Zynerba Pharmaceuticals to Present an Update on the Zygel™ Development Program at the 17th NFXF International Fragile X Conference Research Roundup

July 22, 2020

- New Data Show Statistically Significant Improvements in Caregiver Impression of Change in Fragile X Behaviors Including Social Avoidance in Patients with Fully Methylated FMR1 genes -

DEVON, Pa., July 22, 2020 (GLOBE NEWSWIRE) -- Zynerba Pharmaceuticals, Inc. (NASDAQ:ZYNE), the leader in innovative pharmaceutically-produced transdermal cannabinoid therapies for rare and near-rare neuropsychiatric disorders, will present an overview of its Zygel™ (ZYN002) development program in Fragile X syndrome (FXS) and additional caregiver-reported data from its 14-week 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 during the 17th NFXF International Fragile X Conference Research Roundup. The multi-national, randomized, double-blind, placebo-controlled trial assessed the efficacy and safety of Zygel™ CBD gel as a treatment for behavioral symptoms of Fragile X syndrome (FXS) in 212 patients; topline results were announced on June 30, 2020. (Press release).

The presentation entitled, “Zygel (ZYN002) Development Program in Fragile X Syndrome” will take place at 3:45PM ET today, July 22, 2020. Additional information on the conference and registration are available here: https://fragilex.org/get-involved/international-fragilex-conference/. A copy of today’s presentation will be made available prior to the time of presentation on the Zynerba corporate website at http://zynerba.com/publications/.

“I am very pleased to participate in today’s Fragile X Research Roundup on Fragile X Awareness Day,” said Joseph M. Palumbo, MD, FAPA, MACPsych, Chief Medical Officer of Zynerba. “We believe that the caregiver data that we are presenting today further support the statistically significant improvement we achieved in the primary endpoint of social avoidance in patients with full methylation of their FMR1 gene. We look forward to discussing these and other data with the U.S. Food and Drug Administration as soon as possible regarding a potential regulatory path forward.”

Qualitative Caregiver Reported Behavioral Survey

Figure 1. Results of Qualitative Caregiver Reported Behavioral Survey

Caregiver Global Impression - Change from Baseline to Week 12

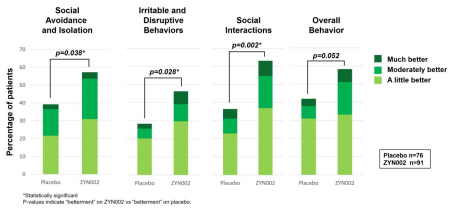

Figure 2. Results of Caregiver Impression - Change: Full Methylation Group

Qualitative Caregiver Reported Behavioral Survey

Consistent with guidance from the FDA on capturing the voice of the patient in drug development, the Company collected qualitative data on the importance of various FXS behaviors to caregivers entering the trial. Utilizing the Qualitative Caregiver Reported Behavioral Survey, caregivers were asked to describe their most important behavioral challenges at baseline. The results of the survey indicate that caregivers found anxiety, socially avoidant behaviors (including elopement and isolation seeking), and disruptive behaviors (including aggression and temper tantrums) to be the most challenging.

Figure 1. Results of Qualitative Caregiver Reported Behavioral Survey is available at https://www.globenewswire.com/NewsRoom/AttachmentNg/67243db8-e2cb-48f4-9ba9-71f82b6355c8

Caregiver Global Impression - Change from Baseline to Week 12

Using the Caregiver Global Impression - Change survey, caregivers were asked to complete a questionnaire rating how their child’s behavior changed with respect to social avoidance and isolation, irritable and disruptive behaviors, social interactions, and the child’s overall behavior at the end of the 12 week treatment period compared to the beginning of the trial, utilizing a seven point scale from ‘much worse’ to ‘much better’. The results of this survey show a broad shift toward global improvement from baseline to week 12 for patients with full methylation of their FMR1 gene (FMet patients), with three of the four behavioral domains showing a statistically significant change in favor of patients on Zygel and the fourth domain trending toward significance.

Figure 2. Results of Caregiver Impression - Change: Full Methylation Group is available at https://www.globenewswire.com/NewsRoom/AttachmentNg/87e1db62-97e8-4dc6-9655-db036a073f20

These statistically significant Caregiver Global Impression - Change data in socially avoidant behavior support the statistically significant improvement observed in the CONNECT-FX primary endpoint of social avoidance in FMet patients who received Zygel compared to placebo (p=0.020).

About Fragile X Syndrome (FXS)

Fragile X syndrome is a rare genetic developmental disability that is the leading known cause of both inherited intellectual disability and autism spectrum disorder, affecting 1 in 3,600 to 4,000 males and 1 in 4,000 to 6,000 females. It is the most common inherited intellectual disability in males and a significant cause of intellectual disability in females, and the leading genetic cause of autism spectrum disorder (ASD). The disorder negatively affects synaptic function, plasticity and neuronal connections, and results in a spectrum of intellectual disabilities and behavioral symptoms, such as

social avoidance and irritability. In the US, there are about 71,000 people suffering with FXS, approximately 60% of whom have full methylation of the FMR1 gene.

FXS is caused by a mutation in FMR1, a gene which modulates a number of systems, including important effects on the endocannabinoid system, and most critically, codes for a protein called FMRP. This protein helps regulate the production of other proteins and plays a role in the development of synapses, which are critical for relaying nerve impulses, and in regulating synaptic plasticity. The FMR1 mutation manifests as multiple repeats of a DNA segment, known as the CGG triplet repeat. In most neurotypical people, the FMR1 gene correctly codes for the FMRP protein. In neurotypical individuals, there are CGG repeats, but these repeats only occur between 5 and 40 times. As a result, FMRP is manufactured at levels that enable control over behaviors like social avoidance and anxiety. In people with full mutation of the Fragile X gene, the CGG segment is repeated more than 200 times and in most cases causes the FMR1 gene to not function. However, the methylation of the FMR1 gene also plays a role in determining functionality of the gene. At greater than 90% methylation, which is considered “full methylation”, the FMR1 gene is silenced, therefore, no FMRP is produced, and the systems and processes that are expected to be affected by FMRP become dysregulated.

People with genetically confirmed full mutation Fragile X and full methylation of their FMR1 gene are generally the most severely impacted by the disorder.

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.

Zynerba Contact
William Roberts, Vice President, Investor Relations and Corporate Communications
Zynerba Pharmaceuticals
484.581.7489
robertsw@zynerba.com

Media contact
Molly Devlin
Evoke KYNE
215.928.2199
Molly.Devlin@evokegroup.com