Zynerba Pharmaceuticals Announces Publication of Results of Phase 2 BELIEVE Open-Label Study of Zygel™ in Children and Adolescents with Developmental and Epileptic Encephalopathies (DEE) in JAMA Network Open

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DEVON, Pa., Sept. 07, 2021 (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 publication of results from the Company's open-label Phase 2 BELIEVE (Open La **b**el Study to Assess the Safety and **E**fficacy of Zygel™ (ZYN002) Administered as a Transderm**a**l Gel to Ch**i**ldren and Adol**e**scents with De**v**elopmental and **E**pileptic Encephalopathy) study in the *Journal of the American Medical Association (JAMA) Network Open*.

The article, titled "*Safety and tolerability of transdermal cannabidiol gel in children with developmental and epileptic encephalopathies: A nonrandomized controlled trial*" can be accessed at HERE.

The article describes the positive results from BELIEVE, the first trial of a non-oral formulation of cannabidiol in children and adolescents with DEEs, and concludes that cannabidiol transdermal gel was safe, well tolerated, and was associated with reductions in focal impaired awareness seizures (FIAS) and tonic-clonic seizure (TCS) frequency and disease burden.

"DEEs are the most severe group of epilepsies and are usually drug-resistant. Antiseizure medications are usually administered orally, which can be extremely challenging in children with behavioral and cognitive problems. Non-oral therapies are needed to provide an alternative route to deliver medications to control seizures and improve developmental outcomes," said Ingrid E. Scheffer, MBBS, PhD, FRS, Laureate Professor, and chair, Pediatric Neurology Research, University of Melbourne, and the lead investigator in the BELIEVE study. "The data from the BELIEVE study are promising and suggest that Zygel may be a safe and well-tolerated option to improve seizure control, challenging behaviors and other symptoms associated with DEEs."

Forty-eight (48) patients with a mean age of 10.5 years were enrolled in BELIEVE and included in the safety analysis. Sixty-percent (60%) had at least one treatment-related adverse event (AE) over the 6.5 month trial period and 96% of these AE's were mild or moderate. During the treatment period, 10 patients (21%) reported serious adverse events (SAEs). Two SAEs were considered to be possibly treatment related: nonconvulsive status epilepticus and lower respiratory tract infection, in separate patients. All SAEs resolved, and none resulted in alteration of study medication.

The authors indicated that the incidence of AEs in this study, particularly related to infections, was likely due to the high baseline rate of complex morbidities and seizure severity of these patients at study onset, and to the relatively long, 6.5 month duration of the trial over which events were collected.

From an efficacy perspective, the analysis of the 33 patients with FIAS and TCS showed a 58% median monthly reduction in seizures at month 5, and 43.5% reduction over the 6.5 month study period (the primary efficacy endpoint). The percent of ≥50% responders in the FIAS and TCS group ranged from 42.4% at month 2 and peaked at 62.5% at month 5. Parents/caregivers noted improvements in social or interpersonal engagement and irritability (33/43 [77%]); alertness, energy and sleep (23/43 [53%]); and cognition or concentration (20/43 [47%]).

About Zynerba Pharmaceuticals, Inc.

Zynerba Pharmaceuticals is the leader in innovative 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 expectations, projections and estimates regarding expenses, future revenue, capital requirements, incentive and other tax credit eligibility, collectability and timing, and availability of and the need for additional financing; 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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