FDA Approves FINTEPLA® (fenfluramine) for the Treatment of Seizures Associated with Dravet Syndrome

June 26, 2020

- *FINTEPLA® significantly and substantially reduced convulsive seizure frequency in patients whose seizures were not adequately controlled on other medications, as observed in two phase 3 placebo-controlled clinical trials*
- *Commercial launch planned for July 2020*
- *Zogenix to host an investor call tomorrow, June 26, at 8:30 AM ET / 5:30 AM PT*

EMERYVILLE, Calif., June 25, 2020 (GLOBE NEWSWIRE) -- Zogenix, Inc. (NASDAQ: ZGNX), a global pharmaceutical company developing rare disease therapies, today announced that the U.S. Food and Drug Administration (FDA) has approved FINTEPLA® (fenfluramine) oral solution, CIV for the treatment of seizures associated with Dravet syndrome in patients 2 years of age and older. FINTEPLA will be launched through a restricted distribution program, called the FINTEPLA Risk Evaluation and Mitigation Strategy (REMS) Program, and is expected to be available through Zogenix's specialty pharmacy partner by the end of July.

"The approval of FINTEPLA by the FDA is a significant milestone we are proud to celebrate with the patients and families living with Dravet syndrome," said Stephen J. Farr, Ph.D., President and Chief Executive Officer of Zogenix. "We began this global development program nearly six years ago after researchers in Belgium recognized the potential of fenfluramine, a drug with distinct pharmacology from all other anticonvulsant agents, to treat intractable seizures in Dravet syndrome. Our heartfelt gratitude goes to the patients, families, and everyone who supported the rigorous development program that led to FINTEPLA's approval."

Dravet syndrome is a rare childhood-onset epilepsy marked by frequent and severe treatment-resistant seizures, associated hospitalizations and medical emergencies, significant developmental and motor impairments, and an increased risk of sudden unexpected death (SUDEP).

"There remains a huge unmet need for the many Dravet syndrome patients who continue to experience frequent severe seizures even while taking one or more of the currently available anti-seizure medications," said Joseph Sullivan, M.D., Director of the Pediatric Epilepsy Center of Excellence at the UCSF Benioff Children's Hospitals and the Principal Investigator for FINTEPLA in Dravet syndrome. "Given the profound reductions in convulsive seizure frequency seen in the FINTEPLA clinical trials, combined with the ongoing, robust safety monitoring that will be part of its use, I feel FINTEPLA will offer an extremely important treatment option for Dravet syndrome patients."

The FDA's approval of FINTEPLA in Dravet syndrome was based on data from two randomized, double-blinded, placebo-controlled Phase 3 clinical trials, published in *The Lancet*[1] and *JAMA Neurology*[2], and safety data from an open-label extension trial in which many patients received FINTEPLA for up to three years. When added to existing treatment regimens, FINTEPLA significantly reduced the monthly convulsive seizure frequency compared to placebo in study patients whose seizures were not adequately controlled on one or more antiepileptic drugs. In addition, most study patients responded to treatment with FINTEPLA within three to four weeks and effects remained consistent over the treatment period.

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.

FINTEPLA will be available to certified prescribers in the U.S. in July. Zogenix is launching Zogenix Central™, a comprehensive support service that will provide ongoing product assistance to patients, caregivers, and their medical teams. Further information is available at www.FINTEPLA.com to assist patients and their families.

"Having a new FDA-approved treatment option is so important because it improves our ability to optimize each patient's treatment," said Mary Anne Meskis, Executive Director of the Dravet Syndrome Foundation. "Moreover, because families living with Dravet syndrome never know when the next seizure is going to occur, whether they will end up in the E.R., or what the consequences might be following the seizure, having a strong support program like Zogenix Central to reduce the strain on families is very welcome. This will allow family members to remain focused on providing the best care of their loved one with Dravet."

Conference Call

Friday, June 26, at 8:30 AM Eastern Time / 5:30 AM Pacific Time
Toll Free: 877-407-9716
International: 201-493-6779

Conference ID: 13706215
Webcast: http://public.viavid.com/index.php?id=140519

Multimedia components are available with this press release here: https://www.multivu.com/players/English/8722951-zogenix-fda-approval-dravet-syndrome/.

About Dravet Syndrome
Dravet syndrome is a rare childhood-onset epilepsy marked by frequent debilitating seizures, lifelong developmental and motor impairments, and an increased risk of sudden death. Despite existing therapies, there remains a great unmet need in Dravet syndrome to reduce convulsive seizures that can lead to medical emergencies, hospitalizations, and SUDEP (sudden unexpected death in epilepsy). 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 FINTEPLA® (fenfluramine) oral solution, CIV
FINTEPLA is an approved treatment, in the U.S., for seizures associated with Dravet syndrome in patients 2 years of age and older. Across multiple clinical studies, FINTEPLA demonstrated significant and sustained reduction of convulsive seizures associated with Dravet syndrome. In two pivotal Phase 3 trials, the reduction in convulsive seizure frequency per 28 days was statistically significantly greater for all dose groups of FINTEPLA compared to placebo.

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)

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.

Glaucoma

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.

About Zogenix
Zogenix is a global pharmaceutical 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 has been approved by the U.S. FDA and is under review in Europe for the treatment of seizures associated with Dravet syndrome, a rare, severe childhood onset epilepsy. In addition, the company has two late-stage development programs underway: one for FINTEPLA for the treatment of seizures associated with Lennox-Gastaut syndrome, a rare childhood-onset epilepsy and one for MT1621, an investigational novel substrate enhancement therapy for the treatment of TK2 deficiency, a rare genetic disorder. MT1621 is being developed through Modis Therapeutics, a Zogenix company.

Forward Looking Statements
Zogenix cautions you that statements included in this press release and the conference call 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: FINTEPLA providing a treatment option for patients with Dravet syndrome; and Zogenix's plans to commercialize FINTEPLA, including the timing of the launch of the restricted distribution program, FINTEPLA REMS Program, and the launch of Zogenix Central and the availability of product assistance to patients, caregivers, and their medical teams. 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: Zogenix's ability to successfully launch FINTEPLA, including establishing the restricted distribution program, FINTEPLA REMS Program, and Zogenix Central, and the timing thereof; the COVID-19 pandemic may disrupt Zogenix's business operations, impairing the ability to commercialize FINTEPLA and Zogenix's ability to generate product revenue; unexpected adverse side effects or inadequate therapeutic efficacy of FINTEPLA that could limit commercialization, or that could result in recalls or product liability claims; Zogenix may not be successful in executing its sales and marketing strategy for the commercialization of FINTEPLA; Zogenix's dependence on third parties for the manufacture of FINTEPLA; Zogenix's ability to achieve and maintain adequate levels of coverage and reimbursement for FINTEPLA; the scope and validity of patent protection or regulatory exclusivity protection for FINTEPLA and Zogenix's ability to commercialize FINTEPLA without infringing the patent rights of others; 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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[1] *The Lancet,* Volume 394, Issue 10216, P2243-2254, December 21, 2019
[2] JAMA Neurol. 2020 Mar; 77(3): 300–308.

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