



Zynerba Pharmaceuticals Initiates CONNECT-FX, a Pivotal Clinical Trial of ZYN002 in Fragile X Syndrome

July 9, 2018

Study will Evaluate the Efficacy and Safety of Transdermally-Delivered Cannabidiol (CBD) in Children and Adolescents with Fragile X Syndrome

Top Line Results Expected in Second Half of 2019

Zynerba to host conference call and webcast today at 8:30 am

DEVON, Pa., July 09, 2018 (GLOBE NEWSWIRE) -- Zynerba Pharmaceuticals, Inc. (NASDAQ:ZYNE), the leader in innovative pharmaceutically-produced transdermal cannabinoid therapies for rare and near-rare neuropsychiatric disorders, today announced the initiation of a multi-national, randomized, double blind placebo controlled Clinical study of Cannabidiol (CBD) in Children and Adolescents with Fragile X (CONNECT-FX). The CONNECT-FX trial will evaluate the efficacy and safety of ZYN002 (CBD Gel) in children ages three to 17 with full mutation Fragile X syndrome (FXS). FXS is a genetic condition that causes intellectual disability, behavioral and learning challenges and is the most common known single gene cause of autism spectrum disorder. Top line results are expected in the second half of 2019.

"We are excited to initiate CONNECT-FX, the first-of-its-kind clinical study evaluating transdermally-delivered ZYN002 as a treatment for the debilitating behaviors associated with Fragile X syndrome," said Armando Anido, Chairman and Chief Executive Officer of Zynerba. "We look forward to demonstrating the clinical effects of ZYN002 in treating some of the most common behavioral symptoms of Fragile X syndrome. If successful, ZYN002 has the potential to become the first product indicated for the treatment of behavioral symptoms of Fragile X syndrome and help address the ongoing needs of the children and families impacted by this syndrome."

The CONNECT-FX study is a multi-national randomized, double-blind, placebo-controlled, 14-week study that will assess the efficacy and safety of ZYN002 for the treatment of children and adolescents with FXS. Approximately 200 male and female patients with Fragile X syndrome, confirmed with the full mutation of the FMR1 gene, will be enrolled at approximately 20 clinical sites in the United States, Australia, and New Zealand. Patients will be randomized 1:1 to either trial drug or placebo. Randomization will be stratified by gender, weight, and investigator geographic region. The primary endpoint is the change from baseline to the end of the treatment period in the Aberrant Behavior Checklist-Community FXS Specific (ABC-C_{FXS}) Social Avoidance subscale. Key secondary endpoints are the change from baseline to the end of the treatment period in the ABC-C_{FXS} Irritability subscale score, the ABC-C_{FXS} Socially Unresponsive/Lethargic subscale score, and improvement in Clinical Global Impression - Improvement (CGI-I) at the end of the treatment period. Based on discussions with the U.S. Food and Drug Administration (FDA), the Company will anchor the CGI-I scale to behavioral symptoms of FXS. Consistent with recent guidance from the FDA on capturing the voice of the patient in drug development, additional qualitative data on the clinical relevance of various FXS behaviors to caregivers and patients will be collected. With positive results from this trial, Zynerba will request a meeting with the FDA to determine the acceptability of these data as the basis for an NDA filing.

"Children with Fragile X syndrome are dramatically impacted by this genetic condition and its debilitating behavioral and emotional challenges, including anxiety, social withdrawal, irritability, inattention and aggression," said Elizabeth M. Berry-Kravis, M.D., Ph.D., Professor of Pediatrics, Neurological Sciences and Biochemistry at Rush University Medical Center. "In patients with Fragile X, augmentation of endogenous cannabinoid availability has the potential to positively impact social avoidance behaviors and anxiety during social interactions. I am excited to participate in a double-blind placebo-controlled study of cannabidiol in Fragile X. I hope to be part of the effort to move what may be the first product indicated specifically for Fragile X syndrome toward availability for my patients."

Conference call information

Zynerba management will host a live conference call and webcast today at 8:30 am Eastern Time to discuss the initiation of CONNECT-FX. The call can be accessed by dialing (866) 573-0180 (U.S. and Canada) or (430) 775-1345 (international) and referencing conference ID 7163869. To access the live webcast or the replay, visit the investor page of the Company's website at <http://ir.zynerba.com/>. The webcast will be recorded and available on the Company's website for 30 days.

About Fragile X syndrome

Fragile X syndrome is a rare genetic developmental disability that is the leading known cause of both inherited intellectual disability and autism spectrum disorder, affecting 1 in 3,600 to 4,000 males and 1 in 4,000 to 6,000 females. It is the most common inherited intellectual disability in males and a significant cause of intellectual disability in females. It is caused by a mutation in the Fragile X Mental Retardation gene (FMR1) located on the X chromosome and leads to dysregulation of the endocannabinoid pathway including the reduction in endogenous cannabinoids (2-AG and anandamide). The disorder negatively affects synaptic function, plasticity and neuronal connections, and results in a spectrum of intellectual disabilities and behavioral symptoms, such as social avoidance and irritability. In the US, there are about 71,000 patients suffering with FXS.

About Our Technology

Cannabinoids are a class of chemical compounds that occur naturally in the human body and in the Cannabis plant and interact with numerous signaling systems and receptors in the central nervous system, giving them wide potential therapeutic application. The two primary cannabinoids contained in Cannabis are cannabidiol, or CBD, and Δ^9 -tetrahydrocannabinol, or THC. Clinical and preclinical data support the potential for CBD in treating epilepsy and Fragile X syndrome. Zynerba is developing therapeutic medicines that utilize innovative transdermal technologies that, if successful, may allow for sustained and controlled delivery of therapeutic levels of CBD. Transdermal delivery of cannabinoids may have benefits over oral dosing because it allows the drug to be absorbed through the skin directly into the bloodstream. This avoids first-pass liver metabolism, potentially enabling lower dosage levels of active pharmaceutical ingredients with a higher bioavailability and improved safety profile. Transdermal delivery also

avoids the gastrointestinal tract, lessening the opportunity for GI related adverse events and the potential degradation of CBD by gastric acid into THC, which may be associated with unwanted psychoactive effects. Using an established pharmaceutical process for manufacturing, Zynerba replicates the CBD found in the Cannabis plant. We believe that this will allow us to meet stringent global regulatory agencies' standards while ensuring that we can efficiently supply the amount of product required to meet the demand of the markets that we are targeting.

About ZYN002

Zynerba's ZYN002 CBD gel is the first and only pharmaceutically-produced CBD formulated as a patent-protected permeation-enhanced transdermal gel and is being studied in children and adolescents with Fragile X syndrome and developmental and epileptic encephalopathies, and in adult epilepsy patients with focal seizures. ZYN002 is a clear, permeation-enhanced gel that is designed to provide controlled drug delivery transdermally with once- or twice-daily dosing.

About Zynerba Pharmaceuticals, Inc.

Zynerba Pharmaceuticals is the leader in pharmaceutically-produced transdermal cannabinoid therapies for rare and near-rare neuropsychiatric disorders. We are committed to improving the lives of patients and their families living with severe, chronic health conditions including Fragile X syndrome and refractory epilepsies. Learn more at www.zynerba.com and follow us on Twitter at @ZynerbaPharma

Cautionary Note on Forward-Looking Statements

This press release contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. We may, in some cases, use terms such as "predicts," "believes," "potential," "proposed," "continue," "estimates," "anticipates," "expects," "plans," "intends," "may," "could," "might," "will," "should" or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements. Such statements are subject to numerous important factors, risks and uncertainties that may cause actual events or results to differ materially from the Company's current expectations. Management's expectations and, therefore, any forward-looking statements in this press release could also be affected by risks and uncertainties relating to a number of other factors, including the following: the Company's cash and cash equivalents may not be sufficient to support its operating plan for as long as anticipated; the Company's ability to obtain additional funding to support its clinical development programs; the results, cost and timing of the Company's clinical development programs, including any delays to such clinical trials relating to enrollment or site initiation; clinical results for the Company's product candidates may not be replicated or continue to occur in additional trials and may not otherwise support further development in a specified indication or at all; actions or advice of the U.S. Food and Drug Administration and foreign regulatory agencies may affect the design, initiation, timing, continuation and/or progress of clinical trials or result in the need for additional clinical trials; the Company's ability to obtain and maintain regulatory approval for its product candidates, and the labeling under any such approval; the Company's reliance on third parties to assist in conducting pre-clinical and clinical trials for its product candidates; delays, interruptions or failures in the manufacture and supply of the Company's product candidates the Company's ability to commercialize its product candidates; the size and growth potential of the markets for the Company's product candidates, and the Company's ability to service those markets; the Company's ability to develop sales and marketing capabilities, whether alone or with potential future collaborators; the rate and degree of market acceptance of the Company's product candidates; and the Company's expectations regarding its ability to obtain and adequately maintain sufficient intellectual property protection for its product candidates. This list is not exhaustive and these and other risks are described in the Company's periodic reports, including the annual report on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K, filed with or furnished to the Securities and Exchange Commission and available at www.sec.gov. Any forward-looking statements that the Company makes in this press release speak only as of the date of this press release. The Company assumes no obligation to update forward-looking statements whether as a result of new information, future events or otherwise, after the date of this press release.

Investor Contacts

Will Roberts, VP Investor Relations and Corporate Communications
Zynerba Pharmaceuticals
484.581.7489
robertsw@zynerba.com

 [Primary Logo](#)

Source: Zynerba Pharmaceuticals, Inc.