Zynerba Pharmaceuticals Announces Positive Top Line Results from Exploratory Open Label Phase 2 BRIGHT Trial of Zygel in Autism Spectrum Disorder

May 27, 2020

- The BRIGHT Trial Achieved Statistically Significant and Clinically Meaningful Improvements from Baseline in All Subscales of the Aberrant Behavior Checklist -

- Safety Data Reinforce Excellent Tolerability Profile of Zygel -

- Zynerba to host conference call and webcast today, May 27, 2020 at 8:30 am ET -

DEVON, Pa., May 27, 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 positive top line results from the exploratory, open label Phase 2 BRIGHT (An Open-La**b**el Tole**r**abi**l**ity and Efficacy Study of ZYN002 Administered as a Transdermal **G**el to C**h**ildren and Adolescen**t**s with Autism Spectrum Disorder) trial.

The trial was designed to assess the safety, tolerability and efficacy of Zygel™ in pediatric and adolescent patients with autism spectrum disorder (ASD). Zygel was administered to patients with moderate-to-severe symptoms of ASD as add-on therapy to their standard of care utilizing a variety of efficacy assessments. Key findings from the trial disclosed today include:

- All five subscales of the Aberrant Behavior Checklist – Community (ABC-C) as well as the Parent Rated Anxiety Scale - Autism Spectrum Disorder (PRAS-ASD) showed both statistically significant and clinically meaningful improvements at 14 weeks of treatment from baseline;
- The results observed in other efficacy outcome measures, including Clinical Global Impressions - Improvement scale (CGI-I), support the subscale results observed in the ABC-C;
- Zygel was well tolerated in this trial with no serious or severe adverse events reported.

“We are very encouraged by the compelling top line results of the BRIGHT trial and we expect to meet with the FDA to discuss the clinical pathway for developing Zygel for the treatment of behavioral symptoms of ASD in the second half of this year,” said Armando Anido, Zynerba’s Chairman and Chief Executive Officer. “Our goal is to develop Zygel for patients suffering from debilitating neuropsychiatric disorders including ASD, Fragile X syndrome, 22q and DEE. I want to thank the patients, families, physicians, clinical staff, and the Zynerba team for their support of this key study in ASD."

Study Design

The 14-week exploratory, open label Phase 2 BRIGHT trial enrolled 37 patients with ASD at a single clinical site. The trial was designed to evaluate the safety, tolerability and efficacy of Zygel in children and adolescents ages three to 17 with ASD as confirmed by DSM-5 diagnostic criteria. Enrolled patients received weight-based doses of 250 mg or 500 mg daily of Zygel.

Patient Disposition and Baseline Demographics

Thirty-seven (37) patients were enrolled in the trial and are included in the safety analysis. One patient was lost to follow up with no post-treatment efficacy evaluation and, as a result, thirty-six (36) patients are included in the efficacy analyses. Twenty-eight (28) patients completed the 14-week trial. The discontinuation rate is consistent with other trials in ASD.

The mean age of patients enrolled in the trial was 9.2 years and thirty-four (92%) of the patients were male. Patients weighed between 15 and 108 kilograms (mean=41.6; median=30.2). The mean time to diagnosis in this population was 5.4 years. Using the Autism Diagnostic Observation Schedule (ADOS-2), 94% of enrolled patients had moderate-to-severe symptoms of ASD. The mean baseline ABC-C Irritability subscale score of 30.3 further supports the severity of the enrolled patient population. Ninety-two percent (92%) of patients entered the trial with the use of at least one underlying medication. Sixty-five percent (65%) of patients were on at least one psychotropic medication, for example, anti-depressants, anxiolytics and antipsychotics.

Top-line Efficacy Results

The trial evaluated multiple efficacy assessments, including the ABC-C, PRAS-ASD, Autism Parenting Stress Index, Autism Impact Measure (AIM), and Clinical Global Impression – Severity (CGI-S) and Improvement (CGI-I). The ABC-C irritability subscale was used as the basis for approval for the two atypical antipsychotics indicated for ASD.

Results from each of the subscales of the ABC-C after 14 weeks of treatment with Zygel are as follows:

ABC-C Subscale	Baseline (n=36)	Week 14 (n=28)	Mean % improvement	p Value
Irritability	30.3	18.2	39.1%	<0.0001*

Inappropriate Speech	7.4	5.2	42.5%	0.0002*
Stereotypy	12.3	7.9	39.1%	<0.0001*
Social withdrawal	25.1	16.5	36.4%	<0.0001*
Hyperactivity	37.0	23.9	35.6%	<0.0001*

*Statistically significant

The results of other efficacy assessments reinforce the results demonstrated in the ABC-C. For example, patients on Zygel experienced a mean improvement of 46% at week 14 from a baseline score of 40.8 as measured by the PRAS-ASD ($p<0.0001$) and 57% of patients were assessed as "very much improved" or "much improved" at week 14 as measured by the CGI-I.

"I am very impressed with the improvements my patients made over the 14-week treatment period while receiving Zygel; the reduction in irritability, communication deficits, and repetitive movements were especially noteworthy since some of these are core autistic behaviors," said Helen Heussler, FRACP, Associate Professor at Children's Health Queensland, Medical Director Child Development and principal investigator in the BRIGHT trial. "The magnitude of effect on autistic behaviors in this trial is significant, including hyperactivity and stereotypy, which are among the most difficult behaviors to improve with therapeutic intervention. The results of this study strongly suggest the potential of this drug as an important treatment for ASD and I look forward to participating in future clinical studies with Zygel."

Safety and Tolerability

Zygel was very well tolerated, and the safety profile was consistent with previously released data from other Zygel clinical trials. Less than half (49%) of the patients experienced any adverse event (whether unrelated or related to study drug), all of which were mild (75%) or moderate (25%). Only 14% of patients experienced an adverse event that was deemed to be treatment-related, all of which were application site-related; most were mild and transient. There were no severe or serious adverse events reported during the study. Eighteen (18) patients who completed the BRIGHT trial have rolled into the open label extension.

Conference call information

Zynerba management will host a live conference call and webcast today at 8:30 am Eastern Time to discuss the results of this clinical trial. The call can be accessed by dialing (866) 573-0180 (U.S. and Canada) or (430) 775-1345 (international) and referencing conference ID 6196218. To access the live webcast or the replay, visit the investor page of the Company's website at http://ir.zynerba.com/. The webcast will be recorded and available on the Company's website for 30 days.

About Autism Spectrum Disorder (ASD)

Autism Spectrum Disorder is a developmental disorder that affects communication and behavior in approximately one million pediatric and adolescent patients between the ages of five and 17 in the U.S. It refers to a range of conditions characterized by anxiety, repetitive patterns of behavior, impairments in social communication including verbal and non-verbal communication, and deficits in developing and maintaining relationships. Although autism can be diagnosed at any age, it is said to be a "developmental disorder" because symptoms generally appear in the first two years of life. Research suggests that genes can act together with influences from the environment to affect development in ways that lead to ASD. Newer studies suggest that ASD is linked to disruption in the endocannabinoid system.

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