Zynerba Pharmaceuticals Provides Clinical Update and Announces Two New Clinical Indications

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- Company Will Focus on Four Childhood Neuropsychiatric Disorders: FXS, DEE, Autism Spectrum Disorder and 22q11.2 Deletion Syndrome -

- Cash Runway Now Extends into the Second Half of 2020 -

- Conference Call to be Held Today at 8:30 am Eastern Time -

DEVON, Pa., Dec. 17, 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 provided an update on its clinical progress.

- Zynerba remains on track to report top line results from the CONNECT-FX (**C**linical study **o**f Ca**nn**abidiol (CBD) in Childr**e**n and Adoles**c**en**t**s with **F**ragile **X**) study in Fragile X Syndrome in the second half of 2019;
- The Company has completed enrollment in its Phase 2 BELIEVE 1 (Open La**b**el Study to Assess the Safety and **E**fficacy of ZYN002 Administered as a Transdermal Ge**l** to Ch**i**ldren and Adol**e**scents with De**v**elopmental and **E**pileptic Encephalopathy) clinical trial in children and adolescents with developmental and epileptic encephalopathies (DEE). Top-line results will be reported in the third quarter of 2019;
- Zynerba has expanded its pipeline with the addition of two new childhood neuropsychiatric clinical targets for ZYN002: Autism Spectrum Disorder (ASD) and 22q11.2 Deletion Syndrome (22q Deletion Syndrome; 22q), a rare genetic syndrome leading to significant impairments, including neuropsychiatric disorders. The Company expects to initiate open label Phase 2 studies in these indications in the first half of 2019 and report top-line results in first half 2020;
- The Company has postponed the initiation of its clinical trial in adult epilepsy until after the completion of the four childhood neuropsychiatric studies; and
- As a result, Zynerba expects to extend its cash runway into the second half of 2020.

“Our aspirations and expectations are clear: To work closely with the U.S. Food and Drug Administration to expand the opportunity for pharmaceutically-developed CBD treatments that meet their rigorous medical and manufacturing standards, and in doing so, continue toward our goal of addressing significant unmet medical needs in neuropsychiatric disorders,” said Armando Anido, Chairman and Chief Executive Officer of Zynerba. “With the new indications of ASD and 22q, in addition to FXS and DEE, we now have four shots on goal to show the clinical benefit of ZYN002 transdermal gel in patient populations that have few, if any, therapeutic options available.”

Fragile X Syndrome Pivotal Data Expected in 2H2019

Enrollment is progressing in CONNECT-FX, a pivotal, multi-national, randomized, double blind, placebo-controlled study evaluating the efficacy and safety of ZYN002 in three through 17-year old FXS patients with full mutation of the FMR1 gene. 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. Clinical investigative sites are enrolling patients in the United States, Australia, and New Zealand. Patients who have completed the double-blind phase are now enrolling into the 12-month open label phase. The Company is on track to report top line data in the second half of 2019; there are currently no approved products indicated for FXS.

Completion of Enrollment in BELIEVE 1

The Company has completed enrollment in BELIEVE 1, an open label multi-dose Phase 2 clinical trial evaluating the efficacy and safety of ZYN002 in children and adolescents (three through 17 years) with developmental and epileptic encephalopathies (DEE), as classified by the International League Against Epilepsy (ILAE) (Scheffer et al. 2017). Children and adolescents with a variety of DEEs have been enrolled in BELIEVE 1 from sites in Australia and New Zealand. Once completing a four-week baseline period to determine seizure frequency, patients are treated with ZYN002 for 26 weeks, initially receiving weight-based doses of 250 mg or 500 mg daily of ZYN002 CBD gel during a two-week titration period, followed by maintenance doses of 250 mg up to 1,000 mg daily for 24 weeks. The primary efficacy assessment is reduction in seizure frequency at week 26 compared to baseline. Patients successfully completing the study may elect to enter a 6-month extension study. The Company expects to announce topline data from this study in the third quarter of 2019.

DEE is a heterogeneous group of rare and ultra-rare epilepsy syndromes that manifest with seizures, behavioral disturbances, or EEG abnormalities that can directly worsen cognition and behavior. These disorders are often progressive and are highly resistant to treatment. The syndromes involve significant developmental impairment (developmental encephalopathies) or regression of developmental progress (epileptic encephalopathies). DEEs include a number of epilepsy syndromes, including Doose, Dravet, Lennox-Gastaut, and Ohtahara (early infantile epileptic encephalopathy); and early-onset epilepsy syndromes caused by variants of genes including SYNGAP1 and SCN1A, among others.

Autism Spectrum Disorder (ASD) in Pediatric Patients

ASD is a developmental disability defined by anxiety, the presence of restricted, repetitive patterns of behaviors, impairments in social communication and interactions, deficits in verbal and non-verbal communication, and deficits in developing, understanding and maintaining relationships. This near-rare neuropsychiatric disorder affects approximately one million pediatric and adolescent patients (five to 17 years of age) in the U.S. Recent studies suggest that ASD may be associated with a disruption in the endocannabinoid system; clinical and anecdotal data show that modulation of the endocannabinoid system with CBD has shown therapeutic potential in ameliorating certain behaviors associated with ASD, including social avoidance

and anxiety. The Company expects to initiate an open label Phase 2 study in pediatric patients with ASD in Australia in the first half of 2019.

22q11.2 Deletion Syndrome (22q)
22q is the most common chromosomal known contiguous gene deletion syndrome. This syndrome is associated with congenital anomalies, cognitive deficits, and neuropsychiatric symptoms including anxiety disorders, ADHD, developmental delays, cognitive impairment and psychoses. Early onset of neuropsychiatric symptoms disrupts development and quality of life, and is thought to heighten the risk of development of psychotic disorders later in life. This rare disorder affects approximately 81,000 patients in the U.S. CBD may treat the neuropsychiatric symptoms of 22q due its activity as an agonist at serotonin 1A receptors, an antagonist at GPR55 receptors, and a modulator of the endocannabinoid system. The Company expects to initiate an open label Phase 2 study in pediatric patients with 22q in Australia in the first half of 2019.

Adult Refractory Focal Epilepsy
The Company will postpone the initiation of its planned Phase 2B study of ZYN002 in adult refractory focal seizures until after reporting data from the four childhood neuropsychiatric studies.

Financial Outlook
Management believes its current cash and cash equivalent position is sufficient to fund operations and capital requirements into the second half of 2020, past data readouts from the CONNECT-FX pivotal trial in Fragile X Syndrome, the BELIEVE 1 Phase 2 trial in DEE, and the planned Phase 2 trials in both ASD and 22q.

Conference call information
Zynerba management will host a live conference call and webcast today at 8:30 am Eastern Standard Time to provide a corporate update. The call can be accessed by dialing (866) 573-0180 (U.S. and Canada) or (430) 775-1345 (international) and referencing conference ID 6892856. 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 ZYN002
Zynerba's ZYN002 CBD gel is the first and only pharmaceutically-manufactured CBD formulated as a patent-protected permeation-enhanced clear gel, designed to provide controlled drug delivery into the bloodstream transdermally (i.e. through the skin).

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 a heterogeneous group of rare and ultra-rare epilepsies known as developmental and epileptic encephalopathies (DEE). 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.

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