Zynerba Pharmaceuticals Announces that Results from Phase 2 STOP Trial Support Continued Development of ZYN002 in Osteoarthritis

August 14, 2017

Zynerba to host conference call and webcast today, August 14 at 8:30 am ET

DEVON, Pa., Aug. 14, 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 reported top line results from its Phase 2 STOP (**S**ynthetic **T**ransdermal Cannabidi**o**l for Treatment of Knee **P**ain due to Osteoarthritis) clinical trial evaluating ZYN002 (cannabidiol [CBD] gel). The study did not meet its primary endpoint of reduction from baseline in the weekly mean of the 24-hour average worst pain score at week 12 for either dose. However, statistically significant results were achieved for a number of secondary endpoints. Importantly, the composite responder analysis (defined as a ≥30 percent reduction in worst average daily pain scores and a ≥20 percent improvement in the WOMAC physical function score) for 250 mg daily of ZYN002 4.2% CBD gel achieved statistical significance (p=0.016). A trend toward statistical significance was observed in other secondary endpoints.

“Many osteoarthritis patients using currently available medicines do not experience relief from pain and improved physical functioning, or cannot tolerate them due to side effects,” said Daniel Clauw, M.D., Professor of Pain Management and Anesthesiology at the University of Michigan, and Director of the Chronic Pain and Fatigue Research Center. “The STOP trial results are encouraging and suggest that ZYN002 can play an important role in impacting the pain and impaired physical function associated with osteoarthritis, with a well-tolerated safety profile. I am particularly impressed with the composite analysis result which accounts for both pain and physical function. I believe that ZYN002 may provide a promising treatment option for OA, and I look forward to participating in future studies.”

“The results from this study are very encouraging and for the first time suggest that CBD has a clinically meaningful impact in osteoarthritis, which affects approximately 31 million people in the United States,” said Armando Anido, Chairman and Chief Executive Officer of Zynerba. “In recent years, as the opioid epidemic has worsened, doctors, patients and their families have continued to emphasize the need for new, non-opioid pain medications, especially those with more favorable side effect profiles than NSAIDs or COX-2 inhibitors.”

Anido continued, “Data from the STOP trial will help shape future studies with ZYN002 in osteoarthritis. We will request an end of Phase 2 meeting with the U.S. Food and Drug Administration, which we believe will take place before the end of this year, and plan to move quickly to our pivotal Phase 3 program for ZYN002 in OA. I want to thank the participating patients, physicians, study coordinators, and the Zynerba team for their support of this important study.”

Three hundred and twenty (320) patients aged 41 to 78 years of age with confirmed osteoarthritis of the knee were randomized in the double-blind, multi-center STOP trial. Patients who completed the one-week washout and the seven-to-10-day baseline phase were randomized 1:1:1 to receive either 250 mg of ZYN002 4.2% CBD gel daily, 500 mg of ZYN002 daily, or placebo, for 12 weeks. Enrolled patients had a mean worst knee pain score of 6.9 on a scale of 1 to 10 during baseline.

- **Primary Endpoint Data:** Across all participants, patients on 250 mg of ZYN002 daily achieved a 2.64 mean reduction from baseline in average worst knee pain scores at week 12; patients on 500 mg of ZYN002 daily achieved a 2.83 mean reduction from baseline in average worst knee pain scores at week 12; and patients on placebo achieved a 2.37 mean reduction from baseline in average worst knee pain scores at week 12. These results were not statistically significant.
- **Secondary Endpoint Data:** Statistically significant results were achieved for a number of key secondary endpoints, including the composite responder analysis for 250 mg of ZYN002 daily (p=0.016), and the responder rate based on ≥30% reduction in worst pain severity at week 8 for 250 mg of ZYN002 daily (p=0.037). A trend toward statistical significance was observed in other secondary endpoints.
- **Post Hoc Analysis (Gender):** Men on 250 mg of ZYN002 daily achieved a 1.65 mean reduction from baseline in average worst knee pain scores at week 4 compared to a 1.19 mean reduction from baseline in men on placebo (p=0.156); a 2.30 mean reduction from baseline in average worst knee pain scores at week 8 compared to a 1.56 mean reduction from baseline in men on placebo (p=0.066); and a 2.68 mean reduction from baseline in average worst knee pain scores at week 12 compared to a 1.70 mean reduction from baseline in men on placebo (p=0.049). Females had a higher placebo rate and did not achieve significance in the endpoint.
- **Post Hoc Analysis (Pain Severity):** In an evaluation of patients with a baseline pain score of ≥7, there were 101 patients on ZYN002 and 48 patients in the placebo arm at baseline. Patients on ZYN002 achieved a 2.17 mean reduction from baseline in average worst knee pain scores at week 4 compared to a 1.6 mean reduction from baseline in patients on placebo (p=0.029); a 3.02 mean reduction from baseline in average worst knee pain scores at week 8 compared to a 2.22 mean reduction from baseline in patients on placebo (p=0.054); and a 3.29 mean reduction from baseline in average worst knee pain scores at week 12 compared to a 2.52 mean reduction from baseline in patients on placebo (p=0.086).
- **Safety Data:** ZYN002 was shown to be very well tolerated and the safety profile was consistent with previously released data from clinical trials. Of the patients in the safety database, 50% (n=106) of the patients on ZYN002 had at least one treatment emergent adverse event, compared to 42% (n=45) of patients on placebo. There were only two treatment

emergent/treatment related adverse events that exceeded 3% of the patients on ZYN002 and were greater than placebo: application site dryness (3.8%, n=8; placebo 0.9%, n=1) and headache (3.3%, n=7; placebo 1.9%, n=2). There was one (0.5%) treatment related serious adverse event on ZYN002 and three (2.8%) treatment related serious adverse events reported on placebo. Discontinuation from the study was 22.5% (n=48) for patients on ZYN002 and 33.6% (n=36) for patients on placebo. There were twelve (5.6%) patients that discontinued due to adverse events on ZYN002 and 8 (7.5%) that discontinued due to adverse events on placebo.

- **Pharmacokinetic Data:** ZYN002 500 mg and 250 mg daily dose median plasma concentrations were dose proportional, with the 500 mg dose levels being approximately two times the plasma concentration of the 250 mg dose.

Additional ongoing studies of ZYN002

Zynerba is also currently evaluating the utility of ZYN002 in its exploratory Phase 2 FAB-C (Treatment of **F**ragile X Syndrome **A**nxiety and **B**ehavioral Challenges with **C**BD) study in children with Fragile X syndrome (FXS). Top line data from this study are expected by the end of September 2017. In addition, epilepsy patients with focal seizures continue to be dosed in the 52-week STAR 2 (**S**ynthetic **T**ransdermal C**a**nnabidiol for the T**r**eatment of Epilepsy) open label extension trial.

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 70071749. 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 Osteoarthritis

Osteoarthritis is a degenerative joint disease that leads to wear and tear of the joints and affects the cartilage, joint lining, ligaments and bone. It is the most common form of joint disease and tends to occur most often in the hand joints, spine, hips, knees and great toes. It is characterized by the breakdown of the joint cartilage, bony changes in the joints and deterioration of the tendons and ligaments leading to pain and inflammation of the joint lining. Approximately 31 million patients in the US suffer from osteoarthritis.

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, 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 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. 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. 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.

Zynerba Contacts
Jim Fickenscher, CFO and VP Corporate Development
484.581.7483
fickenscherj@zynerba.com

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

Media contact
Theresa Dolge
Tonic Life Communications
Office: 215-928-2748
Theresa.Dolge@toniclc.com

Primary Logo

Zynerba Pharmaceuticals, Inc.