Zogenix and Leading Experts to Present New Rare Epilepsy Data at AES 2020

December 1, 2020

- New long-term safety, efficacy, and durability data for FINTEPLA® (fenfluramine) oral solution in Dravet syndrome
- Full results from Phase 3 study of FINTEPLA in Lennox-Gastaut syndrome
- New data from investigator-initiated study in CDKL5 Deficiency Disorder

EMERYVILLE, Calif., Dec. 01, 2020 (GLOBE NEWSWIRE) -- Zogenix (Nasdaq: ZGNX), a global biopharmaceutical company developing and commercializing rare disease therapies, announced that data from eleven poster presentations related to FINTEPLA® (fenfluramine) oral solution in Dravet syndrome, Lennox-Gastaut syndrome, and other rare epilepsies will be presented at the American Epilepsy Society (AES) Annual Meeting, being held virtually from December 4-8, 2020. Zogenix will also host a virtual scientific exhibition room and sponsor a continuing medical education (CME) symposium during AES 2020.

“We are honored to collaborate with leading international epilepsy experts to broaden our understanding of how FINTEPLA, a drug recently approved by the FDA to treat seizures associated with Dravet syndrome, may improve the lives of epilepsy patients and their families,” said Zogenix’s Chief Medical Officer Bradley S. Galer, M.D. “With new long-term data in Dravet syndrome, full results from our Lennox-Gastaut syndrome Phase 3 trial, and data from investigator-initiated studies, we are eager to continue advancing FINTEPLA as a potential new treatment option for additional rare epilepsies.”

Main Conference
Full data for the FINTEPLA posters presented in the main conference will be available on the AES 2020 conference site starting this Friday, December 4, at 9:00 a.m. Eastern Time and will be available after AES on the Zogenix Newsroom site. Authors will be available to discuss their data with attendees during the following times:

- Efficacy and Tolerability of Adjunctive FINTEPLA (Fenfluramine Hydrochloride) in an Open-Label Extension Study of Dravet Syndrome Patients Treated for Up to 3 Years
  Scheffer, Devinsky, Perry et al
  Poster #978
  Authors available: Monday, December 7, 1:30 – 3:00 PM ET

- Treatment with FINTEPLA (Fenfluramine) in Patients with Dravet Syndrome has no Long-Term Effect on Weight and Growth
  Gil-Nagel, Ceulemans, Wirrell et al
  Poster #977
  Authors available: Monday, December 7, 1:30 – 3:00 PM ET

- Fenfluramine (FINTEPLA) Provides Comparable Clinical Benefit in Adults and Children with Dravet Syndrome: Real-World Experience from the US Early Access Program
  Perry, Knupp, Wirrell, et al
  Poster #1057
  Authors available: Monday, December 7, 1:30 – 3:00 PM ET

- The Long-Term Effects of Fenfluramine on Patients with Dravet Syndrome and Their Families: A Qualitative Analysis
  Jensen, Salem, Gammaitoni et al
  Poster #418
  Authors available: Sunday, December 6, 12:00 – 1:30 PM ET

- University of Washington Caregiver Stress Scale Translations
  Amtmann, Bamer, Salem et al
  Poster #287
  Authors available: Sunday, December 6, 12:00 – 1:30 PM ET

- Fenfluramine (FINTEPLA) in Dravet Syndrome: Results of a Third Randomized, Placebo-Controlled Clinical Trial
  Sullivan, Lagae, Cross et al
  Poster #853
  Authors available: Monday, December 7, 9:00 – 10:30 AM ET
- Efficacy and Tolerability with FINTEPLA (Fenfluramine) in Adult Patients with Dravet Syndrome: A Case Series of Patients Participating in Phase 3 Studies
  Miller, Devinsky, Auvin et al
  Poster #849
  Authors available: Monday, December 7, 9:00 – 10:30 AM ET

- Fenfluramine for the Treatment of Patients with Lennox-Gastaut Syndrome: A Randomized, Double-Blind, Placebo-Controlled Clinical Trial
  Knupp, Lagae, Arzimanoglou et al
  Poster #852
  Authors available: Monday, December 7, 9:00 – 10:30 AM ET

- Fenfluramine to Treat Convulsive Seizures in Patients with CDKL5 Deficiency Disorder
  Devinsky, King, and Price
  Poster #1060
  Authors available: Monday, December 7, 1:30 – 3:00 PM ET

Scientific Exhibit Room
All posters from the main conference above, plus the two additional Scientific Exhibit Room posters, will be available in the Zogenix Scientific Exhibit Room. Questions regarding data in the Scientific Exhibition Room will be answered during a live discussion on Sunday, December 6, from 8:00 – 11:00 a.m. Eastern Time.

- Impact of FINTEPLA (Fenfluramine) on the Incidence Rate of SUDEP in Patients with Dravet Syndrome
  Cross, Galer, Gil-Nagel et al

- Fenfluramine Prevents Audiogenic Seizures in a 129/SvTer Mouse Model of Sudden Unexpected Death in Epilepsy (SUDEP)
  Martin, Biraben, Harnandez et al

Satellite Symposium:
Zogenix is proud to sponsor the Industry CME Satellite Symposium: An Update on Rare Childhood-Onset Epilepsies, which will be held on Sunday, December 6, from 6:00 – 7:30 p.m. Eastern Time with the following speakers and topics:

- Epileptic Encephalopathies: Phenotypic Evolution
  Elaine Wirrell, M.D., FRCPC (Program Chair)

- Mechanisms of Epileptogenesis in a Zebrafish Model of Dravet Syndrome
  Camila V. Esguerra, Ph.D.,

- An Update on Sunflower Syndrome: Clinical Features and Treatment Challenges
  Elizabeth Thiele, M.D., Ph.D.

- An Update on CDKL5 Deficiency Disorder: Clinical Presentations, Genetic Variation, and Approaches to Treatment
  Orrin Devinsky, M.D.

About Dravet Syndrome
Dravet syndrome is a rare and devastating infant-onset epilepsy highly correlated with a mutation in the SCN1A gene. The disease is marked by frequent debilitating seizures, lifelong developmental and motor impairments, and an increased risk of sudden death (SUDEP). In addition to its impact on the patient, the severity and unpredictability of the disease, coupled with around-the-clock concern for the diagnosed child’s well-being, can present significant emotional and logistical challenges for all members of the family.

About Lennox-Gastaut Syndrome
Lennox-Gastaut Syndrome (LGS) is a rare and devastating lifelong childhood-onset epilepsy that can arise from multiple different causes. LGS is characterized by many different seizure types, including many that result in frequent falls and injuries and that often don’t respond to currently available seizure medications. The intellectual and behavioral problems associated with LGS, as well as around-the-clock care requirements, add to the complexity of life with this disease.

About CDKL5 Deficiency Disorder
CDKL5 deficiency disorder is a rare developmental epileptic encephalopathy caused by mutations in the CDKL5 gene. The hallmarks are early-onset, intractable epilepsy and neurodevelopmental delay impacting cognitive, motor, speech, and visual
function. Although rare, it one of the most common forms of genetic epilepsy.

About FINTEPLA® (fenfluramine) oral solution
FINTEPLA (fenfluramine) oral solution is approved in the United States, has received a positive CHMP opinion in Europe, and is in development in Japan for the treatment of seizures associated with Dravet syndrome, and is being investigated as a potential treatment for Lennox-Gastaut syndrome (LGS) and other rare and severe childhood-onset epilepsy disorders.

United States

IMPORTANT SAFETY INFORMATION

Boxed WARNING: VALVULAR HEART DISEASE and PULMONARY ARTERIAL HYPERTENSION

- There is an association between serotonergic drugs with 5-HT2B receptor agonist activity, including fenfluramine (the active ingredient in FINTEPLA), and valvular heart disease and pulmonary arterial hypertension.
- Echocardiogram assessments are required before, during, and after treatment with FINTEPLA.
- FINTEPLA is available only through a restricted program called the FINTEPLA REMS.

Contraindications
FINTEPLA is contraindicated in patients with hypersensitivity to fenfluramine or any of the excipients in FINTEPLA and with concomitant use of, or within 14 days of the administration of monoamine oxidase inhibitors because of an increased risk of serotonin syndrome.

WARNINGS AND PRECAUTIONS

Valvular Heart Disease and Pulmonary Arterial Hypertension (see boxed Warning)
Because of the association between serotonergic drugs with 5-HT2B receptor agonist activity, including fenfluramine (the active ingredient in FINTEPLA), and valvular heart disease and pulmonary arterial hypertension, cardiac monitoring via echocardiogram is required prior to starting treatment, during treatment, and after treatment with FINTEPLA concludes. Cardiac monitoring via echocardiogram can aid in early detection of this condition. In clinical trials of up to 3 years in duration, no patient receiving FINTEPLA developed valvular heart disease or pulmonary arterial hypertension.

Monitoring
Prior to starting treatment, patients must undergo an echocardiogram to evaluate for valvular heart disease and pulmonary arterial hypertension. Echocardiograms should be repeated every 6 months, and once 3-6 months post-treatment with FINTEPLA.

If valvular heart disease or pulmonary arterial hypertension is observed on an echocardiogram, the prescriber must consider the benefits versus the risks of initiating or continuing treatment with FINTEPLA.

FINTEPLA REMS Program (see boxed Warning)
In the United States, FINTEPLA is available only through a restricted distribution program called the FINTEPLA REMS program. Prescribers must be certified by enrolling in the FINTEPLA REMS program. Prescribers must Counsel patients receiving FINTEPLA about the risk of valvular heart disease and pulmonary arterial hypertension, how to recognize signs and symptoms of valvular heart disease and pulmonary arterial hypertension, the need for baseline (pretreatment) and periodic cardiac monitoring via echocardiogram during FINTEPLA treatment, and cardiac monitoring after FINTEPLA treatment. Patients must enroll in the REMS program and comply with ongoing monitoring requirements. The pharmacy must be certified by enrolling in the REMS program and must only dispense to patients who are authorized to receive FINTEPLA. Wholesalers and distributors must only distribute to certified pharmacies. Further information is available at www.FinteplaREMS.com or by telephone at 1-877-964-3649.

Decreased Appetite and Decreased Weight
FINTEPLA can cause decreases in appetite and weight. Decreases in weight appear to be dose related. Most patients resumed the expected measured increases in weight by the end of the open-label extension study. Weight should be monitored regularly during treatment with FINTEPLA and dose modifications should be considered if a decrease in weight is observed.

Somnolence, Sedation, and Lethargy
FINTEPLA can cause somnolence, sedation, and lethargy. Other central nervous system (CNS) depressants, including alcohol, could potentiate these effects of FINTEPLA. Prescribers should monitor patients for somnolence and sedation and should advise patients not to drive or operate machinery until they have gained sufficient experience on FINTEPLA to gauge whether it adversely affects their ability to drive or operate machinery.

Suicidal Behavior and Ideation
Antiepileptic drugs (AEDs) increase the risk of suicidal thoughts or behavior in patients taking these drugs for any indication. Patients treated with an AED for any indication should be monitored for the emergence or worsening of depression, suicidal thoughts or behavior, or any unusual changes in mood or behavior.
Anyone considering prescribing FINTEPLA or any other AED must balance the risk of suicidal thoughts or behaviors with the risk of untreated illness. Epilepsy and many other illnesses for which AEDs are prescribed are themselves associated with morbidity and mortality and an increased risk of suicidal thoughts and behavior. Should suicidal thoughts and behavior emerge during treatment, consider whether the emergence of these symptoms in any given patient may be related to the illness being treated.

**Withdrawal of Antiepileptic Drugs**

As with most AEDs, FINTEPLA should generally be withdrawn gradually because of the risk of increased seizure frequency and status epilepticus. If withdrawal is needed because of a serious adverse reaction, rapid discontinuation can be considered.

**Serotonin Syndrome**

Serotonin syndrome, a potentially life-threatening condition, may occur with FINTEPLA, particularly with concomitant administration of FINTEPLA with other serotonergic drugs, including, but not limited to, selective serotonin-norepinephrine reuptake inhibitors (SNRIs), selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants (TCAs), bupropion, triptans, dietary supplements (eg, St. John’s Wort, tryptophan), drugs that impair metabolism of serotonin (including monoamine oxidase inhibitors [MAOIs]), which are contraindicated with FINTEPLA, dextromethorphan, lithium, tramadol, and antipsychotics with serotonergic agonist activity. Patients should be monitored for the emergence of signs and symptoms of serotonin syndrome, which include mental status changes (eg, agitation, hallucinations, coma), autonomic instability (eg, tachycardia, labile blood pressure, hyperthermia), neuromuscular signs (eg, hyperreflexia, incoordination), and/or gastrointestinal symptoms (eg, nausea, vomiting, diarrhea). If serotonin syndrome is suspected, treatment with FINTEPLA should be stopped immediately and symptomatic treatment should be started.

**Increase in Blood Pressure**

FINTEPLA can cause an increase in blood pressure. Significant elevation in blood pressure, including hypertensive crisis, has been reported rarely in adult patients treated with fenfluramine, including patients without a history of hypertension. Monitor blood pressure in patients treated with FINTEPLA. In clinical trials of up to 3 years in duration, no patient receiving FINTEPLA developed hypertensive crisis.

**Glucoma**

Fenfluramine can cause mydriasis and can precipitate angle closure glaucoma. Consider discontinuing treatment with FINTEPLA in patients with acute decreases in visual acuity or ocular pain.

**Adverse Reactions**

The most common adverse reactions (incidence at least 10% and greater than placebo) were decreased appetite; somnolence, sedation, lethargy; diarrhea; constipation; abnormal echocardiogram; fatigue, malaise, asthenia; ataxia, balance disorder, gait disturbance; blood pressure increased; drooling, salivary hypersecretion; pyrexia; upper respiratory tract infection; vomiting; decreased weight; fall; status epilepticus.

**Drug Interactions**

Strong CYP1A2 and CYP2B6 Inducers: Coadministration with rifampin or a strong CYP1A2 and CYP2B6 inducer will decrease fenfluramine plasma concentrations.

Consider an increase in FINTEPLA dosage when coadministered with rifampin or a strong CYP1A2 and CYP2B6 inducer.

**Use in Specific Populations**

Administration to patients with moderate or severe renal impairment or to patients with hepatic impairment is not recommended.

Please see full Prescribing Information, including Boxed Warning, for additional important information on FINTEPLA.

**About Zogenix**

Zogenix is a global biopharmaceutical company committed to developing and commercializing therapies with the potential to transform the lives of patients and their families living with rare diseases. The company’s first rare disease therapy, FINTEPLA® (fenfluramine) oral solution, C-IV is approved by the U.S. FDA, has received positive CHMP opinion in Europe, and is in development in Japan for the treatment of seizures associated with Dravet syndrome, a rare, devastating infant-onset epilepsy. FINTEPLA is also in development for the treatment of seizures associated with Lennox-Gastaut syndrome, another rare and devastating childhood-onset epilepsy. Through its subsidiary Modis Therapeutics, Zogenix is developing MT1621, an investigational novel deoxynucleoside substrate enhancement therapy for the treatment of TK2 deficiency, a rare genetic disorder.

**Forward Looking Statements**

Zogenix cautions you that statements included in this press release and 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 statements include Zogenix’s development plans for FINTEPLA in Lennox-Gastaut syndrome (LGS) and
CDKL5 deficiency disorder and for MT1621, and the potential clinical value that FINTEPLA provides for Dravet syndrome, LGS and CDKL5 deficiency disorder patients and their families. 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 due to the risks and uncertainties inherent in Zogenix’s business, including, without limitation: the timing of enrollment or results of Zogenix’s clinical trials; the COVID-19 pandemic may disrupt Zogenix’s business operations, impairing the ability to complete the planned studies of MT1621; unexpected adverse side effects or inadequate therapeutic efficacy of FINTEPLA or MT1621 that could limit development or commercialization, or that could result in recalls or product liability claims; additional data from Zogenix’s ongoing studies may contradict or undermine the data reported for Dravet syndrome or other indications; and other risks described in Zogenix’s prior press releases as well as in public periodic filings with the U.S. Securities & 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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