

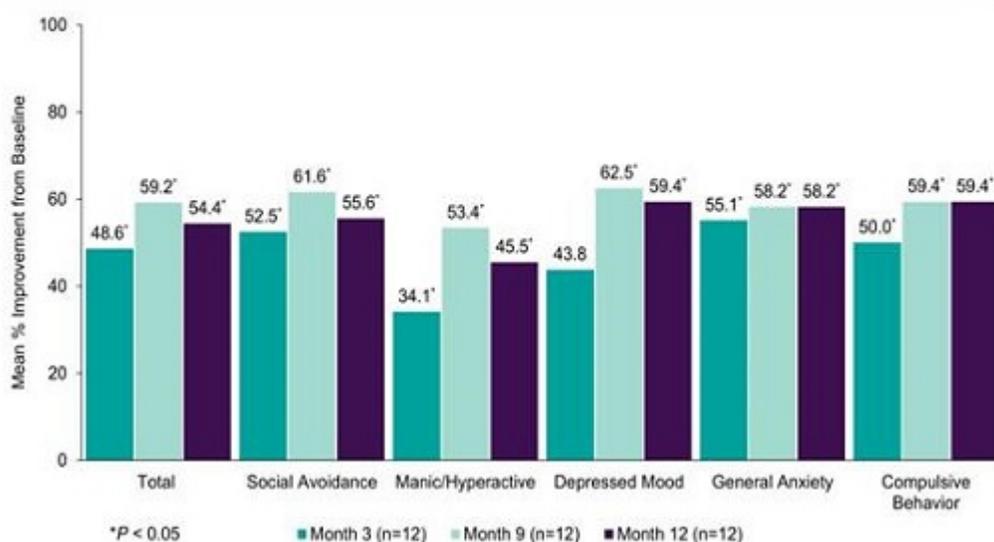
Zynerba Pharmaceuticals Announces Sustained Improvements in Emotional and Behavioral Symptoms of Fragile X Syndrome through 12 Months of Treatment with ZYN002

December 12, 2018

- Patients Experienced a 77% Improvement in Aberrant Behaviors Associated with Social Avoidance Compared to Baseline after One Year of ZYN002 Treatment -

FAB-C Month 12 – Extension Phase Data

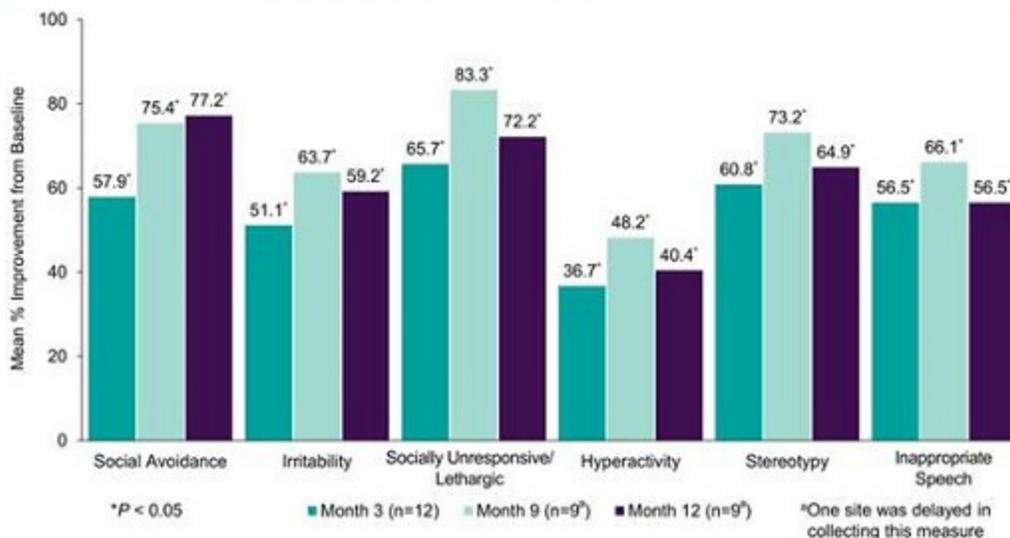
ADAMS Percent Improvement from Baseline



FAB0C Month 12: ADAMS Percent Improvement from Baseline with ZYN002

FAB-C Month 12 – Extension Phase Data

ABC-C_{FXS} Percent Improvement from Baseline



FAB-C Month 12: ABC-C_{FXS} Percent Improvement from Baseline with ZYN002

- Presentation Today at the 57th Annual Meeting of the American College of Neuropsychopharmacology -

DEVON, Pa., Dec. 12, 2018 (GLOBE NEWSWIRE) -- [Zynerba Pharmaceuticals](http://zynerba.com), Inc. (NASDAQ:ZYNE), the leader in innovative pharmaceutically-produced transdermal cannabinoid therapies for rare and near-rare neuropsychiatric disorders, is reporting new 12-month open label clinical data describing the long term impact of ZYN002 on emotional and behavioral symptoms of Fragile X Syndrome (FXS) in a poster presentation at the 57th Annual Meeting of the American College of Neuropsychopharmacology. The presentation is taking place today from 5:30 to 7:30 PM EST in poster session III at the Diplomat Beach Resort in Hollywood, Florida. A copy of the presentation and poster are available on the Zynerba corporate website at <http://zynerba.com/publications/>.

In a poster entitled, "Transdermal Cannabidiol (CBD) Gel for the Treatment of Fragile X Syndrome (FXS)," Steven Siegel, M.D., Ph.D., Professor and Chair of the Department of Psychiatry and the Behavioral Sciences at the Keck School of Medicine, University of Southern California, is presenting new 12-month data from the open label Phase 2 FAB-C (Treatment of Fragile X Syndrome Anxiety and Behavioral Challenges with CBD) trial of ZYN002 in children and adolescents with FXS. The data demonstrate that treatment with ZYN002 improved core emotional and behavioral symptoms of FXS with statistical significance versus baseline across multiple measures of efficacy at month three, and that these improvements were sustained through 12 months of treatment. ZYN002 continues to be well tolerated; no serious adverse events were reported, and no clinically meaningful trends in vital signs, ECG, or clinical safety laboratories, including liver function tests, were observed.

In the Social Avoidance subscale of the Aberrant Behavior Checklist for Fragile X (ABC-C_{FXS}), patients completing 12 months of treatment with ZYN002 experienced a 77.2% improvement in social avoidance behaviors versus baseline, compared to a 57.9% improvement at three months of treatment. Both results are statistically significant compared to baseline. The Social Avoidance subscale of the ABC-C_{FXS} is the primary endpoint of the ongoing pivotal CONNECT-FX study of ZYN002.

"I am encouraged to see that improvements in FXS-associated emotional and behavioral symptoms after 12 months of treatment with ZYN002 are consistent with those seen at three and nine months; these data continue to suggest the potential for sustained responses that may be conserved over extended use of the drug," said Dr. Steven Siegel of the Keck School of Medicine. "Improvements in these behaviors may enhance the child's capacity for interaction and engagement with their peers, families, teachers and caregivers. These data are promising, and I am enthusiastic about the potential opportunity for ZYN002 in these patients. I look forward to the results of the double blind, placebo-controlled CONNECT-FX study next year."

Study design

Twenty patients (3:1 males) aged six through 17 years of age (median = 9) with Fragile X Syndrome were enrolled in the open label FAB-C study. All patients had genetic confirmation of the full mutation of the FMR1 gene. ZYN002 was added to other medications being administered. The first six weeks were designed to titrate dosing in patients. Dosing was initiated at 50 mg daily and could be increased to 250 mg daily. Weeks seven through 12 was a maintenance period where patients were treated at the dose established at week six. At the completion of week 12, thirteen patients elected to enter into the extension study for up to 24 months. To date, 11 patients remain in the study and have now exceeded 12 months of therapy with ZYN002.

The primary endpoint of the FAB-C trial was the Anxiety, Depression, and Mood Scale (ADAMS) Total Score. Key secondary endpoints included the ADAMS subscale scores for Social Avoidance, Manic/Hyperactive Behavior, Depressed Mood, General Anxiety, and Compulsive Behavior; and the Aberrant Behavior Checklist FXS Factor Structure (ABC-C_{FXS}) subscale scores of Social Avoidance, Irritability, Socially Unresponsive/Lethargic, Hyperactivity, Stereotypy, and Inappropriate Speech.

Long Term Efficacy: 12 months

The following data show the improvement in various efficacy measures for the patients who completed three months, enrolled in the extension trial, and have completed 12 months of treatment.

Anxiety, Depression, and Mood Scale (ADAMS)

Scale: ADAMS	Group Mean Percent Improvement from Baseline					
	Month 3 (n=12)	P-value vs Baseline	Month 9 (n=12)	P-value vs Baseline	Month 12 (n=12)	P-value vs Baseline
ADAMS Total Score	48.6	0.0001	59.2	<0.0001	54.4	<0.0001
Social Avoidance	52.5	0.0013	61.6	0.0007	55.6	0.0004
Manic/Hyperactive Behavior	34.1	0.0012	53.4	0.0002	45.5	0.0014
Depressed Mood	43.8	0.0831	62.5	0.0372	59.4	0.0032
General Anxiety	55.1	<0.0001	58.2	<0.0001	58.2	<0.0001
Compulsive Behavior	50.0	0.0295	59.4	0.0247	59.4	0.0213

A photo accompanying this chart is available at: <http://www.globenewswire.com/NewsRoom/AttachmentNg/95ff728a-4470-41b3-9659-5b1c336c148b>

Aberrant Behavior Checklist – Community: FXS Specific (ABC-C_{FXS})

Scale: ABC-C _{FXS}	Group Mean Percent Improvement from Baseline					
	Month 3 (n=12)	P-value vs Baseline	Month 9 (n=9)	P-value vs Baseline	Month 12 (n=9)	P-value vs Baseline
Social Avoidance	57.9	0.0040	75.4	0.0013	77.2	0.0013
Irritability	51.1	0.0012	63.7	0.0003	59.2	0.0007
Socially Unresponsive/Lethargic	65.7	0.0024	83.3	0.0016	72.2	0.0035
Hyperactivity	36.7	0.0119	48.2	0.0012	40.4	0.0037
Stereotypy	60.8	0.0048	73.2	0.0019	64.9	0.0012
Inappropriate Speech	56.5	0.0002	66.1	<0.0001	56.5	<0.0001

A photo accompanying this chart is available at: <http://www.globenewswire.com/NewsRoom/AttachmentNg/fced1b83-4584-4d28-9a38-f6945e0bc98b>

Safety Summary

ZYN002 was well tolerated, and the safety profile was consistent with previously reported clinical data, with no serious adverse events (SAEs) reported. Through month 12, patients reported 43 treatment-emergent adverse events (TEAEs), all of which were mild or moderate. Two out of 20 patients, who were siblings, discontinued during the initial three-month period; one discontinued due to worsening eczema (not considered treatment related) and the other discontinued for administrative reasons. In the ongoing open label extension, there has been one discontinuation for administrative reasons. The most common TEAEs were gastroenteritis (14%) and upper respiratory tract infection (12%). One patient developed moderate skin rash (alternate etiology reaction to antibiotics) and one patient developed mild dry skin; both resolved and the patients remained in the study. There has been no THC detected in plasma. There have been no clinically meaningful trends in vital signs, ECGs or clinical safety labs, including liver function tests.

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). Enrollment is ongoing in a multi-national, randomized, double blind placebo controlled Clinical study of Cannabidiol (CBD) in Children and Adolescents with Fragile X (CONNECT-FX), a pivotal clinical trial of ZYN002 in FXS (ClinicalTrials.gov/CONNECTFX); topline data from CONNECT-FX are expected in the second half of 2019. Additionally, Zynerba expects to complete enrollment in its Phase 2 Open Label Study to Assess the Safety and Efficacy of ZYN002 Administered as a Transdermal Gel to Children and Adolescents with Developmental and Epileptic Encephalopathy (BELIEVE 1) clinical trial before year-end 2018.

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. 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 and refractory epilepsies. 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.

Investor Contact

Will Roberts, VP Investor Relations and Corporate Communications
Zynerba Pharmaceuticals
484.581.7489
robertsw@zynerba.com



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