Zogenix Announces Positive Top-line Results from Second Pivotal Phase 3 Clinical Trial of ZX008 in Dravet Syndrome

July 12, 2018

Primary Endpoint Achieved - Statistically Significant Convulsive Seizure Reduction for ZX008 versus Placebo for Adjunctive Treatment of Seizures

ZX008 Also Demonstrated Statistical Significance in All Key Secondary Endpoints

U.S. and EU Regulatory Submissions on Track for Fourth Quarter of 2018

Zogenix to Host Conference Call and Live Webcast Today at 8:30 AM Eastern Time/5:30 AM Pacific Time

EMERYVILLE, Calif., July 12, 2018 (GLOBE NEWSWIRE) -- Zogenix, Inc. (NASDAQ:ZGNX), a pharmaceutical company developing therapies for the treatment of rare central nervous system (CNS) disorders, today reported positive top-line results from its second confirmatory Phase 3 study (Study 1504) for its investigational drug, ZX008 (low-dose fenfluramine hydrochloride), for the treatment of children and young adults with Dravet syndrome. The study results, which are consistent with those reported in Study 1, Zogenix's first pivotal Phase 3 study, successfully met the primary endpoint and all key secondary endpoints, demonstrating that ZX008, at a dose of 0.5 mg/kg/day (maximum 20 mg/day), is superior to placebo when added to a stiripentol regimen.

Key Findings

- Patients taking ZX008 achieved a 54.7% greater reduction in mean monthly convulsive seizures compared to placebo (p<0.001). The median reduction in monthly convulsive seizure frequency was 62.7% in the ZX008 group compared to 1.2% in placebo patients.
- ZX008 also demonstrated statistically significant improvement versus placebo in both key secondary measures, including patients with clinically meaningful reductions (>50%) in seizure frequency and longest seizure-free interval.
- ZX008 was generally well-tolerated in this study with the adverse events consistent with those observed in Study 1 and the known safety profile of fenfluramine. No patient exhibited cardiac valvulopathy or pulmonary hypertension at any time in the study.

"These impressive study results show the significant impact the addition of ZX008 made in reducing the burden of convulsive seizures for patients who are not adequately controlled using stiripentol, the standard of care for the treatment of Dravet syndrome in Europe," said Professor Rima Nabbout, M.D., Ph.D., Department of Pediatric Neurology, Reference Center for Rare Epilepsies, Necker Enfants Malades Hospital, and Principal Investigator of Study 1504. "If approved, ZX008 has the potential to be a transformative treatment for Dravet syndrome, a rare and serious form of epilepsy with few available treatment options."

Secondary endpoints assessed ZX008 compared to placebo in terms of the proportions of patients who achieved ≥50% reductions and ≥75% reductions in monthly convulsive seizures, as well as the median of the longest convulsive seizure-free interval. These results are shown in the following table.

	ZX008 0.5 mg/kg/day (N=43)	Placebo (N=44)
Patients with ≥50% reduction in monthly convulsive seizures*	53.5% (p<0.001)	6.8%
Patients with ≥75% reduction in monthly convulsive seizures	32.6% (p=0.004)	2.3%
Longest seizure-free interval (median)*	22 days (p<0.005)	13 days

**Key secondary endpoints*

"Patients with Dravet syndrome can often experience frequent, severe convulsive seizures that dramatically impact quality of life for them and their families," said Linda Laux, M.D., Associate Professor, Pediatrics – Neurology, Ann & Robert H. Lurie Children's Hospital of Chicago. "For patients who continue to have significant seizures and need new treatments to reduce seizure frequency and improve quality of life, ZX008 may be an exciting and important new treatment option."

ZX008 was generally well-tolerated in this study, with the adverse events consistent with those observed in Study 1 and the known safety profile of fenfluramine. The incidence of treatment emergent adverse events was similar in both the treatment and placebo groups, with 97.7% (n=42) of patients receiving ZX008 experiencing at least one treatment emergent adverse event compared to 95.5% (n=42) of patients in the placebo group. The most common adverse events in the ZX008 group were decreased appetite, diarrhea, pyrexia, fatigue, and nasopharyngitis.

The incidence of serious adverse events was similar in both the treatment and placebo groups, with 14% (n=6) of patients in the ZX008 group experiencing at least one treatment emergent serious adverse event compared to 15.9% (n=7) of patients in the placebo group. Two patients in the ZX008 group had an adverse event leading to study discontinuation compared to one in the placebo group.

Prospective cardiac safety monitoring throughout the study did not identify clinical or echocardiographic evidence of cardiac valvulopathy or pulmonary hypertension in any patient. This confirms the observations from Study 1 which also reported no valvulopathy or pulmonary hypertension in any patient. Furthermore, approximately 300 patients are currently enrolled in the ongoing open-label safety extension study (Study 1503), some of whom have been treated with ZX008 on a daily basis for over 2 years. In all studies, no safety signal of any cardiovascular abnormality has been identified to date.

The double blind, placebo controlled, Phase 3 study (Study 1504) randomized 87 patients, with a median age of 9 years (range, 2-19 years), across sites in Europe, the United States,

and Canada. Following a six-week baseline observation period, patients were assigned to one of two treatment groups in which ZX008 (n=43) or placebo (n=44) was added to their stable background regimen of stiripentol plus other antiepileptic drugs. The ZX008 dose of 0.5 mg/kg/day (20 mg maximum daily dose) in this study accounted for a drug-drug interaction between stiripentol and ZX008 and was designed to approximate the 0.8 mg/kg/day dose evaluated in Study 1 where stiripentol use was not permitted. The mean baseline convulsive seizure frequency across all treatment groups in Study 1504 was approximately 25 seizures per month. Patients were titrated to their target dose over three weeks and then remained at that fixed dose for 12 weeks.

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. Earlier this year, Zogenix conducted a positive meeting with the U.S. Food and Drug Administration (FDA) regarding the ZX008 clinical development program and planned New Drug Application (NDA) submission in Dravet syndrome in which FDA affirmed Study 1 and Study 1504 were suitable as the clinical basis for the NDA submission.

“I would like to extend my gratitude to the patients, families and investigators involved in Study 1504,” said Stephen J. Farr, Ph.D., President and CEO of Zogenix. “Based on these highly compelling top-line results from both of our pivotal studies, we are now focused on submitting applications for regulatory approvals in the U.S. and Europe in the fourth quarter of 2018. We are excited about ZX008’s potential to have a major impact in the treatment of patients with Dravet syndrome and their families.”

Conference Call Details
Thursday, July 12 @ 8:30 AM Eastern Time/5:30 AM Pacific Time
Toll Free: 877-407-9208
International: 201-493-6784
Conference ID: 13681129
Webcast (with slides): http://public.viavid.com/index.php?id=130286

Audio Replays, available through July 26, 2018:
Domestic: 844-512-2921
International: 412-317-6671
Replay PIN: 13681129

About Zogenix
Zogenix, Inc. (Nasdaq:ZGNX) is a pharmaceutical company dedicated to developing therapies for people living with severe central nervous system (CNS) disorders who have limited or no treatment options. Led by a team of experts in rare disease development and CNS conditions, Zogenix is rapidly advancing the clinical investigation and development of ZX008 (fenfluramine hydrochloride) for patients with severe, rare epilepsies, including Dravet and Lennox-Gastaut syndromes.

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 Zogenix's current beliefs and expectations. These forward-looking statements include statements regarding ZX008’s potential to be a transformative treatment for Dravet syndrome; and the projected timing of the Zogenix’s applications for regulatory approvals of ZX008 in the U.S. and Europe. 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 top-line 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 top-line data may not accurately reflect the complete results of the trial, and the FDA may not agree with Zogenix’s interpretation of such results; unexpected adverse side effects or inadequate therapeutic efficacy of ZX008 may limit regulatory approval and/or commercialization, or may result in recalls or product liability claims; 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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