Zynerba Pharmaceuticals Announces Presentation of Phase 2 BELIEVE Safety, Efficacy and Quality of Life Data in Developmental and Epileptic Encephalopathies (DEE) at the 2020 American Academy of Neurology (AAN) Science Highlights Virtual Session

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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, is presenting two posters on the safety, efficacy and quality of life results of the Phase 2 BELIEVE (Open La**b**el Study to Assess the Safety and **E**fficacy of Zygel™ (ZYN002) Administered as a Transderma**l** Gel to Ch**i**ldren and Adol**e**scents with De**v**elopmental and **E**pileptic Encephalopathy) clinical trial. These data are being presented 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 posters are also available on the Zynerba corporate website at http://zynerba.com/publications/. The top line results of the 26-week Phase 2 BELIEVE trial were initially announced in September 2019. (Press release)

"These BELIEVE data continue to build on the strong safety and tolerability profile of Zygel that we've seen across our clinical trial programs, and provide evidence of its anti-seizure activity in children and adolescents suffering from developmental and epileptic encephalopathies, or DEEs," said Zynerba's Chief Medical Officer, Joseph M. Palumbo, MD, FAPA, MACPsych. "These data are particularly exciting because they also suggest its potential to improve behavioral, cognition and mood deficits in these children and adolescents, which may improve the quality of life for these children and their family."

The first poster entitled *Cannabidiol Transdermal Gel in Children and Adolescents with Developmental and Epileptic Encephalopathies: An Open-Label Clinical Trial* further describes the safety and efficacy of Zygel in children and adolescents with developmental and epileptic encephalopathies (DEE) who participated in the Phase 2 BELIEVE trial.

Forty-eight (48) patients with a mean age of 10.5 years were enrolled in BELIEVE and included in the safety analysis. Nearly three-quarters of patients (73%) had a diagnosis other than LGS or Dravet syndrome. Patients with DEE are medically fragile. Clinically important comorbid conditions were present in all patients and included gait and movement disorders (46%), sleep disturbances (40%), chronic respiratory conditions/infections (38%), and PEG/feeding tube (15%). The modified intent-to-treat (mITT) population comprised 46 patients; 33 patients in the mITT population had consciousness-impairing seizures (focal impaired awareness seizures [FIAS]; or convulsive, or tonic-clonic, seizures [TCS] including generalized tonic-clonic seizures [GTCS] and focal to bilateral tonic-clonic seizures [BTCS]) at baseline and constituted the population in which the primary efficacy endpoint was measured.

As described in the poster, the study met its primary efficacy objective: Over the BELIEVE 26-week treatment period, the median percentage reduction from baseline in monthly frequency of FIAS and TCS was 43.5% (primary efficacy endpoint). Reduction from baseline in monthly (28-day) seizure frequency was ≥44% from month two onwards using monthly seizure frequency normalized to 28 days (SF28). Monthly (28-day) reductions from baseline in seizure frequency ranged from 44% to 58% from month two of the treatment period onward. When analyzed by seizure type, the median reductions from baseline at month six for FIAS, GTCS, and BTCS were 45.3%, 59.5%, and 58.7%, respectively.

At six months of treatment in the BELIEVE trial, 62% of patients achieved a ≥35% reduction in FIAS and TCS from baseline, and 55% of patients achieved a ≥50 reduction in FIAS and TCS.

FIAS, focal impaired awareness seizures; mITT, modified intent-to-treat; TCS, tonic-clonic seizures.
Month = SF28

Safety

Zygel was well tolerated in this 26 week Phase 2 study. Adverse events (AEs) are common in this medically fragile patient population, and expected in a 26-week trial. All events in the six-month period, whether unrelated or related to study drug, were reported as AEs (e.g.: influenza, infections, scrapes, etc.). As a result and as anticipated, most patients experienced an adverse event during the 26-week BELIEVE trial. No safety signal was identified. The most common treatment-related adverse events occurred in only four patients each: application site dryness, application site pain, and somnolence (all four patients exhibiting somnolence were taking concomitant clobazam). Ten (10) patients reported a serious adverse event (SAE); most were infection-related and unrelated to study drug. Of the 10, two patients experienced an SAE that was determined to be possibly related to treatment (nonconvulsive status epilepticus and lower respiratory tract infection, both of which are common in patients with DEE). All SAEs recorded during the study resolved and did not require dose alteration. There were no clinically significant changes in vital signs, ECGs, or laboratory findings.

No drug-related increases in liver function tests (LFTs) were observed.

The authors of the poster concluded that:

- These data suggest meaningful reductions in FIAS and TCS with Zygel treatment beginning as early as month two and sustained through 26 weeks;
- Zygel was well tolerated over 26 weeks of treatment in a medically fragile patient population of children and adolescents with DEEs;
- The positive benefit/risk profile of Zygel in this trial supports further study in patients with DEEs and FIAS and TCS.

The second poster entitled *Quality of Life and Qualitative Caregiver Assessments in Children and Adolescents with Developmental and Epileptic Encephalopathies Treated With Cannabidiol Transdermal Gel: An Open-Label Clinical Trial* builds on the previously disclosed data suggesting the potential of Zygel to improve the quality of life of patients living with DEE.

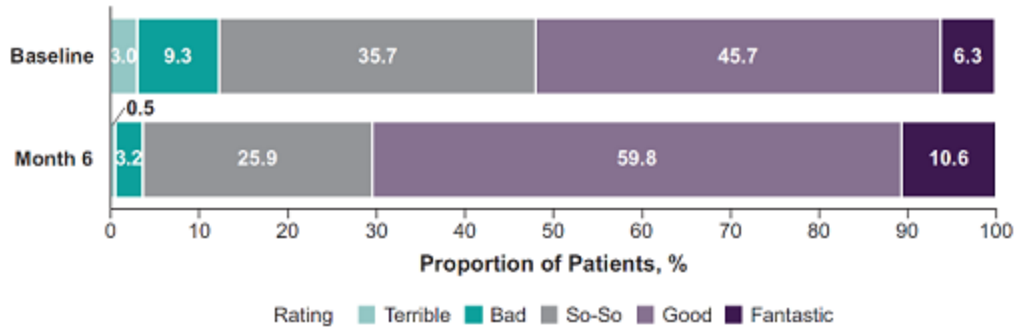
The key assessments for Quality of Life (QoL) in the open label BELIEVE trial included the Epilepsy and Learning Disabilities Quality of Life (ELDQOL) scale - modified version, daily “good day/bad day” questionnaire, and qualitative caregiver assessment.

ELDQOL

Statistically significant reductions from baseline in mean ELDQOL-modified subscale scores for seizure severity, behavior, and mood were observed at week 26 ($P < 0.01$ for all measures).

Good Day/Bad Day Assessment

At month six, the combined proportion of “good day” and “fantastic day” reports increased from 52% at baseline to 70%, and the combined proportion of “terrible day” and “bad day” reports decreased from 12% at baseline to 4%.



[a]Modified intent-to-treat (mITT) population, observed cases during the 4 weeks of month 6.

Qualitative Caregiver Feedback

The qualitative caregiver assessment was administered to parents/caregivers for 43 patients. Improvement in summary measures of qualitative assessments was observed in most patients for most measures:

- Any improvement: 84% (n = 36)
- Improved vitality: 58% (n = 25)
- Improvement in seizures: 51% (n = 22)
- Improved cognition/concentration: 47% (n = 20)
- Improved socially avoidant behaviors: 44% (n = 19)
- Improvement in irritability: 33% (n = 14)
- School improvement: 28% (n = 12)
- Medical improvement: 14% (n = 6)

The most frequent positive qualitative statements were in the domains of (1) behavior, cognition, and mood, and (2) seizures. Some caregivers reported difficulty in applying gel (26%) and mild skin reaction issues (19%).

The authors concluded that treatment with Zygel may be associated with clinically meaningful improvements in social behaviors and cognitive symptoms and increased QoL in children and adolescents with DEEs and their families.

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.

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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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