Zogenix Announces New Efficacy and Safety Data for ZX008 in Treatment of Seizures in Lennox Gastaut Syndrome & Dravet Syndrome

December 5, 2016

- *New Clinical Data Presented at 70th Annual American Epilepsy Society Meeting*
- *Posters Highlighting Potential Protective Effect of ZX008 in Pre-Clinical Model of Sudden Unexpected Death in Epilepsy (SUDEP) and Results of Roundtable Discussions Evaluating Burden of Illness on Caregivers in Dravet Syndrome Also Presented*
- *Company Evaluating Potential Phase 3 Program for ZX008 in Lennox Gastaut Syndrome*

EMERYVILLE, Calif., Dec. 05, 2016 (GLOBE NEWSWIRE) -- Zogenix, Inc. (NASDAQ:ZGNX), a pharmaceutical company developing therapies for the treatment of orphan and central nervous system (CNS) disorders, today announced new data demonstrating effectiveness and cardiovascular-related safety for patients treated with ZX008 (low-dose fenfluramine) as an adjunctive therapy for seizures associated with Lennox Gastaut Syndrome (LGS), and continued effectiveness and safety for the on-going open-label patients with Dravet syndrome. The data were presented at the 70th Annual American Epilepsy Society (AES) meeting, taking place this week in Houston, Texas (see study data here and here).

The LGS data presented were from an interim analysis of the first 13 patients to have completed at least 12 weeks of a Phase 2 open-label, dose-finding investigator-initiated study, led by 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. Patients enrolled in the study were 3-18 years of age diagnosed with LGS with at least four convulsive seizures and on at least two anti-epileptic drugs (AEDs) at stable doses in the four weeks prior to study initiation. Participants were treated with ZX008 as an add-on therapy for up to 20 weeks starting at 0.2mg/kg/day. The dose could be titrated at four-week intervals based on treatment response up to a maximum of 0.8 mg/kg/day (maximum daily dose in the trial could not exceed 30mg/day) if the patient did not reach at least a 50% reduction in major motor seizure frequency. It is important to note that, per protocol, dose escalation stopped when a patient's major motor seizure frequency was reduced by ≥50% of baseline. The mean age of participants was 11.4 years (± 4.4) and they had failed a median of five antiepileptic therapies (range: 3-7) prior to this study. At study initiation, patients were receiving a median of four antiepileptic therapies. The median number of major motor seizures (defined as generalized tonic-clonic, tonic, atonic, and focal seizures with a motor component) during the four-week baseline period was 60 (range 21-1360). In the Intent-to-Treat (ITT) patient population (n=13), there was a median 50% reduction in seizure frequency over the entire treatment period compared to baseline (range: +74% to –90%), with seven patients (54%) to date achieving a ≥ 50% reduction (range: 50% to 90%) in the number of major motor seizures in this step dose study.

There were no cardiovascular-related adverse events observed. The most common treatment-related adverse events were decreased appetite (n=3), decreased alertness/fatigue (n=3) and insomnia (n=2). Three patients withdrew due to adverse events (decreased alertness (n=2) and insomnia (n=1) and one patient withdrew due to lack of effect (the patient was initially a responder, but lost response after undergoing surgery during the trial).

"These initial results for ZX008 in LGS are quite compelling for this refractory group of patients," said Professor Lagae. "A significant unmet medical need currently exists in the treatment of LGS and these initial data indicate that ZX008 has the potential to be a safe and effective adjunctive treatment for this rare pediatric epilepsy condition. I look forward to continuing to evaluate ZX008 in this ongoing Phase 2 open-label study."

The Dravet syndrome data highlighted updated results from the ongoing prospective study in Belgium with the new patient cohort (n=9). All of these patients began add-on treatment with low-dose fenfluramine (5 mg to 20 mg per day) at various starting points between 2010 and January 2016. Median treatment duration was 2.1 years (range 0.8 to 5.6 years). During the 90-day run-in period prior to initiating low-dose fenfluramine treatment, the median frequency of major motor seizures (defined as tonic, clonic, tonic-clonic, atonic, and myoclonic seizures lasting >30 seconds) was 15.0 per month (range 0.4 to 39.7). Over the entire observation period, the median frequency of major motor seizures was reduced to 1.9 per month, and the median decrease was 76% (range 20-95%). Six of the nine patients (67%) had at least a 70% reduction in major motor seizures. In addition, regarding durability of effect, six of the nine patients (67%) experienced a ≥50% reduction in seizure frequency for at least 90% of the months they were being treated.

Treatment with low-dose fenfluramine continues to be generally well-tolerated. The most common treatment-emergent adverse events were mild-to-moderate somnolence (n=5) and anorexia (n=4). No evidence of cardiac valvulopathy or pulmonary hypertension was observed in any patient on any echocardiogram. There were no patient discontinuations.

Two additional posters were also presented in the main exhibit hall at the AES meeting. One poster presented pre-clinical data suggesting that there may be a protective effect of fenfluramine in an accepted pre-clinical model of Sudden Unexpected Death in Epilepsy (SUDEP) (see study data here). In this SUDEP animal model, the administration of fenfluramine significantly ($p<0.05$) reduced the susceptibility of the mice to have seizure-induced respiratory arrest (S-IRA) 30 minutes post-dosing (20 or 30 mg/kg i.p.) and maintained significance through 24 hours. The prolonged effect of fenfluramine in the present study was not consistently observed with other serotonergic agents tested. These data provide the first evidence of a protective effect of fenfluramine in a mammalian model of SUDEP.

The second poster highlighted the findings from roundtable discussions with parents and caregivers of children with Dravet syndrome that sought to identify those aspects of caregivers' lives that are most impacted by caring for a child with Dravet syndrome (see study data here). These roundtable discussions identified significant impacts on the lives of these families in four overarching areas: physical, mental, social, and financial. Future work by this group will focus on developing a validated measure of caregiver burden in Dravet syndrome.

"The Zogenix team is extremely pleased with all of the data presented at this year's AES meeting," said Stephen J. Farr, Ph.D., President and CEO. "Based on the strength of the LGS data generated, we are currently evaluating a move into a Phase 3 program of ZX008 in this indication. In Dravet syndrome, our confidence in the potential of ZX008 as a safe and effective treatment for seizures associated with Dravet syndrome continues to strengthen with the meaningful reduction in seizure frequency and sustained cardiovascular safety that remain consistent in the results observed in the new cohort of patients. Additionally, the preliminary data generated in the animal model of SUDEP, which suggests a protective effect of fenfluramine against seizure-induced respiratory arrest, is an interesting finding that we intend to explore further."

Zogenix also hosted a Scientific Exhibit Room at the AES meeting entitled, "*Evolution of Low-Dose Fenfluramine in the Treatment of Epileptic Encephalopathies: New Understandings of the Mechanisms, Basic Science, and Clinical Data.*" In this Scientific Exhibit Room, the Company highlighted important ZX008-related research conducted over the last year, including multiple scientific posters that were not presented in the main poster session of the AES meeting. These posters can be found here.

Zogenix's Phase 3 program for Dravet syndrome continues to enroll patients in the U.S. and internationally, and the Company expects the availability of Phase 3 top-line data in

Dravet syndrome in the second quarter of 2017, and potential regulatory submissions for approval to occur by year-end 2017. ZX008 is designated as an orphan drug in both the U.S. and Europe, and also received Fast Track designation in the U.S., for the treatment of Dravet syndrome.

About Zogenix
Zogenix, Inc. (Nasdaq:ZGNX) is a pharmaceutical company committed to developing and commercializing CNS therapies that address specific clinical needs for people living with orphan and other CNS disorders who need innovative treatment alternatives to improve their daily functioning.

For more information, visit www.zogenix.com.

Forward Looking Statements
Zogenix cautions you that statements included in this press release 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 statements are based on the company's current beliefs and expectations. These forward-looking statements include statements regarding ZX008's potential as a treatment for seizures associated with Dravet syndrome or LGS and treatment for SUDEP; the enrollment of patients in the two on-going Phase 3 clinical trials of ZX008 for patients with Dravet syndrome; the continued evaluation of patients in the open-label Phase 2 clinical trial of ZX008 for patients with LGS and the potential to move into a Phase 3 program for LGS; the timing of any submission of a new drug application to the U.S. Food and Drug Administration or comparable market authorization filing in Europe; and the further exploration of fenfluramine in SUDEP. 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 due to the risks and uncertainties inherent in Zogenix's business, including, without limitation: the uncertainties associated with the clinical development and regulatory approval of product candidates such as ZX008, including potential delays in the commencement, enrollment and completion of clinical trials; 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 manufacture commercial supplies of its drug products, if approved; 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; Zogenix's ability to fully comply with numerous federal, state and local laws and regulatory requirements, as well as rules and regulations outside the United States, that apply to its product development activities; Fast Track designation may not result in an expedited regulatory review process; 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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