Zynerba Pharmaceuticals Presents New Data in Two Posters at the 2020 Annual Meeting of the American Epilepsy Society (AES)

December 4, 2020

- New Efficacy Data Describe Strong Evidence of Seizure Reduction over 12 Months of Treatment, Including a 73% Median Reduction from Baseline in Monthly Seizure Frequency at Month 12 -

- Zygel™ Improves the Profound Sleep Disturbance Often Experienced by Developmental and Epileptic Encephalopathy (DEE) Patients Enrolled in the BELIEVE Trial -

DEVON, Pa., Dec. 04, 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 describing the efficacy, safety 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** **i**Gel to Ch**i**ldren and Adol**e**scents with De**v**elopmental and **E**pileptic Encephalopathy) clinical trial at the 2020 virtual annual meeting of the American Epilepsy Society (AES). Both posters are available on the Zynerba corporate website at http://zynerba.com/publications/.

"These newly reported data are exciting as they describe the compelling anti-seizure activity of Zygel in children and adolescents suffering from developmental and epileptic encephalopathies, or DEEs, through twelve months of treatment," said Zynerba's Chief Medical Officer, Joseph M. Palumbo, MD, FAPA, MACPsych. "This is particularly exciting, as this trial was conducted in a refractory seizure population in which patients failed to show adequate response despite taking as many as four anti-seizure drugs. Additionally, we observed an equally compelling seizure reduction in children with a coexisting diagnosis of autism spectrum disorder."

The first poster entitled, "*ZYN002 Cannabidiol Transdermal Gel in Children and Adolescents With Developmental and Epileptic Encephalopathies: An Open-Label Clinical Trial [BELIEVE (ZYN2-CL-025)]*" describes the evidence of tolerability and efficacy of Zygel observed in children and adolescents with developmental and epileptic encephalopathies (DEE) who participated in the Phase 2 BELIEVE trial treated for up to 12 months.

As shown in Figure 1, new results presented today include 12-month treatment data showing improvements in the median percentage reduction from baseline in monthly frequency of consciousness-impairing seizures (focal impaired awareness seizures, or FIAS, and tonic-clonic seizures, or TCS, including generalized tonic-clonic seizures [GTCS] and focal to bilateral tonic-clonic seizures [FBTCS]), ranged from 44% at month three to 73% at month 12.

Figure 1: Median Percentage Reduction From Baseline in 28-Day Frequency of FIAS and TCS by Time Point, Patients With FIAS and/or TCS at Baseline

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When analyzed by seizure type, median reductions from baseline at month six for FIAS, GTCS, and FBTCS were 45%, 60%, and 59%, respectively. At month 12, the median reductions for FIAS, GTCS and FBTCS were 100%, 83% and 59% respectively.

Additionally, as shown in Figure 2, a substantial percentage of patients achieved ≥35% and ≥50% reduction in FIAS and TCS by month three (58% and 46%, respectively), and these reductions in seizures continued through month 12 (89% and 83%, respectively).

Figure 2: Percentage of Patients With 35% and 50% Reduction in FIAS and TCS by Time Point, Patients With FIAS and/or TCS at Baseline

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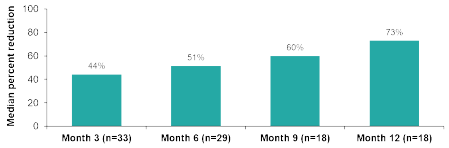
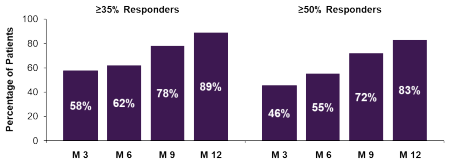
Epileptic encephalopathies represent a particularly severe form of epilepsy, associated with cognitive and behavioral deficits, including impaired social-communication and restricted, repetitive behaviors that are the hallmarks of autism spectrum disorder (ASD)[1]. Zynerba conducted an exploratory analysis to evaluate the efficacy of Zygel in reducing seizures in DEE patients with coexisting ASD enrolled in BELIEVE.

Figure 1: Median Percentage Reduction From Baseline in 28-Day Frequency of FIAS and



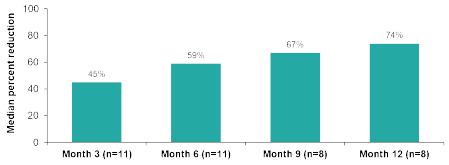
Median Percentage Reduction From Baseline in 28-Day Frequency of FIAS and TCS by Time Point, Patients With FIAS and/or TCS at Baseline

Figure 2: Percentage of Patients With 35% and 50% Reduction in FIAS and TCS



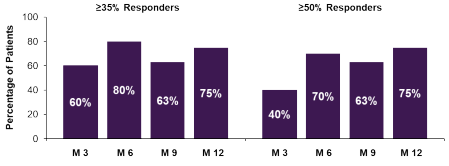
Percentage of Patients With 35% and 50% Reduction in FIAS and TCS by Time Point, Patients With FIAS and/or TCS at Baseline

Figure 3. Median Percentage Reduction From Baseline in 28-Day Frequency of FIAS and TCS, Patients With Coexisting ASD



Median Percentage Reduction From Baseline in 28-Day Frequency of FIAS and TCS by Time Point, Patients With Coexisting ASD at Baseline

Figure 4: Percentage of Patients With 35% and 50% Reduction in FIAS and TCS, Patients With Coexisting ASD



Percentage of Patients With 35% and 50% Reduction in FIAS and TCS by Time Point,

As seen in Figure 3, over the 12-month treatment period, the median percentage reduction from baseline in monthly frequency of consciousness-impairing seizures (FIAS or TCS) in patients with DEE and ASD improved over time, and these reductions in seizures ranged from 45% at month three to 74% at month 12.

Figure 3. Median Percentage Reduction From Baseline in 28-Day Frequency of FIAS and TCS by Time Point, Patients With Coexisting ASD at Baseline

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As seen in Figure 4, a substantial percentage of patients achieved ≥35% and ≥50% reduction in FIAS and TCS by month three (60% and 40%, respectively), and these reductions continued through month 12 (75%).

Figure 4: Percentage of Patients With 35% and 50% Reduction in FIAS and TCS by Time Point, Patients With Coexisting ASD at Baseline

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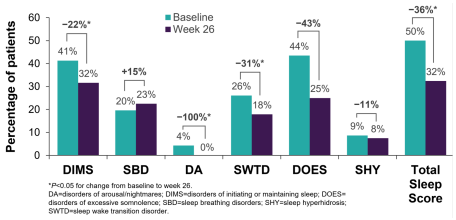
Patients With Coexisting ASD at Baseline

Figure 5: The Sleep Disturbance Scale for Children (SDSC) – Percentage of Patients Above Threshold for Clinically Significant Sleep Problems at Baseline and Week 26



The Sleep Disturbance Scale for Children (SDSC) – Percentage of Patients Above Threshold for Clinically Significant Sleep Problems at Baseline and Week 26

Zygel was well tolerated in BELIEVE. Most treatment-emergent adverse events (any event, whether unrelated or related to study drug) were mild or moderate. There were no clinically significant changes in vital signs, ECGs, or laboratory findings except for one patient with a transient, benign, isolated elevation of alkaline phosphatase at week 26 that was not considered related to study medication.

The authors of the poster concluded that:

- These data suggest meaningful reductions in FIAS and TCS with Zygel treatment which is maintained through to 12 months of treatment with Zygel;
- In the subgroup of patients with ASD, Zygel demonstrated meaningful reductions in FIAS and TCS seizures, with most children reaching either the 35% or 50% responder threshold by month three and month six respectively;
- Zygel was well tolerated over 18 months of treatment in a medically fragile patient population of children and adolescents with DEEs; and
- 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 Sleep Assessments in Children with Developmental and Epileptic Encephalopathies Treated With ZYN002 (CBD) Transdermal Gel: BELIEVE (ZYN2-CL-025)*" describes the impact of Zygel on profound sleep disturbances experienced by DEE patients enrolled in the BELIEVE trial.

Dr. Palumbo continued, "These new data highlight the impact Zygel has on the profound sleep disturbance often experienced by DEE patients in this trial. Importantly, disrupted sleep in children with epilepsy has previously been reported to be associated with negative outcomes in overall family functioning. The Sleep Disturbance Scale for Children (SDSC) utilized in the BELIEVE trial shows that half of the enrolled children exhibited clinically significant sleep problems at study baseline, which improved while receiving Zygel."

The Sleep Disturbance Scale for Children (SDSC) is a 26-item scale completed by caregivers that assesses six different sleep categories. The authors of the poster concluded that treatment with Zygel may be associated with improvements in disorders of initiating and maintaining sleep, disorders of arousal/nightmares, sleep wake transitions, and overall sleep, as well as clinically meaningful improvements observed in vitality, cognition/concentration, socially avoidant behaviors, seizure severity, behavior, and mood.

As shown in Figure 5 and Table 1 below, statistically significant improvements from baseline in sleep scores were observed in the Total Sleep Score (p=0.012), Disorders of Initiating or Maintaining Sleep (DIMS; p=0.006), Disorder of Arousal/Nightmares (DA; p=0.031), and Sleep Wake Transition Disorder (SWTD; p=0.030).

Figure 5: The Sleep Disturbance Scale for Children (SDSC) – Percentage of Patients Above Threshold for Clinically Significant Sleep Problems at Baseline and Week 26

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Table 1. Change From Baseline in the SDSC

SDSC Factors	*t*-Score Mean (SD)	Change (negative number is improvement)	*P* value
Total Score			
Baseline (n=46)	71.6 (12.68)		
Week 26 (n=37)	63.9 (13.40)	−5.1	**0.012***
Disorders of Initiating and Maintaining Sleep (DIMS)			
Baseline (n=46)	69.6 (14.67)		
Week 26 (n=38)	63.2 (15.76)	−5.1	**0.006***

Sleep Breathing Disorders (SBD)			
Baseline (n=46)	60.6 (15.46)		
Week 26 (n=40)	58.9 (15.08)	0.40	0.797
Disorders of Arousal/Nightmares (DA)			
Baseline (n=46)	51.5 (9.91)		
Week 26 (n=39)	49.0 (5.07)	−1.7	**0.031***
Sleep Wake Transition Disorder (SWTD)			
Baseline (n=46)	65.0 (13.09)		
Week 26 (n=39)	60.2 (13.78)	−4.6	**0.030***
Disorders of Excessive Somnolence (DOES)			
Baseline (n=46)	68.5 (16.76)		
Week 26 (n=40)	63.1 (13.82)	−3.6	0.100
Sleep Hyperhidrosis (SHY)			
Baseline (n=46)	52.7 (12.28)		
Week 26 (n=40)	50.6 (9.95)	−2.8	0.154

*P<0.05 for change from baseline to week 26; statistically significant

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

Media contact
Molly Devlin
Evoke KYNE
215.928.2199
Molly.Devlin@evokegroup.com

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[1] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5481888/