

## Autism Spectrum Disorder, Fragile X Syndrome, and 22q11.2 Deletion Syndrome Share a Constellation of Sociobehavioral Symptoms

September 5, 2019

- Preliminary Evidence Shows that CBD May Prove to be Effective in Managing the Spectrum of Behavioral Symptoms Associated with these Conditions –

- New Data Presented Today at the Society for the Study of Behavioural Phenotypes (SSBP) Research Symposium -

DEVON, Pa., Sept. 05, 2019 (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 data today describing the results of a retrospective literature review on patients with autism spectrum disorder (ASD), Fragile X syndrome (FXS), and 22q11.2 deletion syndrome (22qDS) conducted to determine symptomatic overlap between these disorders. The data indicate that patients with ASD, FXS, and 22qDS share a constellation of sociobehavioral symptoms and that the pharmacology of CBD is broad, continues to be defined, and may prove to be beneficial in addressing important behavioral symptoms of these conditions.

The poster, entitled *Common Behavioral Features of Autism, Fragile X Syndrome, and 22q11.2 Deletion Syndrome*, is being presented on September 5<sup>th</sup> and 6<sup>th</sup> at the 22<sup>nd</sup> Society for the Study of Behavioural Phenotypes (SSBP) Research Symposium at Aston University in Birmingham, UK. A copy of the poster is available on the Zynerba corporate website at <http://zynerba.com/publications/>.

Honey Heussler, MBBS, FRACP, MRCPCH, PGCAP, DM, Associate Professor, University of Queensland and Medical Director Child Development, Children's Health Queensland is presenting data showing that patients with ASD, FXS, and 22qDS share a constellation of sociobehavioral symptoms that includes anxiety, which may lead to social avoidant behavior, aggression, irritability, attention deficits, and poor communication. Dr. Heussler is presenting the poster from 12:40 – 1:45 British Summer Time (BST) on September 5<sup>th</sup> and 6<sup>th</sup>, 2019.

"Those of us who care for patients and families contending with certain neuropsychiatric dysfunction understand that there are significant shared sociobehavioral symptoms between such disorders, though until now no review has been conducted to examine or clarify the overlap," said Dr. Heussler. "These data on the shared behaviors between ASD, FXS and 22qDS are important to understanding disease impact, patient care, and the development of potential treatments. One such potential treatment being studied in well-controlled clinical trials is a proprietary gel formulation of CBD, which has diverse pharmacologic effects and may prove to be important in these neuropsychiatric disorders."

Based on insights from Company data, a search of the PubMed database was conducted using the terms "behavior," "behavioral symptoms," "autism spectrum disorder," "ASD," "Fragile X Syndrome," "FXS," "22q11.2 deletion syndrome," "parents," "caregivers," and "CBD and treatment of anxiety" with no restriction on date or publication type. Records were then analyzed for relevance. The most common behavioral manifestations across all conditions are anxiety-related, such as social avoidance, aggression, irritability, attention deficits, stereotypy, poor communication, and social unresponsiveness.

### ASD

Anxiety-related symptoms are common in patients with ASD with up to 84% of children experiencing some degree of debilitating anxiety. Rates of physician-diagnosed anxiety disorders in these patients range from 42% to 55% and may include simple phobias, generalized anxiety disorder, separation anxiety disorder, obsessive-compulsive disorder, and social phobias. Comorbid anxiety disorders can be associated with behaviors such as aggression/irritability and isolation from same-age peers (due to bullying/victimization in school). Inattention and hyperactivity are often present in Attention Deficit-Hyperactivity Disorder and ASD.

### FXS

In FXS, severe cognitive and social impairments are more common in males than in females. FXS usually has profound effects on the life of patients (comorbid conditions, social impairment) as well as their caregivers and families (mental health, absence from work/school). Anxiety and social avoidance are considered core features of FXS; further, anxiety can be thought of as a foundational precipitant to social avoidance. Social avoidance encompasses behaviors that may include seeking isolation, lack of interaction, social escape, and gaze avoidance that distance the individual from his/her social counterparts.

### 22qDS

The most common behavioral/psychiatric diagnoses in children with 22qDS were ADHD, ASD, and anxiety. Up to one-third of patients with 22qDS will develop schizophrenia or schizo-affective disorder by late adolescent and early adulthood. The emergence of social deficits during adolescence can represent a major source of disability in some individuals with 22qDS. Cross-sectional studies (observational research that analyzes data collected at one given point of time across a sample population) show that children with 22qDS are withdrawn and shy, and have social impairments which may be less of a concern to the individual.

### *The Potential Role of CBD in Managing Behavioral Symptoms Associated with ASD, FXS, and 22qDS*

The authors conclude that preliminary evidence, including findings from the Phase 2 open-label FAB-C study in children and adolescents with FXS and a retrospective literature review based on insights from that Company data, shows that CBD improves social anxiety and associated behavioral manifestations suggesting that it may prove to be effective in managing the spectrum of behavioral symptoms associated with these conditions.

**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](http://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](http://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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