Zynerba Reports Positive Results for ZYN002 CBD Gel in Phase 1 Studies at 70th Annual Meeting of the American Epilepsy Society

December 5, 2016

ZYN002 CBD gel was shown to be safe and well-tolerated across range of doses tested in healthy subjects and adult epilepsy patients with focal seizures
No impairment in cognitive performance or changes in psychological health were observed

DEVON, Pa., Dec. 05, 2016 (GLOBE NEWSWIRE) -- Zynerba Pharmaceuticals, Inc. (NASDAQ:ZYNE), a clinical-stage specialty pharmaceutical company dedicated to the development of innovative transdermal synthetic cannabinoid treatments, today announced additional results from Phase 1 randomized, double-blind, placebo-controlled single and multiple ascending dose studies of ZYN002 cannabidiol (CBD) gel. These results, which assessed safety, tolerability, and effects on cognition and mood, of ZYN002 CBD gel in both healthy adults and adult epilepsy patients with focal seizures, were reported at the 70th Annual Meeting of the American Epilepsy Society (AES) in Houston, Texas. ZYN002 CBD gel is a patent-protected, synthetic CBD that is formulated as a permeation-enhanced gel for transdermal delivery in development for the treatment of epilepsy, osteoarthritis and Fragile X syndrome.

“In these first human clinical studies of CBD via transdermal delivery, we are very encouraged that results further demonstrated that ZYN002 CBD gel is safe and well-tolerated in both healthy subjects and adult epilepsy patients with focal seizures across a wide range of doses and concentrations,” said Armando Anido, Chairman and CEO of Zynerba. “Further, we did not observe any difference in cognitive performance or mood changes after treatment with ZYN002 CBD gel. Enrollment in our STAR 1 clinical trial in adult epilepsy patients with focal seizures is continuing and we remain on track to report top-line results in the first half of 2017.”

In a poster reported at AES, entitled *Neuropsychological Effects of ZYN002 (Synthetic Cannabidiol) Transdermal Gel in Healthy Subjects and Patients With Epilepsy: Phase 1, Randomized, Double-Blind, Placebo-Controlled Studies* (Poster #3.237), results from a Phase 1 randomized, double-blind, placebo-controlled single ascending dose study involving 32 healthy adults demonstrated that ZYN002 CBD gel was safe and well-tolerated at all dose levels ranging from 50 mg (n = 6), 100 mg (n = 6), 125 mg (n = 6) to 250 mg (n = 6), in comparison to placebo (n = 8), and demonstrated no impairment on the Trail Making test. In a seven-day multiple-dose study, healthy volunteers received ZYN002 CBD gel at doses of 200 mg (n = 6), 250 mg (n = 6), and 500 mg (n = 6) or placebo (n=6) and were assessed for neuro-cognitive effects based on several tests. On the Trail Making Test and Paced Auditory Serial Addition Task (PASAT), a test that measures working memory and focused attention, there were no effects of drug condition or drug-time interactions. These results indicate that ZYN002 did not produce impairment in critical areas of cognitive functioning that are often impacted by CNS drugs. In addition, there were no adverse changes in mood symptoms as assessed by the Inventory of Depression and Anxiety Symptoms (IDAS) and the Positive and Negative Affect Schedule (PANAS), indicating that ZYN002 CBD gel was not associated with any declines in these psychological measures.

In a second poster, entitled *Safety and Tolerability of ZYN002 (Synthetic Cannabidiol) Transdermal Permeation-Enhanced Gel in Healthy Subjects and Epilepsy Patients: Three Phase 1, Randomized, Double-Blind, Placebo-Controlled Studies* (Poster #2.214), results from three Phase 1 studies including a single ascending dose study, a seven-day multiple rising dose study and a 14-day repeat application study in healthy adults and epilepsy patients with focal seizures were reported. A total of 96 healthy adults and 22 epilepsy patients received 50 mg (n = 6), 100 mg (n = 6), 125 mg (n = 6), 200 mg (n=6), 250 mg (n = 43), 395 mg (n=8) 500 mg (n=12) and 504 mg (n=8) of ZYN002 CBD gel versus placebo (n=34). Studies tested once-daily and twice daily application of ZYN002 CBD gel at three concentrations of CBD (1%, 2.5%, and 4.2%, and four volumes of gel (4.7, 5, 6, and 10 g) Application was on clean, dry intact skin of the upper arms and shoulders or upper thighs. Standard safety measures across three studies included physical exams, vital signs, ECGs, safety labs, Columbia Suicide Severity Rating Scale (C-SSRS), adverse events and daily examination of skin for erythema at application site using a 5-point scale.

Transdermal application of ZYN002 administered once or twice daily was safe and well-tolerated at all dose levels tested. Mild, transient, application site events were common for both ZYN002 and placebo gel. Overall, the incidence of adverse events associated with ZYN002 CBD gel was similar to placebo in both healthy volunteers and adult epilepsy patients with focal seizures. After 14 days of ZYN002 administration, there were no reports of somnolence, fatigue or decreased appetite, with one gastrointestinal adverse event reported (nausea). There were also no clinically significant drug related changes during physical exams, on ECG, in vital signs, or in clinical labs.

ZYN002 CBD gel is being evaluated in the ongoing STAR1 (**S**ynthetic **T**ransdermal C**a**nnabidiol for the T**r**eatment of Epilepsy) Phase 2 multi-center, double-blind, placebo-controlled, multi-dose clinical trial designed to evaluate the efficacy and safety of ZYN002 in patients with refractory focal seizures. Enrollment is continuing and top-line results are anticipated in the first half of 2017. A multi-center, open-label extension clinical trial, STAR 2, for ZYN002 CBD gel has also launched allowing epilepsy patients with refractory focal seizures who complete the STAR 1 study to receive treatment with ZYN002 CBD gel for up to 52 weeks. A second Phase 2 clinical trial of ZYN002 CBD gel, STOP (**S**ynthetic **T**ransdermal Cannabidi**o**l for the Treatment of Knee **P**ain due to Osteoarthritis (OA)), is enrolling patients and is also expected to report top-line results in the first half of 2017. Initiation of a third Phase 2 clinical trial of ZYN002 CBD gel in patients with Fragile X syndrome is planned before year-end 2016 and top line results are anticipated to be released in the first half of 2017.

To view the posters reported at the Annual Meeting of the American Epilepsy Society, please click here for access to the Publications portion of the Zynerba website.

About ZYN002 CBD Gel
Zynerba’s ZYN002 CBD gel is the first and only synthetic CBD formulated as a patent-protected permeation-enhanced gel and is being studied in refractory epilepsy, Fragile X syndrome and osteoarthritis. ZYN002 is a clear, permeation-enhanced gel that is designed to provide consistent,

controlled drug delivery transdermally with convenient twice-daily dosing. Transdermal therapeutics are absorbed through the skin directly into the systemic circulation, avoiding first-pass liver metabolism and potentially enabling lower dosage levels of active pharmaceutical ingredients and rapid and reliable absorption with high bioavailability. In addition, transdermal delivery avoids the gastrointestinal tract and potential stomach acid degradation of CBD into THC (associated with psychoactive effects), as demonstrated in a Zynerba in vitro study.

About Epilepsy
Epilepsy is a disease characterized by an enduring predisposition to generate epileptic seizures (transient symptoms due to abnormal neuronal activity in the brain) and by the neurobiological, cognitive, psychological and social consequences of the condition. Focal seizures usually start in a small area of the temporal lobe or frontal lobe of the brain and quickly involve other areas of the brain that affect alertness and awareness. Approximately 2.2 million patients in the United States and 3.1 million in Europe and Japan battle epilepsy. Focal seizures are the most common type of seizure, with 1.5 million of the 2.2 million adults with epilepsy in the US suffering from focal seizures.

About Zynerba Pharmaceuticals, Inc.
Zynerba Pharmaceuticals (NASDAQ:ZYNE) is a clinical-stage specialty pharmaceutical company focused on developing and commercializing proprietary next-generation synthetic cannabinoid therapeutics formulated for transdermal delivery. Zynerba is developing therapeutic candidates based on proprietary transdermal technologies that, if successfully developed, may allow sustained, consistent and controlled delivery of therapeutic levels of two cannabinoids: cannabidiol (CBD), a non-psychoactive cannabinoid, and tetrahydrocannabinol (THC). Transdermal delivery has the potential to reduce adverse effects associated with oral dosing. ZYN002, the Company's CBD gel, is the first and only synthetic CBD formulated as a patent protected permeation-enhanced gel. In June 2016, the company initiated the Phase 2 STAR1 (Synthetic Transdermal Cannabidiol for the Treatment of Epilepsy) clinical trial of ZYN002 CBD gel in adult refractory epilepsy patients with focal seizures and has also launched the STAR2 open-label extension trial which allows patients who complete STAR1 to receive treatment with ZYN002 gel for up to 52 weeks. In August 2016, the Phase 2 STOP (Synthetic Transdermal Cannabidiol for the Treatment of Knee Pain due to Osteoarthritis) clinical trial in patients with knee pain due to OA was initiated. A Phase 2 clinical trial in Fragile X syndrome (FXS) is expected to initiate in the second half of 2016. Zynerba is also developing ZYN001, which utilizes a synthetically manufactured pro-drug of THC. A Phase 1 clinical trial for ZYN001 is planned to begin in the first half of 2017. 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. 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. These and other risks are described in the Company's periodic reports, including the annual report on Form 10K, quarterly reports on Form 10Q 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.

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