Zynerba Pharmaceuticals Presents Data Supporting FMR1 Methylation Status as a Correlate to Fragile X Syndrome Severity at the Virtual Joint 16th International Child Neurology Congress (ICNC) & 49th Annual Child Neurology Society (CNS) Meeting

October 15, 2020

DEVON, Pa., Oct. 15, 2020 (GLOBE NEWSWIRE) -- Zynerba Pharmaceuticals, Inc. (NASDAQ:ZYNE), the leader in innovative pharmaceutically-produced transdermal cannabinoid therapies for rare and near-rare neuropsychiatric disorders, is presenting a poster describing data 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**) trial describing the role of *FMR1* methylation status in children and adolescents with Fragile X syndrome (FXS) as a correlate to disease severity and as a prognostic biomarker. These data are being presented at the virtual Joint 16th International Child Neurology Congress (ICNC) & 49th Annual Child Neurology Society (CNS) Meeting. These data will also be presented as an oral presentation during the "Research Pipeline: New Findings on Diagnostic and Therapeutics" session of the virtual American Academy of Child and Adolescent Psychiatry (AACAP) 2020 Annual Meeting on Friday, October 23rd, 2020.

Figure 1: Greater Percentages of Participants Achieved Meaningful Change in ABC-CFXS Social Avoidance and Irritability with ZYN002 vs Placebo

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A copy of the poster entitled, "*ZYN002 Cannabidiol Transdermal Gel in Children and Adolescents With Fragile X Syndrome: Role of Methylation Status as a Correlate to Disease Severity and as a Prognostic Biomarker*" is available on the Zynerba corporate website at http://zynerba.com/publications/.

"We are excited to provide an update on the potential role of methylation status of the *FMR1* gene as a predictive biomarker of preferential response to Zygel™ (ZYN002) in the treatment of the behavioral symptoms of FXS," said Zynerba's Chief Medical Officer, Joseph M. Palumbo, MD, FAPA, MACPsych. "These new data demonstrate that in patients diagnosed with FXS with a fully methylated *FMR1* gene significantly more patients who received Zygel achieved a clinically meaningful improvement in their behavioral symptoms compared to patients who received placebo."

CONNECT-FX is a randomized, double-blind, multinational, 14-week pivotal study to evaluate the efficacy and safety of Zygel in children/adolescents aged 3 to 17 years. Although the CONNECT-FX full analysis set did not achieve statistical significance in its endpoints, building on current scientific evidence, a pre-planned ad hoc analysis of patients having at least 90% methylation ("full methylation" or FMet) of the impacted *FMR1* gene, representing 80% of the overall study population, was performed. The results, including the achievement of statistical significance (p=0.020) in the primary endpoint of improvement at 12 weeks of treatment in the Social Avoidance subscale of the ABC-C_{FXS} compared to placebo, suggest that Zygel may have benefit in patients with full methylation of the *FMR1* gene.

Zynerba utilized psychometric analyses to determine what constitutes a clinically meaningful change from baseline as measured by subscales of the ABC-C_{FXS}. New results described today include the results of these analyses which support the definition of a clinically meaningful treatment response over 12 weeks of treatment as an improvement of three points or greater for the Social Avoidance subscale, nine points or greater for the Irritability subscale, and five points or greater for the Socially Unresponsive / Lethargic subscale. The Company determined that 58.2% of FMet patients receiving Zygel achieved a clinically meaningful change in their socially avoidant behavior compared to 40.6% of patients receiving placebo (statistically significant; p=0.031), and 40.3% of patients receiving Zygel achieved a clinically meaningful change in Irritability compared to 23.8% of patients receiving placebo (statistically significant; p=0.036).

Figure 1: Greater Percentages of Participants Achieved Meaningful Change in ABC-C_{FXS} Social Avoidance and Irritability with ZYN002 vs Placebo

https://www.globenewswire.com/NewsRoom/AttachmentNg/d8cf2270-883e-4618-9515-82b29393a6dc

The authors of the poster concluded that:

- To our knowledge, CONNECT-FX is the largest controlled study ever performed in FXS.
- These results may represent an important step forward in biomarker-driven prediction of response in FXS and neuroscience.
    - Zygel was well tolerated, and the safety profile was consistent with previously reported clinical trials.
    - In the FMet group, Zygel was superior to placebo in multiple analyses, including:
        - Statistically significant mean change in Social Avoidance vs placebo;
        - Proportion of patients attaining threshold of clinically meaningful change in Social Avoidance and Irritability;
        - Caregiver reported improvements, including statistically significant improvements in Social Avoidance and Isolation, Social Interaction, and Irritable and Disruptive Behaviors.
- Zynerba will be meeting with the FDA in the fourth quarter of 2020 to discuss these data.

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, autism spectrum disorder, 22q11.2 deletion syndrome, and a heterogeneous group of rare and ultra-rare epilepsies known as developmental and epileptic encephalopathies. 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; the Company’s expectations regarding its ability to obtain and adequately maintain sufficient intellectual property protection for its product candidates; the timing and outcome of current and future legal proceedings; and the extent to which health epidemics and other outbreaks of communicable diseases, including COVID-19, could disrupt our operations or adversely affect our business and financial conditions. 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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