# Zynerba Pharmaceuticals Announces that Enrollment is Nearing Completion in Pivotal CONNECT-FX Trial in Fragile X Syndrome

January 13, 2020

**– Company Confirms Expectation of Topline Results in the Second Quarter of 2020 –**

DEVON, Pa., Jan. 13, 2020 (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 the pivotal 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 of Zygel™ in children and adolescents with Fragile X syndrome (FXS) in advance of this week's investor meetings in San Francisco.

Enrollment is nearing completion in CONNECT-FX, a pivotal, multi-national, randomized, double blind, placebo-controlled trial evaluating the efficacy and safety of Zygel in treating common behavioral symptoms of FXS in three through 17-year old patients with FXS. As of January 10, 2020, 178 patients of the 204 targeted for enrollment in the trial have been randomized into the trial. There are also 15 patients who have been screened but not yet randomized. The Company anticipates that screening for the trial will close near the end of January.

"We have made great progress throughout our pipeline in recent months," said Armando Anido, Chairman and Chief Executive Officer of Zynerba. "We are nearing completion of enrollment in our pivotal CONNECT-FX study in patients with Fragile X syndrome, and we expect to report results from this trial late in the second quarter of 2020. We believe that the prospective inclusion criteria have enabled us to execute on a rigorous clinical trial of Zygel in a more severely impacted population of children and adolescents than included in our Phase 2 FAB-C study, which should enhance the study's ability to demonstrate a strong signal of activity and minimize response variability. With key milestones expected from each of our clinical programs in the first half of this year, 2020 has the potential to be a compelling and exciting year."

*Baseline Data for Patients Randomized Through January 10, 2020*

The primary endpoint for this trial 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. Key secondary endpoints include the change from baseline to the end of the treatment period in the ABC-$C_{FXS}$ Irritability subscale score, and the ABC-$C_{FXS}$ Socially Unresponsive/Lethargic subscale score and the Clinical Global Impression – Improvement scale (CGI-I) anchored to FXS behaviors evaluated at the end of the treatment period.

As intended and prospectively designed, the trial has enrolled a more severely affected population than that enrolled in the previously completed Phase 2 FAB-C trial as measured by baseline behavioral symptoms, enabling the study to potentially demonstrate the anticipated full range of efficacy of Zygel in several behavioral domains. The ABC-$C_{FXS}$ mean baseline scores for patients randomized through January 10, 2020 in the CONNECT FX trial in comparison to the FAB-C trial are as follows (higher baseline scores denote more severe behaviors):

- Social Avoidance subscale (primary endpoint): 7.2 in CONNECT-FX vs 5.1 in FAB-C;
- Irritability subscale (key secondary endpoint): 28.1 in CONNECT-FX vs 18.2 in FAB-C;
- Socially Unresponsive/Lethargic subscale (key secondary endpoint): 13.2 in CONNECT-FX vs 8.7 in FAB-C;
- Hyperactivity subscale: 18.5 in CONNECT-FX vs 14.5 in FAB-C;
- Stereotypy subscale: 9.4 in CONNECT-FX vs 7.9 in FAB-C; and
- Inappropriate Speech subscale: 6.9 in CONNECT-FX vs 6.1 in FAB-C.

During screening, caregivers of patients in the trial are informed that their participating child may have the opportunity to receive Zygel in an open label extension trial following the child's compliant completion of CONNECT-FX, regardless of their child's perceived response or actual blinded drug assignment in CONNECT-FX. To date, 96% of the 141 patients who have completed CONNECT-FX have enrolled in the open label extension trial.

Of the 178 patients randomized as of January 10, 2020, 135 (76%) are male and the mean age in the study is 9.6 years.

The Company expects to disclose topline results of this study late in the second quarter of 2020. If the results are positive, the Company expects to meet with the U.S. Food and Drug Administration (FDA) to determine acceptability of the data as a basis to submit its New Drug Application (NDA) for Zygel in FXS in the second half of 2020, with potential approval by mid-year 2021.

***Other Corporate Updates***

- As announced in a separate press release earlier this morning, the Company has achieved its enrollment target of 36 patients in the Phase 2 BRIGHT trial of Zygel for the treatment of pediatric and adolescent patients with autism spectrum disorder (ASD). Topline results are expected in the second quarter of 2020;
- Zynerba remains on track to report top line results from the Phase 2 INSPIRE study of Zygel in 22q11.2 deletion syndrome (22q) in the second quarter of 2020;
- The Company expects to meet with the FDA in the first half of 2020 to discuss the clinical path forward for Zygel in the treatment of developmental and epileptic encephalopathies (DEE);
- As of September 30, 2019 Zynerba had $77.5 million in cash and cash equivalent, which it believes is sufficient to fund its

operations and capital requirements into the second half of 2021.

**About Zygel™**
Zygel (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). Recent studies suggest that Fragile X syndrome (FXS) and other neuropsychiatric conditions including ASD may be associated with a disruption in the endocannabinoid (EC) system. Clinical and anecdotal data suggest that CBD may modulate the EC system and improve certain core social and behavioral autism-related symptoms, including social avoidance and anxiety.

**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. For example, there can be no guarantee that the Company will obtain approval for Zygel from the U.S. Food and Drug Administration (FDA) or foreign regulatory authorities; even if Zygel is 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 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 FDA 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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