

# Zogenix Presents Positive Clinical Study Results for Investigational Treatment for TK2 Deficiency

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- Safety and efficacy data from a global, retrospective Phase 2 study (RETRO) support potential for deoxynucleoside substrate enhancement therapy (SET) to treat TK2 deficiency, an often-fatal mitochondrial DNA depletion disorder
- Highly significant impact on survival probability ( $p < 0.0006$ ) for treated patients compared to untreated natural history control subjects; all treated patients remain alive
- Most (~95%) treated patients experienced improvement (68%) or disease stabilization (26%)
- Among clinical responders, profound responses, such as re-acquiring previously lost motor milestones, were measured in a subset of treated patients

EMERYVILLE, Calif., Oct. 07, 2019 (GLOBE NEWSWIRE) -- Zogenix, Inc. (NASDAQ: ZGNX), a global pharmaceutical company developing rare disease therapies, and its wholly-owned subsidiary, Modis Therapeutics, presented positive top-line results from its pivotal Phase 2 RETRO study at the recent World Muscle Society congress in Copenhagen. The data from RETRO form the basis of Zogenix's ongoing investigational MT1621 program and support the safety and efficacy of pyrimidine nucleoside substrate enhancement therapy (SET) for the treatment of *Thymidine Kinase 2 deficiency (TK2d)*, a rare, debilitating, and often fatal genetic disorder that primarily affects infants and children and for which there are currently no approved therapies. *The poster can be found [here](#).*

"*TK2d* is an inherited mitochondrial DNA depletion disorder that causes severe muscle weakness that progresses until patients, typically children, lose the ability to stand, walk, eat, and breathe independently," said Michio Hirano, M.D., Chief of the Division of Neuromuscular Medicine at Columbia University, New York. "This is a landmark study demonstrating that nucleoside therapy provided meaningful clinical benefit to patients across the spectrum of TK2 deficiency."

## Study Design

RETRO is a global retrospective study of SET, a fixed combination treatment of two pyrimidine nucleosides (dC/dT), in 38 pediatric and adult patients with TK2 deficiency (median age of disease onset, 2.5 years) treated at eight clinical sites in three countries (U.S., Spain and Israel). Subjects received SET for a median of 77 weeks (range 92 days – 7 years). Each subject was scored across motor, respiratory, and feeding domains according to pre-defined response criteria and was compared to pre-treatment status to assess whether responses improved, remained stable, or worsened.

Parallel to RETRO, the Company compiled a comprehensive, global TK2d Natural History dataset from published studies and individual case reports to document untreated patients' disease course. From this natural history dataset, 68 patients reflecting the range of disease severity, age, and age of disease onset, were selected as a control group for treated patients in the RETRO study.

## Key Efficacy Findings

- All treated patients remain alive. A survival analysis using a time-dependent Cox regression model showed that the difference in probability of survival between treated patients and untreated natural history control patients was highly statistically significant ( $p < 0.0006$ ).
- In addition to the survival benefit, the vast majority of treated patients (94.7%) had either improved (68%) or stabilized (26%) responses in major functional domains.
- Among clinical responders, a subset demonstrated profound responses, in some cases re-acquiring previously lost motor milestones, as described below:

- Ambulation: Three patients who had lost the ability to walk prior to treatment regained ambulation; one patient who had never walked gained ambulation.
- Respiratory Function: One patient receiving 24 hours/day of invasive mechanical ventilation prior to treatment discontinued all respiratory support.
- Feeding Support: Eight patients were on feeding tubes at study start; three of these patients had their feeding tubes removed.

### **Safety & Tolerability**

Safety data from RETRO indicated that SET is generally safe and well-tolerated. Most reported adverse events were considered not related to study drug (199 of 292), with mild or moderate diarrhea being the most common treatment-related adverse event, occurring in 63% of patients.

Serious AEs (SAEs) were reported in 14 subjects (37%). The majority of SAEs were deemed related to TK2d; two patients experienced three events related to study drug alone (kidney stone, kidney stone removal, diarrhea).

Two adult-onset patients stopped treatment due to asymptomatic increases in aminotransferase liver enzymes (no increase in bilirubin levels), which resolved upon discontinuation of treatment.

“The results from this study demonstrate the potential of our investigational drug, MT1621, to improve outcomes in patients with TK2d and to significantly alter the course of disease,” said Joanne Quan, M.D., Chief Medical Officer at Modis Therapeutics. “We look forward to continuing the development of MT1621, with the goal of bringing it to patients as quickly as possible.”

### **About MT1621 and TK2 Deficiency**

MT1621 is a proprietary investigational deoxynucleoside substrate enhancement therapy in late-stage development for the treatment of TK2 deficiency (TK2d), a genetic disorder that results in mitochondrial dysfunction and leads to inadequate energy production in cells. TK2d presents as severe and progressive muscle weakness that profoundly impairs movement, breathing, eating, and other normal functions, and is often fatal. There are currently no approved therapies for this disease.

Deoxynucleoside combination therapy has been shown to improve mitochondrial functions and prolong survival in preclinical models, and data from initial clinical studies suggest it may meaningfully alter the course of disease in patients with TK2d.

### **About Zogenix**

Zogenix is a global pharmaceutical company whose mission is to develop and commercialize therapies that transform the lives of patients and their families living with rare diseases. The company has two late-stage development programs underway: FINTEPLA® (ZX008, fenfluramine) for the treatment of seizures associated with Dravet and Lennox-Gastaut syndromes, two rare and often-catastrophic childhood-onset epilepsies, and MT1621 combination deoxynucleoside substrate enhancement therapy for the treatment of TK2 deficiency.

Zogenix recently resubmitted its New Drug Application for FINTEPLA® for Dravet syndrome to the U.S. Food & Drug Administration; its application for FINTEPLA for Dravet syndrome is under review by the European Medicines Agency. Zogenix expects top-line data from its Phase 3 study of FINTEPLA in Lennox-Gastaut syndrome in the first quarter of 2020. FINTEPLA is also in development in Japan. Zogenix acquired Modis Therapeutics and MT1621 in September 2019.

### **Forward-Looking Statement**

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 include: the

potential for MT1621 to significantly improve outcomes in patients with TK2d; and Zogenix's expectations that the RETRO study will serve as a pivotal study for FDA review of MT1621 for treatment of TK2d. 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: risks associated with the acquisition of Modis Therapeutics, Inc. (Modis) and integration of Modis' operations into Zogenix's business, including an increase in near and long-term expenditures, exposure to unknown liabilities and diversion of Zogenix's management's time and attention; the inherent risks of clinical development of MT1621; the data Modis 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 trial and such data may not accurately reflect the complete results of the trial; risks associated with relying on a retrospective analysis for pivotal efficacy and safety data for MT1621; Breakthrough Therapy and PRIME designations do not guarantee that the FDA or EMA will approve MT1621 or expedite its review of MT1621; the FDA may refuse to accept the re-submitted NDA for FINTEPLA the FDA may not agree with Zogenix's interpretation of the results of the clinical trials of MT1621 or FINTEPLA; 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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The logo for Zogenix, featuring the word "ZOGENIX" in a bold, purple, sans-serif font. A green swoosh underline is positioned beneath the letters "O" and "G".

Source: Zogenix, Inc