Zynerba Pharmaceuticals Announces New Two-Year Data from Open Label Extension of the Phase 2 FAB-C Trial in Patients with Fragile X at 2020 American Academy of Neurology (AAN) Science Highlights Virtual Session

May 26, 2020

- Robust Response Sustained through Two Years of Treatment with Zygel™ in Patients from Phase 2 FAB-C Trial -

- Top Line Results of Pivotal CONNECT-FX Trial Expected Late in the Second Quarter of 2020 -

DEVON, Pa., May 26, 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 announced the availability of a poster describing 116-week (two-year) data from the Phase 2 FAB-C (Treatment of **F**ragile X Syndrome **A**nxiety and **B**ehavioral **C**hallenges with CBD) trial of Zygel™ (CBD transdermal gel; ZYN002) in pediatric and adolescent patients with Fragile X syndrome (FXS). The data in the poster show that the statistically significant improvements from baseline that were observed at week 12 were sustained in each subscale score of the Aberrant Behavior Checklist for Fragile X (ABC-C_{FXS}) through two years for patients who participated in the open label extension.

The poster entitled *Cannabidiol Transdermal Gel for the Treatment of Fragile X Syndrome: Post Hoc Analysis and Pattern of Efficacy on Domains of the Aberrant Behavior Checklist-Community for FXS (ABC-C_{FXS}) Through 116 Weeks of Treatment* is available at the 2020 American Academy of Neurology (AAN) Science Highlights Virtual Session. The Virtual Session is online at http://www.aan.com/2020science. A copy of the poster is also available on the Zynerba corporate website at http://zynerba.com/publications/.

“It’s very exciting to see that the observed early benefits of Zygel appear to be sustained for over two years in patients who enrolled in the open label extension of FAB-C; these data suggest the potential for a sustained and measurable benefit for those patients who experience an early response,” said Zynerba’s Chief Medical Officer, Joseph M. Palumbo, MD, FAPA, MACPsych. “It’s also reassuring to see these responses in the context of a strong tolerability profile. We look forward to the results of our pivotal CONNECT-FX study in children and adolescents with FXS late this quarter.”

Open Label Phase 2 FAB-C Trial Background

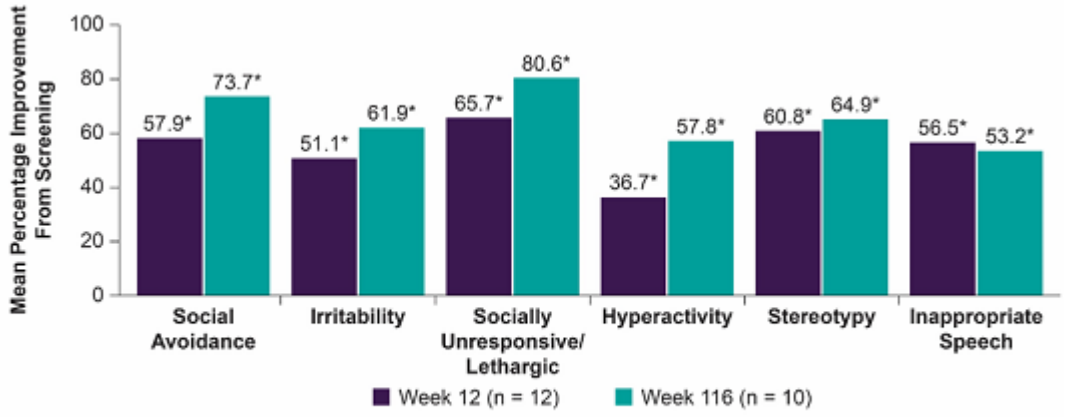
The 12-week treatment results of the Phase 2 FAB-C trial were initially announced in September 2017. These data were published in the August 2nd, 2019 online edition of *Journal of Neurodevelopmental Disorders*. (Press release)

Twenty patients aged 6 to 17 years of age with Fragile X as confirmed by molecular documentation of FMR1 full mutation were enrolled in the open label FAB-C study. Zygel was added on to other medications being administered. At the completion of the 12-week study (Period 1), patients could enter an extension study (Period 2).

Thirteen patients who completed the Period 1 rolled into Period 2. One patient who withdrew during Period 2 for reasons unrelated to safety or efficacy had no efficacy data post week 12 and therefore was not included in the analyses. Ten patients exceeded two years of therapy.

Sustained Improvement in Core FXS Behaviors over Two Years of Treatment with Zygel

Statistically significant improvements from baseline were observed at week 12 in all six subscale scores of the ABC-C_{FXS} in Period 1 and these statistically significant improvements were sustained through two years in subjects who entered Period 2. The persistence of effect over the two-year period is as follows.



ABC-C_{FXS}, Aberrant Behavior Checklist-Community for FXS.
*P < 0.05 for mean change from screening in subscale score.
P values were calculated by within group t test (null hypothesis: no change from baseline).

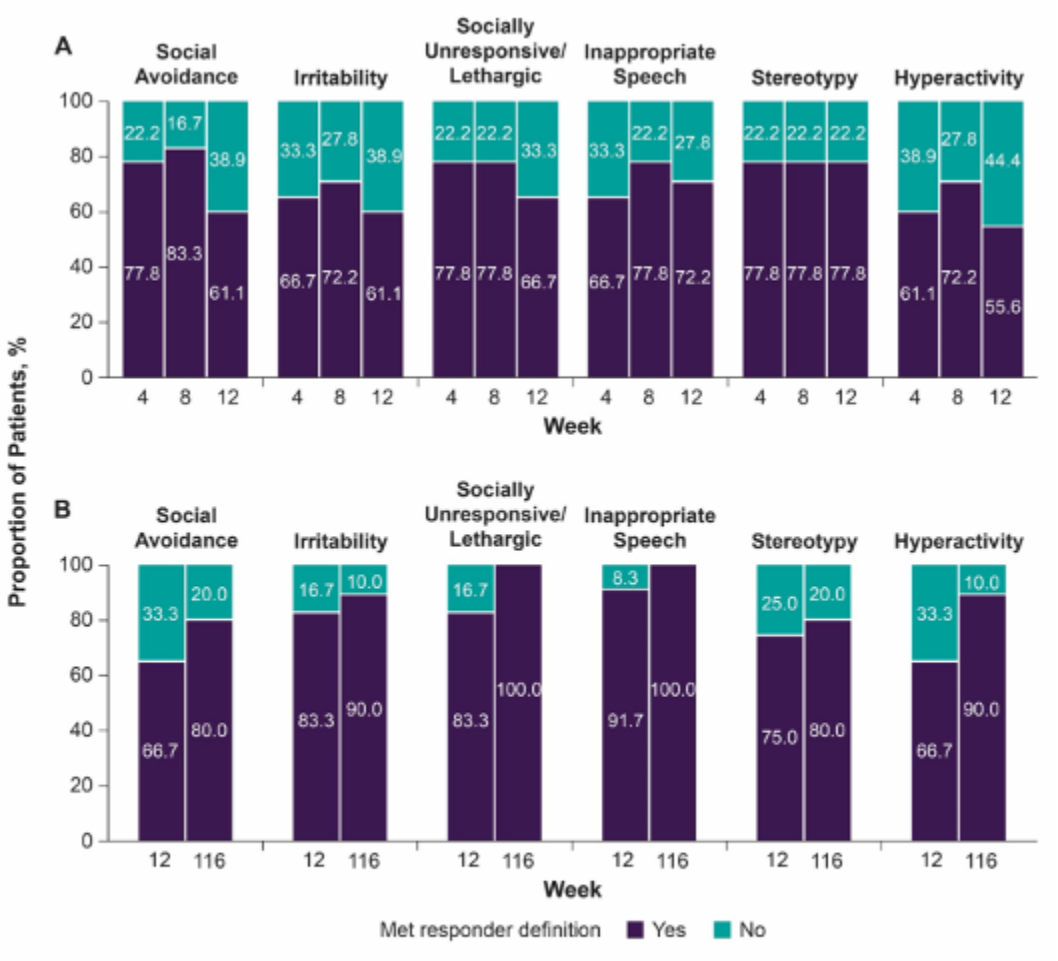
In addition, statistically significant improvements from baseline were observed at week 12 in the total score and all five subscale scores of ADAMS and

these statistically significant improvements persisted to two years.

Responder Analysis

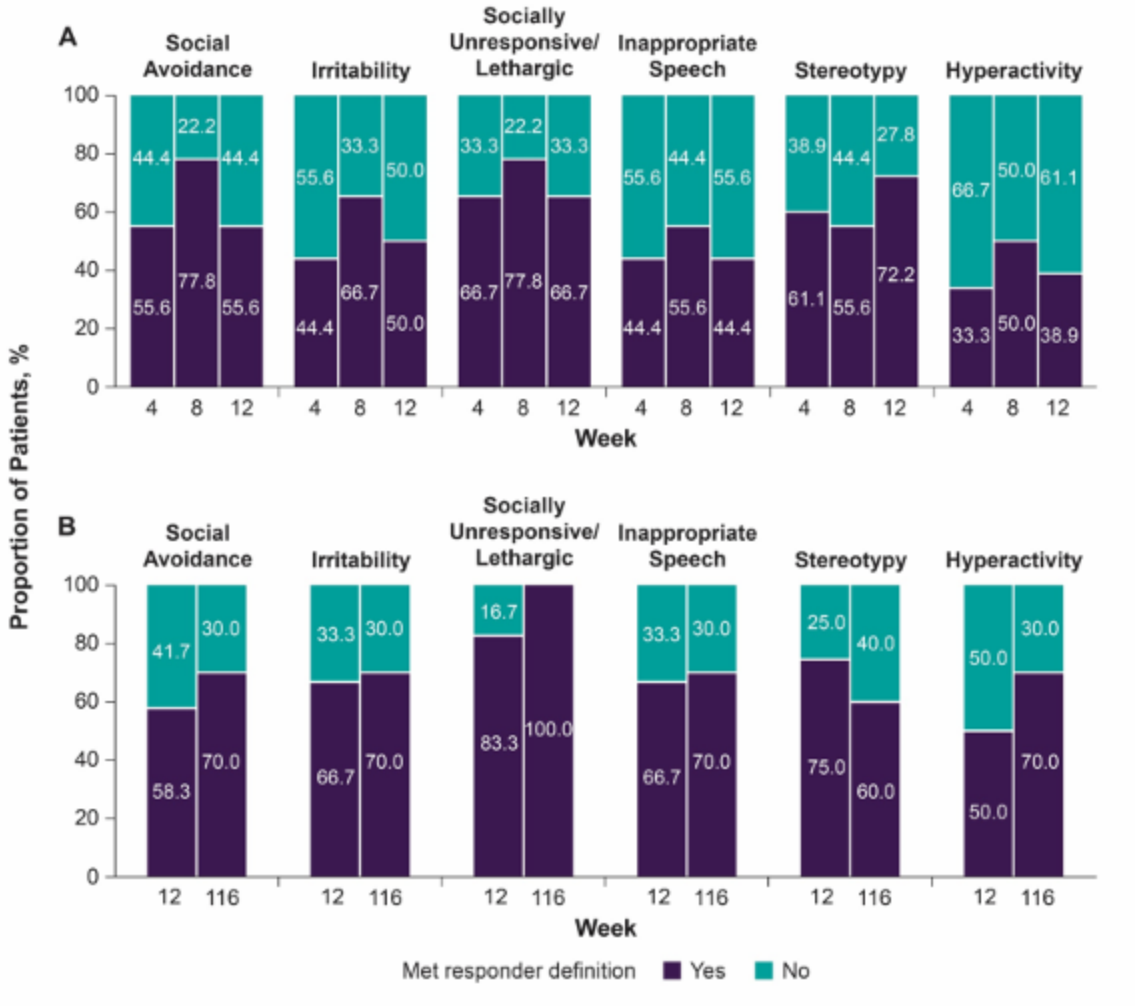
Zynerba performed responder analyses for patients achieving at least a 25% and 50% improvement from baseline for each subscale of the ABC-C_{FXS}.

Maximal 25% responder rates for each ABC-C_{FXS} domain at any visit in patients who completed Period 1 ranged from 72.2% to 83.3% and emerged by week 8 for all domains. Most patients who entered Period 2 met criteria for response at weeks 12 (≥66.7%) and 116 (≥80%).



ABC-C_{FXS}, Aberrant Behavior Checklist-Community for FXS.
N = 18 for weeks 4, 8, and 12 (patients who completed period 1).
N = 12 for patients who were evaluated in period 2.
N = 10 for week 116.

Maximal 50% responder rates for each ABC-C_{FXS} domain at any visit ranged from 50.0% to 77.8% in patients who completed Period 1 and were observed at week 8 for all domains except stereotypy. Among patients who entered Period 2, 50% responder rates ranged from 50% to 83.3% at week 12. At week 116, the range of 50.0% responder rates was observed to be descriptively higher, ranging from 60% to 100% across the six ABC-C_{FXS} domains.



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N = 18 for weeks 4, 8, and 12 (patients who completed period 1).
N = 12 for patients who were evaluated in period 2.
N = 10 for week 116.

Evidence of Global, Multi-domain, and Sustained Reduction in Behavioral Symptom Burden

Radar charts were created to visualize the proportional effect of Zygel across the six ABC-C_{FXS} subscales. The boundaries of the polygon at screening and endpoint allow visualization of change across all domains cross-sectionally and over time. These radar charts suggest global and sustained reductions in severity with Zygel treatment in patients who entered Period 2.

Tolerability of Zygel over Two Years of Treatment

Zygel was well tolerated in the FAB-C trial over two years. Treatment-emergent adverse events (TEAEs) – any event occurring during a trial period whether unrelated or related to study drug - are common in children and expected over a two-year period. Of the 66 TEAEs reported in 19 patients, all were either mild (85%) or moderate (15%), and 91% were determined to be unrelated to treatment. No treatment-related TEAEs occurred in more than one patient. Only one serious adverse event (constipation) was reported over two years of treatment and was not related to treatment.

The authors of the poster concluded that:

- In this post hoc analysis, the majority of patients who completed Period 1 met important criteria for therapeutic response (≥25% or ≥50% improvement from baseline in ABC-C_{FXS} domains) at weeks 4, 8, and 12 of the Phase 2 FAB-C trial; this response was sustained or continued to improve through two years in patients who entered Period 2;
- Simultaneous visualization of change across all ABC-C_{FXS} domains at baseline and endpoint through radar charts provided additional evidence for global, multi-domain, and sustained reduction in behavioral symptom burden among patients who entered Period 2;
- Zygel was well tolerated through two years; all AEs were mild or moderate and most were considered unrelated to treatment; and
- Together, these data may suggest evidence of the clinical efficacy and favorable safety and tolerability of Zygel in children and adolescents with FXS when added to stable standard of care therapies. A double-blind, placebo-controlled study of Zygel in FXS called CONNECT-FX is currently in progress and will extend the knowledge gained from this Phase 2 study.

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). FXS is caused by a mutation in the Fragile X Mental Retardation gene (FMR1) located on the X chromosome and leads to dysregulation of the endocannabinoid pathway including the reduction in endogenous cannabinoids (2-AG and anandamide). 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 patients suffering with FXS.

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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