 7828122
Webcast: http://public.viavid.com/index.php?id=127211

Audio replays available through December 18, 2017:

Toll-Free: 844-512-2921
International: 412-317-6671
Replay PIN: 7828122

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, refractory epilepsies, and LGS; 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 FDA may not agree with Zogenix's interpretation of the results of the Study 1 and other data; the uncertainties associated with the clinical development and regulatory approval of product candidates such as ZX008; 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.

Disclaimer
Lieven Lagae, Berten Ceulemans, and the KU Leuven University/Antwerp University Hospital may benefit financially from a royalty arrangement that is related to this research if Zogenix is successful in marketing its product, fenfluramine. The terms of this arrangement have been reviewed and approved by the KU Leuven University/Antwerp University Hospital.

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