



## Zynerba Pharmaceuticals Announces Top-Line Results from Phase 2 STAR 1 Trial of ZYN002 in Adult Epilepsy Patients with Focal Seizures

August 7, 2017

**Company to host conference call and webcast today, August 7 at 8:30am ET**

DEVON, Pa., Aug. 07, 2017 (GLOBE NEWSWIRE) -- [Zynerba Pharmaceuticals](#), Inc. (NASDAQ:ZYNE), a clinical-stage specialty pharmaceutical company dedicated to developing and commercializing innovative transdermal pharmaceutically-produced cannabinoid treatments, today announced top-line results from its double-blind placebo controlled Phase 2 STAR 1 (Synthetic Transdermal Cannabidiol for the Treatment of Epilepsy) clinical trial evaluating ZYN002 (cannabidiol [CBD] gel) in adult epilepsy patients with focal seizures. ZYN002 did not demonstrate a statistically significant reduction of focal seizures during the treatment period compared to the baseline period for either the high or low dose cohorts compared to placebo.

"We are very disappointed that the STAR 1 trial did not meet its primary endpoint in this patient population," said Armando Anido, Chairman and Chief Executive Officer of Zynerba. "We are continuing to evaluate this study and the ongoing STAR 2 open label study to determine next steps with ZYN002 in adult epilepsy patients with focal seizures. I'd like to thank the patients, coordinators and investigators, as well as the development team at Zynerba, for their time and energies in conducting this very important trial."

Anido continued, "Importantly, today's results demonstrated ZYN002 to have a very favorable safety and tolerability profile, which is an encouraging fact as we look to develop ZYN002 as a treatment for a wide range of indications. We are excited that we will present top-line data from our ZYN002 STOP trial in osteoarthritis soon, followed by top-line data from our FAB-C study in Fragile X syndrome by the end of September."

In the double-blind, multi-center STAR 1 trial, 188 patients were randomized to receive (i) 195 mg of ZYN002 4.2% CBD gel every 12 hours, (ii) 97.5 mg of ZYN002 4.2% CBD gel every 12 hours or (iii) placebo gel every 12 hours for 12 weeks. Patients aged 18 to 71 years old with confirmed refractory epilepsy with focal seizures with or without secondary generalization were enrolled in this study. Enrolled patients had a median monthly seizure frequency of 10.6, and were on an average of 2.5 anti-epileptic drugs (AEDs). The primary endpoint assessed the median percentage change in seizure frequency over the 12-week treatment period compared to the 8-week baseline period. Secondary endpoints included proportion of patients with  $\geq 50\%$  reduction from baseline in seizure frequency, percent change from baseline in seizure frequency, change from baseline in seizure frequency, seizure-free days, and 100% seizure free. Safety and tolerability were also evaluated. The study was conducted at 14 sites in Australia and New Zealand. The efficacy analysis included 186 patients.

- **Primary Endpoint Data:** Patients on the low dose of ZYN002 (n=63) achieved an 18.4% median reduction in focal seizures during the treatment period compared to baseline; patients on the high dose of ZYN002 (n=62) achieved a 14.0% median reduction in focal seizures during the treatment period compared to baseline; and patients on placebo (n=63) achieved an 8.7% median reduction in focal seizures during the treatment period compared to baseline.
- **Secondary Endpoint Data:** None of the secondary endpoints showed statistically significant differences between ZYN002 and placebo.
- **Safety Data:** ZYN002 was shown to be very well tolerated and the safety profile was consistent with previously released data from the Phase 1 trials. Of the 188 patients in the safety database, 50% of the patients on ZYN002 (n=63) had at least one treatment emergent adverse event, compared to 41% (n=26) of patients on placebo. Two treatment emergent adverse events occurred in greater than 5% of the patients on ZYN002: fatigue (5.6%, placebo, 1.6%) and headache (5.6%, placebo, 3.2%). There were no treatment related serious adverse events reported. The discontinuation rate in the trial for ZYN002 was 10.4% compared to 1.6% in placebo.
- **Pharmacokinetic Data:** ZYN002 high and low dose median plasma concentrations were dose proportional, with the high dose levels being approximately two times the concentration of the low dose. Despite the dose proportionality, there was no correlation between plasma levels and efficacy.

### Additional studies of ZYN002

Zynerba is evaluating the utility of ZYN002 in other indications. Enrollment is complete in its Phase 2 STOP (Synthetic Transdermal Cannabidiol for Treatment of Knee Pain due to Osteoarthritis) study in patients with osteoarthritis, and in its exploratory Phase 2 FAB-C (Treatment of Fragile X Syndrome Anxiety and Behavioral Challenges with CBD) study in children with Fragile X syndrome (FXS). Delivery of top line data from these studies is on track for August and by the end of September 2017, respectively.

### Conference call information

Zynerba management will host a live conference call and webcast today at 8:30 am Eastern Time to discuss the results of this clinical trial. The call can be accessed by dialing (866) 573-0180 (U.S. and Canada) or (430) 775-1345 (international) and referencing conference ID 64535355. 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 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  $\Delta 9$ -tetrahydrocannabinol, or THC. Clinical and preclinical data support the potential for CBD in treating epilepsy, arthritis and Fragile X Syndrome, and THC has positive effects on treating pain. 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 chemical 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 gel and is being studied in adult epilepsy patients with focal seizures, in osteoarthritis and in children with Fragile X Syndrome. 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 dedicated to improving the lives of people with severe health conditions where there is a high unmet medical need by developing and commercializing pharmaceutically-produced transdermal cannabinoid medicines designed to meet the rigorous efficacy and safety standards established by global regulatory agencies. Through the discovery and development of these life-changing medicines, Zynerba seeks to improve the lives of patients battling severe, chronic health conditions including epilepsy, Fragile X syndrome, osteoarthritis, fibromyalgia and peripheral neuropathic pain. 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 or ZYN001 from the U.S. Food and Drug Administration (FDA) or foreign regulatory authorities; even if ZYN002 or ZYN001 are approved, the Company may not be able to obtain the label claims that it is seeking from the FDA 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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