



## Zynerba Pharmaceuticals Announces Positive Meeting with U.S. Food and Drug Administration and Plans to Conduct a Single Pivotal Study of ZYN002 in Fragile X Syndrome to Support an NDA Filing

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### Company Expects to Initiate Pivotal Study Mid-Year 2018 and Deliver Top-line Data in 2019

DEVON, Pa., March 05, 2018 (GLOBE NEWSWIRE) -- [Zynerba Pharmaceuticals](#), Inc. (NASDAQ:ZYNE), a clinical-stage specialty neuropsychiatric pharmaceutical company dedicated to developing and commercializing innovative pharmaceutically-produced transdermal cannabinoid treatments for rare and near-rare neurological and psychiatric disorders with high unmet medical needs, today announced the results of a positive meeting held with the U.S. Food and Drug Administration (FDA) regarding its planned development strategy for ZYN002 in Fragile X syndrome (FXS). FXS is a rare genetic developmental disability that is the leading known cause of both inherited intellectual disability and autism spectrum disorder.

ZYN002 is the first and only pharmaceutically-produced cannabidiol (CBD) formulated as a patent-protected permeation-enhanced transdermal gel. Zynerba has received U.S. Orphan Drug designation for the use of CBD as a treatment of FXS. Currently, there are no approved therapies to treat FXS or its most common symptoms.

Based on the company's dialogue with the FDA, the Company expects to initiate a single pivotal study mid-year 2018 to support a New Drug Application (NDA) for ZYN002 in FXS. The FDA and the Company are in agreement that the primary and key secondary endpoints for the study should assess observable behaviors in patients with FXS as reported by the caregiver using the validated Aberrant Behavior Checklist in Fragile X syndrome (ABC-FXS). If the pivotal trial meets its endpoints, approval for an indication encompassing the treatment of behavioral symptoms associated with Fragile X syndrome may be granted.

"The FDA meeting was an important milestone for us as we advance the development of ZYN002 for patients and their families suffering with the profound behavioral symptoms of Fragile X syndrome," said Armando Anido, Chairman and Chief Executive Officer of Zynerba. "We are pleased with the outcome of the discussion and the guidance on trial design, and believe we now have a path forward to advance the development of ZYN002 to an NDA. We look forward to initiating the pivotal study mid-year, and potentially providing FXS patients and their families an effective and well tolerated therapy to treat the complex behavioral symptoms of Fragile X syndrome."

Zynerba plans to initiate a pivotal 14-week randomized, double blind, placebo controlled clinical trial in approximately 200 pediatric and adolescent patients in the U.S., Australia and New Zealand. Patients will be randomized 1:1 to receive either one of two weight based doses of ZYN002, or one of two matching administrations of placebo. Zynerba anticipates initiation of this pivotal clinical trial mid-year 2018. Additional protocol details will be shared at that point. All patients will be eligible to enroll in a 12-month open label extension after completing dosing in the pivotal study.

"We believe that ZYN002 may address core behavioral symptoms of FXS and improve the quality of life for patients and their families," said Dr. Liza Squires, Zynerba's Chief Medical Officer. "There are currently no drugs indicated to address behavioral symptoms in the FXS population. We believe we have designed an efficient pivotal program that includes endpoints that measure clinically relevant and observable behaviors in patients with FXS, and if successful, positions us to bring the FXS community its first targeted treatment designed with patients' symptoms in mind."

#### 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 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, social anxiety and memory problems. In the US, there are about 71,000 patients suffering with FXS.

#### About Our Technology

Cannabinoids are a class of chemical compounds found in the Cannabis plant. The two primary cannabinoids contained in *Cannabis* are cannabidiol, or CBD, and ?9-tetrahydrocannabinol, or THC. Clinical and preclinical data support the potential for CBD in treating epilepsy and Fragile X syndrome, and THC has positive effects on treating symptoms of Tourette 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 and THC. 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 and THC 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 large 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 (NASDAQ:ZYNE) is a clinical-stage specialty pharmaceutical company dedicated to developing and commercializing innovative pharmaceutically-produced transdermal cannabinoid treatments for rare or near-rare neuropsychiatric diseases with high unmet medical needs. We are dedicated to improving the lives of people with severe health conditions by developing cannabinoid medicines designed to meet the rigorous efficacy and safety standards established by global regulatory agencies. Through the discovery and development of these potentially life-changing medicines, Zynerba seeks to improve the lives of patients battling severe, chronic health conditions including Fragile X syndrome, refractory epilepsies, Tourette Syndrome, and other neuropsychiatric disorders. Learn more at [www.zynerba.com](http://www.zynerba.com) and follow the Company 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. For example, there can be no guarantee that the Company will obtain approval for ZYN002 from the U.S. Food and Drug Administration (FDA) or foreign regulatory authorities; even if ZYN002 are approved, the Company may not be able to obtain the label claims that it is seeking from the FDA. In addition, the Company’s cash and cash equivalents may not be sufficient to support its operating plan for as long as anticipated. 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 success, cost and timing of the Company’s product development activities, studies and clinical trials; the success of competing products that are or become available; 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](http://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.

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